RESEARCH ARTICLE

In-silico Analysis of FANCD2 Mitochondrial Localization Signal Sequence and its Role in Multiple Cancer Developments

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ABSTRACT

All Fanconi Anemia complement protein play significant role in the fixed of nuclear inter cross link damage DNA. Crucial steps of this FANCD2 activation through addition Ubiquitin of single unit in the D2 protein. From *In-Silico* analysis of Fanconi anemia complement protein D2 unique mitochondrial localization signal sequence at N-terminal of D2 which is 30AA long. The cosmic database analysis of 30 AA residues of MLS establishes the important role of FANCD2 in Mitochondria. Mutations within MLS linked to the development of various cancer types.

Keywords: Fanconi Anemia, Mitochondria, Mitochondrial Localisation Signal, Cancer, DNA Repair.

INTRODUCTION OF FANCONI ANEMIA

FA concern with any one genetic loss or non functional mutation of FA complements proteins which regulate the correction of intercross link DNA Damage. It is rare kind of autosomal recessive genetic disease. Consequences are that showing many uncommon symptoms during teen age conformation of Fanconi anemia disease from observation cellular ICL DNA in response of oxidative stress. The consequences of accumulation of random mutation in the entire genome because of lacking ICL repair mechanism which is functional in normal cell. The deposition of random mutation may lead to the developments of cancer in different organs. For detail study of how developed cancer in multiple organs this disease is most suitable model. In present 19 genes known to contribute to achieve common goal that is repair inter cross link DNA damage. The interesting fact is the FANCD2 protein is effectors to operate ICL DNA after activation through addition of one unit of ubiquitine.

FA leads to the developed cancer in the different organ. One of the common symptom is development of blood cells in the bone marrow if failure/reduced or form faulty/transform cells. In the fanconi anemia patient's common defective organ is concern with the actively dividing cells. In the organ having actively dividing cells maximum probability of accumulation of mutations and leads to transformations. Because of mutation is random in many organs in the fanconi anemia give a very good opportunity to scientist to investigate real roadmap of transformations. FA pathways prevent from tumour development by repairing inter cross link DNA damage. More than 19 proteins member linked with FA pathways. Eight member of FA core complex (FANCA, FANCB, FANCC, FANCE, FANCF, FANCG, FANCL and FANCM) senses the ICL Damage along with accessory proteins FAAP100 and FAAP24 work in the nucleus. FA core member FANCL acts as the E3 Ubiquitin ligase [1] which activates the effectors FANCD2-I by monoubiquitination.

Interaction of FANCD2 with nuclear protein

FANCD2 and FANCI both respond against DNA damage and both are monoubiquitinates on Lysine 561 and Lysine 521 respectively. Ubiquitination of FANCD2-I leads to its localization to chromatin foci in association with FANCJ and FANCN. These foci are considered to be DNA repair structures because they contain repair factors such as Rad51, BRCA1, BRCA2, NBS1, PCNA, or γH2AX. The mechanisms that mediate these transitions, as well as the function of ubiquitinated FANCD2-I in these foci, are currently unknown. In response to Infra red, FAD2 is phosphorylated by ATM on Ser 222, leading to the activation of an S phase checkpoint response [2]. These observations suggest that FANCD2 has two discrete functions in response to DNA damage. Recently, ATR-dependent phosphorylation of FANCD2 and FANCI has been shown by the induction of the interstrand cross linking reagents. Besides acting on FANCD2 and FANCI, ATR also phosphorylated FANCA after induction of DNA cross links and this event is required for the nuclear localization of FANCA and for efficient crosslink repair [3]. FANCG is also phosphorylated to promote repair [4]. Recent studies suggest that a high molecular weight FA complex is found in both the nucleus and cytoplasm [5]. This suggests that the complex may function in more than one cellular compartment. In addition, the FANCC protein has been found to interact with molecular chaperones GRP94 and HSP70, NADPH cytochrome P450 reductase, involved in xenobiotic biotransformation, glutathione S-transferase (GSTP1) involved in redox metabolism, and STAT1 involved in signaling [6,7]. FANCA is a phosphoprotein which associates with the IκB kinase (IKK) signal some via interaction with IKK2, promoting NF-κB signaling, which can impact apoptosis [8].

MATERIASLS AND METHODS

***In-Silico* Analysis of FANCD2 for Mitochondrial Localization Signal (MLS)**

Mito Prot (*https://urgi.versailles.inra.fr/predotar/predotar.html*)

Predotar is an online tool aimed for efficient screening of large groups of proteins for identifying signal sequences with very low rate of false positives. Predotar recognizes the NTD Signal sequences of the query proteins. For each protein sequence, Predotar tool provides a probability approximation about the protein sequence weather it contains a MLS (mitochondrial localization signal) sequence, plastid targeting sequence or ER targeting sequence. The probability threshold value above 0.2 is well indicating a targeting sequence. The FASTA format of the query proteins are given to the query box by selecting the source of the protein.

COSMIC v99, released 28-NOV-23:

COSMIC, the Catalogue of Somatic Mutations in Cancer is the world's largest and most comprehensive resource for exploring the impact of somatic mutations in human cancer. The gene view histogram is a graphical view of mutations across FANCD2_ENST00000383807. These mutations are displayed at the amino acid level across the MLS 30 amino acid region of FANCD2 NTR. (https://cancer.sanger.ac.uk/cosmic/gene/analysis).

RESULTS AND DISCUSSION

All 19 FA proteins analyzed by various *in-silico* tools for MLS and NLS.

A comprehensive analysis of all 19 FA proteins was conducted using various *In-silico* tools to identify mitochondrial localization signals MLS and nuclear localization signals NLS the findings are presented in the tables. The FANCD2 protein is known to bind directly to damage DNA playing a crucial role in the repair process. Notably FANCD2 also possesses an MLS contributing to the repair of mitochondrial DNA damage. This *In-silico* analysis revealed the presence of mitochondrial localization signals in both the FANCD2 and FANCG proteins as detailed in tables 1 and 2. Through utilizing online tools such as IPSORT a signal sequence of 30 amino acids was identified at the N-terminal of both FANCD2 and FANCG the MLS provides significant insights for subsequent analyses table 3 highlights the 30 amino acid sequences of the MLS in fancd2 serial number 5 and FANCG serial number 8 in green.

Mutation in FANCD2 associated with disease analyzed by using database.

The FANCD2 protein demonstrates a significant degree of conservation, which reflects its critical importance. The MLS of FANCD2 is extensively conserved across a range of organisms; further supporting the assertion that fancd2 is vital for mitochondrial functionality. Additionally, found mutation within MLS of FAD2 lined with disease has been analyzed through various databases. the cosmic database along with other databases created by rockefeller university regarding fanconi anemia complement proteins was employed to identify patients with mutations at the N-terminus of their FAD2 emphasizing the importance of the FAD2 MLS. The cosmic database recognized as a comprehensive mutation database for cancer reveals that mutations occurring within the MLS at many positions of FAD2 are implicated in cancers affecting various primary tissues (refer to fig 2 table 5).

CONCLUSIONS

FancD2 Complement protein of FA Pathways target mitochondria. MLS of FANCD2 play important role in targeting. FAD2 MLS highly conserved among various other species. Mutation in MLS of FAD2 causes transformation in tissue of urinary tract, skin, stomach, lungs, pancreas etc. Cosmic database clearly say FANCD2 MLS mutation involved in carcinoma, chronic mylomonocytic leukaemia and malignant melanoma. Like nuclear DNA Damage response FANCD2 may responsible in mitochondrial DNA damage response and repair it.

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23. https://cancer.sanger.ac.uk/cosmic/gene/analysis

Table 1. In-silico characterization of FA proteins for their localization into the mitochondria by TargetP 1.1, MitoProt II – v1.101, iPSORT, Predotar, TPpRED2.0. Maximum probability of the mitochondrial localization of FA proteins is showed in bold. mTP: mitochondrial Targeting Peptide; RC: reliability class; SP: Signal Peptide; MLS:

PROTEIN	TargetP 1.1		MitoProt II – v1.101		iPSORT		Predotar	TPpRED2.0	
	mTP	RC	probability	Charge	SP	MLS			
FANCA	0.223	3	0.0897	-15	NO	NO	0.00	NO	0.98
FANCB	0.061	1	0.0732	-05	NO	NO	0.00	NO	0.99
FANCC	0.059	2	0.0590	-15	NO	NO	0.00	NO	0.99
FANCD1	0.115	2	0.0169	-30	NO	NO	0.01	NO	0.99
FANCD2	0.182	2	0.2296	-42	NO	YES	0.03	NO	0.99
FANCE	0.090	1	0.0070	-20	NO	NO	0.00	NO	0.99
FANCF	0.056	2	0.1802	+06	NO	NO	0.00	NO	0.72
FANCG	0.212	3	0.4097	-13	NO	YES	0.02	NO	0.92
FANCI	0.054	1	0.1082	-03	NO	NO	0.00	NO	0.99
FANCJ	0.093	2	0.0758	-11	NO	NO	0.00	NO	0.98
FANCL	0.321	4	0.1797	-05	NO	NO	0.02	NO	0.85
FANCM	0.875	2	0.5774	-41	NO	NO	0.29	YES	0.97
FANCN	0.088	1	0.0090	-01	NO	NO	0.00	NO	1.00
FANCO	0.577	4	0.3127	-02	NO	NO	0.20	NO	0.89
FANCP	0.061	2	0.0081	-27	NO	NO	0.00	NO	0.93
FANCQ	0.050	3	0.0699	-07	NO	NO	0.00	NO	0.99
FANCR	0.059	1	0.0159	-13	NO	NO	0.00	NO	0.99
FANCS	0.087	2	0.0248	-86	NO	NO	0.00	NO	0.98
FANCT	0.346	4	0.2180	5	NO	NO	0.04	NO	0.98

Table-2: In-silico characterization of FA proteins for their localization into the mitochondria by RSLpred, Iloc-Animal, MultiLoc. Bold represents the maximum

FA Protein	RSLpred In Mito.	Iloc-Animal		MultiLoc	
		Mito.	Nucleus	SVMTarget	SVMaac
FANCA	-0.362414	NO	NO	NO	NO
FANCB	0.167961	Yes	NO	NO	NO
FANCC	-0.163899	Yes	NO	NO	NO
FANCD1	-0.081539	Yes	NO	NO	NO
FANCD2	-0.582377	YES	YES	YES	YES
FANCE	-0.107736	NO	NO	NO	NO
FANCF	0.2794675	Yes	Yes	NO	NO
FANCG	-0.394209	Yes	Yes	NO	NO
FANCI	0.0149994	NO	NO	NO	NO
FANCJ	-1.321411	NO	NO	NO	NO
FANCL	-0.859685	NO	NO	NO	NO
FANCM	-1.530589	NO	NO	NO	NO
FANCN	-0.866173	NO	NO	NO	NO
FANCO	0.766075	YES	YES	NO	NO
FANCP	-1.845464	NO	NO	NO	NO

FANCQ	-0.140815	NO	NO	NO	NO
FANCR	1.324080	YES	NO	NO	NO
FANCS	-0.958446	NO	NO	NO	NO
FANCT	-0.912399	NO	NO	NO	NO

Table-3: Through iPSORT prediction clearly identify the 30 AAs sequence of FANCD2 and FANCG at N terminal of protein having mitochondrial localization signal.

S.NO	FANC PROTEIN	N-TERMINAL SEQUENCE	MLS
1	FANCA	MSDSWVPNSASGQDPGGRRRAWAELLAGRVK	NO
2	FANCB	MTSKQAMSSNEQERLLCYNGEVLVFQLSKG	NO
3	FANCC	MAQDSVDLSCDYQFWMQKLSVWDQASTLET	NO
4	FANCD1/BRCA2	MPIGSKERPTFFEIFKTRCNKADLGPISLN	NO
5	FANCD2	MVSKRRLSKSEDKESLTEDASKTRKQPLSK	YES
6	FANCE	MATPDAGLPGAEGVEPAPWAQLEAPARLLL	NO
7	FANCF	MESLLQHLDRFSELLAVSSTTYVSTWDPATV	NO
8	FANCG	MSRQTTSVGSSCLDLWREKNDRLVRQAKVA	YES
9	FANCI	MDQKILSLAAEKTADKLQEFLQTLREGDLT	NO
10	FANCJ/BRIP1	MSSMWSEYTIGGVKIYFPYKAYPSQLAMMN	NO
11	FANCL	MAVTEASLLRQCPLLLPQNRSKTVYEGFIS	NO
12	FANCM	MSGRQRTLFQTWGSSISRSSGTPGCSSGTE	NO
13	FANCN/PALB2	MDEPPGKPLSCEEKEKLKEKLAFLKREYSK	NO
14	FANCO/RAD51C	MRGKTFRFEMQRDLVSFPLSPAVRVKLVSAG	NO
15	FANCP/SLX4	MKLSVNEAQLGFYLGSLSHLSACPGIDPRS	NO
16	FANCQ/ERCC4	MESGQPARRIAMAPLLEYERQLVLELLDTD	NO
17	FANCR/RAD51C	MAMQMQLEANADTSVEEESFGPQPISRLEQ	NO
18	FANCS/BRCA1	MDLSALRVEEVQNVINAMQKILECPICLELI	NO
19	FANCT	MQRASRLKRELHMLATEPPPGITCWQDKDQM	NO

Table.4: Similarity of MLS of FANCD2 in different species: Other than human, dog and chicken also having mitochondrial localization signal. It represents the importance of mitochondrial function of FANCD2

S. No	Name Of Species	References	AMINO TERMINAL AMINO ACID OF FANCD2.
1	*Homo sapiens*	NCBI Reference Sequence: NP_001018125.1	MVSKRRLSK SEDKESLTEDASKTR KQPLS KKTKKSHIANEVEEN DSIFVKLLKISGIILK
2	*Canis lupus familiaris* (dog)	XP_005632230.1	MVSKRRLSKSEDKESLTEDASKARKQPLSK
3	*Gallus gallus* (chicken)	NP_001034350.3	MVSKRKLSKIDAAEESSKTDLQSRCPETKR
4	*Saimiri boliviensis boliviensis*	NCBI Reference Sequence: XP_003927119.1	MVSKRRLSKSEDKDNLTEDASKTRNQSLSKKTKKSQVLNEVEEN DSIFVNFLKTSGIILKTG
5	*Ophiophagus hannah*	GenBank: ETE70717.1	MEGLKASTSILTATICCTGYRYSIVLFLKMYLGYPNHDMSTPVMA SKRKLFKPHFYSENLI
6	*Mus musculus*	NCBI Reference Sequence: NP_001028416.2	MISKRRRLDSEDKENLTEDASKTMPLSKLAKKSHNSHEVEENGS VFVKLLKASGLTLKTG

7	*Rattus norvegicus*	NCBI Reference Sequence: NP_001001719.1	VKMVSKRSRLDFEDKETLAEDASKIMKQPLSKLAKKSCGSHEVEE NGSVFVRLLKASGLT
8	*Xenopus laevis*	NCBI Reference Sequence: NP_001089160.1	MVAKRKLSRSDDREESFTADTSKNKKCRTSSKKSKALPQDGVVE NDSIFVQLLKSSGMTL
9	*Danio rerio*	GenBank: AAI63598.1	
10	*Bombyx mori*	NCBI Reference Sequence: NP_001233147.1	MMRKKKRSSVTVDEDPTLDVSKAKKSKSSGRSTKSSVQDSCQDS VFVQFLKESGVTLTPGS
11	*Drosophila melanogaster*	GenBank: AAN13836.2	MGPKKNKSQLSQVSYVSPNKRARKENKDNYLYICLRDSGLTLKD PPEKNCASRESIQII

Table- 5: Shows mutation at different position within 30AA residue of MLS in FANCD2. Many mutations in MLS part of FANCD2 associated with cancer (global mutation data base for cancer)

Mutation in MLS	Genomic Mutation ID	AA mutation	CDS mutation	Primary Tissue	Primary Histology	Pubmed ID, references
S3F	COSV107286679	p.S3F (Substitution - Missense, position 3, S→F)	c.8C>T (Substitution, position 8, C→T)	Skin	Malignant melanoma	36219477, [9]
S3T	COSV104599290	p.S3T (Substitution - Missense, position 3, S→T)	c.7T>A (Substitution, position 7, T→A)	Skin	Malignant melanoma	28467829, [10]
R5T	COSV55036087	p.R5T (Substitution - Missense, position 5, R→T)	c.14G>C (Substitution, position 14, G→C)	Urinary tract	Carcinoma	32321774, [11]
R6I	COSM7946246	p.R6I (Substitution - Missense, position 6, R→I)	c.17G>T (Substitution, position 17, G→T)	Skin	Malignant melanoma	-----
R6G	COSV105155845	p.R6G (Substitution - Missense, position 6, R→G)	c.16A>G (Substitution, position 16, A→G)	Lung	Carcinoma	29535388, [12]
E11E	COSV104599166	p.E11= (Substitution - coding silent)	c.33G>A (Substitution, position 33, G→A)	Prostate	Carcinoma	31874108, [13]
E14D	COSV55046760	p.E14D (Substitution - Missense, position 14, E→D)	c.42G>C (Substitution, position 42, G→C)	Lung	Carcinoma	22980975, [14]
S15I	COSM9995230	p.S15I (Substitution - Missense, position 15, S→I)	c.44G>T (Substitution, position 44, G→T)	Lung	Carcinoma	32321774, [15]
S15R	COSV105155867	p.S15R (Substitution - Missense,	c.45C>A (Substitution, position 45, C→A)	Prostate	Carcinoma	32268276,

		position 15, S→R)				[16]
D19Y	COSV55047680	p.D19Y (Substitution - Missense, position 19, D→Y)	c.55G>T (Substitution, position 55, G→T)	Urinary tract	Carcinoma	-------
T23T	COSV55036868	p.T23= (Substitution - coding silent)	c.69C>T (Substitution, position 69, C→T)	Stomach	Carcinoma	--------
Q26H	COSV55036019	p.Q26H (Substitution - Missense, position 26, Q→H)	c.78A>C (Substitution, position 78, A→C)	Haematopoietic and lymphoid Prostate	Chronic myelo monocytic leukaemia	26648538, [17] 31874108, [18]
P27T	COSV105156026	p.P27T (Substitution - Missense, position 27, P→T)	c.79C>A (Substitution, position 79, C→A)	Pancreas	Carcinoma	26804919, [19]
S29F	COSV55048072	p.S29F (Substitution - Missense, position 29, S→F)	c.86C>T (Substitution, position 86, C→T)	Skin	Carcinoma	25759019, [20]

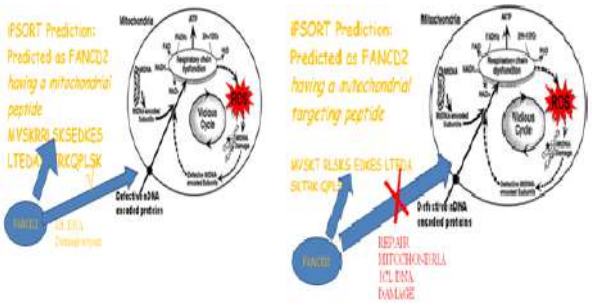

Figure.1: Represents FANCD2 localize in mitochondria and involve in mt.DNA damage repair (left). Mutant MLS of D2 unable to localize, repair mt.DNA (right) cause increase ROS level and DNA damage.

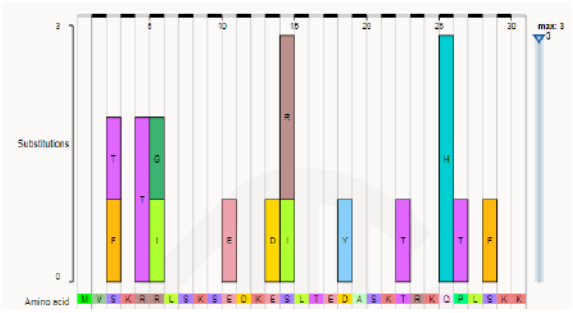

Figure.2: Mutations in MLS part of FANCD2 (Cosmic global mutation data base for cancer)

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RESEARCH ARTICLE

Current Status and Future Prospects of Vegan Foods

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ABSTRACT

Current day's people are giving more priority to the food, in this concern this article was reviewed and this is not related to one particular region, it is a universal concept. Among the changing scenario of food habits vegan food is one among them. Vegan food is focusing more attention in current days due to its personal and potential health benefits have uplifted the overall health consciousness among consumers, regarding unease on planetary sustainability, and the ethical animals' treatment. In a couple of years, there has been a great demand of vegan population around the globe specifically in developed countries. Vegans also avoid eating food products that are sources of animal products like milk, dahi and also some wines. The global vegan food market is projected to number of restaurants catering to the vegan community and the increasing penetration of global companies, the global vegan food market is expected to witness a further growth in the forecast period of 2022-2027, thereby boosting the growth of India vegan food market.

Keywords: Demand, Market, Products, Health, Awareness

INTRODUCTION

The nourishment that conquers includes an expansive impact on our environment significantly between different diets. It may impact on demographic change, population growth involve an increasing stipulate for animal products predominantly meat, dairy products and crops. Meanwhile several beliefs and concerns were raised in recent days about animal welfare and also climate change and greenhouse gas emissions have recently started to become a point

of interest **(**Weber and Matthews 2008**)**. Modern food systems, chiefly the agriculture sector, have a decidedly indefensible collision on the environment; sustainable cut down is one with production by the environmental impact. Gaining additional interest or looking forward towards the nutritionally safe, healthy, economic and ethnically acceptable food/diet and also less impact on biodiversity of ecosystems. When compared the managing of plant and animal origin foods, animal husbandry require a large inputs along with more detrimental have an effect on of environment. While there is no universally established system for measuring these effects quantitatively, a broadly used method is the Life Cycle Impact Assessment technique (LCAs). LCAs can deduce the ecological impacts of generation, transport, handling, storage, waste disposal of food production Chai *et al*. (2019).

History of Vegan Foods:

Donald Watson, an animal rights campaigner and co-founder of The Vegan Society, pretend the term "vegan" in 1944. However, the data at hand points to ancient Indian and eastern Mediterranean communities as the origins of the idea of avoiding flesh. Around 500 BCE, the Greek philosopher and mathematician Pythagoras of Samos made the first reference to vegetarianism, a less harsh type of veganism, as an advocate he showed his kindness toward all species (16) every year on November 1st, the society celebrates World Vegan Day to honour its creation. In November 1944, Donald Watson, the secretary of the Leicester Vegetarian Society, established the new quarterly publication "Vegan News." He chose the term "vegan" on his own. Indian religions including Jainism, Buddhism, and Hinduism have all been influenced by the Indian concept of ahimsa, which has been crucial to the formation of Vegan Studies. Mahatma Gandhi, a staunch proponent of ahimsa, strongly condemns the cruelty and suffering inflicted on animals in his book My Experiments with Truth. He emphasises vegetarianism and avoiding milk. One Indian religion, Jainism, has a lot in common with ethical veganism. According to Jainism, the entire natural world is alive. They hold that every element of the natural world-from rocks and trees to gods-contains an eternal soul, or Jiva. The thought that the spirit of veganism has been present in Indian cultural memory since the beginning is additional supported by the fact that the asastriya vratas of Hinduism are inherently vegan. A. The first of its two main goals is to study critically the geo-cultural growth of veganism in India. Second, it considers how new vegan theory and critique could influence the narratives that make up contemporary Indian culture **(**Wright 2021**)**. However, some people are extremely interested in the concept and are incorporating more and more plant-based foods into their diet. Such individuals are the target of a variety of vegan and plant-based products since they facilitate their transition and the market for vegan consumers is rapidly expanding.If properly followed, the vegan diet is healthful, and its popularity and awareness are rising. There are already a number of items available in India, so adhering to one of the many acceptable diets that include a variety of vegetables, cereals, pulses, and other foods is not very difficult **(**Tonstad *et al*,.2009**)**.

The biggest difference between vegetarians and vegans is that, despite not eating any meat (including that from cows, pigs, fowl, or fish), vegetarians do consume dairy products, eggs, or both. All foods containing components from animals are forbidden in the vegan diet. People who follow a vegan diet must carefully plan their meals in order to prevent nutritional deficiencies because some food sources are removed from the diet. Before starting a vegan diet, people may want to consult a doctor or dietitian, especially if they already have a health concern. (16).

Before the broad COVID-19 upheaval a year previously, demand for vegetarians was increasing; vegan, vegetarian, and flexitarian diets were on the rise. Concerns about planetary sustainability, personal wellbeing, and the ethical treatment of animals sparked this expanded interest in plant-based diets, and it now appears that the general public has effectively nurtured this trend. Similar to a vegan diet, a vegetarian diet excludes meat and animal products. Veganism and vegetarianism differ in that the vegetarian diet may occasionally include animal products such as dairy, milk, eggs, cheese, and honey **(**Gallagher 2022**)**.

Types of Vegans

A vegan diet consists solely of plant-based meals. This diet forbids the consumption of any animal products, such as meat, dairy, and eggs. Others refrain from consuming honey. Being vegan is a lifestyle decision for some people while it is a dietary choice for others. (Gupta and Bhatia 2016**)**. The four core types of vegans are ethical vegans, environmental vegans, health vegans, and religious vegans.

Ethical Vegans – Those who have adopted a vegan lifestyle because they are adamantly opposed to animal cruelty are known as ethical vegans. They are all living things with the desire to survive and are conscious. The only way ethical vegans can see to protect the short and miserable lives of creatures produced for our plates is by avoiding from all animal products.

Environmental Vegans – Environmental vegans think that by choosing a vegan diet, they may minimize their impact on deforestation, reduce greenhouse gas emissions, and reduce pollution by refusing to support animal agriculture.

Health Vegans –Health vegans include another sizable category of vegans. Health vegans are the second most widespread form of vegan, after ethical vegans.

Religious Vegans – For instance, Jainism is a religion whose adherents strictly adhere to a vegan diet. It is a tradition from ancient India. All forms of violence are abhorred by Jainism. "One's ultimate religious duty is non-violence". This extends to their diet meaning they consume a non-violent vegan diet. Vegetables, fruits, legumes, nuts, and seeds are frequently found in large quantities in vegan diets. These foods offer a wide range of essential vitamins, minerals, healthy fats, and protein when consumed in a variety. To ensure that one has access to all necessary nutrients, especially those derived from animal sources, such as iron, protein, calcium, vitamin B-12, and vitamin D, enough planning is necessary. **(**Katz 2014**)**.

Major nutrients that reflect vegan diet

Vitamin B-12 is usually found in products made from animals. Red blood cells and neurons are both protected by it. This vitamin can be obtained from plants in the form of yeast spreads, nutritional yeast, and fortified plant milks and cereals.

Iron is vital for the health of the blood. Dark leafy vegetables and beans are also excellent sources. Extract additional vegan foods high in iron.

Calcium for maintaining bone health. Tahini, tofu, and leafy greens are foods that can help maintain healthy calcium levels. Incorporation of plant-based foods high in calcium.

Vitamin D helps build the bones and teeth while offering protection against cancer and several other long-term health issues. Regular consumption of foods fortified with vitamin D and exposure to sunlight can raise vitamin D levels.

Omega-3 fatty acid - There are three forms of omega-3 fatty acids: EPA, DHA, and ALA, which are crucial for the health of the heart, eyes, and brain. Walnuts and flaxseeds are rich sources of ALA, but the only plant sources of EPA and DHA are seaweeds and algae.

Zinc is crucial for the repair of DNA damage and the immune system. High zinc foods include oats, beans, nutritional yeast, almonds, and nuts.

Iodine is critical for thyroid health. Seaweeds and fortified meals are examples of plant-based sources.

Vegan diets are increasing awareness of plant-based eating, which has been associated to a numeral of health advantages. According to reports, a well-planned vegan diet can provide all the nutrients desirable for good health (Haas *et al*, 2019). However, there is still some dispute regarding the nutritional value of vegan diets and the possibility of nutritional deficiencies, particularly with regard to some important micronutrients like vitamin B12, vitamin D, iron, calcium, iodine, omega-3 fatty acids, selenium, and zinc in inadequately adapted or unfortified vegan diets. A classic vegan diet is one that excludes all foods that are wholly or moderately sourced from animals. More whole grains, pulses, fruit, and vegetables are highlighted in the diet.**(** Key *et al.* 2006**)**

Status of Food Industry

The food sector is increasingly taking notice of the rising demand for vegan cuisine. By 2023, it is predicted that the market for meat substitutes would have grown to over £22 billion. It shows that vegan dietary preferences are being influenced by the vegan food sector. The health advantages of plant-based diets, according to Fardet and Boirie, are directly related to the fact that these foods require the least amount of processing **(**Petre 2019**)**.

Vegan Food Prototype

Foods that are produced from plant-based sources and are often free of dairy or meat are known as vegan foods. Products that taste, flavour, and look like real meat but are healthier than meat are called meat replacements. These goods are increasingly used as alternatives to traditional meat and meat-based items. The popularity of vegan food in India has been largely attributed to a variety of writings on Indian vegan recipes. Vegan e-commerce is booming, and many restaurants have started designating their menu items as "vegan" and "veganizable." Dairy substitutes, meat substitutes, and other goods are the three primary categories of vegan products that are offered on the market. **(**Gerke and Janssen 2017**)**. In 2020, the dairy substitute category dominated the market. The number of components utilized to make milk substitutes has significantly increased in the dairy substitutes industry. These ingredients include soy, oat, coconut, almond, rice, hemp, etc. The greater diversity of ingredients allows customers to choose from a wider range of flavors and ensures that their nutritional needs are addressed. The market is divided into Almond, Soy, Oats, Wheat, and Others, according on the source. The segment's market share is increasing as a result of soy's expanding applications. Many food products, including meat substitutes, frozen desserts, soups, salads, nondairy creamers, breakfast cereals, newborn formula, cheese, whipped cream, pasta, bread, and pet meals, include soy proteins**(**Guha *et al*. 2020**)**.

Based on product type, the market is divided into:

Dairy Alternatives
Meat Substitutes
Egg Alternative
Vegan Bakery
Confectionery
Plant-Based Snacks
Others

Upward wakefulness towards Veganism Market Demand

Due to a growing middle class, increased awareness of global trends, the need for protein transitions for human and planetary health, as well as deeply ingrained cultural views on meat consumption among India's diverse population, plant-based foods are well-positioned to bridge the socio-cultural divides in that country. The expansion of eateries that serve the vegan community is anticipated to further fuel the market's expansion in India. (8). The extension of the worldwide vegan food market, which reaches a value of USD 15.4 billion in 2020 and was fuelled by mounting consumer awareness of healthy lifestyles, is opinionated the growth of the vegan food market in India. The global vegan food market is anticipated to prolong growing in the forecast period of 2022–2027, growing at a Compound Annual Growth Rate (CAGR) of 26%, thereby boosting the growth of the India vegan food market. This growth will be aided by the growing number of restaurants catering to the vegan community and the increasing penetration of global companies. (9). The Indian consumer, like the rest of the world, is well-travelled and knowledgeable about current events. The main factors influencing the market in India are the shifting dietary trends and the rising health consciousness among the large population. These individuals are capable of identifying the rising prevalence of chronic lifestyle diseases like cancer, diabetes, obesity, and cardiovascular issues. In addition, the Indian government is making positive moves to encourage the adoption of sustainable plant-based diets to combat climate change and other environmental problems brought on by fisheries and animal husbandry. The demand for vegan food has increased as consumers become more aware of its health benefits, grow more concerned about animal cruelty, and become more knowledgeable about its nutritional advantages **(**Petre 2019**)**. The expansion of vegan businesses in the nation has been fuelled by the rising demand for plant-based substitutes. Indian start-ups are now selling a range of items to help consumers embrace a vegan lifestyle, from a variety of plant-based dairy products to vegan meat substitutes. The country's expanding vegan population has also caught the attention of large international Fast-Moving Consumer Goods (FMCG) companies, who are now launching vegan items to capture a piece of this booming market.The American journal of Lifestyle Medicine found that (83%) respondents believe that a plant-based is safe and health-promoting diet. The plant-based diet pattern reduce the risk of cardiovascular disease (83%), type 2 diabetes (79%), and cancers (63%) as well as avoid and care for various chronic diseases (58%). Several industries like

defence, military, healthcare, manufacturing, automotive and aerospace contributing their share to vegan foods market growth. Another contributing factor is the increasing investments in biodegradable electrostatic discharge packages in the country are projected to release doors to advantageous opportunities for the expansion of the market throughout the forecast period **(**Sethi *et al.*, 2016**)**. Consumption of meat and poultry products is linked to an increased risk of diabetes, cardiovascular illnesses, and several malignancies, according to a recent study published in Bio Med Central (BMC) Medicine. Meat has been linked in numerous previous studies to high mortality rates, and the World Health Organization has classified meat as human carcinogenic (cancer-causing). People all throughout the world are gradually switching to plant-based diets as awareness of the negative impacts of meat consumption grows **(**Guha 2020**)**. In essentially, veganism is a philosophy and way of life that aims to exclude and eliminate animal exploitation and cruelty in all forms of animals used for food, clothing, or any other purpose, as far as it is possible and practical to do so. By extension, it promotes the development and use of animal and cruelty-free alternatives for the benefit of animals, humans, and the environment. In terms of nutrition, it refers to the practise of avoiding any goods that are entirely or partially produced from animals. **(**Weber and Matthews 2008**)**

CONCLUSIONS

The trend of eating pattern is slowly changing from consumption of Non vegetarians or vegetarians to vegans because of the health consciousness, animals and environment saver's. This article provides basic information regarding the Vegan foods. Further interest is on the vegan food products and its processing, which is going to be a vast area of food research and development.

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REVIEW ARTICLE

Insightful Reviews on Varicose Veins

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ABSTRACT

Twisted, dilated, and tortuous veins are known as varicose veins, and they typically affect the lower limbs. Varicose veins are a consequence of venous reflux brought on by ineffective valve closure. Although varicose veins are usually not fatal, they can lead to a number of issues that can negatively impact a person's life and perhaps result in life-threatening consequences. Varicose veins can cause pain, itching, leg restlessness, swelling, ulceration, and a burning feeling. Several factors such asage, gender, occupation, pregnancy, and obesity can increase the likelihood of developing varicose veins. The primary cause of the higher risk of vein varicosities has been determined to be prolonged standing and pressure on the venous valves in the lower extremities. The techniques for diagnosing varicose veins that rely on ultrasonography are doppler ultrasound and duplex scanning technique. These procedures are carried out following a physical assessment. The most widely applied technique is colour doppler ultrasound. Conservative management techniques, such as compression therapy, dietary and lifestyle changes, and medication, can be used to treat varicose veins without surgery. It also comprises the sclerosant and foam-based sclerotherapy treatment approach. Phlebectomy, radiofrequency ablation, and endovenous laser ablation are the minimally invasive therapy options. Procedure of operation Subfascial endoscopic perforator vein surgery identifies and repairs the lower limb's injured perforating vein using a laparoscopic device. The varicose veins treatment methods help to eradicate the venous reflux in saphenous veins, that relieve symptoms of venous incompetence, prevent complications, lower recurrence rates and if feasible, short recovery time. This review article aims to put a light on varicose veins, including its etiopathology, diagnosis, treatment options, and risk factors.

Keywords: Varicose veins; Chronic venous insufficiency; CEAP classification; Colour doppler; Endovenous laser ablation; Sclerotherapy; Subfascial Endoscopic Perforator Vein Surgery (SEPS)

INTRODUCTION

Varicose veins are protuberant or popping veins that are larger indiameter than 3mm. Varicose veins along with telangiectasias (spider veins), reticular veins, pigmentation, lipodermatosclerosis, oedema, atrophie blanche and venous ulcerations subsumes under the medical condition known as *chronic venous insufficiency (CVI)*[1,2]**.**Varicose veins can occur due to the condition called venous reflex. Varicose veins can occur due to the condition called venous reflex, in which blood can flow in both forward and backward direction as a result of failure of valves to close properly or the stretching of veins near the skin surface (superficial veins). The venous reflex leads to twisting and popping of veins and eventually leads to varicose veins (Fig 1). The superficial veins comprise of the great saphenous vein (GSV) and small saphenous vein (SSV), in which varicose vein eventuate. The body's lower extremities are more susceptible to vein varicosities than additional body parts as standing and walking increases the pressure within the lower body's veins [3].The patients with varicose veins experiences pain, itchiness, burning sensation and swelling in lower legs. However, varicose veins can occur all over the legs but the symptoms are more eminent near the knees and ankle region[4].

CEAP Classification

The Clinical – Etiology – Anatomy – Pathophysiology (CEAP) classification is a widely used method for confirming patients with chronic venous disorders [5]**.** CEAP proposed by John Peter, developed in 1993, updated in 1996 and revised in 2004, is a classification system based on clinical expression of chronic venous disorders, on the basis of current understanding of Etiology, the involved anatomy and the underlying venous pathology [6]**.** Clinical (C) Classification In the advanced revision of CEAP, the recurrence of venous ulcer and varicose veins was represented by adding the subscript 'r' in C_2 and C_6, classifying newly as 'C_{2r}' and 'C_{6r}' respectively. Also, corona phlebectatica was classified separately as 'C_{4c}' by sustaining pigmentation/eczema as 'C_{4a}' and lipodermatosclerosis/atrophie blanche as 'C_{4b}' (TABLE1)[7,8]. Clinical research reveals that varicose veins develop gradually. Leg pain, itching, a feeling of heaviness in the legs, swelling, and restlessness accompany the first stage of vein swelling. As the condition progresses, a patient may reach the stage of telangiectasias, during which they may have severe leg discomfort, a burning feeling, and blue, purple, or red veins that form thin lines or web-like networks. Additionally, varicose veins can bleed and develop ulcers in some areas of the veins. Other symptoms at this point include discoloration, discomfort, swelling, and heaviness. The loosening and leaking of the valves during the edema stage might cause blood to collect in the legs. Prolonged standing might cause pain and swelling in the patient's legs. The condition then advances to the pigmentation/eczema stage, where skin stiffening and colour changes from reddish to tan or reddish-brown occur. Corona phlebectatica is the progressing stage and is thought to be an early indicator of advanced vein disease. Other symptoms at this stage may include lipodermatosclerosis, atrophie blanche, and decreased ankle mobility. The last stage is known as active venous ulceration, during which an open sore may develop at the site of the injury. If the ulcer is infected, pus may drain from the wound and it might have bad odour. The chance of getting blood clots in deep veins increases at this point [4,6]**.**

Etiology (E) classification

Etiology domain in 2004 revision was classified into congenital, primary, secondary and no cause identified. In the advanced revision of CEAP classification, the class E_S was bifurcated into ESi for intravenous secondary causes and E_{Se} for extravenous secondary causes of disease. The subscript 'n' is used to describe the patients report in whom no venous abnormality is identified. E_{Si} is interpreted as any intravenous condition that cause internal damage to venous wall and venous valve, and includes the conditions like Deep Vein Thrombosis (post-thrombotic changes), traumatic arteriovenous fistulas, primary intravenous sarcoma or any other luminal internal changes in the veins. Conversely, E_{Se}interprets the conditions that affects the venous hemodynamics rather than internal venous wall or valve damage

(Table 2)[5,6]. *Anatomy (A) classification* In 2004 CEAP classification system amendment, the anatomic sites for venous diseases were classified as superficial (A_s), deep (A_d) and perforating veins (A_p) [5]**.** In the new advanced CEAP system modification, the 18 numerical classification was used to describe the venous segment of pelvis, abdomen and lower extremities (Table 3)[6,9]**.** *Pathophysiology (P) classification* The basic 2004 revision of *pathophysiology* (P) classification of CEAP system differentiates between reflux (P_r), obstruction (P_o), both ($P_{r,\ o}$) and no venous pathophysiology (P_n) (Table 4)[5,10]**.**

Causes

Chronic venous hypertension, vessel dilation and the rigidity of extracellular matrix leads to the venous wall inflammation in the lower extremity and also cause damage to the endothelial cells leading to increased endothelial cell permeability/injury [11]**.** The damaged endothelial cells in both conditions, ischemia and the extravasation of blood in vein wall, releases matrix metalloproteinases, inflammatory mediators, growth factors, intracellular adhesion molecule-1 (ICM-1) and vascular cell adhesin molecule-1 (VCAM-1), and also the increased concentration of fibrin and hemosiderin in tissues, all of which results in further inflammation and endothelial cell activation [12]**.**The additional cellular processes that more prominently leads to development of varicose veins are: oxidative stress caused by oxygen-free radical reaction due to iron accumulation [13]**,**blood flowing through the superficial vein to the deep vein and changes in the saphenous vein valves [14]**,**increased venous reflux, capillary hypertension and leakage [12]andhypoxia, uncontrolled apoptosis and wall remodelling [15]**.**

Risk Factors

The pressure on the lower limb veins is one of the key reasons of varicose veins development. The development and occurrence of varicose vein disease are linked to a number of important risk factors – Age, gender, family history, pregnancy, occupation, obesity, and genetic factors [3,11,16,17]**.**

Age: One of the main risk factors for the development of varicose veins discovered is age. Varicose veins occur more frequently as people age because of a number of causes, including decreasing venous valve flexibility, changes in the vein matrix's composition and crippling of the calf muscles [16]**.**

Gender: Women are more likely than men to develop varicose veins. The primary causes of the higher frequency of varicose veins in women are pregnancy and the concentration of the sex-steroid hormones, estrogen and progesterone [16]**.** A study showed that the chances of varicose veins to develop are higher in women, than in men [18]**.** However, the results of chronic venous insufficiency (CVI) were found not to be consistent. Another study demonstrated that men are more likely than women to have chronic venous insufficiency[19,20]**.**

Pregnancy: The physiological changes such as increase in weight, hormonal changes, vasodilation, fetal development, rise in blood volume and increased pressure on blood vessels, that occur in woman during pregnancy may result in symptoms leading to venous disease. According to the evidences obtained, the prevalences of varicose veins development in women are: multiparous woman (having more than one pregnancy) > parous woman (having one previous pregnancy) > nulliparous woman (no previous pregnancy), showing that the frequency of venous varicosities development increases as parity increases [16,21]**.** Relaxin, a vasodilator hormone, secreted during pregnancy by corpus luteum, functions in relaxing the pelvic ligaments and preparing cervix for delivery, was found to increase the pressure on venous valves in lower limbs leading to lessening of valves flexibility [22]**.**

Occupation: The occupations such as teachers, clerks, labourers, nursing staffs, street cleaners, that are linked to extended standing have an increased chance of developing varicose veins. Prolonged standing increases the pressure on venous valves and vessel walls leading to chronic venous diseases [16,18]**.** The research conducted on the frequency of varicose veins development in teachers and found that 42% of the teachers were positive for having varicose veins in which the incidence was higher in women in teaching profession [23]**.** A cross-sectional investigation conducted in 2022 among nurses of two hospitals in Saudi Arabia, concluded that the frequency of

venous varicosities in nurses and medical staffs of other departments vary from 15% to 40% based on working hours and time period [24].

Obesity: Blood reflux in veins is caused by obesity, which raises pressure on the vein wall and valves.However, obesity is not a compulsory factor and is not constantly associated with the emergence of persistent venous insufficiency [16].

Genetic factors: The genetic factors include the genes which on mutation are responsible for venous diseases. These genes are *FOXC2* and *THROMBOMODULIN (TM).*FOXC2 (Forkhead Box Protein C2) gene on mutation results in lymphedema distichiasis, a hereditary disorder caused by venous valves failure in both saphenous and deep veins of lower limbs [25,26].Thrombomodulin (TM) is an endothelial cell surface-expressed glycoprotein that bind to thrombin with a high affinity, was discovered to be related to varicose veins [27].

Diagnosis

Clinical diagnosis is the primary method used to diagnose chronic venous insufficiency and varicose veins. Varicose veins might show differently in each individual and sometimes cause no symptoms at all [28]. The assessment of symptoms, risk factors and physical examination results aids in determining the diagnosis of size and distribution of varicose veins, presence and type of edema, skin discoloration and ulceration. Doppler ultrasound imaging is the technique considered for clinical diagnosis of varicose veins [10,11].

Doppler ultrasound

Doppler ultrasonography is a simple, painless, non-invasive method that can be used to assess patients with symptomatic varicose veins or asymptomatic visible varicose veins considering treatment. It can also show the presence of blood clots or obstruction in the veins [11]. The other aims of doppler ultrasonography that helps to demonstrate both the anatomical patterns of veins and abnormalities of venous blood flow in the limbs are to determine the saphenous junctions that are incompetent, diameter of the junction and intensity of the veins reflux [29].There are four techniques for imaging that use the Doppler approach: *Continuous Wave (CW) Doppler:* The method involves two piezoelectric transducer crystals, both contained on a single head. One transducer crystal always functions in transmitting a constant audio signal at a frequency of 3-8 Hz, while the second transducer crystal continuously operates to receive the returning frequency and records it automatically by deducting the first signal from the returned signal. This method only detects the blood flow, but fails to give information about depth, direction and velocity of flow [11,30,31]. *Pulse Wave (PW) Doppler:* With this technique, the depth of a returning signal oriented at any point along the ultrasonic beam's axis can be obtained. For the purpose of identifying such mobile structures, three fundamental technical parameters are: high pulse repetition frequency, optimum transducer frequency and correct insonation angle (less than 60°) [30]. Since the pulse wave (PW) doppler does not provide information on the structure or place of echo origin, it is typically utilised in conjugation with B-mode or 2-dimensional mode imaging. This is called Duplex Ultrasound scanning [32]. *Colour Doppler:* Colour Doppler is also called as colour flow imaging (CFI). Ultrasonic colour doppler is an imaging technique that generates colour-coded chart of tissue velocity superimposed on grey-scale (pulse-echo) image of the anatomy of tissues by combination of anatomical information obtained using ultrasonic pulse-echo technique and velocity information obtained using ultrasonic doppler technique. In the resulting image of colour doppler, the red-orange colour depicts the flow towards the robe and blue colour depicts the flow away from the probe [30,33,34][Fig. 2 (a) and (b)]. *Power Doppler or Energy Mode Imaging:* Power doppler is a method that evaluates the power i.e. the amplitude/strength of the doppler signal in colour, instead of the velocity or direction of the flow as in conventional doppler methods. This variable is basically different from the mean frequency shift of the echoes [11]. The velocity of red blood cells determines frequency, but the quantity of blood present determines power. The advantages of power doppler over the conventional doppler methods are: high sensitivity to flow, better edge definition and depiction of continuity of flow [35].

Duplex scanning technique

Standing position is required to perform the duplex ultrasonography with most of the patient's weight on the contralateral limb. This position is beneficial as: 1. It is most accurate physiological position for examination of venous insufficiency and reflux, and 2. It ensures maximum venous inflation as it relaxes the muscles of the leg to be examined. Both the great saphenous vein (GSV) and small saphenous vein (SSV) are examined. During GSV evaluation, the affected leg is flexed turned slightly outward with the patient's heel against the ground. During SSV evaluation, the patient is turned away from the operator and the knee is slightly flexed and the muscles are relaxed to prevent venous compression [36,37]**.** Six venous segments of the lower limb are scanned using a colour duplex scan using a QAD-1 duplex scanner and a 5MHz probe: the common femoral vein, superficial femoral vein, greater saphenous vein, deep femoral vein, popliteal vein and the posterior tibial vein. *Valsalva maneuver*and *Distal pneumatic deflation*in two positions (RT-15 and standing) are the techniques employed for the examination.Valsalva maneuver is performed to check the adequacy by placing a manometer into the mouth of the patient's generating a pressure of at least 40 mmHg. The distal pneumatic deflation described by Van Bemmelen et al. uses an automatic cuff inflator for rapid inflation and deflation of cuffs placed in the distal position to the level of examination [36, 37].

Treatments

The prevailing varicose veins treatments available includes non-operative therapy (conservative management and sclerotherapy), minimally invasive therapy (endovenous laser ablation, radiofrequency ablation and phlebectomy) and surgical treatment (subfascial endoscopic perforator vein surgery [SEPS]) [11,40]**.** The treatment to be given is selected by considering the symptoms, location, severity and cause [17]**.** The methods for treatment are discussed in detail below.

Non-operative therapy:

Conservative management:

Treatment of chronic venous insufficiency and varicose veins with conservative management includes *compression therapy, diet and lifestyle modifications*and *pharmacotherapy*[41]**.**Compression therapy is suggested to prevent swelling of limb and as an effective way for treating discomfort. Compression stockings not only improve the symptoms but also improves venous hemodynamics by decreasing reflux of veins and hypertension. Although, compression stockings impact is only for the time period it is worn [17]**.** Individuals with vein varicosities are recommended to bring lifestyle changes such as avoiding prolonged standing or sitting, elevating the legs, lose weight and exercising to improve calf muscle function to avoid swelling and pain. Several foods such as blackberries, garlic, ginger, chia seeds, grapes, dark-coloured fruits and vegetables and medical herbs and supplements are recommended to include in daily routine to increase the efficacy of treating varicose veins [11,41,42]**.**The components used as pharmacotherapeutics to treat varicose veins are low-dose diuretics, topical steroid cream or ointment (fluocinolone acetonide or triamcinolone), antibiotics (generally covering *Staphylococcus* and *Streptococcus sp.*) and herbal supplements (horse chestnut seed extract, micronized refined flavonoid fraction, French maritime pine bark extract and rutosides). These helps to treat stasis ulcers and reduce inflammation [43,44]**.**

Sclerotherapy:

Sclerotherapy is the method that involves intravenously injecting the liquid or foam sclerosant that prompt cellular damage in venous lumen via inflammatory, toxic or physical means causing the removal of varicose veins [41,45]**.** Several sclerosants (chemical agents that are used in sclerotherapy treatment are called sclerosants) used for giving therapy are ferric chloride, hypertonic saline, polidocanol, iodine, glycerine and sotradecol (sodium tetradecyl sulphate, STS). STS is most widely used detergent sclerosant for saphenous varicosities that binds to the lipid membrane of the innermost endothelium of the vein, damaging the exposed cells and inducing an inflammatory reaction. Polidocanol stimulates nitric acid pathway and cellular calcium channel signalling leading to cell death [11,46,47]**.** Sclerotherapy treatment mainly aims at ablation of varicose veins, prevention and treatment of complications of chronic venous disorder and impaired venous functions [45]**.** Some complications and risks may occur during or after the sclerotherapy treatment are anaphylaxis, extensive tissue necrosis, vision disorders, headache and migraine, stroke and transient ischemic attack and hyperpigmentation [48,49]**.** The sclerotherapy

treatment can be provided to patient either in form of foam sclerotherapy or liquid sclerotherapy. The procedure involves the mixing of sclerosing agent with a gas generally air or medical carbon dioxide and then injecting it as a foam. This causes removal of blood from the infected vein by gas with sufficient endothelial damage at low concentration and low quantities of sclerosing agent (Fig 3). The advantage of this method is that it slowly migrates the sclerosing agent so that it can be compressed relatively slowly following injection [50,51].

Minimally invasive therapy

Endovenous laser ablation

The endovenous laser ablation method was introduced in 1999 to treat superficial venous reflux and varicose veins, after receiving permission in the United States. Endovenous laser ablation treatment is a minimally intervening method that has a short and pain-free postoperative recovery period leaving no scar on patient's body and with low recurrence rates (reducing neovascularization by avoiding surgical disruption of sapheno-femoral junction) [11,52]. The most commonly used laser device, also called a laser diode, is 1320nm diode; however, the newer generation diode of 1470nm provides more safety and higher efficacy towards specificity of interstitial water in the venous wall [53]. The process of endovenous laser treatment initiates with the vein mapping and the laser catheter is adjusted at the correct position (at the end inside the vein's lumen). The great saphenous vein is punctured at 2-3 cm below the knee level with 18-gauge cannula in reverse Trendelenburg position (patients are placed in supine position, which is inclined at 30°, so that the head is higher than the pelvis and the leg is lower than hip). The rest of the process is carried out by changing the position to Trendelenburg (patients are placed by elevating the feet and legs of the patient above the heart level in supine position). J-tip 0.035-inch guide wire is inserted at the sapheno-femoral junction using ultrasonography guidance. A 5-F long introducer sheath ranging from 36-50cm depending on the length of GSV to be treated is placed over the guide wire. The bare-tipped fibre of 600-µm diameter connected to a 980-nm laser diode is introduced through the sheath. The device was set with low power and with duration of 2 seconds ON and 1 second OFF. Peri-venous tumescent anaesthesia is then injected into the fascial space of GSV under ultrasound guidance. The tumescent anaesthesia is composed of 20-25 ml lidocaine 2% buffered with 1.4% sodium bicarbonate in 500cc saline 0.9%. Then, laser energy is fired and laser fibre and sheath are gradually drawn back till 1cm above the punctured site to avoid skin burn (Fig 4 (a) and (b))[11,41,54].

Radiofrequency ablation

Radiofrequency ablation (RFA) generates thermal energy destroying endothelium and causing subsequent fibrosis. Radiofrequency ablation (RFA) devices produce truncal ablation, with minimal discomfort and short recovery period [41,55]. Majorly, the procedure involved in radiofrequency ablation and endovenous laser ablation are comparable. Before starting the treatment, the patient is positioned in reverse Trendelenburg position. The procedure initiates with vein mapping followed by injecting a local anaesthesia guided by ultrasonography prior to placement of endoluminal sheath. The catheter is inserted and advanced, under ultrasound guidance, to the target saphenous junction. The position is changed to Trendelenburg for vein emptying. The tumescent anaesthesia solution is injected around the catheter within the saphenous fascia. The catheter is retracted slowly and the venous wall is heated by a bipolar electrode, resulting in the immediate shrinkage and occlusion of the vein. The treatment progresses from the target saphenous junction to the site of venous access. Multi-layer compression bandage is applied to the treated limb and is suggested for about 1 week after the completion of treatment [43,44,55]. The complications of the radiofrequency procedures include haematoma, thrombophlebitis, venous thrombosis, vessel perforation, thermal injury to adjacent nerves, skin burn and pigmentation [56].

Phlebectomy

Phlebectomy technique was developed in 1950s. the varicose veins are mapped by palpation and ultrasound. The patient is kept in standing position and marked prior to the treatment [11]. The area of treatment is made numb and soft tissues are percutaneously hydro-dissected by injecting local anaesthetics. Small incisions are made at regular intervals along the entire length of affected vein [41]. The varicose veins are trapped using phlebectomy hook and forceps are used to obstruct and remove affected veins after ligation. The technique is used at each incision until the varicose veins and feeder vessels are removed [57].

Surgical treatment

Subfascial Endoscopic Perforator Vein Surgery (SEPS)

Subfascial endoscopic perforator vein surgery (SEPS) was introduced in 1985 by G. Hauer. This is a novel method for identifying perforator veins (the blood vessels that links superficial and deep veins are called perforator veins) directly by visual means using an endoscope in the subfascial space. It involves cutting and closing off damaged perforator veins in the leg [58]**.** SEPS is performed using laparoscopic instrument (firstly reported by O' Donnell) with two endoscopic ports for CO_2 infusion to enlarge the subfascial plane and a thigh torniquet is employed to obtain a bloodless field and to prevent gas embolism [59]**.** The perforating veins are mapped with duplex scanning prior to operation and the veins are clipped and divided either by endoscopic scissors or by ultrasonic harmonic scalpel. The perforating veins are divided from the proximal third of the calf down to the ankle, anteriorly to the edge of the tibia and posteriorly to the midline. All perforating veins in the subfascial compartment were then ligated. If the patient has superficial venous incompetence, then stripping of the saphenous vein from the groin to just below the knee and varicose veins removal is performed through small stab wounds [59,60]**.** Patients are generally allowed to move from first postoperative day and are treated with ambulatory compression therapy until the ulcer is healed. Elastic stockings are prescribed for lifetime whenever ulcer occurs [58,60]**.**

CONCLUSION

Varicose vein is the chronic venous disease that could lead to serious damage of veins and excessive bleeding with pain, itchiness, burning sensation and swelling of veins in lower limbs.Varicose veins are diagnosed by physical examination, followed by a vascular ultrasound. The treatment methods include both non-operative and operative approach. From various literature studies, it was found that the various preventive measures such as regular exercise, physiotherapy, maintaining healthy weight, avoiding prolonged sitting or standing, hydration, healthy diet and wearing compression stockings regularly, can be taken to decrease the chances of occurrence of varicose veins. The study of varicose veins holds various future scopes, driven by the advancements in medical science, technology, and a deeper understanding of the condition.

Author Contributions

AA: Drafting the manuscript, **SP**: Revising and editing the manuscript

Competing Interests

The author declare that they have no competing interests.

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Table 1: CEAP Clinical (C) Classifications[5,7]

Clinical Classes	Description
C_0	No obvious symptoms of venous disorder
C_1	Telangiectasias (1mm diameter)
C_2	Varicose veins (3mm diameter)
C_{2r}	Reappearing varicose veins
C_3	Edema (increase in fluid volume in skin)
C_4	Skin and subcutaneous tissue changes resulting from chronic venous disorders
C_{4a}	Pigmentation/eczema
C_{4b}	Lipodermatosclerosis or atrophie blanche
C_{4c}	Corona phlebectatica
C_5	Healed ulceration
C_6	Venous ulcer is in active state
C_{6r}	Active venous ulcer recurring

C_0 – C_6 classes represents the stages of progression of venous disease. Each clinical class sub characterized by a subscript indicates the presence (symptomatic, s) or absence (asymptomatic, a) of symptoms attributable to venous disease.

Table 2: CEAP ETIOLOGY (E) CLASSIFICATIONS[5]

Etiological Notations	Category
Ep	Primary venous disease
E_S	Secondary venous disease
E_{Si}	Secondary – Intravenous (post-thrombotic changes) venous disease
E_{Se}	Secondary – Extravenous (venous hemodynamics) venous disease
E_c	Congenital venous disease
E_n	Cause unknown

Table 3: CEAP ANATOMY (A) CLASSIFICATIONS[5,9]

Segment Number	Area of Anatomic Involvement
AS Superficial veins	
1.Tel	Telangiectasias
2.GSVa	Great saphenous vein above knee
3.GSVb	Great saphenous vein below knee
4.SSV	Small saphenous vein
5.NSV	Nonsaphenous vein
A_d Deep veins	
6.IVC	Inferior vena cava
7.CIV	Common iliac vein
8.IIV	Internal iliac vein
9.EIV	External iliac vein
10.PELV	Pelvic vein
11.CFV	Common femoral vein
12.DFV	Deep femoral vein
13.FV	Femoral vein
14.POPV	Popliteal vein
15.TIBV	Crural (Tibial) vein
16.MUSV	Muscular vein
Ap Perforator veins	
17.TPV	Thigh vein
18.CPV	Calf vein
A_n	No visible venous anatomical site found

Table 4: CEAP PATHOPHYSIOLOGY (P) CALSSIFICATIONS[6,10]

Path physiological Notations	Conditions
P_r	Reflux
P_o	Obstruction
$P_{r, o}$	Reflux and obstruction
P_n	No pathophysiology was found

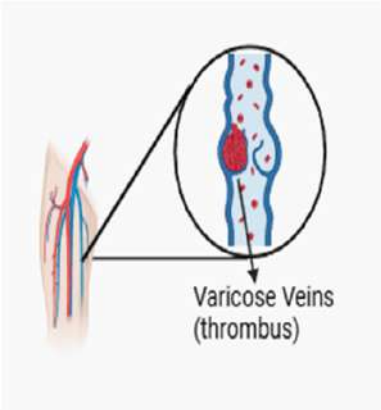

Figure.1: Varicose veins: Bulging veins with diameter larger than 3 mm and loose valves that causes venous reflux and venous thrombosis.

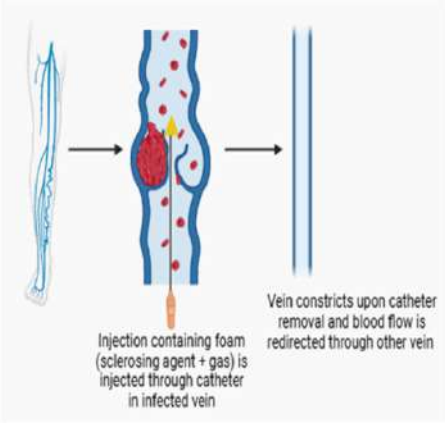

Figure.2: The sclerosing agent is injected as foam after mixing with the gas. The foam pushes the blood out of the infected vein and the blood flow is diverted through the other vein. A sclerosing agent affects the vein's diseased vascular lining, causing the vein to collapse.

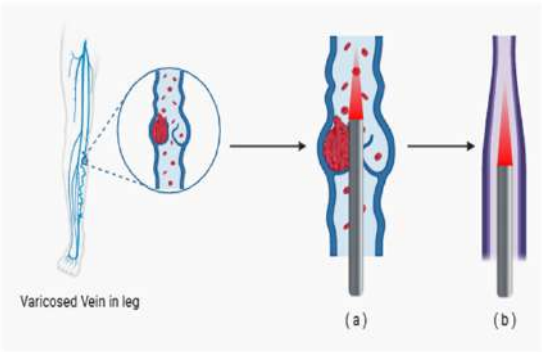

Figure.3:Endovenous laser ablation.(a) Using ultrasonography, the laser fibre is placed into the infected vein. Through the fibre's tip, the laser energy is fired into the infected vein. (b) As the fibre is drawn back, the heat generated causes the vein to collapse, stopping the flow of blood from the infected vein and redirecting it through a different vein.

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REVIEW ARTICLE

Microalgae and its Application - Antibacterial and Antibiofilm Activity of Nanoparticles Biosynthesized with Micro Algal Extract– Review

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ABSTRACT

Microbes are crucial to the environment's ability to function. Some species operate in a way that counteracts the drawbacks of another creature. The anti-inflammatory, antiviral, antibacterial, and antioxidant capabilities of microalgae and cyanobacteria represent only a few of their benefits. Microalgae are eukaryotic unicellular cells with several advantages for creating biotechnological applications, including high biodiversity, photosynthetic yield, growth, productivity and metabolic plasticity that may be directed by culture conditions. The bioactive of microalgae which include several polysaccharides, lipids and secondary metabolites are the reason for their high economic value. These characteristics of microalgae can be increased with Nanotechnology. Bio films are organized communities of microbes that exist within self-produced 'Extra polymeric substances' (EPS) that adhere to the surface. They are hydrogels with viscoelastic behavior that work through Quorum Sensing. Due to their Extra polymeric substance, they have high anti-microbial and multidrug resistance. This is a result of the factor

called 'Biofilm Virulence', which is the root cause of many acute to chronic diseases. The biofilm-inhibiting ability of microalgae and cyanobacteria employing nanotechnology will be the main emphasis of this review.

Keywords: Microalgae, Cyanobacteria, Biofilm inhibition, Antibacterial activity.

INTRODUCTION

Microbes are an essential part of the functioning of the environment. Their continued existence and operation may have both positive and negative effects. In all microbes like bacteria, fungi, viruses, archaea, algae, molds, prions, lichens, etc., some species operate in a way that counteracts the drawback of another creature. Bacterial diseases are caused by the virulent effect of the organism on cells and the resulting immune response. The role of bacteria has a predominant effect as organ-specific which targets a specific part of the body and causes infection. Patients with secondary infections caused by bacteria are prone to high morbidity and mortality rates [1] [2]. The active principle molecules against the bacterial pathogen can fight and the substances selectively eradicate them or restrict their growth without causing any damage to the tissues surrounding them. Antibiotics have come into existence to control bacterial infections and their long-term effects due to over dosage of repeated antibiotics show severe effects on the body because the bacteria gets antibiotic resistance. To overcome these antibiotic resistances, a safe selection of treatment is needed where the prescribed dosage depends on pharmacokinetics, its side effects, resistance profile, and cost of the drug[3][4][5]. Microalgae play an effective role against inflammation, microbial infections, bio films and oxidation building. Microalgae are eukaryotic unicellular organisms with diverse biotechnological applications, including high biodiversity, photosynthetic yield, growth, productivity, and metabolic plasticity that may be directed by culture conditions. Cyanobacteria and diatoms are types of microalgae which are known for their specialized properties. Microalgae have easy, low-cost growth requirements (free seawater, low-cost nitrogen, phosphorus, and carbon sources), and they develop quickly in the presence of enough light. The inhibitory effect of bacteria is due to the beneficial qualities of microalgae [6]. Microalgae, which include blue-green algae or cyanobacteria, are tiny, single-cell, organisms. Some of them are capable of heterotrophic and photogenic growth. Carbon and radiation energy fuel their metabolism, which is extremely similar to the angiosperm plants which are spotted singly, collectively, or in clusters. Microalgae is rich in nutrition. Some types of microalgae can replace phospholipids in their membranes with non-phosphorus lipids to adapt in phosphorus deficiency [6].

Microalgae are a desirable feedstock for the generation of higher energy-density products like fuels and others. Microalgae are capable of creating several fuels, including hydrogen, lipids, hydrocarbons, and carbohydrates because of their capability to generate various chemical intermediates. They enhance the Sustainable Development strategies that are to be achieved shortly.Microalgae have been found to have anti-biofilm activity against various bio film causing bacteria. [38] In the search for alternative treatments against bacterial infections and to alleviate the capabilities of microalgae, nanotechnology is used. Nanoparticles due to their magical dimensions exhibit specialized characteristics that are manipulated for biotechnological applications. Metallic, non-metallic, carbon-based nanoparticles are known for their anti-microbial properties [46]. Biofilms are organized communities of microbes that exist within self-produced 'Extra polymeric substances' (EPS) that adhere to the surface. They are hydrogels with viscoelastic behavior that work through Quorum Sensing, as was discovered through analysis of the EPS coat present in the biofilm. The EPS are composed of polysaccharides lipids and nucleic acids, which help to tolerate mechanical and various other stress. Biofilms are prevalent in almost all habitats like medical implants, from contact lenses to intrauterine gadgets, pacemakers, prosthetic joints, catheters, and heart valves. Due to their capacity for antibiotic resistance, host defense and other pressures like multi-drug resistance and chemical resistance (Biofilm Virulence), biofilms pose serious health risks like various microbial infections, heart diseases and chronic diseases like osteomyelitis, endocarditis, cystic fibrosis (CF), and periodontitis. It is essential to eradicate biofilm formation for a

healthy disease - free environment for which micro algal bioactive compounds are a solution [33][36]. The Antibacterial and bio film-inhibiting ability of microalgae and cyanobacteria employing nanotechnology will be the main emphasis of this project. Algae are organisms that produce oxygen through photosynthesis and can be found in freshwater, sewage, and aquatic habitats. Algae have the potential to provide the biotechnology sector with innovative chemicals and bioactive substances. Thus, these microalgal species are being innovatively used for various purposes. In addition to being a precursor of bioenergy eco-friendly fuels like bioethanol, manure, nutrients, and other bioactive metabolic compounds, algae also serve as a source of food and as an effective pollution control [6]. Numerous extreme environmental conditions, such as those involving temperature, pH, salinity, osmotic pressure, exposure to UV light, and anaerobic conditions, can cause algae to survive and even flourish [9]. They are capable of protecting their cellular constituents by producing primary metabolites in opposition, including Lutein, vitamin B12, vitamin E, oleic acids and Zeaxanthin. In difficult environments where they may exist, secondary metabolic compounds are also produced. These metabolites are effective against virulent microbes like fungi, acting as antibiotics and antimicrobials [7] [55].

Microalgae

The most prevalent primary unicellular autotrophs are microalgae, which can be found in all aquatic environments, including freshwater, seawater, hypersaline lakes, deserts, and polar habitats. They create biomass, such as sugars, by converting light energy and carbon dioxide (CO_2) [26]. These are resilient in a variety of environments and can adjust to both severe and mild circumstances. Microalgae can synthesize an extensive variety of bioactive chemicals, such as polysaccharides, lipids, carotenoids, and vitamins. Because they have anti-inflammatory, antitumor, antioxidant, antiviral, anticancer, antiallergy and antibacterial characteristics, they are employed in important biological and pharmaceutical sectors [21].

Cyanobacteria, a variety of microalgal species, are recognized as the fundamental organisms for fixing nitrogen and are also responsible for the initial emergence of atmospheric oxygen roughly 2.3 billion years ago. The ability of microalgae to produce useful biocompounds and bioenergy has recently attracted attention. Thus, over the past 20 years, there has been a lot of interest in the production of modified cyanobacteria. A unicellular freshwater cyanobacterium known as *Synechocystis* sp. Is a single-cell model organisms for genetic, and physiological investigations of photosynthesis, and energy research. In 1996, *Synechocystis* sp. PCC 6803, the fourth organism overall and the first prototroph, had its whole genome sequenced. Chlorophyll pigments, carotenes, and phycobilins are the three main categories of algae compounds, which are particularly significant in plant physiology.[32]

Biomass cultivation

Microalgae have simple, cost-effective, developing conditions (no-cost marine water, low-cost carbon, phosphorus, and nitrogen sources), and grow quickly in the presence of enough light. The best method for the creation and manufacture of the following rare products is the high density and extensive cultivation of microalgae. Algae grown in enclosed photo bioreactors or open-pond systems could accomplish this. [26]

In essence, a sealed cultivation environment is used to cultivate the algal species in photoautotrophic environments. The culturing conditions like abiotic factors which comprise the nutrition and temperature influence the development and availability of biomass. While oxygen must be removed, controlled amounts of water, nutrients, and CO_2 are delivered. To achieve ideal culture conditions, all criteria are carefully controlled. When compared with open systems, the pollution level is significantly lower. [26] Controlling culture conditions, such as light, gas transmission, temperature and pH level along with preventing the introduction of contaminants and toxins are the most crucial function and characteristics of the system. [37] [22] [23] [24] [25]

Factors affecting microalgae cultivation

The environment for micro algal cultivation has a significant impact on how these microorganisms function, which in turn affects how the metabolites and bioactives are synthesized are synthesized. In the production of antimicrobial agents, it has been highlighted that the effects of culture conditions like pH and salinity matter. Commercial production of algae has been constrained by contamination from predators and other rapidly developing heterotrophs. The dominance of certain species due to Monosaturated FA is determined by various factors, such as

the rate of microbial growth, the connection of different algal strains, fluctuating external factors, the production of allelopathic toxins (such as Fischerellin and cyanobacteria), reduction in development due to rapacity and drowning, among others are theby products of external membrane breakdown [27].

Effect of pH

The main defenses against contamination by microbes, like other types of microalgae, are pH alterations. Due to the direct impact pH control has on the availability of different chemical elements, for efficient porosity between media contents, pH maintenance is crucial. The depletion of nutrients in media may cause the production of particular bio compounds. [27] [30]

Effect of light

The biomass's metabolic makeup is influenced by irradiation as well. As the incidence of light increases, the fatty acid content can decrease. This is because the majority of chloroplasts are made of lipids, and more light energy requires more activity from chloroplasts. Photosynthesis requires light for cells to proliferate and increase the quantity of cells. Studies have shown that illumination has an impact on the antioxidants found in microalgae especially the 450-490 nm range, during microalgae cultivation. The ability of *S. fusiform* to act as an antioxidant is due to a mechanism in which it alters the protein structure. [27] [30]

Effect of Temperature

The temperature play a dominant role in crucial elements for the development of all living things. The rate of micro algal proliferation is closely associated with the photosynthetic rate.Temperature affects both photosynthesis and respiration, with temperature having an exponential effect on the respiration rate. Temperature significantly influences the synthesis of microalgal metabolic components like phenols and lipids and biomass development. The ideal temperature range for growing microalgae is 35.5 to 37.5 °C. In experiments to determine the culture conditions that encouraged the microalga to produce the most antibacterial compounds, It was discovered that *Synechococcus leopoliens* generated the highest quantity of this bioactive chemical at 35.5 °C and pH.[27] [30] [31].

Microalgae – Health and Nutrition

Due to their great nutritional content, microalgae like *Chlorella*sp., *Hematococcus* sp., etc. are taken as Neutraceutics and Functional dairy foods. Proteins, vital amino acids, carbohydrates (like starch), omega-6,3 fatty acids, and vitamins like A, B, C and E can all be found in microalgae. Large concentrations of minerals, α-linolenic acid, proteins and vitamins are present in *Spirullina* sp., which demonstrated remedial actionson several medical conditions, including cancer, diabetes, arthritis, and cardiovascular illnesses. The single-cell protein is referred to as *spirulina*. The two most significant omega - 3 FA's found in the algal cells include eicosapentaenoic acid and docosahexaenoic acid. These acids are highly nutritious in the development of infant brain and eye development as well as adult nervous system health, blood clotting, and blood pressure regulation. The microalgae, *Schizachyrium* sp., *Crypthecodinium* sp., *Spirulina* sp. And *Haematococcus* sp.is responsible for producing these lipids [10][11]. Polysaccharides derived from microalgae like cyanobacteria are synthesized externally and utilized as moisturizing substances in skincare and medicines and as enhancers in neutraceuticals. Their 'free - radical scavenging activity' is because of several microalgalglycans that are utilizedin moisturizers and salves. Sulfated polysaccharides that are taken out of microalgae also boost the human immune system [11]. Proteins from *Spirulina* sp. may lessen allergies and inflammation, and *C. vulgaris* peptides may guard against cell deterioration. The essential amino acids that are unable to generate naturally in mammals are present in these microalgal cells. The pigments made from polymerized isoprene units are called carotenoids. Important carotenoids found in microalgae include lutein, astaxanthin, lycopene, zeaxanthin and most importantly β Carotenes. Because of its Radical scavenging nature, which lowers oncogenetic development, beta-carotene is used in the therapeutic industry [14]. Another carotenoid found in microalgae, astaxanthin is a free radical scavenger and exhibits remarkable qualities like skin protection, improved immunological function, and defense against cancer and inflammatory illnesses [21].

Diseases like cardiac illness, cancer, eye problems and neurological disorders can be avoided with bioactive compounds synthesized by microalgae. Microalgae due to their cost-effective cultivation and fast multiplication become an appropriate host for the synthesis of recombinant vaccines. Their covalent modifications like Phosphorylation and acetylation are almost the same as mammalian cells [21].

Chlamydomonas reinhardtii is the common model organism used to synthesize recombinant proteins like subunit vaccines, nuclear proteins, antibodies, etc. The Hepatitis B Antibody, Viral protein 28 and α- galactosidase are produced by *D. Salina*, *scenedesmus* etc.[21] Doxorubicin a bioactive from *Spirulina* sp. It is used to create a new fluorescent biomarker. The compound's biodegradability is attributed to its high chlorophyll content and its ability to release drugs in response to changes in pH. The fast half-life period and Liver metabolism render the Diclofenac sodium to encounter challenges. It has an increase in surface area and pore volume because of the *Microporous* sp. episkeleton. Successful oral delivery of *Dunaliella salina* extract was achieved by employing gum arabic (GA)-grafted magnetic nanoparticles (MNPs) as a biocompatible scaffold [37]. Nowadays, the majority of monoclonal antibodies are made in cell lines derived from Chinese hamster ovaries, are quite expensive, and carry a risk of pathogen contamination. Microalgae are regarded as effective alternative host cells because of their advantages. These eukaryotic microorganisms perform post-translational changes of human recombinant proteins better than bacterial cells. They are also chosen over other eukaryotic hosts due to their quick development, easy handling, and straight forward culture. In a study, Hampel et al. created an engineered form of *Phaeodactylum tricornutum* that included an MAb of Immunoglobulin to inhibit the Marburg virus (which causes hemorrhage and fever) [21].

Antibacterial activity of Microalgae

The cure of microbial infections, especially bacterial infections is significantly hampered by antimicrobial resistance. Therefore, finding new antibiotics is crucial. Of the various contents of microalgal cells, lipids are reportedly the major cause of their antibacterial character. Unsaturated fatty acidsand triacylglycerols are among the most polar lipids found in microalgal cells. These phospholipids and glycolipids present as membrane lipids (cell and organelle membrane) activate various metabolisms, thus coding for almost all its economical applications. The most abundant Polyunsaturated FAs, like Eicosapentaenoic Acid, hexadecatrienoic acids, docosahexaenoic acids, etc. play a major role in inhibiting bacterial development [48] [50]. These fatty acids play a crucial role in the functioning of pathways such as the α-Linolenic acid route, n-3 and n-6 pathway by acting as starting or signalling molecules. These VLC-PUFAs because of their therapeutic and neutraceutical value can be effectively used as a bacterial and biofilm inhibiting compound *in vivo* [49]. Other bioactive like terpenes and flavonoids are present as functional groups attached with microalgal TAGs [50] [53].

In a study conducted by Sukhikh *et al* and his co-authors, it was shown that the microalgal lipids had effective inhibitory activity against a variety of Gram positive and Gram negative bacterial strains. Apart from proving to be an effective bactericidal component it has shown antifungal and immunomodulatory properties [51]. Bioactive like phycobiliproteins, vitamins, and carotenoids apart from being metabolically active themselves enhance the functions of these lipids [51][52].

Biofilm

An organized community of microbes called a biofilm is described as microbes existing in viscous matrices made of polymer materials that adhere on various surfaces. Nearly every habitat is discovered to include these microbial collectives. Both biotic and abiotic surfaces may contain biofilms. On liquid surfaces, biofilms have been seen to exist both on and inside the liquid well. Either homogeneous or heterogeneous bacterial communities are present in biofilms, and they are embedded in an EPS matrix. Polysaccharides make up the majority of EPS, but it also contains proteins, lipids, and nucleic acids. Glycopeptides, lipids, and lipopolysaccharides are examples of polymers that create a mold to support the film. Biofilms are hydrogels with viscoelastic behavior, as was discovered. It can tolerate mechanical stress thanks to its characteristics. The nutrients present in the bacteria include the EPS matrix to be bounded and the water molecules that is present in the matrix is effectively bound through H bonds. [33] [34].

Quorum Sensing in Biofilm

Through the signal molecules, bacterial cells in a biofilm coordinate their behavior and communicate with one another. Quorum Sensing, which is a communication method between two cells that extends beyond bacterial cell density, is the name of this mechanism. The majority of the time, QS functions are categorized into four categories:

(1) Synthesis of Extracellular metabolites and iron chelators like Pyochelin and enterobactin for cell differentiation and preservation.

(2) Bacterial Conjugation for gene transport

(3) Production of antibiotics for

(4) Study of Motility and synthesis of Extrapolymeric substances. It has been widely established that microbial cells can build biofilms through the QS pathway.

Quorum sensing uses signal molecules known as Acetyl lactones and peptides, to govern the production of biofilms [35] [36].

Microalgae and its biofilm inhibition capability

Microalgae have been found to have anti-biofilm activity against this bacteria, opening up new therapeutic options for *S. epidermidis* infections [38].The NoMorFilm project in 2019, showed how 3 different polar and nonpolar solvents like MeOH, Hexane, etc. were used in this study's extraction procedure to extract a variety of biological materials. Against *Candida* and *Escherichia* extracts from all solvents were found to have the highest inhibitory ratios. Except for the methanolic fraction of Glaucophyta and hexanoic fraction of Rhodophyta, *Candida*, exhibited strong inhibition rates exceeding 50% in all samples. The minimal biofilm inhibitory concentrations (MBIC) for chlorophyta and charophyta extracts were greater than those for the other phyla. It is commonly known that the Chlorophyta phylum is capable of synthesising a wide range of advantageous compounds, such as lipids and the polyunsaturated fatty acids (PUFAs) that are derived from them. Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are two PUFAs that have been shown to have antibacterial and antibiofilm effects. However, they were not readily apparent in our investigation [39][12] [13][54].

Applications of nanotechnology

Nanotechnology has altered the fate of pharmaceutical, medical, textile, food, and electronic industries. Treatment of many autoimmune disorders, diabetes, heart problems, and other chronic bacterial infections can be cured easily thanks to nanotechnology as it has enhanced the diagnosis, bioimaging, production of scaffolds, transplantations, etc. [40]

Silver nanoparticles and its anti-bacterial activity

The silver ions are known for their antibacterial activity. They are achieved through majorly oxidative dissolution where Silver ions are released. Many studies show that these silver ions are reactive to Sulphides or halides resulting in insoluble salts. This activity is enhanced by nanoparticles by increasing the absorption of ions into biofilm substrates. Thus (Silver Nanoparticles) Ag NPs are very effective as antibacterial systems [41] [42].

Mechanism of Antibacterial Activity

Antibacterial properties to an AgO core's presence. Ag NPs have a propensity to gather and form aggregates at the bacterial membrane when they bind to the microbe. Reactive oxygen species (ROS) production has also been considered a primary route of cytotoxic action. Several studies using Silver NP to study microorganisms revealed a high amount of ROS.They experience excessive levels of free radical damage under these circumstances, which results in cellular inactivation. Radicals are a by-product of metabolism in the natural world. The fact that silver ions have a very strong bonds with NH_3 , phosphate ions especially thiols, with which they form a quasi-covalent bond, is one of the keys to their function [41] [43]

Anti-biofilm activity and silver Nanoparticles

Because biofilms are resistant to antibiotics, novel strategies, such as nanoparticles, have been developed to attack them. AgNPs, a type of metal nanoparticle, are employed extensively because they have antibacterial and antibiofilm

properties. By compromising the strength of the membrane of bacterial cells, AgNPs demonstrated antibacterial action, which caused the bacteria to die and their contents to flow out. Additionally, AgNPs generate ROS which modifies Nucleic acids, fatty acids and peptides in cells, leading to bacterial dysfunction and death.
AgNPs inhibit bacterial cell attachment to surfaces or weaken intermolecular interactions to produce antibiofilm activity. AgNPs were shown to be able to prevent quorum sensing [47] [44].

Synergistic Activity of Silver nanoparticles and Microalgal metabolites
The Nanoparticles are synthesized for their unique characteristics like surface charge, shape, molecular weight, fluorescence properties, etc, [56]. The nanoparticles especially Silver Nanoparticles, in themselves are effective antibacterial agents as discussed above. Upon deep studies, many researchers have reported that the changes undergone by the microalgal cells when exposed to the Silver nitrate are very complex. The Silver nitrate when comes in contact with the microalgal cells, first degrades the cell wall and membrane. This is followed by the binding of microalgal proteins, changes in metabolic functions, mitochondrial metabolism modifications and alterations in all the proteins which are further expressed in the microalgal cells [61] [62]. The various defence strategies carried out by the microalgal cells against the silver nitrate lead to the synthesis of other secondary metabolites, Formation of Reactive Oxygen species, etc, [57]. These function as potent antibacterial agents, together with the aggregate molecules of silver nitrate and bioactive molecules, or the synthesized nanoparticles [59]. These bio molecular and biochemical changes activate a cascade of signaling processes and lead to the stress response in microalgae. The activation of antioxidant mechanisms, alterations in cellular composition, adjustments to organelle activities, and the release of biomolecules to create a barrier against more stress are some of the different defensive tactics [60]. The nanoparticle stress plays an effective role in enhancing the production of bioactive molecules [58]. The activity of these synthesized nanoparticles depends on the dose of silver nitrate administered.

CONCLUSION

Algal species are enigmatic single-celled factories whose benefits are more than they are credited. It has been a subject of research for decades and is still is, due to its molecular and metabolic functions. The metabolites in these species are of a broad range which acts as a precursor for the production of various biorefinery products like biofuel, Neutraceuticals, skincare and cosmetics, medicinal products, etc. The combination of microalgal compounds along with Nanoparticles very much enhances the chance to overcome the challenge of multidrug resistance. The utilization of microalgae cultures for the biosynthesis of AgNPs exemplifies a sustainable and environmentally friendly method for nanoparticle synthesis. These investigations will provide insightful information that will support further research in this area, allowing for a better understanding and possible breakthroughs in the synthesis and use of AgNPs mediated by microalgae.

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RESEARCH ARTICLE

An Appraisal of Human-Wildlife Conflict in the Rajouri and Poonch Districts of the Pir Panjal Himalayan Region, J&K India

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ABSTRACT

This study was conducted in the Rajouri and Poonch districts of the PirPanjal Himalayan region of J&K, India. A few villages prone to human-wildlife conflicts were selected for the study with an aim to look at the current state of conflict, its causes, and potential mitigation measures applied in reducing the conflict. The study was survey-based, and the data was collected through the questionnaire method and semi-structured interviews. It was discovered during the study of the selected villages that the majority of human settlements were located in or near the forests, resulting in conflicts with wild animals. Conflicting wild creatures in the region include wild boars, black bears, leopards, porcupines, jackals, and foxes, among others. Locals lose their land, animals, crops, and occasionally even their lives as a result of man-wildlife conflict. In certain instances, it has even been reported that wildlife is killed to stop future confrontations. To prevent loss of human life and livestock as well as other socioeconomic consequences, the conflict between humans and wildlife in the area needs to be seriously resolved. Additionally, the study makes a few mitigating recommendations that can help lessen human-wildlife interactions in the area.

Keywords: Crop damage, Depredation, Habitat loss, Human-wildlife conflict, Livestock.

INTRODUCTION

Man-animal conflict can be defined as an interaction between humans and wildlife in which negative magnitudes, whether observed or actual, exist for one or both parties when the behavior of one party hurts the other [1]. Human-

animal conflict includes human and wildlife, as well as natural space rivalry [2]. Human-wildlife conflict refers to any contact between humans and animals that has a detrimental influence on human social, economic, or cultural life, the conservation of wildlife populations, or the environment. Even under normal conditions, the presence of humans and wild animals in the same area impacts both, and they can never coexist until their interests collide [3]. Man-wildlife conflict is a severe global issue that has social and economic consequences for people. Many factors, such as geographical circumstances, human activities near wildlife habitats, the proximity of animal habitats and human settlements, and the availability of food assets for wild animals near human settlements, contribute to many forms of conflict [4]. Conflict can take numerous forms, including human and animal deaths or injuries; competition for rare or important resources, and habitat loss or degradation [5, 6]. The nature and scope of human-wildlife conflict vary by region. The nature and extent of the problem, as well as the management solutions to be used, vary substantially depending on the climate, vegetation, wildlife makeup, and socio-cultural setting of people. The Indian subcontinent, particularly the Himalayan region, is rich in biodiversity. It sustains a vast amount of biodiversity and is among the world's most biodiverse areas. The PirPanjal region is one of the western Himalayas' most significant areas, both biologically and culturally. It has a diverse range of vegetation, including conifers and deciduous forests, alpine meadows, temperate grasslands, and subtropical woods, and it supports a high level of biodiversity. The area is not well off socioeconomically, which forces the human population to place additional demands on the nearby forests and wildlife habitations to meet their daily needs. For grazing their livestock, gathering fruit, fodder, and other small forest products, or for any other reason, people frequently enter forests. Man-wildlife conflict incidents are not unusual in the area. People suffer significant losses not only in terms of agricultural destruction, livestock slaughter, or property loss but also in terms of major threats to human life as a result of wild animal assaults. Wildlife, the bulk of which is already endangered or threatened, is also killed, harmed, or threatened in response. Very few studies on the issue were reported from the western Himalayas and none from the PirPanjal region. This study aims to investigate the causes and effects of human-wildlife conflict in the Rajouri and Poonch districts of J&K, India. The study also suggests a few recommendations that help reduce man-carnivore conflict in the region and also help in the conservation of wildlife.

MATERIALS AND METHODS

Study Area

The PirPanjal Region includes the districts of the Rajouri and Poonch, which are located on the southern slopes of the PirPanjal Himalaya in the Indian Union territory of Jammu and Kashmir. Rajouri and Poonch districts serve as a link between subtropical Jammu and temperate Kashmir province. The Rajouri district is located between 32°57' to 33°34' N latitudes and 74°00′ to 74°48′ E longitudes, whereas the Poonch district is situated between 33°28' to 34°00' N latitudes and 73°56′ to 74°32′ E longitudes. There are thirteen tehsils in the Rajouri district, with a total area of 2,630 km2, of which 48.17% are under forests. In contrast, the Poonch district is comprised of six tehsils, with a combined total area of 1,674 km2, of which 56.81% is covered by forests. Both of these districts are heavily undulating to hilly, with the majority of the people residing in remote communities [7]. The landscape is varied, with distinctive physical features; the majority of the farmed land is in upland areas, with maize serving as the local staple food. Both of these districts have a generally subtropical climate, while dry temperate conditions can be observed in the foothills of the PirPanjal range, and alpine and subalpine conditions are more prevalent higher up in the mountains. The majority of the villagers' income comes from agriculture; very few operate small businesses, such as shops and stores, etc. The principal crops farmed in the area include grains such as maize, wheat, paddy some legumes, and vegetables. *Oleacus pidata, Quercus semicarpifolia, Quercus leucotrichophora, Cedrus deodara, Pinus wallichiana, Pinusrox burghii, Acacia modesta, Abies*, and several shrub species make up the region's predominant vegetation. *Pantherapardus, Ursusthibetanus, Susscrofa, Hytricomorph hystricide, Macaca mulatta, Vulpesvulpes, Canisaureus, Presbytis entellus*, and other wild creatures are found in the area. The majority of human settlements are very close to forests, and as a result, the occupants are invading and disrupting the habitat of wild animals either directly or indirectly.

Methodology

For this study, eight villages of the Rajouri and Poonch districts, namely Bedar, Chella-dangri, Mohrabachhi, Upper Phagla, Dassal, Bhattian, Chowkian, and Kotchalwal, that are vulnerable to man-wildlife interactions, were chosen. Both primary and secondary data were used to fulfill the requirements of the study. For the collection of primary data, a questionnaire was prepared on the different aspects of man-wildlife conflict in the area, and a field survey was conducted. For the field study, a random sample of 280 households (20% from each village under study) was chosen, and the distribution of houses was noted before conducting the survey. Data on livestock depredation, crop depredation, attacks on humans by wild animals, the periodicity of livestock depredation, and crop protection strategies were collected from the chosen households by using a questionnaire. The study was conducted from May 2023 to October 2023. Secondary data includes reports on human-wildlife conflict published in newspapers, journals, and online sources.

RESULTS AND DISCUSSION

Through the use of a questionnaire, the general public's perception regarding the human-wildlife conflict, its origins, effects, and mitigation strategies were ascertained. The backgrounds of the respondents ranged widely in terms of education and income. They were fully informed about the study that was being conducted before being asked for their responses. The stated observations and answers were recorded and are presented below.

Socio-Demographics of the Study Area

The socioeconomic attributes of individuals hold great significance, as these metrics offer insights into the state of a community. A sample of 280 households was collected from eight selected villages to determine their responses. Out of these, 210 (75%) were men. The total population of the surveyed households was 1770. Out of 280 participants, 56 percent were literate.

Livestock Profile for Sampled Households

The survey revealed that 80% of the sampled households rely on livestock as a secondary source of income. Furthermore, a total of 1870 individual livestock were reported from the studied households, with sheep and goats accounting for 60%, followed by cow/buffaloes (30%) and horse/mule/ass (10%), respectively.

Livestock Depredation

More than 216 respondents in the study area reported incidents of mammalian predator attacks on their livestock. The bulk of livestock deaths in the area were observed to be caused by leopards and black bears, whereas red foxes and jackals were mostly responsible for killing poultry. It was discovered during the household survey that there had been one hundred and seventeen occurrences of cattle depredation during the last two years. Of these, it was shown that black bears were implicated in twenty-four cases and leopards in a maximum of ninety-three cases [8, 9]. The survey also revealed that the least predated animals are cows and buffaloes, and the most predated species are sheep and goats. The investigation made it clear that the leopards in the area frequently prey on sheep and goats. Sheep and goats accounted for the majority of all livestock killed by leopards in a case study of a similar nature carried out in the Doda district of Jammu and Kashmir, India [10, 11]. It was also discovered that the majority of injuries sustained by people in the area were caused by black bears. The current investigation also found that the majority of animals were slaughtered during the night and early morning [12]. The population decrease and extinction of many carnivore species can be traced back to confrontation with humans caused by livestock depredation [13].

Crop Depredation

The agricultural year in the region is divided into two well-established growing seasons. Rabi season lasts from October to March and involves crops like wheat, barley, mustard, peas, and some fruits and vegetables, whereas kharif season lasts from July to October and harvests maize, paddy, beans, fruits and vegetables, and so on. The survey found that 85% of the respondents reported widespread crop depredation raids by wild creatures in their

fields. Some crops were observed to be damaged from germination to ripening and maturity. 90% of respondents reported substantial crop depredation, beginning with the fruiting stage and continuing until the crop gets mature and ready for harvest. 28% of respondents reported crop depredation occurring throughout the crop's lifecycle. The household survey also revealed that wild boar, black bear, monkey, and porcupine are the most harmful crop-raiding species in all eight surveyed villages (Table 1). Wild pigs have been recorded to destroy crops all over the year, while monkeys, porcupines, and some birds have been reported to harm orchids, fruits, and vegetables at all stages of maturity (Table 2). According to the study, maize was the most depredated crop, followed by vegetables, fruits, and wheat. This indicates that Kharif crops were more susceptible to agricultural raids than Rabi crops [14].

Crop Protection Strategies

The crop protection measures employed by farmers to defend their fields and orchards from wildlife incursions were also investigated. Farmers in the area used a variety of crop protection measures, including shouting at animals, pounding tin canes, using dogs, fencing fields with scarecrows and thorny twigs, and patrolling and guarding agricultural fields. According to interviewees, the most widely adopted crop protection method in the study area was shouting and patrolling (46%), followed by pounding tin cans (32%), field fencing with stones, scarecrows, and thorny twigs (14%), and by using dogs (8%). In a similar nature of study conducted in the Reasi District of Jammu and Kashmir, India, shouting as well as patrolling were shown to be the most commonly employed crop protection measures [15, 16].

The Manifestations of Human Animal Conflict

The manifestations of human-wildlife conflict in the study area were also studied. During the survey, 45% of the respondents reported the destruction of crops and orchards by wildlife, 35% reported that wild animals were responsible for generating an environment of dread, and the remaining 20% reported harm and the loss of human life [17]. The study has found that conflicts between humans and wildlife are becoming more common in the PirPanjal region, especially in recent years as wild animal habitats have been invaded under the guise of development. The well-known Mughal Road, which links the Kashmir valley and the southern part of PirPanjal, has made the issue of habitat fragmentation and increased threat to the current species even worse. During the study, it has been observed that habitat fragmentation, encroachment of forest fringes for agricultural purposes, reliance of people on forests for a variety of needs, retaliation, anthropogenic attractants such as piles of solid waste or unattended cattle, and an increase in the number of wild animals are the potential causes of the human-wildlife conflict in the study area. As a result, according to the respondents, the effects of man-wild life conflict in the area include wildlife attacking people, preying on domestic animals or livestock, wild animals appearing in residential areas, birds nesting in or near residential buildings, killing wildlife in retaliation, and driving wildlife away from natural habitats to thwart further attacks. As per the official data and local reports during the last two years, 58 persons were reported to have suffered serious injuries, one person died, and 117 livestock were killed in different incidents of man-wildlife conflict in the area. In retaliation six black bears and two common leopards were killed by the villagers. More than 28 incidences of bear and leopard attacks have been reported in the Mandi tehsil of Poonch district of Jammu and Kashmir alone.

CONCLUSIONS

The PirPanjal region's economy depends entirely on agriculture and cattle for its subsistence. Wildlife conflicts have a detrimental effect on the community. Wild animal's damage to agricultural crops is a significant issue for farmers in the area. The livelihood patterns of people in the region are impacted by livestock predation and agricultural destruction, as a result of which many people now detest these wild creatures. Unquestionably, human-wildlife conflict is a severe issue in the area that is getting worse day by day. In order to fully understand the situation and consider potential solutions, in-depth scientific research is necessary. To address this issue, a comprehensive scientific research is necessary to determine the true situation and to investigate potential solutions. Consequently, problems involving human-wildlife conflict need to be handled carefully and considered in light of both conservation goals and the requirements of the local community.

Recommendations

The following suggestions are offered in an effort to reduce conflicts between Humans and Wildlife in the area:

1. Fragmentation and alteration of wildlife habitats should be discouraged.
2. In order to prevent locals from infiltrating the forest and fostering conflicts between humans and wildlife, LPG should be made available to individuals, who frequently visit the forest, particularly wildlife habitats, to gather fuel or wood.
3. In order to prevent crop damage from wild animals, crop diversification should be implemented. Specifically, cropping patterns should be modified from traditional, typically consumed crops to more recent; less consumed, or damaged crops like aloe vera, ginger, garlic, turmeric, marigold, and aromatic and medicinal plants.
4. To prevent people from becoming enemies of wildlife, victims of wildlife attacks should receive ex-gratia or compensation as soon as possible. Otherwise, people tend to seek revenge on wild creatures by killing them.
5. To control human-wildlife conflict in the area, a complete predator survey is necessary, as no baseline data on the population of wild animals is available with respect to the region.
6. People living in forested areas should avoid keeping pets, as they attract leopards.
7. Residents in forested areas should avoid walking at dawn and twilight, as wild animal attacks are common during this time.
8. To safeguard natural ecosystems against exploitation and human intrusion in such areas, it is important to implement suitable legislative measures to safeguard natural ecosystems from exploitation and to stop human intrusion in these areas.
9. People's knowledge of the ecology and behavior of wild animals is remarkably restricted, despite years of interacting with nature. Therefore, it is imperative that governments and nongovernmental organizations take the lead in the organization of awareness campaigns on the issue.

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Table 1: Agricultural crops and depredating species active in the study area

Common Name	Botanical Names	Depredating Species	Seasons	Parts depredated
Maize	*Zea mays*	Wild boar, black bear monkey, porcupine	July to October	Young shoots, corn and roots
Paddy	*Oryza sativa*	Wild boar, monkey	July to October	Young shoots
Wheat	*Triticumae stivum*	Wild boar, black bear monkey, porcupine	October -March	Young shoots, grains and roots
Barley	*Hordeum vulgare*	Wild boar, monkey,	October -March	Young shoots and grains,
Common bean	*Phaseolus vulgaris* L	Wild boar, monkeys,	March-May	Whole plant
Fruits and vegetables	--------	Wild boar, monkeys, porcupines and some birds	During the maturity and harvesting stage	Leaves, young shoots, Twigs and fruits

Table 2: Crop depredation happening in the study area as reported by respondents

Wild animal Involved	Crop depredation as reported by respondents (Numbers)
Wild boar*	104
Monkey	98
Black bear	49
Porcupine	14
Others	11

*Remain active throughout the year and cause maximum damage.

RESEARCH ARTICLE

Nanotechnology Meets Nature: Herbal Nanogels in Rheumatoid Arthritis Treatment

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ABSTRACT

Rheumatoid arthritis (RA) known as Chronic autoimmune disease is characterized by inflammation of the synovial joints and degradation of cartilage as well as bones. Currently, RA is treated with a range of clinical drugs. As nanotechnology has advanced technique by which RA is being treated with an increasing number of nano-drugs because of the special chemical and physical characteristics of nanoparticles, which can target injured joint tissue specifically and increase bioavailability. A chronic autoimmune illness called rheumatoid arthritis affects around 1% of the global population. It is believed that between 0.5 and 0.75 percent of adults in India suffer from the condition targeting the complex pathophysiology of RA through the addition of several herbal components into nanogel formulations is a strategy that shows potential. This strategy might result in more tailored and efficient treatment choices. Researchers hope to reduce systemic side effects, increase drug delivery, and improve bioavailability by enclosing plant extracts within nanoscale hydrogel networks. The manufacture, characterization, and effectiveness of herbal nanogels are thoroughly covered in this review, with a focus on the advantages they offer in drug delivery and their potential to improve patient outcomes. After reviewing the current status of RA treatment, including the drawbacks of traditional medicines, we study into the herbal perspective and the developing field of drug delivery using nanogels.

Keywords: Rheumatoid arthritis, herbal, nanogel, drug delivery, nanotechnology, traditional medicine.

INTRODUCTION

Rheumatoid Arthritis (RA) that impacts millions of people globally . This article provides a comprehensive summary of RA, including its causes, symptoms, diagnosis, therapies and impact on people's lives. It is a complex autoimmune disorder that primarily affects joints. Systemic autoimmune disease rheumatoid arthritis mostly affects synovial joints, leading to synovial joint degeneration, persistent inflammation, and severe disability, if treatment is not received. Genetic predisposition, environmental variables, and dysregulated immune responses involving both innate and the etiology of RA involves complex interactions between adaptive immunity.[1] When the immune system attacks the body's own tissues there is occurrence of RA, unlike osteoarthritis which is typically caused by joint wear and tear. This inflammatory reaction causes chronic inflammation of the synovium, the membrane that surrounds joints. RA can affect any body however; Most often, individuals between the ages of 30 and 60 have been diagnosed with it. Women are more probable to be affected it. Cellularly, RA is defined by chronic synovial inflammation, in which the synovium becomes hyperplastic and invasive, resulting in the formation of a pannus that destroys bone and cartilage. Numerous immune cells, such as macrophages, B cells,T cells, and synovial fibroblasts, are responsible for this process. They generate a series of pro-inflammatory cytokines,, IL-6, including TNF-$\alpha$and IL-1β. Cytokines lead to tissue damage and sustain the inflammatory response. Treatments for RA must be both articular and extra-articular, and they must be well-tolerated due to the disease's systemic nature and impact on quality of life. Because of this intricate pathophysiology, there are potential as well as problems in creating novel treatment strategies that target many disease pathways at oncelike herbal nanogels. [2] The application of nanotechnology to treat rheumatoid arthritis (RA) has great potential for improving drugs delivery, reducing side effects and enhancing treatment efficacy. Herbal nanogels are an efficient treatment for rheumatoid arthritis (RA), a chronic inflammatory illness. These nanogels combine the therapeutic potential of many herbal components with the advantages of nanotechnology to provide a targeted and effective treatment for RA. Herbal nanogels are created by combining a variety of extracts from plants or active ingredients with well-known an analgesic ,immune-modulating, and anti-inflammatory substances with nanogel technology. While any herb can be used, some that are recognized to have anti-RA qualities are *frankincense (Boswellia serrata), turmeric (curcumin), ashwagandha, Tridax procumbens* also *ginger*etc. From the early stages of human history, people have utilized traditional herbal treatments to treat illnesses and advance their general health. Natural Phyto-constituent-based products are becoming well-known as pharmaceuticals for the treatment of illnesses diabetes, inflammatory diseases, anxiety, and other diseases. A growing number of people are interested in creating herbal compositions because of their historical origins, commercial feasibility, and customer compliance. Nowadays, a wide range of treatments involving topical, biological and systemic drugs are possible. While some drugs have some unpleasant side effects, they can also assist to reduce the symptoms of an illness. [3] Although topical drugs are less harmful than systemic ones, they frequently have low levels of free drug penetration through the stratum corneum and poor solubility in water. However, in moderate to severe cases, systemic therapy is also required. These compounds may be sealed or conjugated with nanocarriers to overcome the limitations of topical therapy. Depending on their nature, several nanocarriers can be gathered together. Among the various applications of nanomedicine, the intersection of pharmaceuticals, medicine and nanotechnology nanogels have lately come to light as the best means of administering and releasing medication to patients. [4]

Remedies for Rheumatoid arthritis

Rheumatoid arthritis is managed using an integrated approach that includes non-pharmacological tactics, pharmaceutical interventions, and in certain situations surgical therapies. This all-encompassing strategy attempts to reduce inflammation, stop joint degeneration, ease symptoms, and enhance the general quality of life for RA patients. [5] Using pharmaceutical therapies is the primary method of managing RA. The "treat-to-target" paradigm that governs modern treatment aims for minimal disease activity or cure. This approach typically involves the use of disease-modifying antirheumatic drugs (DMARDs) in an early and aggressive manner, frequently in conjunction with symptomatic treatments such short-term glucocorticoids and nonsteroidal anti-inflammatory drugs (NSAIDs).Non-pharmacological methods are extremely important for managing RA. Maintaining muscle strength

and joint flexibility is crucial for pain relief and function preservation. Physical therapy plays a major role in this. Therapists may use methods including hydrotherapy, strength training, and range-of-motion exercises. Occupational therapy helps patients keep their independence by assisting them in adapting to their regular tasks and focusing on joint protection tactics and energy saving procedures. A tailored strategy is needed to integrate these different therapy methods, taking into consideration the unique illness characteristics, comorbidities, and preferences of each patient. Treatments for RA are becoming increasingly specific and efficient as our knowledge of the disease's pathophysiology grows and novel therapeutic options, such as herbal nanogels, become available.[6]

Conventional Therapies

Over the past few decades, there has been a considerable evolution in the pharmacological management of rheumatoid arthritis (RA), with a variety of conventional medicines now available to patients and physicians. By lowering inflammation, delaying the course of the illness, and easing symptoms, these treatments hope to enhance patient's quality of life and ability to work. In order to manage RA symptoms, nonsteroidal anti-inflammatory drugs (NSAIDs) continue to be essential. The mechanism of action of medications like celecoxib, naproxen, and ibuprofen is to suppress the cyclooxygenase (COX) enzymes, which lowers the number of prostaglandins that cause inflammation and pain. Although NSAIDs are useful for temporarily relieving symptoms, they do not change the course of the illness and are usually taken in addition to therapy that modify it. [7] Prednisone and methylprednisolone are two examples of glucocorticoids that are essential for managing RA because of their strong anti-inflammatory and immunosuppressive properties. Since they are capable of controlling symptoms, these medications are frequently used as a bridge to slower-acting DMARDs while the latter take their entire course. For specific therapy, glucocorticoids can be administered intraarticularly, intravenously, or orally. Disease-modifying antirheumatic drugs, are an essential component of RA treatment. The mode of action of conventional synthetic DMARDs, such as leflunomide, hydroxychloroquine, sulfasalazine, and methotrexate vary. The most effective medication for RA is methotrexate, which has various anti-inflammatory properties and functions as a folate antagonist. These drugs can successfully prevent the progression of the disease and are frequently used as first-line therapy, either alone or in combination. Treatment for RA has changed dramatically with the introduction of biological DMARDs, particularly for those patients who do not react well to traditional DMARDs. These drugs specifically target immune system components implicated in the pathophysiology of RA.

Adalimumab, Etanercept, and Infliximab are examples of tumor necrosis factor (TNF) inhibitors, which were the first biologics licensed for RA and are still in widespread use. Other biological DMARDs include the B-cell depleting drug Rituximab, the T-cell stimulation inhibitor Abatacept, the interleukin-1 receptor antagonist Anakinra, and interleukin-6 (IL-6) inhibitors such as Tocilizumab and Sarilumab. In numerous patients who were previously difficult to treat, these drugs have demonstrated extraordinary efficacy in preventing joint injury and reducing disease activity. [8] Targeted synthetic DMARDs have been a significant tool in the RA therapeutic inventory in more recent times. Tofacitinib, Baricitinib, and Upadacitinib are examples of Janus kinase (JAK) inhibitors that impede intracellular signaling pathways related to inflammation. These oral drugs demonstrate similar effectiveness in clinical trials and provide an option to injectable biologics. The main focus of the current RA treatment paradigm is on early, severe management using a treat-to-target strategy. Usually, methotrexate or another conventional DMARD is used as a starting point, and if the response is insufficient, combination therapy or biologic/targeted synthetic DMARDs are rapidly elevated to. The objective is to prevent permanent joint damage and impairment as soon as this is possible by achieving remission or low disease activity. [9]

Limitations of Conventional Therapies

Even though RA treatment has come a long way, traditional medicines still have drawbacks. These drawbacks which range from expensive and practical difficulties to side effects and inconsistent efficacy highlight the necessity for ongoing study into cutting-edge therapy modalities. For many RA treatments, side effects continue to be a major concern. Even while NSAIDs are good at relieving symptoms, they can raise the risk of cardiovascular disease, induce renal impairment, and cause gastrointestinal ulcers when used for extended periods of time. A number of negative effects, such as osteoporosis, diabetes, hypertension, and an increased risk of infection, are linked to the

systemic and prolonged use of glucocorticoids. There are dangers associated with both conventional and biologic DMARDs. Biologic drugs greatly raise the risk of serious infections and in certain situations such as cancers, whereas methotrexate can cause hepatotoxicity and bone marrow suppression. Patients' experiences with RA therapies vary widely, which is indicative of the disease's heterogeneity. Drug response is influenced by genetic and environmental factors, which makes it difficult to anticipate which medication would work best for a given patient. Due to this diversity, a trial-and-error method is frequently required, which may postponethe start of successful treatment and permit the condition to worsen in the meantime. Another drawback is the gradual loss of efficacy or development of drug resistance, which is especially noticeable with biologic DMARDs. Antibodies to these medications may develop in some patients, which would reduce or eliminate their effectiveness. Immunogenicity is a condition that can make treatment plans more complex by requiring patients to switch between different biologics. [13] Many RA medications continue to raise concerns about long-term harm. The long-term implications of using certain modern medications for decades are still unclear, despite the well-documented short-term negative effects.

This is especially important as RA is a chronic condition that frequently needs lifelong care. Many RA treatments have immunosuppressive side effects that can make patients more susceptible to infections and some cancers, even though they are vital for managing the condition. This elevated risk can make therapy more difficult and calls for close observation, particularly in individuals who are undergoing surgery or have coexisting medical conditions. Finally, the underlying immunological dysfunction that causes RA is not addressed by existing medications, despite the fact that they are effective at reducing inflammation and delaying joint destruction. Because of this, the majority of patients need continuous care to keep their diseases under control.[14] These drawbacks of traditional medicine emphasize the necessity of ongoing study into cutting-edge therapeutic modalities. One such cutting-edge tactic is the use of herbal nanogels, which aim to solve some of these issues by providing targeted distribution, possibly decreased side effects, and the combined advantages of several herbal substances. It's critical to take into account how these novel strategies can address the shortcomings of existing treatments while posing their own special advantages and difficulties as we investigate this developing field.

Herbal Perspective

Herbal medicine has a long and rich history of being used to treat rheumatoid arthritis, spanning millennia in a variety of traditional medicinal systems. The need for more natural treatment alternatives and the possibility of fewer side effects as compared to prescription drugs have led to a resurgence of interest in herbal medicines in recent years. A comprehensive approach to treating RA is provided by traditional herbal remedies, which frequently target several components of the illness at once. Numerous herbs have anti-inflammatory, analgesic and immunomodulatory qualities that are useful in the treatment of RA. This multifaceted action may have benefits over single-target conventional medications given its alignment with the intricate pathophysiology of RA.[15] *Turmeric (Curcuma longa)* is one of the herbs for RA that has been investigated the most. *Curcumin* its main ingredient, has shown strong anti-inflammatory properties by blocking important inflammatory signaling pathways like COX-2 and NF-κB. Promising outcomes have been observed in clinical trials, wherein patients report greater function and decreased joint pain. Nevertheless, curcumin's low bioavailability has proven to be a drawback, which makes it a prime option for cutting-edge delivery methods like nanogels.Another herb that has been used for many years to treat inflammatory diseases is *Boswellia serrata*, sometimes known as *Indian frankincense*. The active ingredients in *Boswellia*, known as *boswellic acids*, inhibit the enzyme 5-lipoxygenase, which is involved in the formation of leukotrienes and reduces inflammation. [16] Larger, deeper investigations are required, but some clinical trials have shown improvements in joint discomfort and function in RA patients taking *Boswellia* extracts. Compounds like *gingerols and shogaols*, found in *Zingiber officinale (ginger)*, have demonstrated antioxidant and anti-inflammatory qualities. These substances block the expression of inducible nitric oxide synthase and production of pro-inflammatory cytokines . Although preclinical research has dominated most *ginger* investigations in RA, a few limited clinical trials have shown some minor improvements in joint function and pain management. [17] An essential herb in Ayurvedic medicine is *Withania somnifera*, also known by its popular name, *ashwagandha*. In experimental models of arthritis, it has been demonstrated to inhibit pro-inflammatory cytokines and display immunomodulatory properties. Additionally, because of its adaptogenic qualities, it could be able to lessen the stress and weariness that RA is known to cause.

Numerous factors are driving the increasing interest in herbal treatments for RA. Though it's vital to remember that natural doesn't always mean safe, many patients believe herbal remedies to be safer and more natural than synthetic medications. In situations when resources are scarce herbal remedies may provide better access to therapy because they are frequently less expensive than contemporary drugs. [18] Furthermore, the intricate phytochemical makeup of herbs may be advantageous compared to medications made of a single ingredient. Herbs include a variety of active chemicals that may work in concert to increase therapeutic effects and lower the risk of treatment resistance. The complicated, multifaceted nature of RA is ideally suited for this multi compound strategy. Nonetheless, there are several difficulties while using herbal remedies for RA. Standardization may be challenging because of variations in the potency and quality of herbal medications. Variations in growth conditions, harvesting practices, and processing processes can all impact the amount of active chemicals present. This unpredictability makes research study design and interpretation more difficult and may result in inconsistent clinical outcomes. A noteworthy obstacle is the paucity of clinical data endorsing the application of numerous natural treatments for RA. Research in this area is still being driven by the potential of herbal medications in the treatment of RA, despite these obstacles. Exciting opportunities exist for getting around some of the drawbacks of herbal remedies thanks to the advent of sophisticated drug delivery methods like nanogels. Nanogel formulations have the potential to fully unlock the therapeutic potential of herbal formulations into treatment of rheumatoid arthritis by strengthening targeting to inflamed joints, improving bioavailability, and permitting controlled release of active components.[19]

Nanogel Technology

A novel technique to drug administration, nanogel technology offers special benefits for treating complicated conditions like rheumatoid arthritis. Nanogels are cross-linked hydrophilic polymer networks made of nanoscale hydrogel particles, usually with a diameter of 20-200 nanometers. Because of their unique structure, nanogels can combine the advantageous qualities of hydrogels and nanoparticles, making them extremely effective transporters of medicinal substances, such as herbal extracts. Nanogels' chemistry is essential to how they work and can be modified to meet a variety of therapeutic requirements. Many synthetic and natural polymers can be used to create them. Natural polymers with biocompatibility and biodegradability, such as hyaluronic acid, alginate, and chitosan, are preferred options. Synthetic polymers such aspoly(ethylene glycol) (PEG), poly(N-isopropylacrylamide) (pNIPAM) offer greater control over physicochemical properties and can be designed to respond to specific stimuli. [20] Three-dimensional networks that are able to absorb significant amounts of water without losing their structural integrity define the structure of nanogels. They are biocompatible and can imitate natural tissue conditions in part because of their high-water content. Properties like swelling behavior, drug loading capacity, and release kinetics can be influenced by the formation of cross linking in the polymer network architecture. Nanogels' versatility in functionalizing with different moieties is one of its main advantages. Stimulus-responsive components for regulated drug release, imaging agents for theranostic applications and ligand targeting for improved delivery to certain tissues or cells are a few examples. When treating RA, nanogels can be engineered to react to the acidic environment of inflamed joints or to specifically target inflammatory synovial tissue. Nanogels have several different mechanisms of action when it comes to medication delivery. First, due to increased vascular permeability in inflammatory tissues, their tiny size enables enhanced permeability and retention (EPR) action, which favors the preferred accumulation of nanoparticles. By modifying the surface with particular ligands, active targeting can be added to this passive targeting. Nanogels have a variety of ways to discharge their payload once they reach their target.

This could happen via straightforward diffusion, polymer network breakdown or in reaction to particular triggers like temperature fluctuations, pH shifts, or the presence of particular enzymes. For the treatment of RA, the capacity to create stimuli-responsive nanogels is especially important since it enables site-specific and demand-driven medication release. [21] Multi-herbal nanogels, including several different herbal extracts or chemicals, are a fascinating new development in this sector. By utilizing the synergistic effects of many herbs, these compositions seek to emulate the conventional application of herbal combinations in numerous medicinal systems. Due to the nanogel structure, it is possible to introduce several drugs at the same time, which may enhance the therapeutic effect of these substances combined. For instance, nanogels could potentially be designed to detect early signs of joint inflammation and release anti-inflammatory compounds in response. [22] In conclusion, that nanogel technology

could enhance the delivery and efficacy of herbal medicine used for RA treatment. Regarding the problem of bioavailability, targeting and the controlled release, the application of nanogels can open for the maximum utilization of the opportunities given by the active substances of higher plants. As research in this field advances, herbal nanogels may emerge as a novel and effective approach to managing the complex pathophysiology of rheumatoid arthritis, potentially offering patients a more holistic and personalized treatment option.

Advantages of Nanogels:[23]

Nanogels are an exceptionally promising approach to drug delivery systems because of their high biological compatibility. Elevated biodegradability is critical to avert the collection of nanogel substances in the body's tissues, which may induce side effects and detrimental effects. Nanogels are non-reactive in the bloodstream and body's inner aquatic environment, indicating they didn't elicit any immune reactions. Nanogels are extremely small, which has several benefits, including: Enhanced permeation capability. Preventing rapid renal exclusion, which can lead to prolonged serum half-life. Preventing reticuloendothelial system uptake and phagocytic cell clearance, allowing for passive as well as active pharmaceutical targeting. Able to pass through the blood-brain barrier(BBB) . increased endothelium perforation in areas that are pathogenic, solid tumors, swelling , infracted regions. Tumor tissues having highly capillary permeability, which facilitates the entry and accumulation of nanoparticles within the tissue. Safe transportation of API-loaded nanogel particles into target cells' cytoplasm, which makes them perfect for intracellular drug delivery. Quick response to changes in temperature and pH in the environment. Nanogels can be taken orally, through inhalation, through the nose, intra venously, transdermal and ophthalmic administration. Nanogels also has a high ability; swelling and deswelling, imbibing aqueous medium solvent when placed in water. This is the best advantageous aspect of nanogel as it made them suitable for the accommodation and transference of protein and peptide, bio-multimolecular and even large molecules of drugs. Drug encapsulation capacity remains high in contrast to alternative nano carriers and drug delivery systems in case of nanogels. This is because a number of the functional groups found in polymeric linkage affect the polymer's properties in a definite manner. Thus, in the polymeric network, the presence of weak interactions such as dipole-dipole or van der Waals forces, hydrogen bonds and the presence of functional groups definitely doubles the drug loading capacity of nanogels at the interface of drug or protein. Site specific delivery is possible in nanogels because functional groups that can couple with antibodies and/or drug are available and it minimizes the drug deposition in non-target area such as muscular and adipose tissues. Furthermore, functionalization of nanogels with ligands caused targeted releasing and delivery of the drug. Dispersions of Nanogel are reported to possess and immensely large surface area which is of paramount importance for in vivo applications.

Limitations of Nanogels

As well, in nanogel it is costly to separate the solvent and surfactant at the end of the formulation prepared though the process is not that costly. Possible side effects if any part of the polymers or the surfactant is still present in the system. [24]

Mechanism of Drug Release of the Nanogels

There is various mechanisms to which the release of the API or biomolecule is assign to including: It can be postulated that factors such as, disintegration of nanogel structure, the effect of pH and temperature, simple diffusion, displacement of counterions or their induction because of an external energy source.

pH responsive mechanism

As the name itself suggests, changes in pH in the surrounding environment have an impact on medication release. Stated differently, different physiological variables can lead to varied pH values during medication release. The maximum release will happen at the right pH, suggesting that the release primarily manifests in a pH-specific region of the body. The self-assembly mechanism of a nanogel is based on that the polymers utilized in its manufacture feature pH-sensitive functional groups that deionize within the polymer matrix. De-protonation results in an increase in the polymer's size, porosity, and osmotic pressure, which releases the molecules that are electrostatically bound. [26]

Thermosensitive and volume transition mechanism

which is reached by some nanogels, indicates that the nanogels' volumes change in response to temperature. This mechanism is known as thermosensitivity and volume transition. It is referred to as a switch off if the surrounding medium falls below VPTT; it then swells and releases the drug loaded. Conversely, the nanogel abruptly compresses and the content begins to emerge, reversing the process. Previously, when they expand and increase in volume, the other thermoresponsive nanogels that have been used cut off the cellular network. As a result, fundamental changes were made to thermosensitive drug-bearing nanogels, such as adjusting the polymer percentage to reduce the critical solution temperature. It is biocompatible magnetic field targetability of poly (N-isopropylacrylamide) and chitosan nanogel used in hyperthermic cancer treatment known to be quiet. [27]

Photochemical internalization and photoisomerization

Photoisomerization may be defined as a kind of isomerization process which involves the bond and as a result of exposure to light – some conformational changes take place. Molecules containing at least one double bond serve as good examples; they isomerizecommonly from the trans position to the c is position under the effect of light . The release of therapeutic drugs into the cytoplasm is determined by the oxidation of cellular compartment walls and the creation of two species of oxygen, namely singlet and reactive, when photosensitizer-loaded nanogel is activated. The release characteristics of azodextran nanogel loaded with aspirin were being studied. This observation indicated that the E-configuration of the azo group is formed as a result of the photoregulated c is-trans isomerization of azobenzene. This forms to a good release profile of aspirin than the previous position where it assumed a Z-configuration . [28]

Preparation Methods of Nanogel

The technique of creating herbal nanogels comprises a number of strictly regulated steps intended to combine several herbal extracts into a hydrogel matrix at the nanoscale. To guarantee the final formulation's stability, effectiveness, and repeatability, these procedures must be refined. [29]

Photolithographic techniques

Thus, for the formation of 3D hydrogel particles and nanogels for the delivery of drugs, the photolithography and photochemistry activation/reaction methods are used. The general technique of employing such gels in micro fabrication is as follows, the poly (dimethyl siloxane) (PDMS) stamps are used to create, transfer and stack gels on top of one another to create three dimensions. Surface modification enhances or reduces the ability of a molded gel to adhere to the substrate. It seems that the techniques usually employed to pattern PDMS stamps are generally revealed by hexa (ethylene glycol)-terminated self-assembled monolayers(SAMs), or the adsorbed monolayer of bovine serum albumin (BSA). [30]

Modified pullulan technique :

Hydrophobized pullulan nanogel that has self-assembled is an example that fits these criteria. Pullulans are changed in two steps: hydrophobic 1-hexadecanethiol is added after methacrylate's are used initially. The end product is an amphiphilic material that, upon the addition of water, starts to self-assemble via hydrophobic interactions between alkyl chains. Another example is pullulan nanogel with a cholesterol base. Here, 1.4 cholesterol was used in place of pullulan, and dimethyl sulfoxide and pyridine are simply reacted to create the nanogel. After being freeze-dried, this mixture created nanogel in the aqueous phase, which then combined with W-9peptide, a TNF-alpha and Receptor activator of nuclear factor kappa-B ligand (RANKL) antagonist, to give an osteological problem. Glycidyl methacrylate was reacted with cholesterol pullulan (CHP) to create cholesterol-bearing methacrylol. For every 100 glucose units, the degree of substitution was 6.2 (CHPMA6). CHPMA6 self-assembled as a nanogel in water. [31]

Emulsion polymerization technique

The emulsion polymerization approach was used to generate l-proline functionalized PMMA [poly (methyl methacrylate)] nanogel with a variety of catalyst functionalization (0.5-15 wt%) and cross-linking densities (0-50 wt%). Mechanical stirring creates monomer droplets in the emulsion polymerization process. [32]

Reverse microemulsion polymerization technique

fluorescent dye by utilizing activators to cause inverse nano-emulsion polymerization of water/cyclohexane at environment temperature, which results in atom transfer, and radical polymerization of oligo (ethylene oxide) monomethyl ether methacrylate, rhodamine B or fluorescein tagged nanogels were produced. Functional nanogels were produced by controlling the polymerization process using an ATRP initiator containing hydroxyl. Monomer droplets are created in the O/W mini-emulsion process by applying high shear stress using ultrasonication or a high-pressure homogenizer. Mini emulsion exhibits kinetic stability**.** [33]

Free radical crosslinking polymerization technique

The purpose of drug delivery and cell imaging, a vinyl-containing fluorescent prepolymer was free radical crosslinked to create photo crosslinked biodegradable photoluminescent polymers (PBPLPs) nanogel. The creation of PBPLPs nanogel heralds a new era in the development of nano biomaterials for nanomedicine. [34]

Applications of Nanogels

Local anesthetics (LA)

Jacques E. Chelly, Shiv K. Goel, Jeremy Kearns, Orkun Kopac & Senthilkumar Sadhasivam worked on Local anesthetics and found the drugs that fall into the category of those that cause analgesia, or the removal of pain by blocking voltage-gated Na+ channels, local anesthetics stop nerve impulses in nerve cell membranes, resulting in analgesic effects. The type, intensity, and quiescent membrane potential of the nerve determine the extent of numbness produced by a specific local anesthetic. concentration based on their chemistry, local anesthetics are pharmacologically divided into two classes: amino amides and amino esters. Due to the significant toxicity of overdosing on local anesthetics, there is interest in developing controlled release drug delivery methods for them.[43]

Neurodegenerative disease

Waris A., Ali, A., Khan, A. U. Asim, studied when since there was no known treatment for neurodegenerative diseases like Parkinson's and Alzheimer's, oligonucleotides have drawn a lot of attention as a potential diagnostic or therapeutic tool. Because oligonucleotides are unstable against metabolism, cannot cross the blood-brain barrier, and are quickly excreted by the kidneys, their use in treating neurodegenerative diseases has been severely limited thus far. To enhance the performance of nanogel delivery devices, oligonucleotides were added. Oligonucleotides have an easier time entering the central nervous system and passing through the blood-brain barrier due to the special properties of nanogels.[44]

anti-inflammatory medication

Shah PP, Desai PR, Patel AR, Singh MS, worked on the formulation of non-steroidal anti-inflammatory medication (NSAID) delivery methods applied topically, as well as the management of psoriatic plaque and allergic contact dermatitis, are among the dermatological and cosmetic applications of nanogels. Since they can get around topical delivery systems' main drawback the comparatively little bonding period between active medications and the application sitenanogels are perfect for this use. This was accomplished by producing a homogeneous dispersion of the nanogel and keeping water in the gel matrix. Using a poly-(lactide-co-glycolic acid) and chitosan nanogel, it was possible to effectively distribute two anti-inflammatory medications topically at the same time: ketoprofen and Spantid II. Oleic acid was used to modify the surface. This nanogel technology has the ability to infiltrate well, making it useful for treating a wide range of inflammatory conditions.[45]

Delivery of vaccines

Yuki, Yoshikazu studied the creation of an immune response that is unique to an antigen is the basic idea underpinning vaccination. As a novel, alternative vaccine delivery technique, polymeric nanogels are being employed to boost vaccination performance and efficacy. Nanogels have an advantage over conventional vaccines because of their ability to protect vaccine antigens from enzymatic degradation through the network of nanogels. By

binding antibodies and other ligands to surface-modified nanogels, target specificity of the vaccine administration can be significantly enhanced. [46]

Transdermal drug delivery:

Tariq, Lubnaworked on thattechnique of administration increases patient compliance, prevents the first pass effect, improves the effectiveness of medication, and creates a constant state drug concentration in plasma. To increase the drug's penetration into the site of action, numerous tactics were considered. A possible approach is topically delivering active pharmacological ingredients to the stratum corneum using nanogels. Since oral aceclofenac administration can result in a variety of side effects, such as stomach bleeding and ulcers, transdermal delivery of the drug was looked into as a potential replacement and was shown to have better stability and permeability. We used the emulsion solvent diffusion approach to dissolve aceclofenac.[47]

CONCLUSION

Herbal nanogels are a novel way to treat rheumatoid arthritis (RA), fusing the sophisticated drug delivery capabilities of nanotechnology with the multifaceted therapeutic potential of herbal medicine. This novel approach tackles the delicate interplay between genetic predisposition, environmental variables, and dysregulated immune responses that characterize the complex pathophysiology of RA. This method seeks to solve the drawbacks of both recent RA therapy and traditional herbal medicines by encasing many herbal extracts with anti-inflammatory, analgesic, and immunomodulatory qualities within nanoscale hydrogel networks. High biocompatibility, improved permeability, responsiveness to environmental indicators, and the capacity to administer medication specifically to inflamed joints are just a few of the many benefits of using nanogels. The development of diverse preparation techniques has made it possible to tailor the properties of nanogels to meet certain therapeutic requirements. Although RA is the primary focus, this technique may also be utilized to treat other autoimmune diseases, neurological conditions, and different drug delivery issues. To completely understand the long-term safety, effectiveness, and ideal compositions of herbal nanogels, more investigation is necessary. With further advancements in this sector, RA patients may be able to get more individualized, efficient, and well-tolerated therapy alternatives, which could improve their quality of life and the course of their condition. Combining cutting-edge nanotechnology with conventional herbal knowledge not only demonstrates innovation in the treatment of RA but also emphasizes the need of multidisciplinary approaches in medical research, creating new avenues for the treatment of complex autoimmune conditions.

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Table.1: Drugs Used in Treatment of Rheumatoid Arthritis

Drug Class	Examples	Mechanism of Action	Reference
NSAIDs	Ibuprofen, Naproxen	COX inhibition	[10]
Glucocorticoids	Prednisone, Methylprednisolone	Immunosuppression	[11]
• Conventional	• Methotrexate,	• Various (e.g.,	[12]

DMARDs Biological DMARDs	Sulfasalazine Adalimumab, Tocilizumab	folate antagonism) Cytokine inhibition	

Table.2:Publications of different Novel Approaches for Management of Rheumatoid Arthritis Treatment

Drug Name	Application	Year of Publication	References
Methotrexate	Nanogel formulation for targeted drug delivery	2024	[35]
Curcumin	Nanoparticle-based hydrogel for anti-inflammatory effects	2023	[36]
Tocilizumab	Dual-drug nanogel for improved bioavailability and targeted action	2023	[37]
Boswellic acid	Nano emulsion-based gel for pain relief in rheumatoid arthritis	2023	[38]
Upadacitinib	Hydrogel formulation for sustained release in rheumatoid arthritis	2024	[39]
Baricitinib	Nanofiber-based formulation for improved JAK inhibitor delivery	2022	[40]
Hydroxychloroquine	Nanoparticle suspension for enhanced bioavailability	2021	[41]
Sulfasalazine	Liposome-based formulation for improved drug delivery	2022	[42]

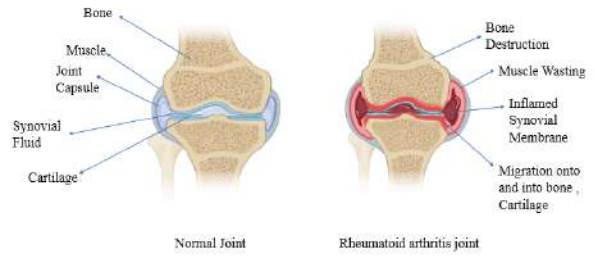

Figure.1 : Difference between Normal Joint and Rheumatoid arthritis Joint.

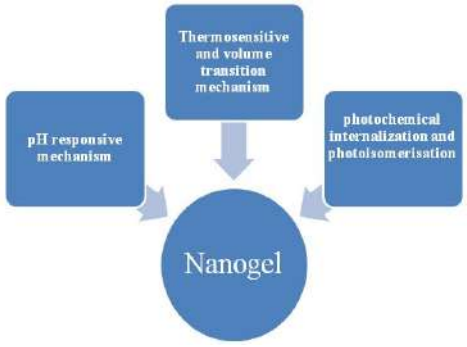

Figure.2 :Mechanism of Drugre lease of Nanogels. [25]

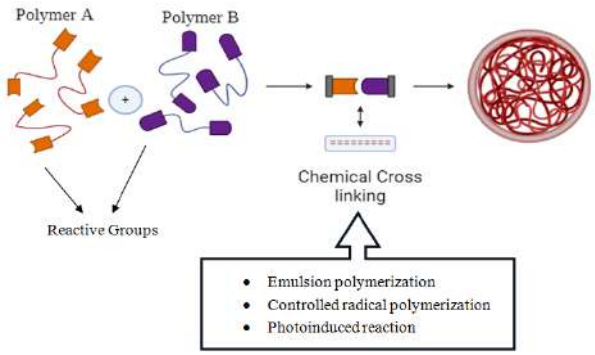

Figure.3 : Chemical Crosslinking reaction

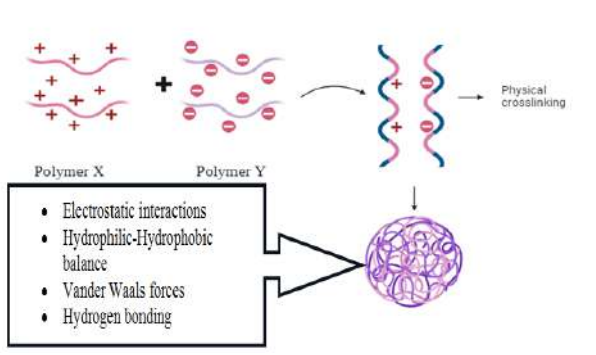

Figure.4 : Physical Crosslinking reaction

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RESEARCH ARTICLE

In-vitro Toxicity Assessment of synthesized silver nanoparticles

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ABSTRACT

Nanomaterials, particularly metallic nanoparticles, exhibit unique properties that make them suitable for various bio-applications, including therapeutics and antimicrobial agents. Silver nanoparticles have shown potential as antimicrobial agents, and their efficacy can be enhanced by combining them with antibiotics. However, evaluating the toxicity of these nanoparticles is crucial to ensure their safety. This study aims to investigate the in-vitro cytotoxicity effects of chemically synthesized silver nanoparticles on the Vero cell line using sulforhodamine B (SRB) assay. At 50 µg/ml silver nanoparticles concentration, the percentage SRB reduction of Vero cells was 57.2%. The results provide valuable insights into the biocompatibility and potential toxicity of silver nanoparticles, which can inform their development as antimicrobial agents and other bio-applications.

Keywords: Silver nanoparticles, Chemical synthesis, Cell lines and Cytotoxicity.

INTRODUCTION

Nanomaterials, defined as materials with dimensions between 1-100 nm, exhibit unique properties that distinguish them from their bulk counterparts, with significant implications for biology and medicine [1,2]. The small size and high surface-to-volume ratio of metallic nanoparticles (NPs) enable them to interact effectively with various biological components [3,4]. At the nanoscale, the activation of surface electrons leads to distinct optical and mechanical properties [5]. Due to their high biocompatibility, nanoparticles are commonly employed in various bio-applications, including therapeutics and antimicrobial agents [6]. The efficacy of silver nanoparticles is influenced by the type of capping agent used [7]. Metallic nanoparticles, such as silver and gold, have been shown to inactivate bacterial enzymes, suggesting their potential as antimicrobial agents. Combining nanoparticles with antibiotics may enhance their effectiveness, as the synergy between the two can lead to improved antimicrobial activity [8]. This

additive effect has been observed in antibiotics against various bacterial strains, indicating the potential for nanoparticles to augment traditional antimicrobial treatments [9]. Evaluating the toxicity of a novel antimicrobial is crucial to ensure its safety for end-users. While traditional experimental models for cytotoxicity and genotoxicity are available, their applicability to antimicrobial nanoparticles is restricted. Toxicity is defined as the potential of a substance to cause harm to humans or animals, and although some medications can be toxic at high concentrations, they can be safe at optimal doses[10]. To evaluate toxicity in biological systems, *in-vivo* studies are essential; however, preliminary *in-vitro* cytotoxicity tests can help minimize unnecessary animal testing and streamline the evaluation process. Cytotoxicity assessments can be performed using both *in-vivo* and *in-vitro* methods, with cell culture experiments being a popular approach for evaluating compound toxicity at the cellular level. *In-vitro* experiments offer several benefits, including rapid results, reduced costs, and minimized ethical concerns, making them the preferred choice for initial cytotoxicity screening [11]. Common in-vitro assays include the MTT and SRB (sulforhodamine B) tests, which evaluate cell membrane integrity. The SRB assay, established in 1990, involves the binding of SRB to proteins in acidic conditions, followed by extraction in basic conditions, providing a reliable measure of cytotoxicity. The present study aims to evaluate *in-vitro* cytotoxicity effects of chemically synthesized silver nanoparticles on Vero cell line.

MATERIALS AND METHODS

Chemical synthesis of Silver Nanoparticles

Silver nanoparticles (Ag NPs) were synthesized using standard protocol with minor modifications. Briefly, 0.01 M aqueous solution of silver nitrate was prepared with Polyvinylpyrrolidone (PVP) (Merck) as a stabilizer. An aqueous solution of 0.03M sodium borohydride ($NaBH_4$), with PVP was prepared. The solution of silver nitrate was kept on magnetic stirrer at 37°C for homogeneous mixing. The solution of $NaBH_4$was added dropwise under vigorous stirring. Slowly, the temperature of solutionwas raised to 50°C after the addition of all reactants. This led to a change in colour of solutions to brown. The solution was kept overnight at room temperature to settle down particles. The purification of synthesized Ag NPs was achieved using centrifugation at 15000 rpm for 15 min. The purified Ag NPs were washed three times with de-ionized water. The synthesizednanoparticles were dried in an oven at 80°C.

Characterization of Nanoparticles

Chemically synthesized silver nanoparticles were subjected for characterization using various biophysical techniques[12]. Nanoparticles (NPs) were scanned in the ultraviolet-visible range using double beam spectrophotometer (Wensar). To verify the reduction of metal ions, the solution was scanned in the range of 200 to 700 nm in an ultraviolet visible spectrophotometer. As nanoparticles have optical properties that are sensitive to size, shape, concentration, agglomeration state, and refractive index near the nanoparticle surface, which makes UV-Visible spectroscopy a valuable tool for identifying, characterizing these materials. The morphology and size of the synthesized silver NPs was determined by Electron Microscope at120 KV (JEOL 2000). Synthesized silver nanoparticles were sent to sophisticated test and instrumentation center (STIC), Cochin. Transmission Electron Microscopy (TEM) was performed to measure the particle size and uniformity. The nanoparticle sample was prepared by depositing a drop onto a carbon-coated copper grid, followed by drying in an oven at 60°C. The dried sample was then transferred to a transmission electron microscope (TEM, JEOL 2000, STIC Cochin, Kerala) for characterization. TEM imaging was achieved by accelerating a beam of electrons through the specimen, generating an image that revealed the size and morphology of the nanoparticles.

Cytotoxicity of Nanoparticles

A cytotoxicity assay of silver nanoparticles was performed on mammalian cell lines. Cell line was procured from National Centre for Cell Science (NCCS), Pune. Toxicity studies were conducted on Vero cell line in CSIR-Central Drug Research Institute, Lucknow with slight modification [13]. Vero cell lines were seeded into 96-well micro titer plate. Synthesized silver nanoparticles were mixed in cell cultures at different concentrations (0, 6.25, 12.5, 25, 50, and 100 µg/ml) and incubated for 24 h. All the stock solutions were sterilized followed by filtration (0.22 µm pore size).

The cells were cultivated in a suitable medium, enriched with 10% fetal bovine serum (FBS) by volume, and supplemented with antibiotics (1% penicillin/streptomycin solution, containing penicillin and 10 mg/ml streptomycin) and 1% L-glutamine (200 mM) from Sigma-Aldrich. The cells were initially incubated in a suitable culture medium at 5% CO_2. They were then rinsed with 5 ml of calcium- and magnesium-free phosphate-buffered saline and treated with 2 ml of 0.05% trypsin/0.5 mM EDTA (Sigma-Aldrich, UK) for 3 minutes at 37°C to facilitate cell detachment. The culture flask was gently tapped, and the detached cells were resuspended using a 1 ml pipette to prevent clumping and achieve a single-cell suspension. To inactivate trypsin, 5 ml of medium with foetal bovine serum (10%) was added. After that, the cell suspension was transferred to a 15 ml tube and centrifuged at 100 x g for another 5 minutes. After discarding the supernatant, the cells were resuspended in culture medium. Silver nanoparticles induced cytotoxicity was assessed by recording the absorbance at 570 nm using an enzyme-labeled instrument, and cell proliferation percentage was calculated.

RESULTS AND DISCUSSION

Chemical synthesis of Silver Nanoparticles

Silver nanoparticles with high stability were synthesized using polyvinylpyrrolidone (PVP) as a capping agent and sodium borohydride as a reducing agent. The synthesized nanoparticles were characterized using various techniques to determine their shape, size, and morphology.

(I) UV-Visible Spectroscopy

UV-visible spectroscopy is a widely accepted technique for analyzing the size and shape of controlled nanoparticles (NPs) in aqueous suspensions. To characterize the synthesized silver nanoparticles, a UV-Visible spectrum was obtained using an optical quality quartz cuvette with a 1 cm path length. The formation of nanoparticles was indicated by a visible color change from colorless to light brown, resulting from surface Plasmon resonance (SPR) vibration. The spectrum was recorded at room temperature, with double distilled water serving as a blank. The sample was scanned across a wavelength range of 200-700 nm, revealing a Surface Plasmon Resonance (SPR) peak at 426 nm, which confirms the presence of silver nanoparticles. The observed UV-Vis absorption band in the visible light region provides evidence for the surface plasmon resonance of the nanoparticles. Similar observation was reported by Kedar et al (2022) [14].

(2)Transmission Electron Microscopy

The size of Silver NPs was in the range of 20 to 40 nm as evident from Transmission Electron Microscopy. Nanoparticles were prominently spherical in shape (Figure 1).

Figure 2 presents the selected area diffraction pattern (SAED) of silver (Ag) nanoparticles, indicating well-crystallized particles. The presence of distinct diffraction rings in the SAED image confirms the face-centered cubic (FCC) crystal structure of the Ag nanoparticles, further supporting their crystalline nature.

Cytotoxicity testing of nanoparticles

Chemically synthesized silver nanoparticles were checked for cytotoxicity assay. Dose-dependent cell toxicity was observed at a highconcentration of AgNPs. As shown in figure, the SRB result demonstrated that higher concentration has generated more toxicity [15]. It was observed that the cell activity has a significant difference between the concentrations of 25 to 50µg/ml for 24 h. The percentage SRB reduction of Vero cells observed at concentration 25 µg to 100 µg/ml was 19.4%, whereas at 50 µg/ml it was 57.2%, and at 100 µg/ml it shows lethality to 82.4% (Table 1 and Figure 3). Similar findings have been reported by Rajasekhar et al (2016) [16].

CONCLUSION

In conclusion, the silver nanoparticles were synthesized using a chemical method, and having size range of 20-40 nm. The synthesized AgNPs exhibitedless toxicity up to 50µg/ml concentration on Vero cell line.

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Table: 1 Percent cell inhibition and cell viability of chemically synthesized silver nanoparticles

Chemically synthesized Silver Nanoparticles			
S. No.	**Concentration**	**Vero Cell Line**	
	(µg/ml)	**% Cell Viability**	**% Cell Inhibition**
1	6.25	95.9	4.1
2	12.5	93.7	6.3
3	25	80.6	19.4
4	50	42.8	57.2
5	100	17.6	82.4

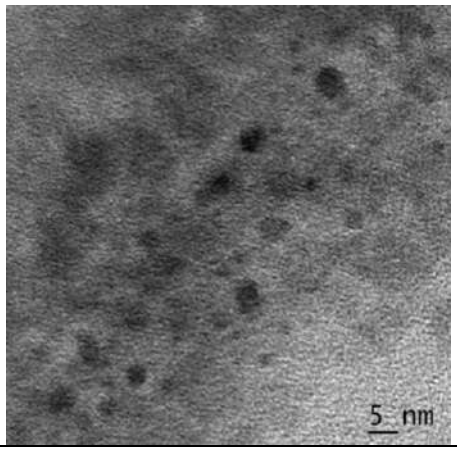


Figure 1: TEM micrograph of Silver nanoparticles synthesized by chemical method

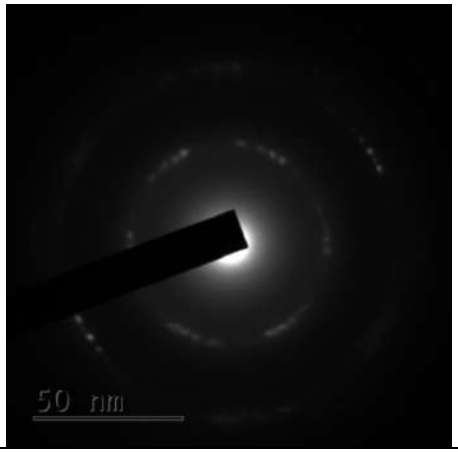
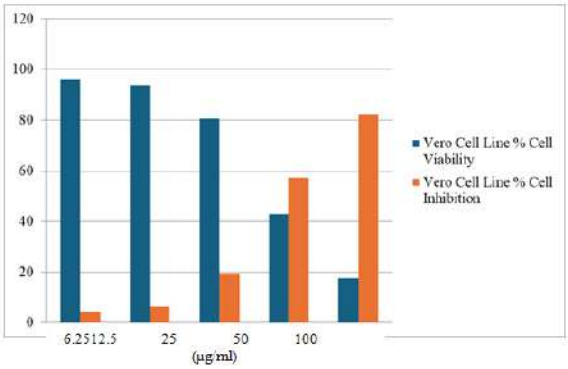


Figure 2: SAED Pattern of Silver nanoparticles synthesized by chemical method.



RESEARCH ARTICLE

Enhancing Salt Tolerance and Osmolyte Accumulation in *Sesamum indicum* L.: by Foliar Application of Humic and Salicylic Acid under Salinity Stress

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ABSTRACT

This study investigates the impact of salt stress and the potential mitigation effects of plant growth regulators on *Sesamum indicum* L. (TMV-4 variety). Plants were subjected to salt stress through soil drenching with NaCl (100 mM) and treated with foliar applications of Salicylic Acid (1 mM) and Humic Acid (500 mg/L). Control groups were included for comparison. The experiment was conducted in pots, with plants sampled on the 35th, 45th, and 55th days after sowing to assess Proline and Amino acid content, results indicated that NaCl stress reduced growth and biomass, and negatively impacted proline and amino acid levels. However, the application of Salicylic acid and Humic acid improved growth and mitigated some of the adverse effects of salt stress. These findings suggest that Salicylic Acid and Humic Acid are effective in alleviating salt-induced stress in *Sesamum indicum* L., highlighting their potential for enhancing plant resilience under saline conditions.

Keywords: *Sesamum indicum*, Osmolytes, Humic acid and Salicylic acid, Saline stress

INTRODUCTION

Soil salinity stands out as a significant driver of soil deterioration, impacting 19.5% of irrigated lands and 2.1% of dry land agriculture worldwide. This issue is particularly noticeable in arid and semi-arid regions, where 25% of irrigated areas suffer from salinity (1). The challenges posed by abiotic stresses on plants have been escalating due to the rapid

changes in global climate (2). To counteract these stresses, plants employ osmotic adjustment through the production of osmolytes small molecules like sugars, polyamines, secondary metabolites, amino acids, and polyolsthat help shield their cellular systems from stress and enhance their resilience (3). These osmolytes, also termed cytoprotectants, play a crucial role in defending cells against environmental stresses (4). Plants have developed sophisticated mechanisms to handle various stresses and ensure their survival (5). Among these mechanisms, the synthesis and accumulation of osmolytes are vital responses to oxidative and osmotic stress (6). The growing unpredictability of climate change exacerbates these stresses, posing significant threats to agriculture (7). To mitigate these issues, targeted environmental adaptation strategies have been devised (8). The overproduction of osmolytes is driven by various stress signaling pathways, including mitogen-activated protein (MAP) kinases, phytohormones, and calcium signalling (9). Research has extensively examined the biosynthesis of osmolytes such as proline and free amino acids to better understand their roles in stress response (10). Sesame *(Sesamum indicum L.),* a key oilseed crop, is widely cultivated around the world, including in India, China, and Turkey. Its oil contains sesamin and sesaminol lignans, which are known for their important roles in improving oxidative stability and antioxidant activity(11).

Salicylic acid plays a crucial role in activating plant defenses against abiotic stresses, such as salinity and osmotic pressure. Research highlights its ability to influence various physiological, biochemical, and developmental processes when applied externally (12). Salicylic acid helps maintain ionic and osmotic balance by boosting the production of stress-related proteins like free proline, glycine-betaine, sugars, and antioxidant enzymes (13). This regulation of osmotic pressure enhances the plant's tolerance to salt stress (14). Humic acid, present in organic humus, is considered a plant bio-stimulant rather than a fertilizer. Its use can greatly improve soil and plant properties, leading to better growth and increased productivity (15). This substance not only helps plants combat both abiotic and biotic stresses but also promotes their overall development, resulting in higher yields and enhanced agricultural output (16). Humic acid's positive effects are linked to improvements in soil qualities such as aeration, aggregation, water retention, and ion availability (17). These enhancements support more effective nutrient and water uptake by plants, boosting the accumulation of photosynthates, especially under water stress conditions (18).

MATERIALS AND METHODS

Sesamum indicum L. specifically the TMV-4 variety was purchased from Tamil Nadu Agricultural University in Coimbatore (TNAU), Tamil Nadu, India. The chemical regulators Humic acid, Salicylic acid, and the analytical reagent sodium chloride (NaCl) were purchased from Sisco Research Laboratories [SRL] based in Chennai India.

Experimental setup

An experimental study on the plant *Sesamum indicum* L. was conducted at the Botanical Garden situated within the Department of Botany at Annamalai University, located in Chidambaram, Tamil Nadu. The geographical coordinates of the experimental site were recorded as 11°23'23.1"N and 79°43'05.3"E. Prior to sowing, the healthy seeds underwent surface sterilization utilizing a 0.2% mercuric chloride solution for 2 minutes, followed by extensive rinsing with sterile double-distilled water to ensure sterility. The seeds of the TMV-4 variety of *Sesamum indicum* were then sown in a total of 90 pots, which were further categorized into six distinct groups. Each group, comprising ten replicates, received a single application of mixed fertilizer combined with manure, with the soil composition maintained at a ratio of red soil, sand, and farmyard manure in a 1:1:1 proportion. Various treatments were administered to the plants, Control, (without treatment) NaCl (100 mM), NaCl (100 mM) + salicylic acid (1 mM), NaCl (100 mM) + Humic acid (500 mg/L), Humic Acid (500 mg/L) and Salicylic acid (1 mM/L). The salinity levels within the pots were meticulously monitored at regular intervals by assessing soil samples from each pot using an Electrical Conductivity Meter. Plant specimens were harvested at specific time points (i.e., at the 35th, 45th, and 55th days after sowing [DAS] to conduct morphological and chlorophyll pigment analyses, thereby evaluating the impact of the different treatments on plant growth and physiological parameters.

Statistical analysis

The statistical analysis of the data was performed using SPSS software (version 22.0) and subsequently subjected to one-way ANOVA. The bars in the graphical representation represent the mean outcomes based on three replicates (n=3), with the standard deviation indicated by (±). The significance level for statistical analysis was set at 0.05%, determined through Duncan's Multiple Range Test (DMRT).

Biochemical Analysis

Determination of Proline Content

Proline was extracted and estimated following the method of Bates *et al.* (1973).

Extraction

To prepare the sample, 500mg of fresh plant material was crushed in a mortar and pestle, followed by homogenization with 10 ml of a 3% (w/v) aqueous solution of 5-sulfosalicylic acid. The resulting homogenate underwent filtration using What man No.1 filter paper. The residue was subjected to re-extraction, and the collected filtrates were combined. The total volume of the filtrates was adjusted to 20 ml with an aqueous sulfosalicylic acid solution, and this resulting extract was utilized for the proline estimation.

Estimation

To initiate the proline estimation, 2 ml of the proline extract was combined with 2 ml of acid ninhydrin and 2 ml of glacial acetic acid. The resulting mixture underwent incubation for one hour at 100°C in a boiling water bath (Technicon). Subsequently, the test tubes were moved to an ice bath to halt the reaction. For extraction purposes, 4 ml of toluene was introduced and vigorously mixed using a test tube stirrer for 15-20 seconds. Following this, the toluene, containing the chromophore (organic phase), was separated from the aqueous phase using a separating funnel, and the absorbance was measured at 520 nm in a UV-vis spectrophotometer (Model-118, Systronic India Limited, Gujarat, India), with a reagent blank. The determination of proline content was based on a standard curve using L-proline as the standard, and the results were expressed in mg g^{-1} dry weight.

Estimation Of Total Free Amino Acid Content

Total free amino acids were extracted and estimated by following the method of Moore and Stein (1948).

Extraction

Five hundred milligrams of fresh plant material were homogenized in a mortar and pestle with 10 ml of 80% boiled ethanol. The extract was centrifuged at 800 g for 15 min. and the supernatant was made up to 10 ml with 80% ethanol and used for the estimation.

Estimation

In a 25 ml test tube, 1ml of ethanol extract was taken and neutralized with 1ml 0.1N NaOH using a drop of methyl red indicator. To which, 1 ml of ninhydrin reagent was added and mixed thoroughly. The whole content was boiled in a water bath for 20min, and then 5ml of diluting solution was added, then cooled under the running tap water and made up to 25ml with distilled water. The absorbance was read at 570nm in a UV-Vis spectrophotometer (Model-118, Systronic India Limited, Gujarat, India) against an appropriate blank. The standard graph was prepared by using leucine as standard and the amino acid content was calculated using the standard graph and the results were expressed in mg g^{-1} dry weight.

RESULT AND DISSCUSION

Proline Leaf

Sesamum indicum L. leaves treated with salt stress had higher proline content overall during all growth stages compared to the control; on the 35th, 45th, and 55th DAS, for example, the proline content was 222.09, 267.59, and

195.48 percent more than the control. On the 55th DAS, the proline content of the leaves rose with individual SA and HA treatments, reaching 144.63 and 150.84 percent over control. In contrast to NaCl stressed plants, individual applications of humic acid (HA) and salicylic acid (SA) reduced the proline content of leaves; however, this reduction was greater than that of the control and was recorded as 171.46 AND 179.31 percent over control, respectively, on 55 DAS. (Fig. 1)Numerous crop varieties, both salt-tolerant and salt-sensitive, have been shown to accumulate proline as a key defense mechanism in response to salt stress [19]. In *Portulaca oleracea* L. [20], *Spinacia oleracea* L. [21], *Vigna unguiculata* L. [22], and *Durantaerecta* L. [23], the proline content of the leaves rose as salt increased. An additive increase in the levels of osmolytes, such as proline, with exogenous SA application under salt stress conditions has previously been observed in *Cucumis sativus* (24), *Cucumis melo* L. (25), and *Solanum lycopersicum* plants (26), respectively, following similar increases in proline by SA treatment (27). All four safflower cultivars' proline concentrations rose when HA was administered foliarly (28). In salt conditions, the benefits of SA on plant growth and productivity are more noticeable (29). According to a study on barley carried out in saline circumstances, applying SA increases proline (30). Another finding by Barley (31) proposed that applying HA to plants of *Hordeum vulgare* L. under Cu metal stress would increase the amounts of amino acids in those plants (32). Exogenously given HA under salt stress had similar outcomes in terms of increased free amino acids as seen in genotypes (33) in maize varieties and Hungarian vetch plants (34).

Stem

Proline content was found to be higher in the stems of NaCl stressed plants when compared to control on all sampling days; on 35, 45, and 55 DAS, it was 296.55, 243.82, and 175.34% over control, respectively; however, the reduction was greater than control. When SA and HA were applied foliarly to non-stressed control plants, proline content of the stem was further enhanced; on 55 DAS, it was 106.84 and 117.12% over control; however, when SA and HA were applied foliarly to non-stressed control plants, proline content of the stem was reduced relative to NaCl stressed S. indicum plants; on 55 DAS, it was recorded 137.67 and 149.31 percent over control. (Fig. 2). Numerous forms of abiotic stress lead to the accumulation of the amino acid proline [35]. Salinity stress raises the proline concentration in the stems of *Solanum tuberosum* L. [37] and *Lupinus termis* L. [36]. As a result, elevated L-proline has a variety of important functions in plants subjected to stressors such salt stress (38). Our findings of lower proline content were consistent with earlier observations from Prosopis alba (39) in mustard, which showed that exogenous SA treatment significantly reduced the levels of osmolyte proline in plants under NaCl stress (40). Salicylic acid in line with that, humic acid's reduction of proline in the stem has been linked to lessening the detrimental effects of salinity on cotton plants (41). Moreover, humic acid has been shown to lessen the effects of salinity on proline accumulation in peppers (42). A study found that foliar application of HA increased proline accumulation in maize stem cultivars, which improved the plant's water relations attributes (43).

Root

In the roots of salt-stressed *Sesamum indicum* L., sodium chloride stress increased the proline content on all sampling days; on 35, 45, and 55 DAS, respectively, it was recorded at 137.87, 145.85, and 167.22 percent over control. When SA and HA were applied topically to unstressed plants, the proline content of the roots increased even more in comparison to the control group, reaching 101.60 and 104.82% on 55 DAS. Nonetheless, when compared to plants under NaCl stress, the proline content of the roots of salt-stressed plants that received individual exogenous applications of SA and HA was reduced; on 55 DAS, this reduction was greater than that of the control, measuring 122.93 and 125.35 percent, respectively (Fig. 3). Compared to the control, plants in the current study that received a NaCl treatment had higher proline levels. In *Cucumis sativus* L. [44], *Triticum aestivum* L. [45], the proline concentration of the roots rose as salinity increased. The greatest amount of proline that SA under stress can accumulate in plant roots may be linked to an increase in proline production as a result of protein hydrolysis [46]. Applying exogenous SA lowers salt stress because *Solanum tuberosum* L. [47] and *Capsicum annum* L. [48] produce more proline. Additionally, using HA increases salt tolerance by increasing osmotic potential and consistently preserving the ideal proline level under stressful circumstances (49). A similar reduction in proline content under exogenous growth regulator cytokinin under copper stress was observed in Bean (50). According to a similar study,

foliar application of HA increased proline accumulation in maize root cultivars, improving the plant's water relations characteristics (51).

Amino acid Leaf

Sesamum indicum L. plants under NaCl salt stress had higher levels of free amino acid in their leaves on all sample days compared to the control group; on DAS 35, 45, and 55, the percentages were 172.87%, 169.00, and 150.51% higher, respectively. Furthermore, when SA and HA were applied topically to non-stressed gingelly plants, the level of free amino acids in the leaves was significantly enhanced in comparison to the control group. On 55 DAS, this improvement was 115.35 and 126.10%, respectively. When compared to NaCl-stressed plants, individual foliar spraying of SA and HA to salt-stressed cowpea plants did, however, result in a lower amount of leaf free amino acid; on 55 DAS, this reduction was recorded to be 141.43 and 146.32 percent higher than control. (fig. 4)Leaf amino acid concentration increased with increasing salinity in *Gossypium hirsutum* L. [52] and Maize [53]. Many plant species use the buildup of soluble organic molecules and low-mass organic solutes, such as osmoregulators, to mitigate the negative effects of water scarcity and salt stress [54]. Under salt stress, overproducing osmolytes proline protected thylakoid membranes and increased the stability of several mitochondrial and cytoplasmic enzymes [55].However, the decline rate was greater than the control. With the age and length of the stress period, foliar spray of SA causes a significant decrease in free amino acid content in NaCl stressed plants compared to NaCl stressed plants alone (56). The highest free amino acid content was discovered after seed priming with a mixture of humic acid. Total free amino acids rose significantly in all of the cultivars investigated in this lentil experiment under saline circumstances (57).

Stem

When compared to the control, free amino acid concentration increased in the stem of NaCl-stressed gingelly plants at all growth stages and sampling days.The increase was 200, 222.52, and 182.29 percent over control on 35, 45, and 55 DAS, respectively. Furthermore, foliar treatment of SA and HA to non-stressed plants resulted in a further increase in stem free amino acid content when compared to the control alone, with values of 101.43 and 111.96 percent higher on 55 DAS, respectively. In contrast, foliar spraying SA on salt-stressed plants resulted in a drop-in stem free amino acid content when compared to NaCl stressed gingelly plants alone, with values of 171.29 and 175.59 percent over control on 55 DAS, respectively. But the decline was greater than the control.(Fig.5).In response to environmental constraints such as salt, many plant species produce amino acid, an organic osmolyte [58]. Salinity stress causes an increase in stem amino acid concentration in plants: (59). SA has a greater favourable influence on plant growth and productivity when salinity is high (60). Several authors showed that NaCl application raised free amino acid levels in various species, including snap bean (61). Humic acid may have had a significant impact on total free amino acids and total phenolics in both wheat cultivars under control and saline conditions (62). Contrary to predictions, triacontanol treatment significantly boosted free amino acid and phenol accumulation in green gram under normal development conditions (63).

Root

Gingelly plants exposed to NaCl stress had an increased free amino acid content in their roots as compared to the control on all sample days, with values of 197.84, 220.89, and 211.29 percent higher on 35, 45, and 55 DAS, respectively. Furthermore, the administration of SA and HA to non-stressed plants resulted in a further rise in amino acid, which was 129.83 and 133.60 percent over the control on 55 DAS.However, individual foliar application of SA and HA to NaCl stressed plants resulted in a substantial fall in root free amino acid content when compared to salt stressed plants, although the reduction was greater than the control, with values of 175.53 and 181.98 percent on 55 DAS, respectively. (Fig.6).Furthermore, free amino acids are osmoregulating chemicals that protect plants from salt stress by decreasing membrane permeability and thereby enhancing membrane tolerance (64, 65, 66). The accumulation of free amino acids is seen as an initial defensive response to salt stress (67). A study on improved free amino acids by SA treatment during salt stress was conducted in mung bean types (68). It was discovered that free amino acid levels increased greatly during salinity stress, and foliar administration of HA resulted in even greater amino acid accumulation under salt stress in flax cultivars (69).

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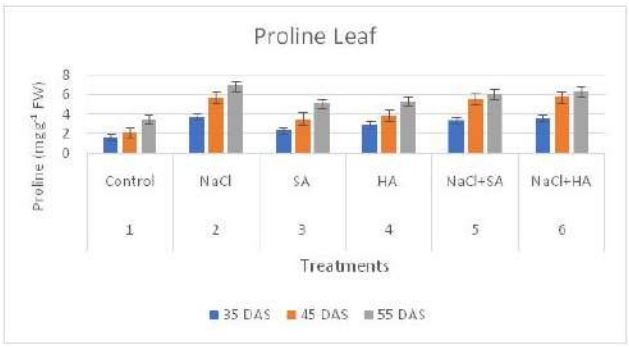

Figure. 1. Effect of foliar application of SA and HA on Proline leaf of *Sesamum indicum* (TMV-4 variety) under 100 mM NaCl stress. Values represented in Bars are mean of three replicates (n=3) and (±) standard error.

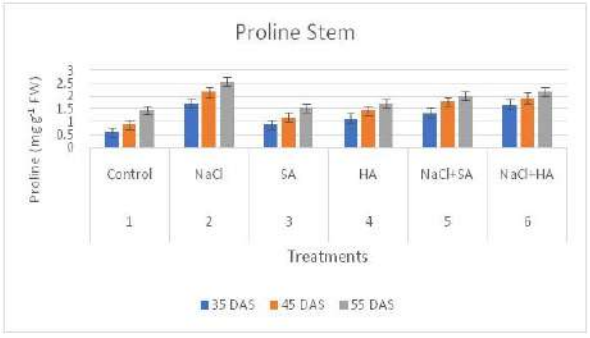

Figure. 2. Effect of foliar application of SA and HA on Proline stem of *Sesamum indicum* (TMV-4 variety) under 100 mM NaCl stress. Values represented in Bars are mean of three replicates (n=3) and (±) standard error.

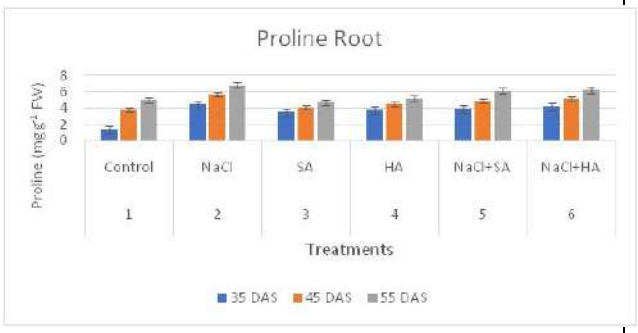

Figure. 3. Effect of foliar application of SA and HA on Proline root of *Sesamum indicum* (TMV-4 variety) under 100 mM NaCl stress. Values represented in Bars are mean of three replicates (n=3) and (±) standard error.

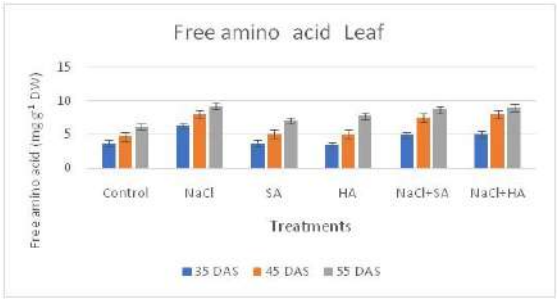

Figure. 4. Effect of foliar application of SA and HA on Amino acid leaf of *Sesamum indicum* (TMV-4 variety) under 100 mM NaCl stress. Values represented in Bars are mean of three replicates (n=3) and (±) standard error.

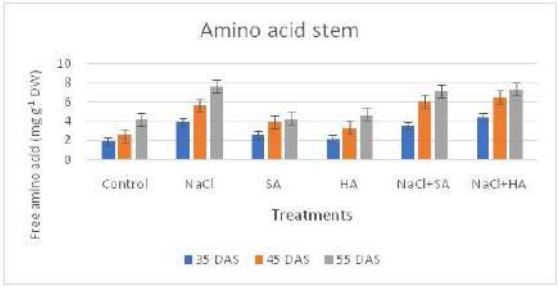

Figure. 5. Effect of foliar application of SA and HA on Amino acid stem of *Sesamum indicum* (TMV-4 variety) under 100 mM NaCl stress. Values represented in Bars are mean of three replicates (n=3) and (±) standard error.

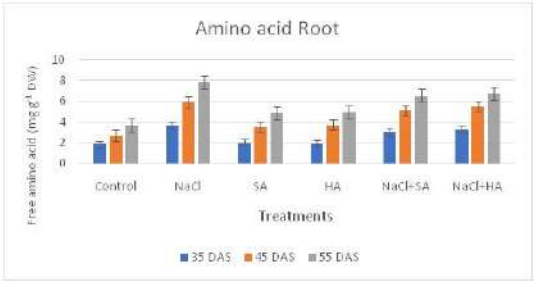

Figure. 6. Effect of foliar application of SA and HA on Stem length of *Sesamum indicum* (TMV-4 variety) under 100 mM NaCl stress. Values represented in Bars are mean of three replicates (n=3) and (±) standard error.

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RESEARCH ARTICLE

Plant Secondary Metabolites - A Weapon for Post-Harvest Disease in Onion

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ABSTRACT

Onion (*Allium cepa*) is a significant seasonal and economically valuable crops around the globe. Lack of ideal storage conditions causes pathogenic fungal infection, which damages and destroys them during storage. The main fungal storage diseases that affect onions are black mold, blue-green mold, fusarium rot, and neck rot. *Aspergillus species*, *Alternaria species*, *Botrytis species*, *Colletotrichum species*, *Fusarium species*, and *Penicillium species* are the main pathogens linked to these conditions. These species prey on bulbous onions during the post-harvest storage stage. Since conventional methods of storage lead to significant damages in stored onions, the implementation of better storage buildings, along with the application of more effective storer types, proper irrigation, fertiliser management, and post-harvest technological advances, are crucial to minimize the damages in stored onions. Biological control is one of the most reliable approaches to protect bulbs from either storage pathogens or other opportunistic microorganisms, which are associated with post-harvest losses. This involves investigating and employing plants' natural defence systems. Such systems are often based on secondary plant metabolites, which are low molecular weight, heterogeneous compounds that make the host plant resistant to pathogens. There are several classes into which secondary metabolites can be divided, including as lignans, alkaloids, phenols, coumarins, flavonoids, saponins, terpenes, quinones, xanthones and others.

Keywords: *Allium cepa*, Post harvest disease, Fungal infection, Secondary metabolites, Antifungal activity.

INTRODUCTION

Onion (*Allium cepa*),which belongs to the family Amaryllidaceae and the genus *Allium* is a major vegetable crop grown and consumed widely across the world. Every year, almost 105 billion pounds of onions are produced worldwide. With 26,738 metric tonnes produced per year, India leads the world in onion production. China comes in second with 23,660 metric tonnes, and the US produces 3,821 metric tonnes annually. Although onions are typically handled as annuals and harvested in their first growing season, they are actually most often biennial or perennial plants. The three main seasons of growth for onions are Rabi, Late Rabi, and Kharif[1]. Onions contain a wide range of chemical compounds, such as diallyl disulphide and diallyl trisulfide, along with allicin, quercetin, and fisetin. At certain quantities, onions and their primary constituents have demonstrated numerous health benefits, including antioxidant and free-radical scavenging characteristics, anticholesterolemic, anti-heavy metal toxicity, antihyperuricemic, antibacterial, anti-gastric ulcer, and anticancer effects [2]. Onions must be stored for a long time in order to provide a consistent supply all year round. A number of fungal diseases that arise during long-term storage are the primary reason behind the decrease in onion yields. To minimise the loss of onions, it is essential that conditions affecting onions are identified early and that efficient management techniques are put in place. A number of factors, including disease and humidity, have been linked to onion quality during the cultivation, production, storage, and distribution processes. Even with recent technological advancements in the production process, postharvest loss during storage remains a significant issue. There are several postharvest conditions that affect onions, including neck rot, brown rot, soft rot, smudge, black mold, and blue mold.Among these, grey mold, blue mold, and black mold are the most common ones that limit international as well as regional trading of onion.Major fungal storage diseases of onion are Aspergillus rot (*Aspergillus flavous*), Black mold (*Aspergillus niger*), Fusarium basal rot (*Fusarium oxysporium*), Rhizopus soft rot (*Rhizopus nigricans*), Pink rot (*Fusarium spp*.), Blue mold (*Penicillium spp*.) and purple blotch (*Alternariaporri*). *Aspergillus* species, particularly *A. niger*, are the most harmful fungal strain in the field and during post-harvest storage[3].

Synthetic fungicides are frequently employed to control post-harvest diseases, which has a detrimental impact on the environment and human health[1]. As antifungal resistance is becoming a significant concern, the investigation for novel bioactive chemicals is essential to prevent excessive usage of fungicides.Biological control is one of the most effective methods for safeguarding bulbs against opportunistic bacteria and storage diseases that are linked to post-harvest losses[4]. This involves investigating and employing plants' natural defence systems. Such systems are often based on secondary plant metabolites, that are low molecular weight, heterogeneous moleculeswhich confer disease resistance on the host plant. In all living systems, theproduction of secondary metabolites is a continuous metabolic pathway. Lignans, flavonoids, coumarins, alkaloids, saponins, terpenes, quinones, and xanthones are a few examples of the several types of secondary metabolites. However, whilst plants, fungi, and bacteria can all synthesise these chemicals, animals lack the pathways necessary for the synthesis of these molecules [5]. An application of these potentially protective compounds requires several steps, starting from the isolation of adequate amounts of purified compounds, followed by the determination of their modes of action, and finally their implementation in a formulation. With the current state of information available on secondary metabolites, this article reviews the potential of plant secondary metabolites as a weapon for post-harvest disease in onion.

PLANT SECONDARY METABOLITES

Metabolites are the byproducts of metabolism. Primary and secondary plant metabolites are essential for the development and survival of plant species [6]. A vast and diverse array of biological molecules are produced by plants, the majority of which do not appear to have any direct impact on how they grow and develop. Suchcompounds are oftenknown as secondary metabolites, and they are particularly significant for defence and environmental interactions [7]. Secondary metabolites are produced biosynthetically from primary metabolites and contain a diverse array of active chemicals. Their range within the plant kingdom is relatively constrained. For a particular type of plant growing in different conditions, they differ in number and function.They are usually generated in smaller amounts and are produced at different developmental stages by specialized cell types. The

biosynthetic routes of secondary metabolites in plants are frequently used to categorize them. Alkaloids, steroids, and flavonoids are the three major chemical families into which they are categorized [8].

TERPENOIDS

Terpenoids, which have approximately 30,000 different structural variations, are the largest class of natural chemicals. They are also known as isoprenoids or terpenes. The majority of these terpenoids originate from plants. Terpenoids have been shown in numerous studies to be capable of eliminating a broad variety of dangerous fungal diseases, including *Aspergillus* species, *Fusarium* species, *Botrytis* species, and others. Carvacrol, thymol, and eugenol are three bioactive terpenoids that have drawn a lot of interest from researchers due to their antifungal properties [9].

Thymol

Thymol (2-isopropyl-5-methylphenol)(Figure 1),is a naturally occurring monoterpenoidwhich is isolated from the species *Thymus vulgaris* L., usually known as thyme, as well as numerous other plants, including *Origanum* L., *Satureja* L. species, *Oliveria decumbens* Vent, *Ocimum gratissimum* L., and *Carum copticum* L [10]. It is a phenolic component found in essential oils. At neutral pH, thymol is less soluble in water but still dissolves in certain organic liquids including alcohols. It possessesantioxidant, antispasmodic, antimicrobial, and anti-inflammatory properties[11]. Thyme essential oil (thymol, 47.59%; γ-terpinene, 30.90%; p-cymene, 8.41%), which is produced from leaves of *Thymus vulgaris*, has thymol as one of its main constituents. Studies have demonstrated that pure thymol inhibits microbial growth about three times more strongly than thyme essential oil[12]. Thymol is effective against *Aspergillus spp*, *Botrytis spp*, *Fusarium spp*[13-15]. Thymol combined with an antimycotic agent not only overcomes pathogen resistance to traditional antifungals but also lowers the toxicity of the antifungal agent and boosts its antifungal efficacy [16]. Thymol inhibits the gene expression related to the calcium transporters, which has a negative impact on intracellular calcium homeostasis. It reduces protein glycosylation by downregulating the gene expression necessary for N-glycosylation. It causes disruption to the synthesis of ergosterol in *Fusarium graminearum* and induces lipid peroxidation. It causes the accumulation of reactive oxygen species (ROS) and compromises the stability of the cell membrane and cell wall by obstructing the genes required for the synthesis of these structures [9]. For long-term storage crops like onions, the thymol solvent fumigation treatment approach is effective for controlling fungal diseases. While the thymol solution spray technique will work well to suppress low-temperature onion pathogens, it is proposed that the thymol solution fumigation technique works better to increase the thymol distribution effect on an industrial level. To effectively apply thymol for postharvest control of pathogens on fields and in remote regions, scaling up studies involving a range of thymol treatment techniques are necessary, as the majority of antifungal tests were conducted in laboratories [3].

Carvacrol

Carvacrol (2-methyl-5-(1-methylethyl) phenol)(Figure 2), is a monoterpenoidpresent in variousspecies of plant including thyme and,to a greater amount in oregano [11]. Many research investigations report carvacrol's antimicrobial, anti-inflammatory, antioxidative, antidiabetic, anticarcinogenic, antinociceptive, neuroprotective, and cardioprotective characteristics. This is because it demonstrates robust antioxidative characteristics in addition to hydrophilic characteristics linked to the phenolic OH group and hydrophobic characteristics linked to the substituted aromatic ring [18]. Carvacrol can be considered as potential antifungal natural compounds to be used against *Aspergillus spp*, *Fusarium spp* and *Botrytis spp* [13-15].It decreases the amount of ergosterol in *A. flavus* and decreases mycelia growth, spore germination, and aflatoxin formation [9].When carvacrol and an antimycotic drug are combined, the antifungal efficiency increases, pathogen resistance to traditional antifungals decreases, and minimizes its toxicity [16].

Eugenol

Eugenol(4-Allyl-2-Methoxyphenol) (Figure 3) is a phenolic monoterpene, belonging to the phenylpropanoid family that possesses potent antimicrobial properties. Its derivatives have demonstrated enhanced antimicrobial activity as

well as non-toxic characteristics [9]. It is effective against *Aspergillus, Penicillium, and Fusarium* species. This compound's antifungal effect has the potential to severely damage the fungal cell wall and membrane, resulting in morphological distortions, conidia disintegration, and hyphae degeneration.The antifungal activity is attributed to the presence of both an aromatic nucleus and a phenolic OH group, which are known to be reactive and create hydrogen bonds with the active sites of target enzymes [20].

PHENOLICS

It has been reported that polyphenols such as phenols, tannins, coumarins, flavonoids, and quinone derivatives have antifungal properties. A polyphenol's ability to inhibit fungal growth can be influenced by the position and amount of hydroxyl groups it contains. They may function by suppressing the activity of enzymes produced by microorganisms, perhaps by less direct interactions with proteins or by reacting with sulfhydryl groups[22]. *Penicillium expanisum* and *Aspergillus flavus* may be susceptible to the antifungal effects of phenolic extracts from *Q. infectoria* galls and *C. colocynthis* fruit. The chemical structures, functional groups, and synergistic interactions among the constituents were primarily responsible for the biological function of these plant extracts. The presence of phytochemical components such as flavonoids and tannins have been reported to be responsible for the disintegration of cell wall and cellular material that ultimately leads to cellular death of the microorganism [23].

Flavonoids

Secondary metabolites like flavonoidshave been classified as major categories of polyphenols which are mostly present in plants. Many beverages, such as green tea, oolong tea, black tea, red wine, and cider, as well as foods like cocoa, onions, apples, bananas, sea buckthorns, grapes, berries, and citrus fruits, are rich sources of these naturally occurring compounds [24]. The general structure of flavonoids (Figure 4) consists of a 15-C skeleton, C6-C3-C6, with two benzene rings (A and B) connected by a 3-carbonated heterocyclic ring.Subclasses of flavonoidslike anthocyanidins, isoflavones, flavones, flavanones, flavonols, and flavan can be distinguished from one another based on modifications to the central carbon ring[25].

Flavonoids exhibit potential antifungal properties against *Aspergillus* species like, *A. flavus, A. parasiticus, A. nomius*[26], *A. fumigatus*[27] and *A. niger*[28].The growth of fungi is frequently suppressed by a number of underlying processes such as, dysfunction of plasma membrane [29], initiation of mitochondrial disintegration, along with inhibition of the following mechanisms like, cell division, formation of cell wall, efflux regulated pumping system and protein& RNA synthesis[30].

Coumarins

The term "coumarin," which comes from the plant *Coumarouna odorata*, refers to a class of molecules known as benzopyrones that are made up of combined benzene and α-pyrone rings. Almost a thousand coumarins have been identified, and they are found in many different parts of the vegetable kingdom, especially in angiosperms. The majority of these are secondary metabolites found in green plants, while some are produced by bacteria and fungus [32]. 4-Acetatecoumarin(Figure 5), also known as Cou-UMB16, is a coumarin derivative that exhibits efficacy against thegrowth of mycelial cells and spore formation for *A. flavus*and *A. fumigatus*. Hyphae and the resulting formation of mycelium is an essential factor of virulencefor *Aspergillus* species. Cou-UMB16 obstructs this crucial virulence factor by showing antagonistic effect on the spore germination of *Aspergillus* species [33]. 7-hydroxy-6-nitro-2 H-1-benzopyran-2-one(Figure 6), also known as Cou-NO2, is a coumarin derivative that can interfere with the virulence of *Aspergillus* species by preventing both the germination and mycelial development of conidia[34].

Tannins

The bark, roots, wood, and seeds of many higher plants contain naturally occurring polyphenolic chemicals called tannins, which are also known as tannic acid (Figure 7). By severely damaging the fungal pathogen's membrane stability and causing its cellular contents to seep out, tannic acid prevents *Penicillium digitatum* from growing. Tannic acid can therefore be utilized as a model compound for producing new fungicides[35].

CONCLUSION

Onion (*Allium cepa*) is a major vegetable crop and has its importance in our diets beyond doubt. Infection by *Aspergillus niger* and other organisms causing post-harvest losses is a frequent occurrence. In recent decades, it has gotten much worse. Since onions are a seasonal crop, they must be stored in low-temperature storage facilities for an extended period of time—more than 11 months—after each harvest. Onions are a crop that can be cultivated in both tropical and temperate climates, so agricultural research and development has given a lot of attention to growing and handling onions. Even with the advances in automated onion harvesting, treatment, and storage, many small- and medium-scale farmers still face significant losses when they cannot afford to use upgraded methods.Post-harvest diseases of onions during storage conditions might result from secondary infections during storage conditions or from latent infections before or after harvest. In order to prevent enormous losses, fungal diseases must be addressed as soon as possible. For example, if onions become contaminated with mold and are stored in excessively humid conditions for an extended period of time, the contaminated onions will infect other healthy onions. Thus, post-harvest losses of onions can be decreased if these diseases are reduced either before or after harvest by various treatments. Improvements in fungicidal formulations can help to minimise these infections. Numerous secondary metabolites have been discovered throughout the years, and researchers have examined their potential resistance against various fungal pathogens. It has also been discovered that a number of phytochemicals may cause microbial cell death or growth suppression. Secondary metabolites can be used to provide biological control against decay, in the field and during storage phase, hence reducing the amount of insecticides and residues applied to post-harvest crops. This is a promising chemical substitute. These improvements must be targeted to prevent any type of health hazard to the consumers and to enhance the well-being of rural farmers, especially women and children who work the majority of the time on subsistence farms.

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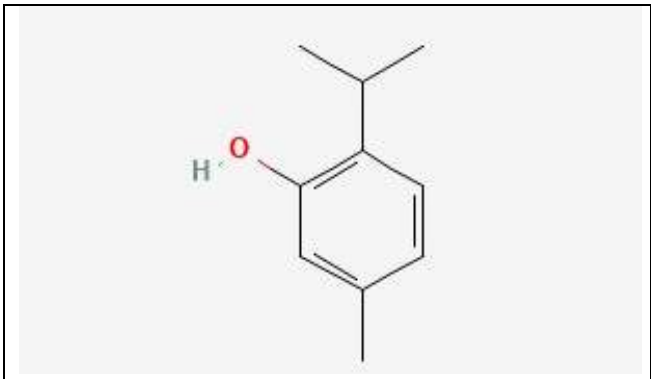

Figure 1. Chemical structure for Thymol [17]

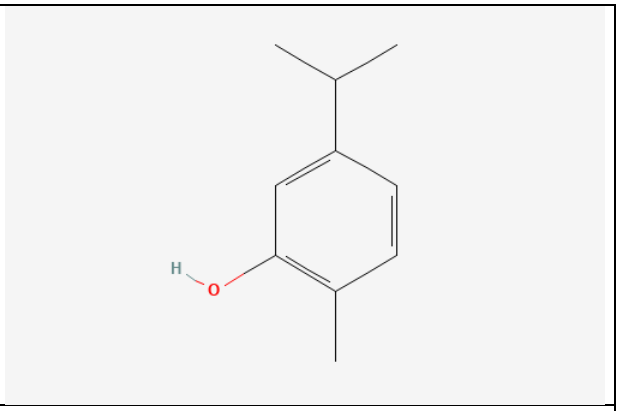

Figure 2. Chemical structure for Carvacrol [19]

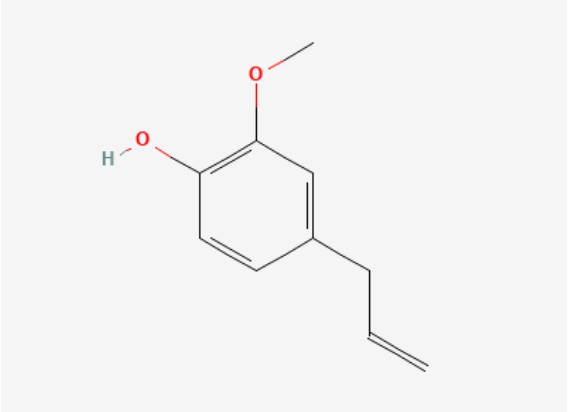

Figure 3. Chemical structure for Eugenol[21]

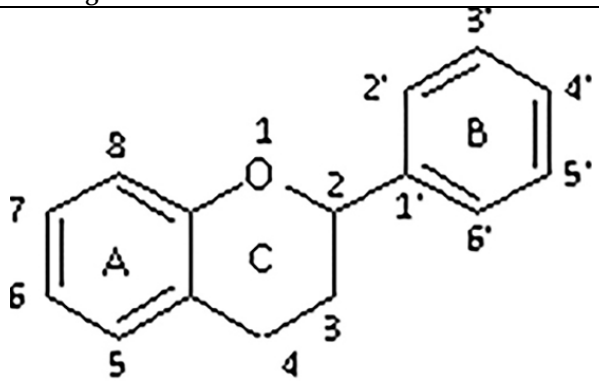

Figure 4. Chemical structure of flavonoid [31]

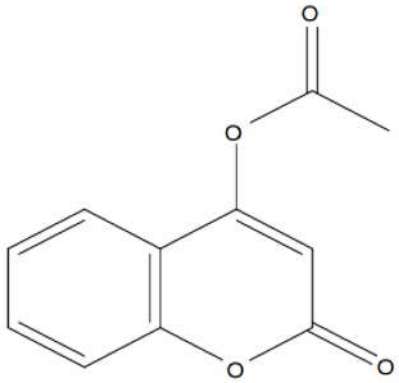

Figure 5. Chemical structure of 4-acetatecoumarin (Cou-UMB16) [33].

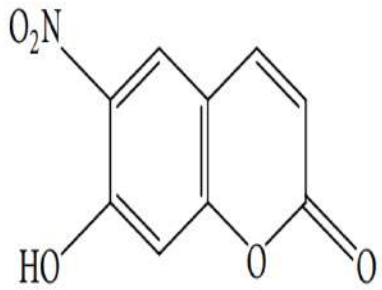

Figure 6. Chemical structure of 7-hydroxy-6-nitro-2H-1-benzopyran-2-one (Cou-NO2)

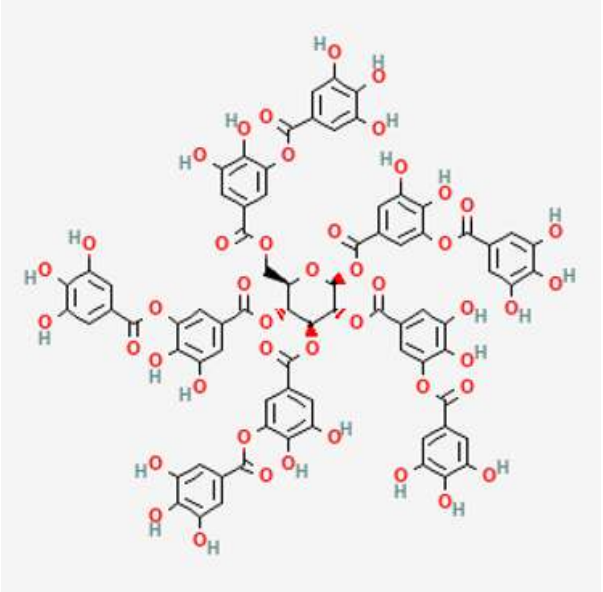

Figure 7. Chemical structure of Tannic acid[36]

RESEARCH ARTICLE

Potential Impacts of Biosurfactant-Coated Zinc Nanoparticle in the Treatment of Wastewater

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ABSTRACT

The chemical production of ZnO nanoparticles was the main focus of this investigation, coating the nanoparticle with the surfactant produced from *Bacillus subtilis* (MTCC441) and checking its efficacy to remediate wastewater. The nanoparticles were synthesized using a wet chemical process. XRD studies revealed that ZnO-NP formed had a spherical structure, with the larger particles having polyhedral form. SEM analysis showed particles showed particles with least agglomeration due to the capping technology. A prominent peak was observed in UV-Vis spectrum at 350 nm and is very unique to ZNPs. SEM revealed that the forms of the produced nanoparticles varied depending on the synthesis process.The obtained emulsification index (E24) was 68% in oil displacement test.The presence of hydrocarbon groups in the surfactant is revealed by FTIR analysis, indicating increased surface activity.It could be concluded from the study that nanoparticle-based treatment ensures environmentally pleasing, economical ways as compared to other procedures. Nanotechnology is increasingly being used in environmental engineering, including wastewater treatment. Because of its hazardous composition, wastewater poses serious risks to natural resources and to man. Capping the biosurfactant produced by microorganisms with the synthesized nanoparticles will improve the bioavailability and bioremediation potential. Hence, this method would have the added advantage of remediating wastewater.

Keywords: capping, biosurfactants, wastewater treatment, and zinc oxide nanoparticles

INTRODUCTION

Materials that range in size around 1 to 100 nm are known as nanoparticles. certain chemical and physical properties of NPs include their enormous surface area and nanoscale size. Due to absorption in the visible area, the optical characteristics vary with size and impart various colours. NPs can be used in both professional and residential settings. They are essential for improving reactions, imaging technology, and applications in medicine and the environment [1]. Recently, researchers discovered a connection between biological species and nanoparticles. It was discovered that a wide variety of microorganisms had the capacity to create inorganic nanoparticles either intracellularly or extracellularly. Due to the variety of accessible core materials and the ability to modify surface properties, these particles are useful for a variety of biotic uses [2]. Zinc oxide nanoparticles are said to damage bacterial cell membranes and reduce how hydrophobic their surfaces are. Zn NPs kill bacteria by triggering the creation of ROS [3]. The unique physiochemical characteristics and surface area, nanoparticles have demonstrated extraordinary antibacterial activity at extremely low concentrations. The majority of the particles, especially metallic and metal oxide nanoparticles, are nontoxic and have antimicrobial capabilities. Their synthesis takes place in a short duration by utilizing standard laboratory equipment and without the need of expensive and sophisticated instruments. Biosurfactants are surface-active biomolecules with emulsifying properties that cause hydrophobic substances to dissolve. These molecules bind between air - air and air- liquid interfaces at different degrees of polarity. Studies on biosurfactants produced by microorganisms has been well documented. Wei and Chu in 2002 reported that *Bacillus subtilis* used solid-state fermentation to produce biosurfactant on a small scale [4]. High surface activity was exhibited by the biosurfactants created using cassava water, which is a crucial characteristic of effective surfactants. Biosurfactant-coated nanoparticles [NPs] have the potential to be effective in blocking dangerous biofilms [5]. The concerted effects of nanoparticles capped with microbial biosurfactants has the added advantage of metallic nanoparticle aggregation and stabilization. Surfactants and other organic colloids cause wastewater to agglomerate more quickly than clean water. With this basic understanding, the current study concentrated on creating zinc oxide nanoparticles chemically and using the biosurfactant made from Bacillus subtilis strain MTCC-441 to cap the manufactured nanoparticle.The zinc nanoparticle coated with biosurfactant as a result was used to remediate the wastewater as per the standard methods.

Production of Zinc Oxide Nanoparticles

The solutions—urea [0.1M] and zinc acetate—were mixed at a 4:1 volumetric ratio. In a water bath, the solution was subjected to heating to 115 °C for 1.5 hours. After forming a white precipitate, the mixture was centrifuged for 10 minutes at 6000 rpm. To get rid of any chemicals that had been absorbed and prevent agglomeration, it was cleaned using distilled water. It was then dried for an entire night to create a ZnO particle-powder. [6].

Analysis of Zinc Oxide Nanoparticles

The physical and chemical properties of the ZnO nanoparticles that were produced were examined. The wavelength range for the UV-Vis spectra was 200–800 nm. Utilizing a scanning electron microscope (SEM), the particle's dimensions and form were investigated. X-ray diffraction (XRD) was employed to confirm the crystallographic phase development of the synthesized nanocrystalline material. [7].

FT-IR is a powerful tool for determining the composition of objects. The sample was made up of dried ZnO and KBr in a 1:3 ratios, and it was then put under an IR spectrometer for analysis.

Biochemical characterization of the Standard Strain Bacillus subtilis MTCC-441

Biosurfactant producing *Bacillus subtilis* strain MTCC-441 was used for the study. In addition to Gram staining, the morphological traits including motility, color, surface area, and cell shape were noted. Using the strain's biochemical properties, microbiological standards were followed in order to identify the strain as *B. subtilis*. [8].

Characterization of the Biosurfactant Produced

Bacillus subtilis culture was incubated at ambient temperature to produce bio-surfactants. The sample was processed to extract cells. The collected supernatant was purified and analysed for the production of biosurfactants using standard techniques [9]. Biosurfactant characterization tests like drop collapse assay, emulsification index was calculated as per the industry standards [10]. The biosurfactant produced was characterized using FT-IR to demonstrate the surface activity.

Treatment of the wastewater with Biosurfactant coated ZnO nanoparticles

The wastewater's initial characteristics, including pH, TDS, COD, color intensity, sulfates, and phosphates, were measured before treatment[11]. The water samples that needed to be treated were combined with biosurfactant and produced ZnO NPs in a 1:1 ratio. ZnO NPs produced at a concentration of 0.1g/100ml were also employed in the treatment. After five days, the concentration of dissolved oxygen (DO) in waste water collected and treated with zinc oxide nanoparticles (ZnO NPs) and biosurfactant coated with ZnO NPs was measured using Winkler's Method[12].

RESULTS AND DISCUSSION

A prominent peak was observed in UV-Vis spectrum at 350 nm [Figure 1] and is very unique to ZNPs. The substantial excitation binding energy of these peaks at room temperature may be the cause of the observed differences in peaks. The band gap widens as particle size decreases, as is widely known from absorption spectroscopy [13]. In earlier research, bulk ZnO experienced absorption about 385 nm. The difference in shift between the synthesized ZNPs and bulk ZnO may be the result of a significant reduction in particle size. A prominent absorption peak at 370 nm, which is ZnO's typical absorption peak, can be observed in the spectrum. The particle size distribution is further supported by this strong peak, which indicates that the particles are nanosized. After synthesis, a heterogeneous powder with very small grains that ranged in size from 100 to 150 nm was observed [Figure 2]. SEM revealed that the forms of the produced nanoparticles varied depending on the synthesis process. The morphology of the ZnO nanopowders is clearly affected in a very intriguing way by the synthesis procedure, as seen by the SEM pictures of samples [14].The larger particles had a polyhedral shape, while the smaller ones were spherical and ranged in size from 10 to 200 nm. The diffraction lines for ZnO can be seen in XRD patterns as peaks [Figure 3]. The broadening of the peaks in this instance can be used to assess the level of crystallinity and the average crystallite size. The XRD patterns verified the poor level of purity of the produced goods, which contained diffraction peaks corresponding to the contaminants. When combinations reach a particular level (often > 1%), XRD reveals structural changes and may allow for the separation of constituents. The typical FTIR spectra of ZnO nanoparticles shows the distinctive absorption of the Zn-O connection, and around 3222 cm-1, hydroxyl absorption is visible. At 865, 1555, and 2922 cm^{-1}, there were multiple tiny absorption bands.

Similar observations were made using ZnO nanoparticles, with absorption peaks ranging from 3437.8 cm^{-1} to 2925.8 cm^{-1} to 1595.8 cm^{-1} to 1383.7 cm^{-1}. The 1595.8 cm^{-1} peak is related to aromatic nitro chemicals and alkyl. The stretching vibration of hydroxyl compounds is shown by the peaks at 2925.8 cm^{-1} and 3437.8 cm^{-1} [15]. The standard microbial strain *Bacillus subtilis* MTCC 441 was analyzed for biosurfactant production. A larger clean area is correlated with higher surface activity in the oil displacement test, which is an indirect indicator of biosurfactant surface activity. The emulsification index (E24) that was attained was 68%.The presence of hydrocarbon groups in the surfactant is revealed by FTIR analysis, indicating increased surface activity. The spectra [Figure 4] show that the CH aliphatic stretch is represented by peaks at 2592 and 2351 cm-1, and the C=C conjugated diene is shown by a peak at 1697 cm-1. The alkene and alkyl benzene surfactant components are significantly more effective, as seen by peaks at 3938 and 3354 cm-1. Novel anionic surfactants are made from alkenes and aromatic or substituted aromatic chemicals. The results of the preliminary characterization has been tabulated in Table1. The addition of surfactants, which are surface-active agents, has clearly cleaned out the solids, and the metal oxide has reduced the BOD level by accelerating the coagulation of solid aggregates. Due to the difficulties in separation, there are some minor drawbacks to employing nanoparticles directly for wastewater treatment [16]. As a result, Coating nanoparticles with

a supporting material, like polymers, will maximize reactivity and reduce release. This method entails creating nanostructures with exceptional properties. During adsorption, the enhanced surface area, in particular, will allow for a strong interaction between the pollutants and the nanocomposites[Figure 5]. Metal oxides, such as zinc oxides (ZnO) [17] have demonstrated high sorption towards organic and inorganic contaminants. The DO concentrated has been represented in Table 2. Results infer that biosurfactant coated nanoparticles are effective in increasing the concentration of DO which in turn will decrease the BOD of the waste water.

CONCLUSION

The study's conclusion might be that biosurfactant-capped nanoparticles can be used in wastewater treatment to disinfect wastewater. Compared with conventional and traditional procedures, it offers an eco-friendly, economical, energy-efficient, and time-saving alternative. When nanoparticles alone are employed it is difficult to separate them. But when these nanoparticles are coated with biosurfactants it exhibits a greater sorption to organic and inorganic pollutants and also increases the amount of dissolved oxygen [DO] for microorganisms to promote decomposition and reduce the BOD and COD in the wastewater. The water after treatment can be discharged in to the water bodies since it will have a reduced pollutant load.

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Table 1:Measurement of BOD in wastewater

Parameter	Quality Standard	Wastewater Untreated	Wastewater treated with surfactant	Wastewater treated with surfactant coated with ZnO NP (0.1g/100ml)
BOD mg/L	60	183.4	178.4	122.3

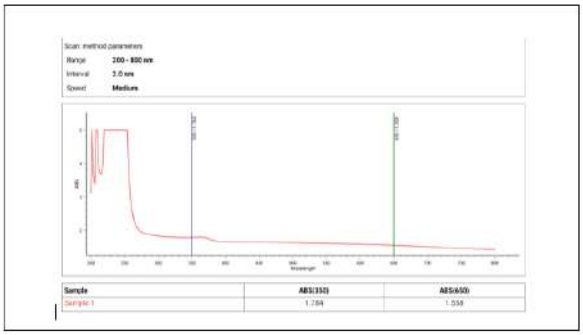

Fig 1. UV-Vis Spectrum of ZnO Nanoparticles

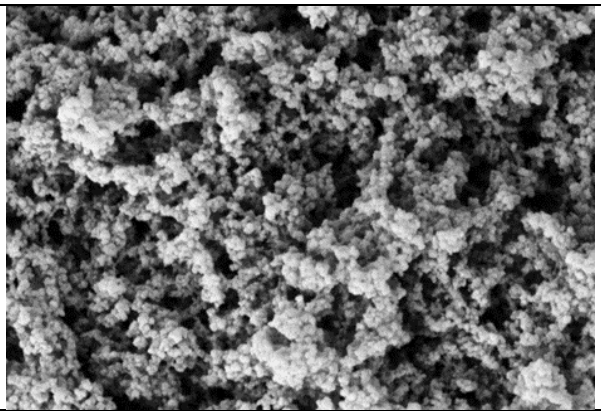

Fig 2. Scanning Electron Micrograph of synthesized ZnO Nanoparticles

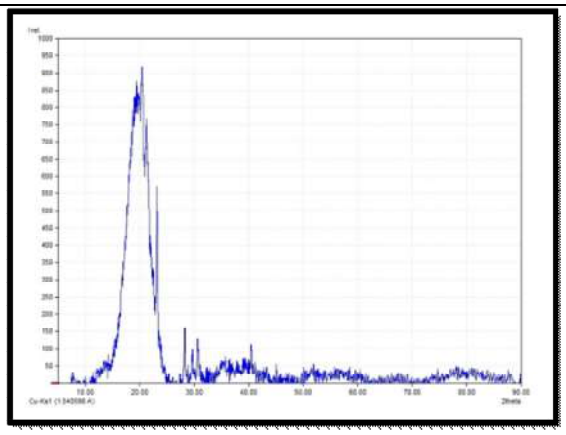

Fig 3. XRD graphs of ZnO nanoparticles

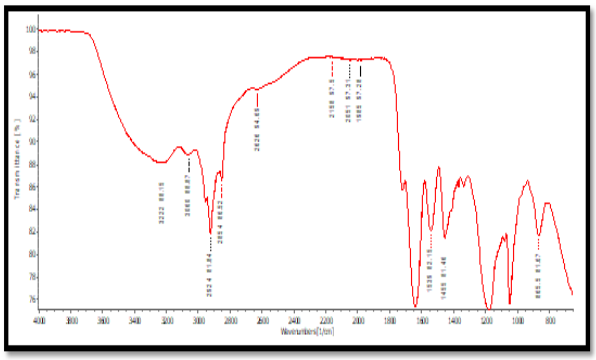

Fig 4. FTIR Spectrum of synthesized ZnO Nanoparticles

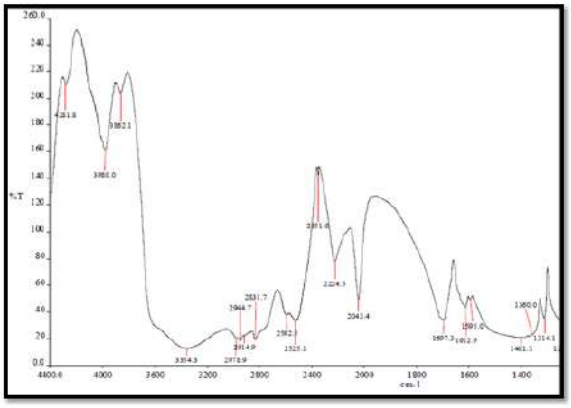

Fig 5. FTIR pattern of Biosurfactant from *B.subtilis*

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RESEARCH ARTICLE

No Siddha Thalidomide : Rising Concerns and Future Prospects

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ABSTRACT

As days go by, human lives are increasingly impacted by various ailments. The treatments offer hope for people's lives, but a daunting challenge lies in adverse drug reactions that occur when drugs are not used judiciously. These adverse effects can only be mitigated by pharmacovigilance. Pharmacovigilance offers a vital safeguard to fight adverse drug reactions. Remarkably the *Siddha* system of medicine developed by visionary *Siddhars* had already identified adverse effects and antidotes for each drug, particularly metals (*thathu*). This exposition aims to illuminate the adverse effects and antidote in *Siddha* pharmacopeia and underscores the potential risks associated with metal-based *Siddha* medicine, unveiling the need for robust pharmacovigilance. This growing pharmacovigilance sector implicates developing safer Siddha medicine practices, more effective ADR monitoring strategies, and improved patient safety. This review bridges the gap between traditional knowledge and modern pharmacovigilance, shedding light on the importance of pharmacovigilance in *Siddha medicine*.

Keywords: Siddha system,*Siddha* Pharmacopoeia, ADR, Antidotes, Pharmacovigilance.

INTRODUCTION

Pharmacotherapy is an important feature of the medical field that relies on the science of pharmacology for continual advancement and on pharmacy for appropriate management. Pharmacovigilance is the science dedicated to reducing the risk of drug-related harm to patients. It deals with the diagnosis, cure, treatment, or prevention of diseases. On

focusing other side, it also extends up to the adverse effects of any kind of drug used. This is termed as Adverse Drug Reactions (ADR). It is highly pronounced locally that the *Siddha* system of medicine has no side effects. but any drugs when handled unseemly result in adverse drug reactions, which can be balanced by pharmacovigilance (PV). Theophrastus Phillipus Auroleus Bombastus von Hohenheim (1493-1541) said, "All things are poison and nothing is without poison; only the dose makes a thing not a poison". The relationship between dose and its effects on the exposed organism is of high significance [1]. Pharmacovigilance is defined as the pharmacological science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem. Although the term 'Pharmacovigilance' does not feature in *Siddha*, it is vivid and highlighted in *Siddha* literature like *Nanjumurivunool*. In *Siddha* literature, there is no absolute equivalent term for adverse effects and pharmacovigilance. As per the *Siddha* concept, Adverse drug reaction (ADR) can be correlated with *NanjuKurigunam* [2-3]. *NanjuMaruttuvam* (*Siddha* toxicology) clearly explains the possible Adverse Drug Reactions (ADRs) of Siddha drugs or toxicities and their management in detail. The drugs are classified as toxic, semi- toxic or to be used with caution, etc. However, it is the need of the hour to prove that these drugs are safe, based on reliable scientific data. *Siddha* medicine is essentially one of the most ancient types of treatment branch wholly based on biotic medium; natural, herbal (*Thavaram*), Inorganic (*Thathu*), and animal products (*Jeevam*) as innovative medicinal resources. In the usage of metals, minerals, and other chemicals, this system was far more advanced than other systems. Manufacturing procedures for *Siddha* drugs are stringent, and adverse reactions are described when safety measures are not taken into consideration while manufacturing and administering these medicines. This review discusses, in brief, the *Siddha* concept of adverse reactions in the *Siddha* system, the need for pharmacovigilance, challenges in introducing pharmacovigilance in *Siddha*, measures to improve pharmacovigilance of herbal medicines, and future suggestions for implementing these elements.

MATERIALS AND METHODS

The information was acquired from various *Siddha* literature like *Gunapadam – thathu, jeevam*, mooligai, *NanjuMurivu*and by literature searching in electronic databases such as PubMed, Embase, Google Scholar, etc[4-8].

Siddha aspect on Adverse drug reaction (ADR)

There is a common misperception that *Siddha* medicines cannot cause adverse effects on the body. In the *Siddha* text, adverse drug reactions are discussed for specific drugs along with their treatment in the context of *NanjuMurivu*. In day-to-day clinical practice, we may encounter adverse reactions to medicine yet fail to accept it. However, it is made very evident in various *Siddha* texts that improper medicine preparation or drug administration (Dose, adjuvant, duration, *pathiyam*) can result in adverse drug reactions. These factors need to be considered while choosing the raw drugs for the preparation of medicines.

RESULTS AND DISCUSSION

Classification of Adverse Drug Reactions

Adverse drug reactions are classified into six types [10].These classifications may also be applied to the *Siddha* system.

Type A (Augmented)

Predicted from the known pharmacology of the drug.

Example: The dose of *Naga parpam* (Nano calcined form of zinc) is the one-sixth weight of Lablab bean. if the dose exceeds, it may cause adverse drug reactions.

Type B (Bizarre)

Reactions are not predicted from the known pharmacology of the drug. Dose independent, as very small doses might already elicit symptoms.

Example: Adjuvant, intake of the drug during a specific season, *pathiyam*if not followed properly type B adverse reaction may occur.

Type C (chronic/cumulative)
It generally has a cumulative effect.
Example: While using *Annabedhichendhuram*, leave an interval of one day after taking it for one week continuously. Otherwise, it will produce constipation and this has a cumulative effect.

Type D (Delayed)
Which appears after many years of treatment.

Type E (End of use)
Occur after drug withdrawal.

Drug-Drug Interactions
The Patients are commonly prescribed more than one drug, have their dietary preferences, and may also be using over-the-counter (OTC) medicines, vitamins, or other nutritional supplements. This polypharmaceutical combination of health care requires caution of potential drug interactions. Drug interactions may lead to altered rates of absorption, altered protein binding or different absorption, altered protein binding, or different rates of biotransformation or excretion of one or both interacting compounds. The pharmacodynamics of a drug may be altered by competition between receptors and nonreceptor. Pharmacodynamic interactions can occur when two drugs have similar actions through different cellular mechanisms. A drug interaction is said to be additive when the combined effect of two drugs equals the sum of the effect of each agent given alone. A synergistic effect is one in which the combined effect exceeds the sum of the effects of each drug given alone. Potentiation describes the creation of a toxic effect from one drug due to the presence of another drug. Antagonism is the interference of one drug with the action of another. It includes of Drug antagonism may confer a therapeutic advantage when one drug is to be used as an antidote for the toxicity of another drug. The Functional or physiological antagonism occurs when two chemicals produce opposite effects on the same physiological function; this is the basis for most supportive care provided to patients treated for drug overdose poisoning. Chemical antagonism or inactivation is a reaction between two chemicals to neutralize their effects such as is seen with chelation therapy. Dispositional antagonism is the alteration of the disposition of a substance (its absorption, biotransformation, distribution, or excretion) so that less of the agent reaches the target organ or its persistence in the target organ is reduced. Receptor antagonism entails the blockade of the effect of a drug with another drug that competes at the receptor site [11].

Need For Pharmacovigilance
Pharmacovigilance is one of the evolving exigencies to ensure
Early detection and exposure of unknown adverse reactions and interactions of drugs.
Detection in frequency of known adverse reactions.
Identification of risk factors and possible mechanisms underlying adverse reactions.
Improve public health and safety concerning the use of medicines.

Challenges in Siddha system of medicine
Adverse effects or toxicities associated with these drugs are challenging. These challenges are not normally encountered in the modern system of medicine. It includes: Ambiguity over nomenclature. Subjective interpretation of traditional descriptions. The *Siddha* curriculum does not address the idea of adverse reaction monitoring or the terminology associated with it, making it impossible to accurately identify adverse reactions. Most of the *Siddha* formulations are polyherbal/Herbo minerals with fixed doses consumed at the same time. Lack of drug safety studies about *Siddha* medicines. Identification of medicinal plants. Patients often use medicines concurrently from other healthcare systems, making it challenging to determine which drug caused which side effects. The quality of available scientific articles is unclear as many are not published in peer-reviewed journals.

Deliberate and native adulteration of herbal medicines Batch-to-batch variation is a challenging issue regarding quality control. Lack of proper knowledge about raw drugs. Liberal use of heavy metals in formulations. Low reporting on ADR and ignorance among *Siddha* physicians about ADRs. The wide prevalence of self-medication amongst users of herbal medicine. Limited pharmacological data on the therapeutic and safety profile. Inadequate and lenient implementation of regulations regarding quality standards for their manufacture, packaging sale, and use. Unpredictable herb-to-herb interactions and herb-food interactions are major contributors to ADR.

Strategies for Success

Raw drugs should be free from adulteration and should be stored in proper storage conditions. Compliance with the WHO's recommendations for the sustainable production of medicinal plants, including Good Manufacturing Practices (GMP), Good Agricultural Practices (GAP), and Good Agricultural Collection Practices (GACP). Instruments should be calibrated periodically. The vessels or utensils used for medicinal preparation and storage should not influence the nature of medicine. In the grinding process, timing should be strictly followed as per literature writings. In the case of *pudam*, the number and duration should be followed. In the case of specifications made in formulation concerning the burial of drugs in particular land and for a particular duration, it should be followed wisely. (eg: *Ayabhringrajakarpam* in *thamaraikulathunilam*; *Arukeeraivithaithailam*-in Slough land for 40 -50 days [12]. The prepared medicines should be quarantined as per the days specified for their better potency. (ex: *Rasa mezhugu*). The adjuvant and the duration of medicine intake should be followed as per the prescription of the physician [13].Promote drug safety studies. Making pharmacovigilance reporting mandatory and introducing pharmacovigilance inspections. Development and validation of gold standard tools to assess the causality of the adverse reactions to Siddha medicines. Creating a clinical trial and pharmacoepidemiologic studies. List all new drug indications by maintaining a standard database for every pharmaceutical company. Buildingand maintaining a robust pharmacovigilance system and pharmacoepidemiologists Education and training of medical students, pharmacists, and nurses in the area of pharmacovigilance. Collaborating with Pharmacovigilance organizations in enhancing drug safety with advancements in information technology. The current global network of pharmacovigilance centers, coordinated by the Uppsala Monitoring Centre, would be strengthened by an independent system of review. This would consider litigious and important drug safety issues that have the potential to affect public health adversely beyond national boundaries [14].

Schemes and Sectors of Pharmacovigilance

The Indian government has established a robust regulatory framework to ensure the safety and efficacy of traditional Indian medicines, including Siddha, Ayurveda, Unani, and Homoeopathy (ASU&H). The Ministry of AYUSH has introduced a pharmacovigilance scheme to monitor adverse reactions and detect potentially unsafe medicines and misleading advertisements. This scheme includes a three-tier network of National Pharmacovigilance Centre (NPvCC), Intermediary Pharmacovigilance Centers (IPvCCs), and Peripheral Pharmacovigilance Centers (PPvCCs) to facilitate reporting, documentation, analysis, and causality assessment of adverse reactions. The National Pharmacovigilance Centre coordinates various activities, while the Intermediary Pharmacovigilance Centers and Peripheral Pharmacovigilance Centers are responsible for reporting, documentation, analysis, and causality assessment. The Pharmacopoeia Commission for Indian Medicine and Homoeopathy (PCIMH) plays a crucial role in developing standards and quality specifications for ASU&H drugs. The PCIMH publishes and revises pharmacopeias, develops standard operating procedures, and funds research projects. The Siddha Pharmacopoeia Committee, functioning under PCIMH, prepares official Formularies and Pharmacopoeias of single drugs and compound formulations. The Committee provides standards for drugs, lays down tests for identity, quality, and purity, and ensures uniformity in physical properties and active constituents. The Committee also provides scientific information on distinguishing characteristics, methods of preparation, dosage, mode of administration, and toxicity of drugs [15]. Siddha Pharmacopoeia Committee functions under the scientific body of PCIMH and the functions of the Siddha Pharmacopoeia Committee are: To prepare official Formularies and Pharmacopoeias of single drugs and compound formulations. To provide standards for drugs and medicines of therapeutic use for pharmaceutical industries. To lay down tests for identity, quality, and purity. To ensure as far as possible uniformity in physical properties and active constituents. To provide all the scientific information regarding the distinguishing

characteristics, methods of preparation, dosage, mode of administration With various *Anupanam* /adjuvant and the toxicity of the drugs. To develop testing methods for various formulations [16].

Processing of Metals and Minerals

The *Siddhars* recognized the potential of minerals in treating chronic conditions and life-threatening cases. To ensure safety and efficacy, they emphasized the importance of precise preparation and purification processes, known as *Suthimuraigal* (Purification process). By meticulously following traditional Standard Operating Procedures (SOPs), Siddha practitioners can create safe and effective remedies that harness the full potential of minerals. This approach involves careful attention to dosing, adjuvants, and treatment duration, all of which are critical factors in achieving successful outcomes.

CONCLUSION

With more wide-based extensive clinical trials and other clinical research activities being conducted, there is an immense need to understand the importance of pharmacovigilance and how it impacts the life cycle of products and patients. *Siddhars* formulated *Nanjumurivu* for formulations in *Siddha* literature. Given this situation, the governing medical body should act quickly to improve pharmacovigilance to integrate good pharmacovigilance practice into the processes and procedures to ensure regulatory compliance and enhance clinical trial safety and post-marketing surveillance. A properly working pharmacovigilance system is essential if medicines are to be used safely. Perhaps pharmacovigilance in *Siddha* medicines has not been considered much yet, but we do not need a "*Siddha* thalidomide" to make the pharmacovigilance community realize how important it is.

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Table No.1: Describes The Adverse drug Reactions of *Siddha* drugs and its *Nanjumurivu*[9].

S.No	Drug	Adverse Effects	NanjuMurivu
1.	*Mercury amalgam* (*Rasam*)	Glossitis, stomatitis, gingivitis, ptyalism, inflammation of oral cavity, dysentery, scabies, erythroderma, tremor	Leaf juice of *Azima tetracanthais* taken orally twice a day for three days. *Indigofera tinctoria* (*avuri*) *karkam*(500mg).
2.	*Hydrargyrum perchloride* (*Veram*)	The taste of verdigris, ulcerative, stomatitis, gastritis, laryngytis, dysphagia, vomiting, watery diarrhoea,puffiness of face ,fissures on skin with oozing serous fluid, morbid thirst, convulsions, syncope ,death	20 ml of Vernonia cinerea (*Neichattikeerai)* juice should be taken twice a day. Tender coconut water, white yolk of egg is mixed with water or milk
3.	*Hydrargyrum subchloride (Pooram)*	Ulcerative gingivitis, glossitis, stomatitis, gastritis, uvulitis, blood-stained diarrhea, miliaria, lumbago	Tulsi juice or Castor oil (*Sitramanakkuennai*) or *Indigofera tinctoria* should be given for 3 to 5 days or till the discharge of pus.
4.	Cinnabar (*Lingam*)	Swelling in the Oral cavity and upper respiratory tract, bad breath, aphasia, saliva is like spoiler toddy or vinegar, pungent taste	Nutmeg, *Piper longum*, Hibiscus root bark, rock candy-4.2gm is turned to *kudineer* and taken twice a day for 48 days.
5.	Sulphur *(Ganthagam)*	Yellowish discoloration of conjunctiva, pallor of face, macules, blackish teeth, profuse hyperhidrosis with yellow discoloration,halitosis,urine appears as goat's urine.	Paste of Lotus seeds in tender coconut water is taken. Decoction of equal parts of *Piper nigrum*, *Indigofera tinctoria*, and *Cuminum cyminum* is taken
6.	Yellow orpiment *(Thalagam)*	Blood clots in the eyes can cause sores, ulcers, and stomach irritation. sudden bleeding from the nose, bad taste in the mouth, nail buds are infected and ulcerated with purulent discharge, acute epistaxis, anorexia, dyspnea, pruritus in scalp lassitude, severe lumbar pain, distended abdomen	*Kudiner of Plumbago rosea (Chithira moola verpattai)* 10g, Piper nigrum (pepper) 10g, Sodium chloride (kariyuppu) 5g is taken
7.	Massicot/lithrage *(Mirutharsingi)*	Mouth ulcers, body rashes, dry throat, stomatitis, gastric ulceration, stomatitis, pruritus with ulcers	Grind 10g of *Indigofera tinctoria* (*avuri*) and take twice a day.
8.	Mica *(Appirakam)*	Wheezing, dyspnea, cough, congestion in chest, flatulence	Use dried ginger (*sukku*), fresh juice of beetle leaves, and *Zingibera officinale* in equal proportion given in a dose of 40 to 80 ml
9.	Calcium	Inflammation of the oral cavity, burning	Coconut milk, buttermilk,

	carbonate *(Sunnambu)*	sensation of the stomach, diarrhea.	dissolved solution of turmeric powder are given
10.	Ghee and honey (When consumed in equal quantity)	Stomach ache and vomiting, body heat, watery secretion in mouth, dysuria,pyorrhoea	Charcoal should be diluted with water and consumed.

RESEARCH ARTICLE

Nutrient Uptake, Use Efficiency and Productivity of Bread Wheat (*Triticum aestivum*L.) As Affected By Different Doses of NPK with Different Farming Practices

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ABSTRACT

In order to maximize agricultural output and quality while lowering fertilizer inputs and avoiding environmental harm, nutrient usage efficiency is essential. The experiments was conducted to study the effect of nitrogen (N), phosphorus (P), potassium (K) and different farming practices on growth, yield, nutrient uptake and nutrient use efficiency of bread wheat during the *Rabi* season of 2021-22 in the Experiment block of the School of Agricultural Sciences, Shri Guru Ram Rai University, Pathribagh, Dehradun, Uttarakhand. Factorial combinations of 12th treatments (03 Main Plot and 04 Sub Plot) were laid out in a split plot design with three replications. The results showed that most parameters *viz* yield, yield attributes, Nutrient uptake and use efficiency revealed significant differences.

Keywords: Agriculture, Nutrient, NPK, Efficiency, *Triticumaestivum*

INTRODUCTION

Next to rice in our nation, wheat (*Triticumaestivum* L.) is the most significant cereal crop for food purposes. Wheat is a rich source of protein (9–10%) and carbs (60–80%) to help meet the body's nutritional needs. Due to its high nutritional content, wheat causes a significant loss of soil nutrients for plants. The crop's production will decrease as a result of this depletion. Extensive farming without balanced fertilization has caused the soil's main and micronutrient levels to decline. (**Prasad, 2006).** The bread wheat (*Triticumaestivum*) is an allopolyploid. *Triticummonococcum*(2n = 14) is believed to be the source of the A genome of wheat and *Triticumtauschi* (2n = 14) is believed to be the source of the genome D, and an unknown source, likely an extinct species, is thought to be the

source of the genome B (2n= 14). *Triticumturgidum* (AABB), the first allotetraploid wheat, is produced by crossing between *Triticummonococcum* (AA) and an unidentified species (BB). Then, hexaploid wheat *Triticumaestivum*(AABBDD) was produced by crossing *Triticumturgidum* (AABB) with *Triticumtauschi*(DD). Thus, the three species genomes are present in two copies in hexaploid wheat. (Prajapati *et al*., 2024). It is a self-pollinated cereal crop of thePoaceae family and the genus *Triticum*, which includes a wide range of staple crops. It is also called as the "King of Cereals" due to its huge land area, outstanding production, and substantial involvement in the global food grain trade. On a worldwide and national level, there are 215.48 and29.65 million hectares cultivated with wheat, respectively, yielding 731.4 and 99.9 million metrictonnes with average productivity of 3390 and 3371kg ha^{-1}(Tiwari *et al*., 2023). While evaluating different crop production systems based on wheat, low productivity, declining soil fertility and health, low nutrient-use efficiency, and loss of sustainability are the main concerns which are causing hurdles in food security. These factors could have a significant impact on fertilizer, soil, and water management, affecting crop production and reducing nutrient losses (Selim, 2020).

Natural farming is a method of farming that doesn't rely on credit and uses little outside inputs. Utilizing resources that are readily available locally, it successfully lowers production costs while raising crop yields. With the help of this strategy, small and marginal farmers will be able to cultivate crops responsibly and without having to worry about high costs. The elements of Natural Farming (NF) are: *Bijamrit*: This is a practice where seeds are coated with a cow dung and urine mixture. It's an all-natural method of improving seed quality and encouraging strong plant development. *Jeevamrit*: This process improves the soil's vitality and enrichment. It's similar to adding more energy to the soil to support crop growth. The main goal of natural farming is to promote the growth of advantageous microorganisms without the use of artificial pesticides or fertilizers from outside sources. Some Indian states, such as Himachal Pradesh and Uttarakhand, have already adopted natural farming methods. This is primarily because of their difficult topography, which restricts access to conventional farming supplies. In Himachal Pradesh, small and marginal farmers rely mostly on agriculture for their living, hence it is imperative to support and expand research and extension initiatives in the area of natural farming (Khurana and Kumar, 2020). Integrating chemical fertilizers with organic manures has been found to be quite promising not only in maintaining higher productivity but also in providing greater stability in crop production. The interactive advantages of combining inorganic and organic sources of nutrients generally proved superior to the use of each component separately (Verma*et al.,* 2020). However, as integrated nutrient management is essential for improving production potential and yield, and preserving soil health while protecting soil, organic manure application as a sustainable source of plant nutrition is becoming more and more popular. Improvements in soil permeability, soil fertility, enzymatic activity, and soil organic carbon and its reserves are one of the many advantages of organic manures *viz*., farm yard manure, vermicomposts, and vermiwash(Sharma and Garg, 2018). Wheat production may be increased by using *Azotobacter*alone or in combination with other biofertilizers (Mahato and Kafle, 2018). *Bijamrit*and *Jeevamrit*, which are sustainable methods of natural farming for not only giving nutrients but also enhancing the soil's nutritional status, are becoming more popular. To increase wheat productivity and correct nutritional deficiencies, farmers employ chemical fertilizers, although doing so increases cultivation costs and has unfavorable environmental implications, including global warming.

MATERIALS AND METHODS

Description of the study site:

The Experiment block of the School of Agricultural Sciences, Shri Guru Ram Rai University (SAS - SGRRU), Pathribagh Dehradun, Uttarakhand, is located in the northwest of the state at an elevation of 450 meters above mean sea level (MSL) and between 29°58' and 31°2'30' North latitude and 77°34'45" and 78°18'30'' East longitude. The field experiment was carried out during *Rabi* 2021–22. The average weekly maximum temperature during 2021-2022 varied between 15.2 ºC to 37.8 ºC, respectively. However, average minimum temperatures were 2.2 ºC to 14.5 ºC, respectively.

Treatments and experimental design

The experiment was laid out in split plot design with three organic nutrient management treatments in main plots *i.e.*, organic farming practices (vermicompost @ 5 t ha-1 + seed inoculation with *Azotobacter* and PSB + 2 sprays of vermiwash at 30 & 45 DAS); Natural farming practices (sieved cow dung @ 2.5 t ha-1 + seed treatment with *Bijamrit*+ *Jeevamrit*@ 200 l ha-1); and absolute control. The sub-plots comprised 100%RDF, 75% RDF, 50% RDF and 25% RDF. The experiment had three replications. The experimental field was ploughed, and then it was adequately prepared with the help of a tractor-drawn leveller. Two cross-wise harrowing were then conducted on the land at the optimal soil moisture state. The wheat variety DBW 173 was sown using the line sowing method on November 14, 2021. The seed rate was 100 kg ha-1, and the row-to-row spacing was 22.5 cm. During field preparation, vermicompost, sieved cow dung, *Jeevamrit*, and different doses of RDF (120: 60: 40 kg NPK ha-1) were added and well mixed into the soil according to the treatments listed in the various blocks. Vermiwash was sprayed at 30–40 DAS, and the seeds were treated with *Azotobacter*, PSB, and *Bijamrit*24 hours prior to planting. The initial irrigation was given in both years during the crown root initiation (CRI) stage, which occurs normally 21–25 days following seeding. The timing of subsequent irrigations was determined by the moisture level of the soil. The crop was manually harvested with a sickle after the grain hardened and reached a moisture level of 18–20%. The collected material was then sun-dried for three to four days in order to separate the grain from the straw.

RESULTS

Yield and Yield components

The data pertaining to the grain yield, straw yield, biological yield & harvest index of the wheat crop during 2021 is presented in Figure 1. Organic farming practices, natural farming practices and application of NPK through fertilizers had significantly influenced the grain yield, straw yield, biological yield and harvest index of the wheat crop. Among different main plot treatments, incorporation of organic farming practices (Vermicompost @ 5 t ha^{-1} + seed inoculation with Azatobacter and PSB + 2 sprays of Vermiwash at 30 & 45 DAS) and natural farming practices (Sieved FYM @ 2.5 q ha^{-1} + seed treatment with *Bijamrit* + *Jeevamrit* @ 200 l ha^{-1} as basal + 5 foliar spray of Jeevamrit @ 1: 10) had significantly higher grain yield, straw yield, biological yield and harvest index of the wheat crop as compared to absolute treatment where no organic manures were applied. However among main plot treatment, significantly higher grain yield, straw yield, biological yield and harvest index was recorded in the plots treated with organic farming practices (Vermicompost @ 5 t ha^{-1} + seed inoculation with Azatobacter and PSB + 2 sprays of Vermiwash at 30 & 45 DAS) as compared to natural farming practices (Sieved FYM @ 2.5 t ha^{-1} + seed treatment with *Bijamrit*+ *Jeevamrit* @ 200 l ha^{-1} as basal + 5 foliar spray of *Jeevamrit* @ 1: 10).

Organic farming practices including application of vermicompost and spray of vermiwash which are the products created by vermicomposting of organic matter from loaded population of earthworms **(Edawrds and Arancon, 2022)** comprises numerous bio compounds viz, hormone, mucous, enzyme, vitamins, proteins, different macro and micronutrients which improve the soil fertility with good aggregation required for efficient uptake of nutrients by the crop plants owing to enhanced growth and yield attributing characters resulted in higher yield. Growth attributes of wheat owing to enhanced yield and production potential of the wheat crop was due to positive effect of vermicompost, which multiplied the population of beneficial soil microorganisms, which were responsible for nitrogen fixation and phosphate solubilization. Similar findings were also observed by (**Verma*et al.*, 2016).** However natural farming practices (Sieved cow dung @ 2.5 t ha^{-1} + seed treatment with *Bijamrit* + *Jeevamrit* @ 200 l ha^{-1}) also had significant higher values of grain yield, straw yield, biological yield and harvest index of the wheat crop as compared to no organic manure application i.e., absolute control. Application of *jeevamrit* and *bijamrit* play important roles for enhancing the production potential of the crop over the absolute control treatments. This may be due to increased availability of nutrients due to build-up of soil micro flora resulting from increased bacteria, fungi, actinomycetes, P solubilizers and N fixer's population in the soil which resulted in high nutrient concentration and better growth and yield. Among different rates of NPK applications, 75 % of the RDF (NPK) had achieved increased values of grain yield, straw yield, biological yield and harvest index of the wheat crop as compared to applications of 100 %, 50 %

and 25 % RDF. Applications of primary nutrients viz. NPK play a vital role in growth and development of the crops in an order to synthesize amino acids and nitrogen, transfer of energy in the form of ATP and also for disease resistance and transfer of carbohydrates. Increasing nitrogen rates using 75 % of RDF had a significant effect on the grain yield while nitrogen application less than 50 % of RDF did not increase the grain yield to a significant extent. Similar findings were also reported by **(Patil*et al.*, 2015).** Application of right amount of nitrogen at a definite time so as to synchronize demand and supply of nitrogen had led to enhancement of yield attributing parameters like dry matter accumulation, number of effective tillers, grain per spike, and the test weight resulting in improved yield.

Nutrient Uptake

The data related to N, P and K contents in grains and strawof wheat cropat harvest stageis presented in **Figure 2 and 3.**Incorporation of organic farming practices and natural farming practices had significantly affected the N, P and K contents and N, P and K uptake by grain and straw at harvest stage in wheat crop. Nitrogen content (%) in wheat grains and straw at the harvest stages during 2021 due to application of different farming practices viz. natural and organic farming had influenced the N, P and K contents. This was significantly increased in the soil where organic farming practices (Vermicompost @ 5 t ha^{-1} + seed inoculation with *Azatobacter* and PSB + 2 sprays of Vermiwash at 30 & 45 DAS) were adopted as compared to natural farming practices. An important characteristic of vermicompost is that many of the nutrients it contains are converted into forms that are more easily absorbed by plants. For example, the addition of nitrate or ammonium nitrogen increased the amount of nitrogen in the soil and the plants, as observed by **(Yan *et al.*, 2019)** in a study. When applied to the soil, vermicompost and vermiwash boost the population of helpful microorganisms like N-fixers and improve the activity of the nitrogenous and urease enzymes, leading to greater and more effective plant metabolism that increases nitrogen content in the plant tissue. According to **(Han *et al.*, 2016)**, the application of organic manure resulted in plants with higher N, P, and K contents than controls, which had no organic manure added to the soil.

This has also shown that the application of organic manure generally results in better nutrient uptake and content in crops because the more organic manure in the soil affects both the availability of nutrients and their availability as a source for plant uptake. Different NPK doses viz. application of different amount of nitrogen, phosphorus and potash through urea, single super phosphate and muriate of potash had significantly influenced the % content and uptake of NPK by grain and straw during both the years of investigation. Highest nitrogen, phosphorus and potassium content in grain and straw of the wheat crop was recorded when 75 % of the RDF was applied followed by 100 %, 50 % lowest The maximum uptake of NPK nutrients in the wheat grain and straw were recorded when nutrients were applied with the application of organic farming practices. Increase in uptake in these nutrients may be due to the increased in fertility levels attributed to the better availability of nutrients and their transport to the plant from the soil. Similar results have been reported earlier **(Salim and Raza, 2020)**. The beneficial effect of application of higher amounts of organic manure through vermicompost, vermiwashetc are not only favored the greater availability of throughout crop growth, fertilizer into different stages resulting in significant improvement in nutrient content and uptake. Since uptake of nutrient is a function of concentration of nutrient and yield/ha at higher fertility levels, nutrient absorption increased resulting in a luxuriant growth and accumulation of nutrients in the grain and straw that might have increased the uptake of nitrogen, phosphorus, and potassium. This might be the main reason behind the higher production of grain and straw yield with maximum nutrient under organic farming practices.

Nutrient Use Efficiency

Agronomic Efficiency

Agronomic efficiency (AE) of N significantly influenced by the main effect of N, P and K fertilizers. Supplying 90 kg ha−1 N produced maximum AE (12.29 kg/kg) where as lowest AE (15.50 kg/kg) was observed at high N levels i.e. S4-25% RDF (5.17 kg N/ha). According to this study, AE grows up to 30 kg N ha−1, after which it decreases. This conclusion is consistent with the findings of **(Fageria and Baligar, 2005)** and **(Solomon and Anjulo, 2017)**, who observed that the highest AE of N was at a lower rate due to decreased losses. The wheat plant used the majority of the nitrogen supplied at the reduced rate to produce grain. The AE result in this investigation was in close agreement

with the results of **(Birke *et al.*, 2019)** who reported 57.1 kg kg−1 at 46 kg ha−1 of N, and **(Derej*eet al,.* 2019)** who reported AE of 50.48 kg kg−1. The AE of K was significantly affected by the interaction effect of N, P and K. The maximumAE (24.58 and36.87 kgkg−1 of P and K, respectively) was recorded from 90 kg N ha−1, 45 kg P/ha and 30 kg K ha−1 and the lowest (10.33 and 15.50 kg kg−1 of P and k, respectively) from 15 kg P/ha and 10 kg K ha−1, respectively. The result had shown that AE of K decreases with the increasing rate of N, P and K.

Physiological Efficiency

Physiological efficiency (PE) of N and K was significantly influenced by different doses of N, P and K fertilizers. The maximum PE of N (60.95 kg kg−1) was recorded from 90 N, 45 P and 30 kg ha−1 and the lowest (19.18 kg kg−1) from Natural farming. Similar results were obtained from **(Brar*et al.*, 2011).** On the other hand, P and K rate above 45 and 30 kg ha−1 led to decline in PE of P and K at all levels of N rates. This illustrated that combination of 90 kg ha−1 N with 45 kh/ha P and 30 kg ha−1 K increased the ability of wheat to absorb applied nutrients which was reflected as increased PE of N, P and K. This result is in line with those of **(Beyenesh*et al.*, 2017)** and **(Mesele, 2017)** who reported that the highest physiological efficiency recorded with the application of 46 kg N ha−1 and K up to 30 kg K ha−1 respectively.

Crop Recovery

Data regarding, RE of N was significantly affected by main effect of N, P and K fertilizer. The highest RE of N (18.20%) was obtained from 30 kg N ha−1and lowest (13.40%) with application of 60 kg N ha−1. The RE of N increases up to 90 kg ha−1 and then showed declining trend. The RE of N obtained in this study is comparable with those obtained 89% by **(Beyenesh*et al.* 2017).** The crop recovery of P and K was significantly affected by the different doses of N, P and K fertilizer rates. The highest apparent recovery efficiency of P and K (13.11% and 85.73%) was obtained with application of 90 N, 45 P and 30 kg K ha−1 and the lowest (-13% and -3.5%) with application of P and K 15 and 10 kg ha−1. The results had shown decreasing trend with increasing N, P and K rates consistently. Similar result was indicated by **(Jackson, 2018)** who reported that RE decreased when the rate of N, P and K increases.

Nutrient Use Efficiency

Nitrogen use efficiency (NUE) of wheat was significantly affected by main effect of N, P and K fertilizer whereas phosphorus and potassium use efficiency (PUE and KUE) was significantly influenced by different doses of N, P and K fertilizers. The highest NUE (983.33%) due to N fertilizer was recorded from 90 kg N ha−1 and the lowest (322.50%) was from 120 kg N ha−1. Application of P and K up to 45 and 30 kg/ha increased NUE. The maximum PUE (799.13%) and KUE (5225.48%) was recorded from 90 kg N ha−1, 45 kg P/ha and 30 kg Kha−1 and the lowest (-509.52%).

CONCLUSION

The experiment's findings showed that applying mineral N, P, and K fertilization increased grain production, nutrient uptake, agronomic efficiency, recoveryand use efficiency. The amount of nutrients absorbed was N > K > P in that sequence. Grain stores more nitrogen and P than straw does, whereas straw stores more K. Farmers in the study region are recommended to apply 90 N, 45 P, and 30 kg K ha−1 for nutrient use efficiency, economy, and agronomy purposes based on the findings of this study. It is also strongly advised to repeat the experiment in other seasons and locations.

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Table:1 Agronomic recovery efficiency

Treatment Details	PE	RE (Nitrogen)	RE (Phosphorus)	RE (Potassium)	AE (Nitrogen)	AE (Phosphorus)	AE (Potassium)	NUE Nitrogen	NUE Phosphorus	NUE Potassium
M_1 Absolute Control	**-**	-	-	-	-	-	-	-	-	-
M_2 Organic	39.54	-	-	-	-	-	-	-	-	-

Farming Practices										
M_3 Natural Farming Practices	19.18	-	-	-	-	-	-	-	-	-
S_1-100 % RDF (120:60:40 kg N, P_2O_5 and K_2O ha^{-1})	45.74	7.05	8.10	43.35	8.21	16.42	24.63	322.50	370.53	1983.03
S_2- 75 % RDF (90:45:30 kg N, P_2O_5 and K_2O ha^{-1})	60.95	16.13	13.11	85.73	12.29	24.58	36.87	983.33	799.13	5225.48
S_3- 50 % RDF (60:30:20 kg N, P_2O_5 and K_2O ha^{-1})	43.16	13.40	1.80	12.95	9.62	19.23	28.85	578.33	77.69	558.91
S_4- 25% RDF (30:15:10 N, P_2O_5 and K_2O)	39.19	18.20	-13.00	-3.50	5.17	10.33	15.50	713.33	-509.52	-137.18

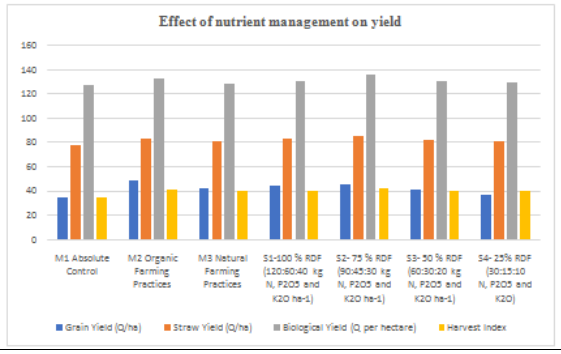

Figure 1. Effect of nutrient management on yield during 2021-22.

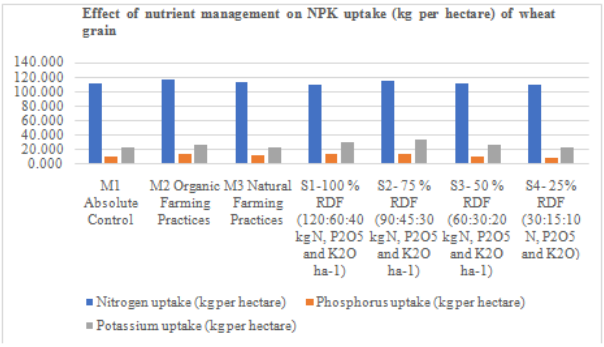

Figure 2. Effect of nutrient management on NPK uptake (kg per hectare) of wheat grain during 2021-22.

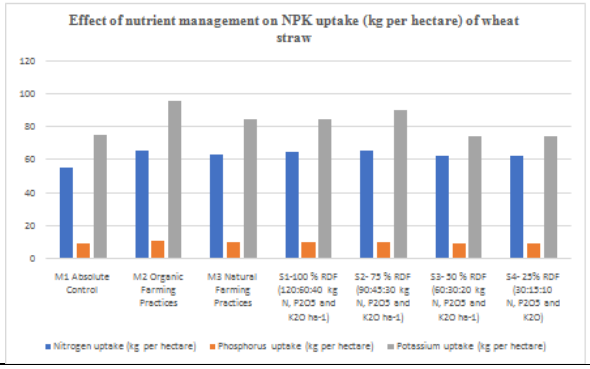

Figure 3. Effect of nutrient management on NPK uptake (kg per hectare) of wheat straw during 2021-22.

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REVIEW ARTICLE

A Review on Useful Applications of Eucalyptus in Diverse Areas

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ABSTRACT

Eucalyptus is an evergreen tall tree that is widely planted all around the world due to its useful applications in diverse areas. It is the native of Australia and Tasmania and belongs to the Myrtaceae family. Eucalyptus oil contains a variety of chemicals that have therapeutic effects such as antibacterial, antiviral, antiseptic, anti-inflammatory, astringent, anti-diabetic, anticancer, anti-oxidative, antitumor, antihistaminic etc. Eucalyptus is widely utilised in the agro forestry industry due to its agronomic features, and it also serves as a raw material for a variety of other industries such as pulp mills, paper mills, textile mills, cosmetics industries, pharmaceutical industries, and so on. It also exhibit herbicide, insecticide, and pesticide properties. The aim of this article is to provide information on the medicinal and other applications of the Eucalyptus tree. Although a number of the health benefits of eucalyptus are widely recognised, further research is needed to investigate other beneficial impacts of this tree and its potential.

Keywords: Eucalyptus, phytochemicals, therapeutics applications.

INTRODUCTION

Various plants and their products have been utilised to cure numerous ailments since ancient times, and eucalyptus is one of them. It is an evergreen tall tree native to Australia and Tasmania, and it belongs to the Myrtaceae family. The genus Eucalyptus has over 700 species, with over 300 of them containing volatile oil in their leaves. Eucalyptus is becoming one of the world's most significant and widely cultivated genera [1]. Eucalyptus has attracted the attentions of many researchers across the world since it is a source of rapidly expanding supply of wood and oil used for a variety of reasons. Antibacterial, antiseptic, antioxidant, anti-inflammatory, and anticancer activities are found in the oil extracted from its leaves, fruits, buds, and bark [2-4]. It is also used to treat respiratory disorders such as the

common cold, influenza, and sinus congestion [5,6]. In the last decade, there has been a surge in the demand for plant-derived products for medicinal purposes [7,8]. Many nations, particularly in rural regions, use aromatic herbs for health care [9], and 80% of the population in developing countries uses these traditional resources [10]. As a result, the use of essential oils isolated from plants for therapeutic purposes is gaining attention in the research world. Several species of eucalyptus are grown specifically in subtropical and warm temperature zones due to their economic benefits. About hundred species of eucalyptus plant have been explored in India, and some of them are under cultivation [11]. Among all eucalyptus species, Eucalyptus globulus, sometimes known as blue gum, has a long history of use due to its numerous therapeutic properties. The herb has antibacterial, astringent, deodorant, diaphoretic, expectorant, inhalant, insect repellent, rubefacient, and suppurative properties, according to many studies [12-14]. Apart from medicinal uses, eucalyptus is widely utilised in the agroforestry and serves as a raw material for a variety of industries such as pulp mills, paper mills, textile mills, cosmetics industries, pharmaceutical industries, and so on.

CHEMICAL COMPOSITION

The leaf, stem, and root of the Eucalyptus tree contain a high concentration of phytochemical compounds such as flavonoids, alkaloids, tannins, and propanoids [2]. Several volatile compounds are detected in both leaves and shoots, including 1,8-cineole (eucalyptol) aromadendrene, α- gurjunene, globulol, ß-pinene, pipertone, α,ß- and γ-terpinen-4-ol, and allo-aromadendrene. Eucalyptol is the primary and most important constituent of eucalyptus (Table 1). It accounts for 79.85% of the entire chemical composition. Other compounds isolated from its fruits include borneol, caproic acid, citral, eudesmol, fenchone, p-menthane, myrecene, myrtenol, α-terpineol, verbinone, asparagine, cysteine, glycine, glutamic acid, ornithine and threonine [15], whereas its flowers are used to extract dextrin, and sucrose [16]. The essential oil also included a significant concentration of oxygenated monoterpenes, with a potential difference in therapeutic effects [17,18] that varies between species.

THERAPEUTIC APPLICATIONS

Anti-allergic activity

Eucalyptus oil has the capacity to limit bacterial activity by functioning as an efflux pump inhibitor, which strengthens the immune system and controls the growth of germs which cause trouble in breathing leading to bronchitis. Similarly, Eucalyptus oil helps in relieving congestion in the airways, lungs, and chest [4,19]. In the case of a sinus infection, Eucalyptus oil reduces inflammation in the nasal canal and the surrounding cavities. Eucalyptus oil can be used as a spray to relieve pain and inflammation produced by an allergic response or any bacterial action by soothing mucous membranes. Asthma is a disorder in which a person has difficulty in breathing due to severe chest discomfort that obstructs the nasal tube. Eucalyptus oil has been used for many years in a variety of treatments, including Vicks VapoRub, which treats coughs and makes breathing easier.

Antiseptic property

Eucalyptus oil has long been used as a potent antibacterial. It has been reported that it contains disinfectant properties and capacity to kill bacteria [20]. Furthermore, Eucalyptus oil is utilised as a stimulant as well as an antibacterial gargle. It reduces sensation when administered locally. It also improves cardiac action [20].

Antihelminthics or Anthelmintic action

Because of the presence of phytochemical compounds in Eucalyptus, such as borneol, cineol, linalool, gernayl acetate, saffrol, and antheol, it has anthelmintic or antihelminthic effect on many parasitic worms [4,21] without causing significant harm to host. In the tropics, one of the treatments for hookworm is Eucalyptus-chloroform solution.

Anti-inflammatory activity

Eucalyptol (1, 8-cineole), the primary components of Eucalyptus oil, is used to treat airway inflammation in bronchial asthma and other steroid-sensitive illnesses [4,22]. Furthermore, the anti-inflammatory activity of eucalyptol is tested in asthma patients, demonstrating the efficacy of this molecule in the treatment of airway illnesses [3,23].

Antiviral activity

It is revealed from the studies that twelve euglobals from Eucalyptus globules and their twenty-six related compounds inhibited Epstein-Barr virus activity in a short term *in vitro* experiment. Euglobals with monoterpene structures, as well as euglobal-III, have been reported to exhibit exceptional inhibitory action. Grandinol and homograndinols have also been demonstrated to have considerable inhibitory effects [4,24].

Antitumor activity

Several compounds in Eucalyptus globulus have antitumor properties. Out of twenty one euglobals, isolated from the leaves of various Eucalyptus species, including E. ampifolia, E. globulus, E. grandis, and E. blakely, block 12-Otetradecanoylphorbol-13-acetate, which acts as a tumour promotor by increasing viral activation. Euglobal G1 and Euglobal III inhibit Raji cells by disrupting their cell cycle. According to the investigations, both of these chemicals can also suppress mouse skin tumour promotion in an in vivo carcinogenesis test [25]. Further more, Euglobal III, also inhibit NF- kappa B cell induction by controlling nuclear translocation which occurs in LPS of THP-1 cells [4,26].

Antifungal activity

Eucalyptus oil is commonly used to treat face demodicidosis, a condition caused by Dematatious fungus that colonise sebaceous gland regions of the skin, producing dryness, redness, rashes, and occasionally erythema. When mixed with glycerol, Eucalyptus oil derived from Eucalyptus globulus can fully treat face demodicidosis [4,27]. Oil derived from Eucalyptus globulus leaves can also be utilised to treat Malassezia furfur fungus (in Sabouraud's destrose agar medium) [4,28], a causal agent of seborrheic dermatitis and tinea versicolor.

Antiplaque activity

The antibacterial and antimicrobial properties of eucalyptus have been harnessed for usage in mouthwash and dental preparations. Eucalyptus appears to be active in combating microorganisms that cause tooth decay and periodontitis, improving dental health. Eucalytus globulus may be effective in preventing the production of dental plaque [4,29].

Inhibitor of cytochrome p450 enzymes

The oil derived from Eucalyptus globulus has been discovered as a cytochrome P450 enzyme inhibitor with IC50 values ranging from 20 and 1000µg/MI [4,30].

Nerve Blocker

Terpineol, a relatively non-toxic, volatile monoterpenoid alcohol, derived from Eucalyptus globulus is used in traditional medicine, aromatherapy, and the perfume industry. Terpineol's effects on the compound action potential (CAP) of the rat sciatic nerve were investigated, it was shown that terpineol generated a dose-dependent blockage of the CAP [4,31].

Antibacterial activity

According to the studies, E. globulus has remarkable antimicrobial activity against both Gram-negative (Salmonella enteritidis, Escherichia coli, and Pseudomonas aeruginosa) and Gram-positive bacteria (Staphylococcus aureus, Enterococcus faecium), as well as bacteriostatic activity against all strains tested (with the exception of Pseudomonas aeruginosa) [32]. This action on bacteria might be attributed to the presence of eucalyptol, which has high antibacterial properties against a variety of diseases [3,33]. As a result, these investigations provided strong support to the use of Eucalyptus oil (particularly, E. globulus and E. bridgesiana) as a natural preservative in the food and pharmaceutical sectors. In natural medicine, it can be a beneficial alternative antibacterial agent for the treatment of many infectious disorders.

Antidiabetic activity

Traditional medicines use the leaves of Eucalyptus globulus to treat diabetes mellitus. The effects of eucalyptus on streptozotocin-induced damage in pancreatic islands were studied using stereological techniques. The investigations show that Eucalyptus globulus improves diabetic conditions in rats by partially restoring pancreatic beta cells and

repairing STZ-induced damage in a dose-dependent manner. The study reveals that eucalyptus has a favourable impact in the treatment of diabetes [2]. Eucalyptus globulus is an excellent antihyperglycemic dietary supplement for the treatment of diabetes and, as such, may be a potential source for the introduction of novel orally active agents for future therapy [34].

Anticancer activity

A monoterpene derivative, phlorogrucinol and euglobal-G1 (EG-1), derived from the leaves of Eucalyptus grandis, has been found to inhibit the promotion of two-stage carcinogenesis induced by both TPA-type and non-TPA-type promoters (fumonisin B 1), as well as pulmonary tumorigenesis induced by 4-NQO and glycerol. As a result, EG-1 has the potential to be a valuable chemoprotective drug in chemical carcinogenesis [4,25].

Inhibition of Intestinal Fructose Absorption

In rats, an extract derived from the leaves of Eucalyptus globulus inhibits intestinal fructose absorption and reduces obesity caused by eating sucrose [4,35].

Anti-hyperglycemic activity

Eucalyptus *tereticornis* exhibit anti-hyperglycemic activitiy when combined with glucose simultaneously [36].

Hepatoprotective activity

Ursolic acid extracted from the leaves of the Eucalyptus hybrid, E. tereticomis, has a dose-dependent (5-20 mg/kg) hepatoprotective effect (21-100%) against thioacetamide, galactosamine, and carbon tetrachloride caused in rats [37].

Myorelaxant effect

The essential oil of Eucalyptus tereticornis has myorelaxant actions in guinea-pig isolated trachea, which is due to a complex interaction between its monoterpenoid constituents [4,38].

Antioxidant Properties

Antioxidants are chemicals that suppress reactive oxygen species, often known as free radicals, and thereby protect cells from harm and death. These free radicals perform several vital functions in biological systems, including energy generation, biomolecule synthesis, phagocytosis, and cell development [3,39]. Oxidative stress is caused by an imbalance between free radical formation and unfavourable antioxidant defence, which results in DNA or tissue damage [40,41]. The demand for natural antioxidant compounds in foods has risen in recent years, and the eucalyptus plant is a rich source of antioxidants.

Agronomic properties of Eucalyptus

Eucalyptus can be grown under broad range of climatic conditions and in a wide variety of soil. It grow best in tropical to temperate regions. It requires 4 to 40 cm annual rain fall, hence it can be cultivated in drought areas and waste lands. In India, eucalyptus tree can be grown in the regions with temperature ranging from 0°C to 47°C. For its best growth and yield, it requires deep, rich and well drained loamy soils with sufficient moisture. Due to a global lack of trendy wood, Eucalyptus is increasingly employed in the furniture industry since it is a quick growing tree with great adaptability to soil and climatic conditions and has desirable wood characteristics. Eucalyptus species become an important hardwood for the pulp industries [42,43]. The Eucalyptus tree also contributes significantly to the reduction of global warming and climate change. Pollution has now become the world's most serious concern. Deforestation of wood trees is currently occurring on a large scale in many nations in order to to increase its economy, population, and urbanisation [6,44]. Because Eucalyptus trees grow quickly, planting more of them might be a solution to this problem. Recent research has discovered that Eucalyptus produces a distinct menthol-like aroma, allowing it to be utilised as an ornamental plant [6,45].

Herbicidal activity

It has been shown that several Eucalyptus species, such as E. citriodora and E. tereticornis oil, can be utilised as herbicides by minimizing the germination of Parthenium hysterophorus when sprayed in vapour form [6,46]. Furthermore, it has been shown that the oil is more effective on Amaranthus viridis due to its smaller size when compared to Raphanus sativus. According to investigations, E. citriodora oil is more toxic than E. tereticornis oil [47]. Herbicidal activity is facilitated by secondary metabolites of oil such as phenolics, tannins, and monoterpenes [48,49]. Several factors influence their commercialization as bioherbicides [50-51] for controlling the growth of unwanted plants and weeds for use in organic farming.

Insecticidal activity

Insects such as gall mites, bagworms, leaf minors, moths, aphids, flies, mosquitoes, earwigs, grasshoppers, and others harm plants by chewing the leaves, draining plant fluids, secreting toxic substances on plant shoots, and creating holes in the leaves, resulting in poor plant growth. Aside from that, they ruin the natural timber fibres. Eucalyptus oil is a natural insecticide [54], with species such as E. globulus and its component 1,8-cineole damaging and killing Pediculus humanus capitis, and it is technically used to kill lice [55]. Eucalyptus globulus leaves have larvicidal efficacy against Culex quinquefasciatus and Culex tritaeniorhynchus [6,56]. E. tereticornis has larvicidal, pupicidal, and adulticidal action against Anopheles stephensi, but E. saligna has repellent activity against Sitophilus zeamais.

Pesticidal activity

The primary component of oil derived from the leaves of many species of eucalyptus are found to have pesticidal activity [1] such as Eucamalol, Pinene, p-cymene, Citronellal, Terpinene, 1,8-Cineole present in E. camaldulensis, E. robusta, E. urophylla, E. saligna, E. citriodora are having pesticidal activity.

CONCLUSION

Because of its medicinal and agronomic properties, the Eucalyptus tree has attracted the attentions of numerous researchers worldwide. Several compounds extracted from this tree have antiviral, antibacterial, anti-inflammatory, antidiabetic, antioxidant, antitumor, anticancer activities. In the last decade, there has been a surge in the demand for plant-derived products for medicinal purposes. The purpose of this article is to provide information on the medicinal and other applications of the Eucalyptus tree. Although a number of the health benefits of eucalyptus are widely recognised, further research is needed to investigate other beneficial impacts of this tree and its potential.

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Table 1: **Major constituents** of **essential oil from** some species of ***Eucalyptus***.

Eucalyptus species	**Major constituents**
E. globulus	Eucalyptol (51.62%) α-Pinene (23.62%) p-cymene (10.0%)
E. camaldulensis	α-Pinene (22.52%) p-cymene (21.69%) aphellandrene (20.08%)
E. robusta	α-Pinene (28.74%) 1,8-Cineole (27.18%)
E. grandis	α-Pinene (29.69%) p-cymene (19.89%) 1,8-Cineole (12.80%)
E. citriodora	Citronellal (29.31%) geraniol (27.63%) β-citronellol (14.88%)
E. saligna	p-cymene (54.20%)
E. maideni	1,8-Cineole (83.59%)
E. astrengens	1,8-Cineole (60.01%)
E. cinerea	1,8-Cineole (79.18%)
E. lehmani	1,8-Cineole (49.07%) α-Pinene (26.35%)
E. bicostata	1,8-Cineole (81.29%)

RESEARCH ARTICLE

Phytochemical Screening, GC-MS Profile and FT-IR Characterization of Bioactive Compounds in *Parmotrema andinum*

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ABSTRACT

Lichens are symbiotic associations of fungi with microalgae and cyanobacteria. *Parmotremaandinum* is one of the type of lichens with several medicinal properties. Hence, *Parmotremaandinum* was selected to identify the important bioactive coumpunds through phytochemical screening and to analyze the compounds using FT-IR and GC-MS techniques. A preliminary analysis of the hydroethanol(HE) extract of *P. andinum* showed the presence of proteins, carbohydrates, glycosides, alkaloids, flavonoids, phenols, sterols, tannins, and saponins. FT-IR analysis of HE extract displayed C-O-H, C-H, C-O, O-H, X-O-C,C=O, C-S, C-N, and P-O-C stretching. Further, GC-MS analysis of the HE extract was used to examine the secondary metabolites in *P. andinum*. From the GC-MS results of *P. andinum* , several metabolites were identified with antimicrobial, anticancer and antioxidant potentials.

Keywords: phytochemistry, GC-MS, FT-IR, characterization, *Parmotremaandinum*

INTRODUCTION

Medicinal plants are source of rejuvenation in regional communities all over the world for thousands of years. It is still used as a primary healthcare method for roughly 85% of the global population and as a commodity for drug development, with 80% of all pharmaceutical and modern chemicals derived from it [1]. Plant-derived phytochemicals have been found to possess anti-inflammatory, antioxidant, anti-aging, antitumor, antiviral, antimutagenic, anticancer, anticarcinogenic, and antibacterial properties, as per epidemiological study. It aids in the

prevention of cancer, cardiovascular diseases, diabetes, and rheumatoid arthritis, as well as lower mortality rates from a variety of diseases [2]. Lichens are nutritionally specialized fungi living in symbiotic association between fungi and algae/cyanobacteria. Many lichen species have been utilized for centuries in traditional medicine and are currently gaining popularity as an alternative treatment for a wide range of illnesses across the globe[3]. Lichens contain 2700 species, including the Parmotrema genus, which contains 300 species. *P. andinum* belongs to the Parmeliaceae family[14] which is widely distributed in the regions like Africa, Asia, and South America. *P. andinum* has been known to have a variety of pharmacological actions against diseases[4]. It have a variety of pharmacological actions and medicinal properties, including sedative, concentrative exhilarant, aphrodisiac, cardiotonic, and stringent properties, and it is used to treat several disorders, including flatulence and anti-inflammatory cardiovascular diseases, stimulating menstrual flow, jaundice, kidney stone, inflammation and so on[5,6]. *Parmotremasp.* produces metabolites such as depsides, depsidones, phenol compounds, polysaccharides, lipids, diphenylethers, and dibenzofurans. These metabolites have been linked to a variety of biological activities, such as the inhibition of antioxidant enzymes, antidiabetic, antihelmintic, anticancer, and anti-inflammatory, antitumor and antifungal effects[7]. Hence, the current work is desinged to assess the qualitative and quantitative phytochemical constituents of HE extracts of*P. andinum*and also to characterize them by FT-IR and GC-MS.

MATERIALS AND METHODS

Plant material

*P.andinum*used in the studywas collected from Ooty, Tamil Nadu.. Wood particles from *P. andinum*was removed and washed to remove dusts, air dried for two weeks, chopped into fine pieces and stored at 25°C in a sealed bottle. Botanical identity of the plant was confirmed by CSIR-National Botanical Research Institute, Lucknow, India.

Sample preparation

About 20 grams of powdered *P.andinum*was weighed accurately and mixed with 200 ml of hydro ethanol(50% water& 50% ethanol*).* It was then left at lab temperature for 72 hours with frequent stirring. Finally the extract was filtered and dried in a hot air oven for 2 hours and the dried powder was taken and stored for further analysis [8].

Phytochemical Screening

Qualitative phytochemical analysis

Phytochemical screening was carried out to access the qualitative chemical composition of crude extracts using commonly employed precipitation and coloration reaction to identify the major natural chemical groups such as alkaloids, saponins, tannins, glycosides, flavonoids, steroids, phenols, proteins and carbohydrates. General reactions in this analysis revealed the presence (or) absence of these compounds in the extracts tested as per standard procedure [9,10**].**

Quantitative Analysis

Biochemical procedures are employed to analyze quantitatively the amount of carbohydrates[11], proteins[12], tannins [14], Flavonoids [15] and total phenol [13,15]. Secondary metabolites are screened using FT-IR and GC-MS analysis.

FT-IR

FT-IR analysis was carried out using a Schimadzu model FT-IR 8300 infrared spectrophotometer on a crude extract of *P. andinum*. To find functional groups (per centimeter), the IR spectrum was examined between wave numbers 500 and 4000.

Gas chrmotography and mass spectroscopy (GC-MS) analysis

The HE extract of *P. andium* was analyzed using the Agilent GC7890A/MS5975C GC-MS apparatus. Helium gas was employed as the carrier gas, with an injection volume of 1µl and a continuous flow rate of 1.5 ml/min. The injector was set at 200°C. Mass spectra with a scan range of 40–1000 m/z were obtained at 70 eV. The duration of the GC was for 35 minutes. Triple Quadruple MS detector software was utilized to manage chromatograms and mass spectra.

RESULTS AND DISCUSSION

Phytochemical analysis of HE extract of *P. andinum* wereanalyzed and quantified. Results showed the presence of bioactive compounds like flavonoids, alkaloids, glycosides, terpenoids, phenols and steroids[Table 1]. Among all other solvents used, hydroethanol (HE) showed maximum amount of secondary metabolites, hence it was chosen for further studies. Quantitative phytochemical estimation of *P. andinum*revealed the presence of the following; carbohydrates(40.901.1mg of GE/mg)[fig 1], proteins(31.201.1mg of GE/mg)[fig 2], phenols(47.901.1mg of GE/mg)[fig 3], tannins(98.011.1mg of GE/mg)[fig 4], flavonoid contents(22.101.1mg of GE/mg)[fig 5]. The FT-IR analysis of HE extract of P. andinum showed that the extract contains alcohols, phenols, aliphatic and aromatic groups with nitro compounds, primary amines and phosphates[Table 2]. They also contain carboxylic acids and conjugated ketones .GC-MS analysis of HE extract of *P.andinum* showed the existence of compounds like orcinol, vanillin, palmitic acid, cis-vaccenic acid[Table 3] with peak areas such as 10.786%, 12.741%, 16.441%, 17.863% respectively. This analysis revealed the abundance of phytochemicals with anti-cancer potential which might be useful in prevention of cancer. Further studies would prove to be useful in the discovery and development of drugs with anticancer potency.

CONCLUSION

The HE extract of *P.andinum* was nfound to have a variety of secondary metabolites with a wide range of pharmacological characteristics. This study revealed several metabolites compounds through GC-MS that might contribute to antibacterial, anti-cancer, anti-inflammatory, anti-oxidant and other properties. C-O-H, C-H, C-O, O-H, X-O-C,C=O, C-S, C-N, and P-O-C stretching were all detected by FT-IR analysis of HE extract. These results indicates *P.andinum* might serve as a potential candidate for further exploitation of its potency against cancer.

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Table.1: Qualitative Phytochemical analysis of *P. andinum*

Phytochemicals	Biochemical test	Solvents					
		Aqueous	Hydro ethanol (50 %)	Ethanol	Acetone	Petroleum ether	Chloroform
Carbohydrates	Molisch's test	++	+++	++	+	-	-
	Fehling's test	++	+++	++	-	+	-
	Benedict's test	++	+++	++	+	-	-
Proteins	Ninhydrin test	-	-	-	-	+	++
Alkaloids	Dragendorff's Test	-	++	++	++	-	++
	Mayer's test	++	++	++	+	_	_
Flavanoids	Alkaline test	-	++	++	-	+	++
	Lead acetate test	-	+++	++	+	+	-
	Shinoda test	++	++	++	-	-	+
Phenols	Ferric chloride test	++	+++	+++	+	+	+

	Lead acetate test	++	++	++	++	-	+
Glycosides	Keller Kilani test	-	++	-	-	+	-
Sterols	Salkowski test	++	++	-	-	-	+
Tannins	Ferric chloride test	++	+++	+++	++	-	-
Saponins	Foam test	++	++	+	-	-	-

Table.2:Characteristic frequencies of functional groups present in HE extract of *P. andinum*

S. No	Absorption frequency (cm^{-1})	Vibration mode range	Functional groups
1.	3849.92	O-H (hydroxy phenol)	Alcohols, Phenols
2.	2931.80	C-H stretch	Aliphatic groups
3.	2862.36	C-H stretch	Aliphatic groups
4.	1681.93	C=O stretch	Quinone or conjugated ketone
5.	1597.06	C-O, C-O-H	Carboxylic acids
6.	1489.05	X-O-C(hetero-oxy)linkage	Aromatic nitro compounds
7.	1365.60	C-S stretch	Sulfonates
8.	1257.59	C-N stretch	Aromatic primary amine
9.	1195.87	P-O-C stretch	Aromatic phosphates
10.	1149.57	C-N Stretch	Secondary amines
11.	833.25	C-O-O- stretch	Peroxides

Table.3: Major phytoconstituents indentified in *P. andinum*

S. No	Peak number	Compound	RT	Peak area	Molecular weight	Molecular formula
1	1	Diglycerol	7.864	0.14	166.17	C_6H14O5
2	3	Orcinol	10.786	13.96	124.14	$C_7H_8O_2$
3	6	Vanillin	12.741	0.17	152.15	$C_8H_8O_3$
4	11	D-Arabinitol	13.263	9.26	152.15	$C_5H_{12}O_5$
5	12	2-Amino-4-acetamino anisole	14.297	6.93	180.2	$C_9H_{12}N_2O_2$
6	17	Palmitic acid	16.441	1.62	256.42	$C_{16}H_{32}O_2$
7	24	Cis-Vaccenic acid	17.863	1.16	282.5	$C_{18}H_{34}O_2$
8	23	9,12-Octadecadienoic acid (Z,Z)-	17.818	1.25	280.4	$C_{18}H_{32}O_2$
9	21	2-Hydroxy-1,8-naphthyridine	17.263	0.06	146.15	$C_8H_6N_2O$
10	26	Linoleic acid ethyl ester	18.018	0.71	308.5	$C_{20}H_{36}O_2$
11	29	Benzothiophene-3-carbonitrile	19.429	0.87	248.39	$C_{14}H_{20}N_2S$

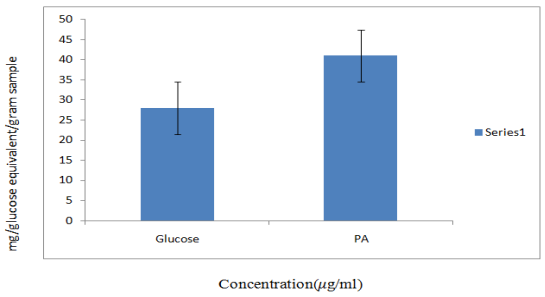

Figure.1: Quantitative estimation of carbohydrates

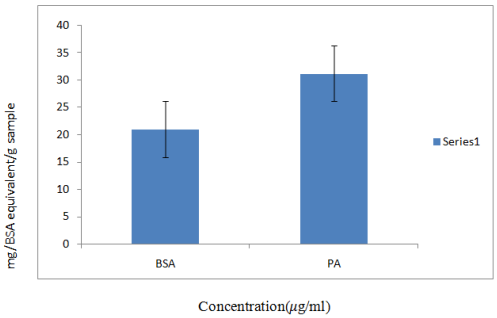

Figure.2: Quantitative estimation of proteins

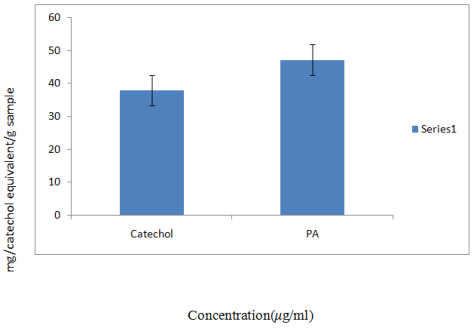

Figure.3: Quantitative estimation of phenols

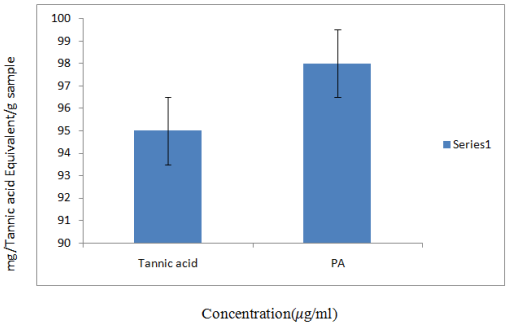

Figure.4: Quantitative estimation of Tannins

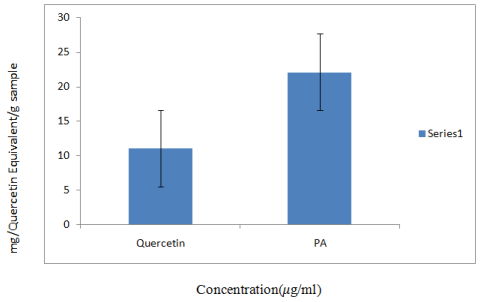

Figure.5: Quantitative estimation of flavonoids

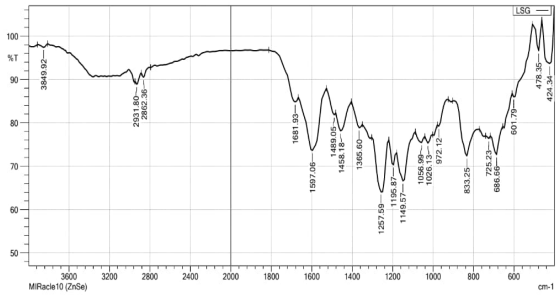

Figure.6: FT-IR characterization of *P. andinum*

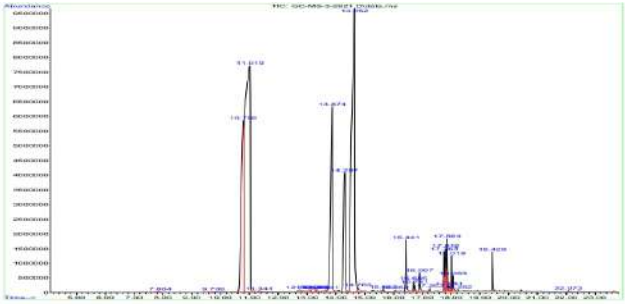

Figure.7:GC-MS analysis of *P, andinum*

RESEARCH ARTICLE

Study of Effect of Integrated Nutrient Management through Inorganic, Organics and Bio-Fertilizers on Grain and Straw Yield and Quality Parameters of *Phaseolus vulgaris*

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ABSTRACT

The population of the country increases day by day. It is necessary to fulfill the need to balance the efficient management of quantitative and qualitative food for humankind. Looking at the economical condition of farmers and the cost of fertilizers, it is essential to adopt new techniques and management practices such as Integrated Nutrient Management like Integrated Pest Management. In the present scenario concept of integrated nutrient management was taken into consideration to increase the qualitative crop yield of *Phaseolusvulgaris* (Rajma)".Standard agricultural practices were adopted as explained in the methodology of the experiment. The field experiment was conducted in *rabi* season with nine treatments and three replications in Randomised Block Design method. It was concluded that the supply of higher quantities of NPK through inorganic fertilizers was more efficient for harvesting the maximum grain yield of Rajma. *Vermicompost* application showed improvement in the physico-chemical properties of soil.

Keywords: *Phaseolus vulgaris (Rajma),* Integrated Nutrient Management, NPK, Integrated Pest Management, fertilizer, etc.

INTRODUCTION

Looking to economic condition of farmer and cost of fertilizers, it is essential to adopt new techniques and management practices as integrated nutrient management. The combined use of organic and inorganic manures not only increases the crop yield but also improves the physical and biological properties of soil. Use of organic manures with optimum rate of fertilizers under intensive farming system increased the turnover of nutrients in the soil plant system (Nambiar, 1989). The organic manures such as FYM and *vermicompost* are not just source of nutrients but also have profound effect on physical properties resulting in a better soil structure, greater water retention in soil and more favourable environment for root growth and better infiltration of water. FYM contains 0.5 per cent N, 0.2 per cent P_2O_5 and 0.5 per cent K_2O (Yawalkar, 1975). Vermicompost application to the soil drastically improves the soil fertility, improves pH, increases water holding capacity, and enhances infiltration, enhancing its exportability (Bhawalkar and Bhawalkar, 1991). It contains 1.60 per cent N, 2.20 per cent P_2O_5 and 0.65 per cent K_2O (Thompson, 1993). The application of inorganic fertilizers along with biofertilizers gives the better results. The application of *Rhizobium* for nitrogen fixation and phosphate solubilizing bacteria (PSB) for phosphorus availability is most advantageous. The number of pods and seed yield plant^{-1} and seeds per pod were noticed to be increased with *Rhizobium* inoculation (Wange *et al*., 1996). Inoculation of *Rhizobium phaseoli* reduced the accumulation of nitrate sulphur in shoot, fruit and roots of plants. PSB possesses the ability to bring phosphorus in soil to soluble forms by secreting glycelic, fumaric and succinic acids and phytase enzymes. Thus, it is increasing phosphorus availability of crops. The inoculation of phosphate solubilizing bacteria increased yield and phosphorus uptake. The organic fertilizers along with biofertilizers help in reducing the dose of inorganic fertilizers, which in turn reduces the cost of cultivation and helps in improving the soil health and therefore the present investigation was taken as "Integrated Nutrient Management" with organic manure and inorganic fertilizers and biofertilizers on yield and uptake of nutrients by French bean with the following objective as, (1).To study the effect of organic and inorganic nutrient sources on yield of Rajma and (2) To study the effect of different nutrient sources on quality of Rajma.

MATERIALS AND METHODS

A field experiment was carried out to study "Integrated nutrient management for Rajma (French bean). The nutrient sources were organic manures, inorganic fertilizers, micronutrients and bio-fertilizers. Effect was studied on yield and uptake of nutrients by French bean". The experiment was conducted in *Rabi* season of 2005-2006 at experiment farm of Department of Agricultural Chemistry and Soil Science, College of Agriculture, Vasantrao Naik Marathwada Krishi Vidyapeeth Parbhani (MS) India. An information regarding the kind of soil, treatment details, design of experiment and number of replications, methods for analysis of quality parameters, crop growth studies, the source of nutrients and statistical analysis are presented. The procedures followed for sampling of soil as well as for plant along with the methods of analysis are also presented here under with suitable sub titles.

Experimental design and treatments

The field experiment was conducted in *rabi* 2005-2006 with nine treatments and three replications in Randomised Block Design. The recommended dose of fertilizer for rajma was 120:60:60 kg NPK ha^{-1}. The treatments in which micronutrients are included, they were applied as 25 kg $ZnSO_4$ and 25 kg $FeSO_4$ per hectare. In treatments where nutrients were applied through organic manures, vermicompost was applied before sowing @ 2.5 or 5.0 t ha^{-1}. The treatments where biofertilizers are included *Rhizobium* and phosphote solubilizing bacteria 250 g each were inoculated per 100 kg of rajma seed. The seed was coated with *Rhizobium phaseoli* and phosphate solubilizing bacteria *Pseudomonas striata* before sowing.

Nutrient sources

Inorganic fertilizer: through urea (46%0, through single super phosphate, through murate of photas (60% K_20).
Micro-nutrient: through $ZnSO_4$, through $FeSO_4$.
Organic fertilizers: Vermicompost applied as par treatment.

Bio-fertilizers: a). *Rhizobium phaseoli* b) phosphate solubilizing bacteria- *Pseudomonas striata*

Table 1 : Details of field experiments, Table 2 :Treatment details

The quality parameters were determined as by below method,

Crude protein in seed

Nitrogen content in grain was determined and it was multiplied by 6.25 to obtain their crude protein content (Chopra and Kanwar, 1976).

Test weight

A random sample of 100 seeds from each net plot produce was drown and its weight was recorded as test weight.

Appearance: Observations on visual appearance i.e. healthy, bold, weak or shriveled seeds was recorded.

Cooking quality

Ten seeds are taken in a 500 ml beaker along with water. Then the beaker was kept on the burner. The time required for cooking the rajma seed was recorded.

Statistical Analysis

The statistical design adopted to obtain relevant and useful information was Randomised Block Design. The statistical analysis of the data was done by the standard statistical methods of analysis of variance (Panse and Sukhatme, 1985). The appropriate standard error (SE $\pm$ (m) for each factor was worked out. The results were tested for their significance by F values. To compare two treatments means the critical difference (C.D.) at 5% level of significance was worked out and is given wherever needed.

RESULTS

Results were presented in three different parts A, B, and C as below,

{A} Effect of inorganic and organic nutrient sources with or without bio-fertilizers on grain and straw yield of Rajma,

{B} Effect of inorganic and organic nutrient sources with or without bio-fertilizers on quality parameters of Rajma AND **{C}** Effect of inorganic, organic nutrient sources and bio-fertilizers on cooking quality and appearance of Rajma

{A} Effect of inorganic and organic nutrient sources with or without bio-fertilizers on grain and straw yield of *Phaseolus vulgaris* (Rajma)":

Effect on grain yield

The data regarding grain yield of rajma as influenced by different treatments are presented in table 3 and fig. 1. The higher grain yields were recorded, when NPK was applied to soil through inorganic fertilizers i.e. T_1, T_2, T_3, T_4 and T_8treatments. High dose of NPK (180:90:90 kg ha^{-1} i.e. 150% RDF) application through inorganic fertilizers recorded 13.17 q ha^{-1} which was highest followed by T_3, T_2, T_8, T_1 application of 2.5 t vermicompost ha^{-1} with 50% RDF of N through urea either at sowing or at flowering recorded significantly lower grain yield as compared to 100% RDF. The results (Table 3 and Fig. 1) indicated that use of organic manure only as 5 t vermicompost ha^{-1} recorded lowest grain yield (i.e. 8.20 q ha^{-1}). The data presented in table 10 indicated that there was no significant increase in grain yield either due to application of biofertilizers or micronutrients. 50% N through urea with 2.5 t vermicompost ha^{-1} applied at sowing or at flowering also had no significant effect on grain yield.

Effect on straw yield

The data from Table 3 and Fig. 1 showed that straw yield of Rajma was higher when NPK was applied to soil through inorganic fertilizers (i.e. T_1, T_2, T_3, T_4 and T_8) treatments. High dose of NPK (180:90:90 kg ha^{-1} i.e. 150% RDF) application through inorganic fertilizers produced 21.18 q ha^{-1} straw which was highest among all treatments. It was

followed by T_3, T_2, T_8 and T_1 treatments. The treatments where 2.5 t of vermicompost ha^{-1} and 50% N (RDF) through urea either at sowing or at flowering were applied recorded significantly lesser straw yields as compared to 100% RDF through inorganic fertilizers.The results from the Table 3 and Fig. 1 also indicated that use of organic manure only as 5 t vermicompost ha^{-1} recorded lowest straw yield i.e 13.35 q ha^{-1} among all the treatments. The data presented in Table 3 also indicated that there was no significant increased straw yield either due to application of biofertilizers or micronutrients. 50% N through urea with 2.5 t vermicompost ha^{-1} either at sowing or at flowering also had no significant effect on straw yield. Table 3: *Effect of Inorganic, Organic, and Bio-fertilizers on Grain and Straw Yield of Rajma*. Fig. 1*Effect of Inorganic, Organic, and Bio-fertilizers on Grain and Straw Yield of Rajma* {B} Effect of inorganic and organic nutrient sources with or without and bio-fertilizers on quality parameters of *Phaseolus vulgaris* (Rajma)":

Effect on percent protein content in grain

The data from Table 4 and fig 2 showed that higher per cent protein content in grain was observed when NPK was applied to soil through inorganic fertilizers. High dose of NPK (180:90:90 kg ha^{-1} i.e. 150% RDF) application resulted in highest protein content i.e. 24.50% in T_4 treatment and was followed by T_3, T_8, T_2 and T_1 treatments. The treatments where 2.5 t vermicompost ha^{-1} with 50% N through urea either at sowing or at flowering with or without micronutirents and biofertilizers recorded in comparatively lesser protein content in grain as compared to 100% RDF. The lowest protein content was observed due to T_9 treatment i.e. (19.68%) where only 5 t vermicompost ha^{-1} was applied. The results also indicated that there was no significant increase in protein content due to bio-fertilizers or micronutrients. 50% N through urea applied at sowing or at flowering had no significant effect on protein content in grain.

Effect on 100 grain weight (g)

The data in table4and fig 2 showed that higher 100 grain weight (g) was observed when NPK was applied to soil through inorganic fertilizers. Application of higher dose of NPK (180:90:90 kg ha^{-1} i.e. 150% RDF) through inorganic fertilizers recorded higher 100-grain weight i.e. 26.30 gms in T_4 treatment followed by T_6, T_8, T_3 and T1. The treatments where 2.5 t vermicompost ha^{-1} +50% N through urea either at sowing or at flowering with or without micronutrients and bio-fertilizers recorded comparatively lesser 100 grain weight as compared to T_4. Treatment T_9 where only 5 t vermicompost ha^{-1} was applied has recorded 100 grain weight 23.79 g which was statistically at par with 100% RDF through in organic fertilizers. The results also showed that the differences in 100 grain weight due to all the treatments were not statistically significant. Table 4: *Effect of Inorganic, Organic, and Bio-fertilizers on quality parameters of Rajm*. Figure 2: Effect of Inorganic, Organic, and Bio-fertilizers on quality parameters of Rajma

{C} Effect of inorganic, organic nutrient sources and bio-fertilizers on cooking quality and appearance of *Phaseolus vulgaris* (Rajma)"

Cooking quality

Treatment wise 100 seeds were taken in 500 ml beaker along with water. Then the beaker was kept on burner. Time required for cooking the rajma seeds was recorded. Rajma seeds from all the treatments showed same cooking quality. The results were non significant.

Colour and Appearanc

There was no marked difference in colour as affected by different treatments. Visual appearance i.e. healthy, bold, weak or shriveld seeds was recorded. All the treatments showed shiny appearance. The results showed that there was no marked change in appearance due to various treatments.

DISCUSSIONS

Effect of inorganic and organic nutrient sources with or without bio-fertilizers on grain and straw yield of *Phaseolus vulgaris* (Rajma):

Grain and straw yield (q ha^{-1}) of Rajma were recorded and results presented in Table 3 and Fig1were discussed below.

Grain yield:

The data pertaining to grain yield indicated that the highest grain yield (13.76 1 ha^{-1}) was observed. Where 150% RDF of NPK ha^{-1} through inorganic fertilizers including micronutrients and biofertilizers were applied. grain yield (Fig. 1) with increasing levels of NPK could be ascribed to the overall improvement in plant growth (Table 3) and vigour as it plays an important role in metabolism Subramanian and Kumarswamy (1989) reported that the addition of N and P resulted in the improvement in root and shoot growth of the crop. Rajpal *et al.* (2003) found that there was increased grain yield due to increased level of nutrients. It might be due to the fact that under adequate availability of nutrients, it might have been taken by plants for greater photosynthesis which ultimately increased plant growth and yield. Deshmukh *et al.* (2005) also reported that the application of 100% RDF of NPK + *Rhizobium* + PSB gave the highest grain yield; it might be due to *Rhizobium* supplied additional nitrogen from the atmospheric nitrogen fixation process and PSB solubilized insoluble phosphate and also enhanced the efficiency of added fertilizer. Sarkar *et al.* (1993) found that *Rhizobium* inoculation resulted in increased grain yield. They also found that N application with *Rhizobium* inoculation might be ascribed to more rapid growth and hence higher grain yield. Similar findings were reported by Takhankhar *et al.* (1998), Boronia (2000), Baboo and Mishra (2001), Mandhare *et al.* (2002), Lanje *et al.* (2005). Lowest grain yield i.e. 8.20 q ha^{-1} in T_9 treatment where only 5t vermicompost ha^{-1} was applied with biofertilizers. This may be due to inadequate supply of nutrients from vermicompost. Similar findings were recorded by Sonboir and Sarwai (2000) they reported that, the lowest grain yield was due to lack of nitrogen and potassium nutrients

Straw yield:

The data pertaining to straw yield presented in Table 3 and Fig. 1 indicated that highest straw yield i.e. 21.18 q ha^{-1} was observed in T_4 treatment where 150% RDF of NPK through inorganic fertilizers with micronutrients and biofertilizers were applied to the soil. Similar observations were found by Rajpal *et al.* (2003). They reported that the increase in straw yield might be due to the fact that under adequate availability of nutrients which might have been taken up by plants and resulted in greater photosynthesis which ultimately increased plant growth and increased straw yield. Sarkar *et al.* (1993) reported that the application of N, or N+P resulted in excessive vegetative growth and increased straw yield. Further, they reported that increase in yield with N or N+P in combination with *Rhizobium* might be due to synergistic effect. Meena (2003) reported that seed inoculation with *Rhizobium* + PSB increased straw yield. The increase in straw yield was due to cumulative effect of increased growth and yield attributes. Patel *et al.* (1994) ascribed the increase in straw yield with increasing level of NPK to overall improvement in plant growth and vigour as it plays an important role in plant metabolism. Tiwari *et al.* (1989) noted that application of 60kg P_2O_5 ha^{-1} along with PSB, *Rhizobium* and micronutrients gave the highest straw yield, which was due to greater availability of macro and micro nutrients and helped in acceleration of various metabolic processes. Similar results were found by Tomor *et al.* (1998), Tiwari and Singh (2000), Sharma (2001), Singh and Varma (2002), Rana *et al.* (2003), Lal (2004) Deshmukh *et al.* (2005). The lowest straw yield i.e. 13.35 q ha^{-1} was observed in T_9 treatment, where only 5t vermicompost was applied alongwith biofertilizers lowest straw yield might be due to an inadequate supply of nutrients, which might have reduced vegetative growth. Similar observations were found by Sonboir and Sarwai (2000). They reported that lower straw yield was due to lack of nitrogen and potassium nutrients in the crop.

Effect of inorganic and organic nutrient sources with or without bio-fertilizers on quality parameters of *Phaseolus vulgaris* (Rajma)

Percent protein content in grain

The data (Table 4) and fig. 2 indicated that highest percent protein content in grain (24.50%) was in T_4 treatment where 150% RDF of NPK with micro nutrient and biofertilizers were applied. Increase in protein yield may be due to application of biofertilizers and the increase in inorganic fertilizers (150% RDF of NPK). Similar observations were found by Ingle *et al.* (2003). They reported highest protein content in *Rhizobium* + Inorganic fertilizer treatment. This may be due to more nitrogen uptake. Turkhede and Giri (1982 reported that application of P with *Rhizobium* inoculation increase the protein content. It might have enhanced the N fixation to be utilized by plants during the grain development stage in synthesis of protein which in turn lead to higher protein. Singh *et al.* (2004) reported that the application of NPK + FYM + Biofertilziers recorded highest protein due to better availability of desired and required nutrients in crop root zone resulting from its solubiliztion caused by organic acids produced from the decreasing organic matter and also increased nutrients by roots due to mycorrhizal filaments. Similar results were also found by Sharma and Namdeo (1999), Meena *et al.* (2001), Mishra, Shailesh Kuma (2003), Jain and Trivedi (2005), Lenje *et al.* (2005). Wandile *et al.* (2005) reported that treatment given i.e. NP with $ZnSO_4$ (micronutrient and inorganics) had no significant effect on protein content in grain. Lowest protein content (19.68%) was observed in T_9 treatment where only 5 tonnes vemicompost was applied. It may be due to less N available and less utilized by plants during grain development stage and resulted in synthesis of protein. Similar results were found by Tukhede and Giri (1982).

Test weight (100 seed wt) gm.

Data from the Table 4indicated that application of inorganic fertilizers with micronutrients, organic manures and bio-fertilizers had no significant effect on 100 grain wt. The highest seed wt 26.30 gm was observed due to T_4treatment, where application of 150% RDF of NPK was applied. Increase in 100 grain wt due to interaction effect of NPK on 100 grain wt. Similar results were found by Mandal *et al.* (1997). They reported that highest 100 grain wt were recorded with 100 kg NPK ha^{-1} applied. Chandel *et al.* (2000), Desai *et al.* (2001), observed that application of 20 kg N and 40 kg P/ha as well as *Rhizobium* + PSB inoculation improved test wt in cow pea. Vishwakarma *et al.* (2002), Lanje *et al.* (2005), Deshmukh *et al.* (2005) also observed similar results.

Colour, Appearance and Cooking quality

There were no differences in the colour and appearance of Rajma grains. Time required for cooking was also same. Hence no differences in cooking quality were observed (Patil *et al.* 1990)

CONCLUSION

The experimental result showed that higher levels of N, P, and K application i.e. 150% RDF through inorganic fertilizers recorded higher available N, P, and K while the absence of inorganic fertilizers i.e. use of only vermicompost showed lower availability in the soil. Application of FeSO4, ZnSO4, and vermicompost showed higher available Fe and Zn. Integrated nutrient management i.e. combination of 2.5 tonne vermicompost with 50 % N through urea was not sufficient to supply the required nutrients to Rajma. *Rhizobium* did notaffect nodulation and thus on other characters and yield of Rajma. It was concluded that the supply of higher quantities of NPK through inorganic fertilizers was more efficient for harvesting the maximum grain yield of Rajma. Vermicompost application showed improvement in the physico-chemical properties of soil.

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Illustrations

Table 1 : Details of field experiments

1	Number of treatments	09
2	Number of replications	03
3	Design of experiment	RBD
4	Gross plot size	4.5m X 3.6 m
5	Net plot size	3.3 X 3.0m
6	Spacing (row to row and plant to plant)	30cm X 15cm
7	Total No.of plots	27.
8	Method of sowing	Dibbling
9	Variety of crop	Araka komal

Table 2 :Treatment details

Symbols	Treatment
T_1	Recommended dose of fertilizer (RDF) i.e. 120:60:60 kg NPK/ha.
T_2	RDF + Rhizobium (*Rhizobium* strain for Rajma will be used i.e. *Rhizobium phaseoli* + PSB (Phosphate solubalizing bacteria).
T_3	RDF + Zn (through 25 kg $ZnSO_4$) + Fe (through 25 kg $FeSO_4$) + *Rhizobium* + PSB
T_4	150% RDF i.e. 180:90:90 NPK kg ha^{-1} + Zn + Fe + *Rhizobium* + PSB
T_5	2.5 t ha^{-1} vermicompost + 50% N through urea at sowing time.
T_6	2.5 t ha^{-1} vermicompost + 50% N through urea + Zn + Fe at sowing + Rhizobium + PSB.
T_7	2.5 t ha^{-1} vermicompost at sowing + 50% N through urea at flowering stage.
T_8	As per soil test NPK application at sowing.
T_9	Vermicompost 5 t ha^{-1} at sowing + *Rhizobium* + PSB

Table 3: ***Effect of Inorganic, Organic, and Bio-fertilizers on Grain and Straw Yield of Rajma***

Treatments	Grain yield (q ha^{-1})	Straw yield (q ha^{-1})
T_1	10.93	16.26
T_2	11.42	17.25
T_3	12.30	18.27
T_4	13.76	21.18
T_5	9.10	15.40
T_6	10.50	16.26
T_7	10.01	16.17

T_8	11.36	16.30
T_9	8.20	13.35
S.E. ±	0.31	0.64
CD at 5%	0.94	1.94

Table 4: ***Effect of Inorganic, Organic, and Bio-fertilizers on quality parameters of Rajma***

Treatments	Protein in grains (%)	100 grains wt. (g)
T_1	21.56	23.61
T_2	22.87	23.70
T_3	23.87	23.70
T_4	24.50	26.30
T_5	20.56	23.05
T_6	21.25	24.43
T_7	21.00	23.06
T_8	22.31	24.40
T_9	19.68	23.79
S.E. ±	0.213	1.213
CD at 5%	0.634	NS

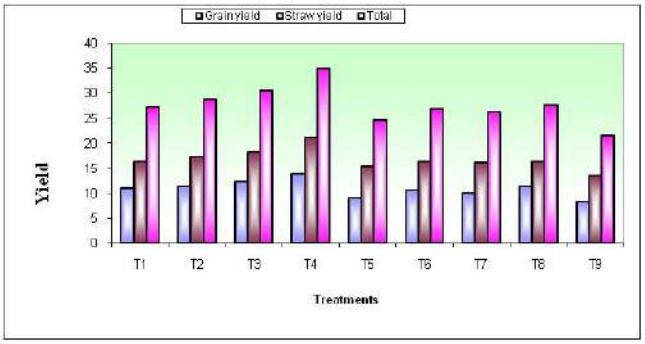

Figure.1:Effect of Inorganic, Organic, and Bio-fertilizers on Grain and Straw Yield of Rajma

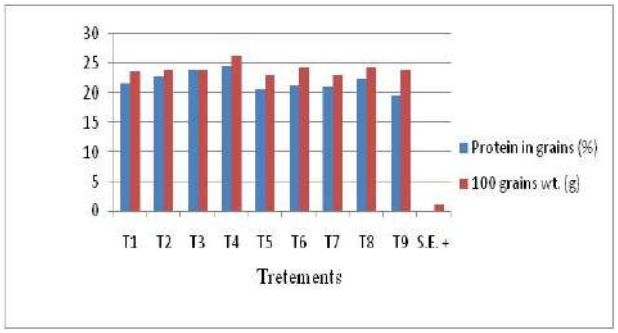

Figure.2: Effect of Inorganic, Organic, and Bio-fertilizers on quality parameters of Rajma

RESEARCH ARTICLE

Effect of Resistance Band Strengthening and Scapular Isometric Exercises on Pain and Function on Adults with Inter-Scapular Pain : An Experimental Study

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ABSTRACT

Effects of Resistance band strengthening exercises and scapular isometric exercises on pain and function in adults with inter-scapular pain: An experimental study. Muscle strain is the most common cause of inter-scapular pain. People strain their muscles through poor posture, overuse, wearing heavy backpacks, or playing sports. Any activity that requires repeated strenuous movements of the arms can inflame bursa and tendons which ultimately, can lead to inter-scapular pain. So purpose of the study is to evaluate "Effect of resistance band strengthening and scapular isometric exercises on pain and function in adults with inter-scapular pain" Total 35 Adults were rrecruited on the basis of Inclusion and Exclusion criteria and divided into 2 groups. Subjects in group A (n=18) received Resistance band strengthening Exercises and subjects in group B (n=17) Received scapular isometric exercises. Age group between 19 to 33 years were included in the study. Intervention was given for 5 days per week, for total 4 weeks. Effects of Resistance band strengthening and scapular isometric exercises was checked using numeric pain rating scale(NPRS) and back pain functional scale respectively for both groups at the beginning and rechecked after the completion of 4 week training sessions. Wilcoxon was used within group analysis and Mann Whitney U test was used for between group analyses. Results of within group analysis revealed a significant difference ($p<0.001$ with level of significance 95%) in pre and post measures of pain and function in the both group. And between groups analysis revealed a statistically significant difference in group A. study concluded that resistance band strengthening exercise are more effective than scapular isometric exercise in pain and function.

Keywords: Resistance band exercises, interscapular pain, scapular isometric exercise

INTRODUCTION

Neck pain is typical repetitive injury in adults. prevalence rate in the world varies between 16.7% to 75.1%.[1] Pain between the shoulder blades or interscapular pain caused by poor Prolonged sitting posture which leads spine to undergo structural derangements which ultimately pain leading in between shoulder blade. crook your back, incline your head down for prolonged duration, or sitting to one side while functioning behind a desk can enfeeble your muscles and give pressure on surrounding structures like spinal discs, bursa and ligaments[2,3]Lifting objects overhead that are too heavy can damage muscles or sprain ligaments, or ultimately injure the shoulder girdle or spine, which can did pain under or near the shoulder blade[3,4] Longer duration work can lead straining of muscle. which can cause pain in the upper back, middle of shoulder blade and spine[5].The shoulder girdle comprised of clavicle and scapula. scapula. coherent with the upper part of humerus. There are Four joints in the girdle it involves glenohumeral joint, sternoclavicular (SC), scapulothoracic joints and acromioclavicular (AC)10. Serratus anterior (SA) is a fan-shaped muscle. Which emerged from first to eighth or ninth ribs and insert at the anterior surface of the scapula. It counterbalanced the scapula and protect the shoulder blades from the ribcage when at rest and during motion. It is the main muscle in scapular protraction and scapular upward rotation.[11] Rhomboid minor, a coulmnar muscle originating from ligamentum nuchae and C7, T1 vertebrae. The insertion is over medial border of scapula, close to scapular spine. Quadrangular muscle Rhomboid major originates from spinous processes of the T2 to T5 vertebra. Its insertion is over medial border of scapula. This group of muscles is important for movement of the upper limb and stabilised the shoulder. It Functions as retractor, elevator and rotator of the scapula[12] Normal scapula humeral rhythm[13] various forces with different intensities and directions that acting over head of humerus. The muscles which conveyed these forces were deltoid, biceps and rotator cuff muscles. key factor of force inclination is muscle orientation. muscles stabilization are influence by postural changes and altered the Scapular stability depends on variation in contractile properties of muscles and connective tissue. Physical therapy for inter-scapular pain:- The physiological changes that happened with injury, disuse and disease, Based on the concept that postural abnormalities cause pain and injury, postural education and correction have been used as treatment approaches for reduce pain and it is important to readjust the scapular in its absolute postural position and to recruit the stabilizing muscles to maintain this position The altered scapular alignment like kyphosis can be problematic. Correct alignment of the thoracic spine can affect position of scapula and reduce muscle imbalance[11].Resistance band strengthening Exercise allows person to exercise in a weight-bearing, functional position that is more effective and easy for most of the persons. Elastic resistance band furnish a unique form of isotonic exexrcise. The actual amount of resistance varies with the amount of stretch applied to the theraband. This is accomplished most effectively by strating a person exercising with some initial slack in the tubing. There by start relatively with low resistance. As the individual enhance the exercise is performed with no slack, increasingly the resistance gradually and safely[24].Numerical Pain Rating Scale (NPRS) for pain may be used to help identify quantify the severity of the condition. The high reliability observed in both subjects of literate and illiterate were 0.96 and 0.95, respectively and the validity, shown to be highly correlated range from 0.86 to 0.95 28.The Back Pain Functional Scale (BPFS) patient's physical function after back pain were measuring by this subjective scale. This scale was developed by Stratford et al. (2000). To check the patient's level of physical independence. This scale comprised of total score of 60. maximum score obtained by individual is indicates the maximum physical abilities of the individual. In addition, this scale also has 'Adjusted score'. Which is ranging from 0 to 60. in that 0 (0%)-unable to perform any activity to 60 (100%)-no difficulty in any activity. This scale had good test retest reliability with an intra-class correlation coefficient of 0.8829,30

Objectives

To study the effectiveness of the Resistance band exercises on pain and function in adult with inter-scapular pain. To check the effectiveness of scapular isometric exercise on pain and function in adult with inter-scapular pain. To compare the effectiveness between Resistance band strengthening and scapular isometric exercises on pain and function in adult with inter-scapular pain.

MATERIALS AND METHODOLOGY

MATERIALS REQUIRED

Resistance band Gym ball , Plinth , Exercise mat , Consent form , Assessment form, Pen, Pencil

CRITERIA FOR SELECTION : INCLUSION CRITERIA[42]:

Age 19 to 33 year old ,Male & Female , NPRS score at least 3 on 0-10 scale ,Willingness of participants, SPECIAL TEST : any 2 positive will be included:

Scapular retraction test

Lateral scapular slide test

Modified lift off test

Rhomboid test

Exclusion Criteria

Subject with upper extremity fracture, radiating pain , abnormal curvature, H/o any shoulder complex injury., Subject with upper extremity fracture, radiating pain , abnormal curvature, neurological abnormalities, mentally retarded patient and any another systemic illness, Not willing to participation., Space occupying lesions, tumour

Methodology

Ethical clearance was received from institutional Ethical committee prior to the study. The subjects from sainath hospital of Ahmedabad were screened. A thorough assessment was done to screen the subjects for inclusion and exclusion criteria. Nature and Purpose of the study was explained to the subjects in detail, in a language they understood. All subjects acknowledgement their understanding of the study and their willingness to participate by providing signed consent. A consent will be taken from the subjects. selection of 35 subjects on the basis of chit method randomization after that allocated into 2 groups. Group A (n=18) Resistance band strengthening exercises and Group B (n=17) scapular isometric exercises. Numerical pain rating scale and back pain functional scale were given to each subject and mean of them were considered. 2 participants from group A and 1 participants from group B discontinue the session due to their inconvenience and their personal reason. In both the groups 3 subjects left the session. After Pre-test measurement, procedure sessions has been started and progression has been done in exercise which has been shown in table A and B. Group A: Resistance band strengthening exercises. Group B: scapular isometric exercises Both groups were asked to perform all exercises with increase in repetition in each week. As well as with progression of exercises. Duration of training session: 20 Sessions 5 Session per week For total 4 weeks

RESULT

Total 32 subjects has been participated in the study, in which 3 participants were dropout. 14 participants in resistance band strengthening exercises sessions and 15 participants in isometric scapular exercises session for 4 weeks. The statistical analyses was done by using software called STATISTICAL PACKAGE FOR SOCIAL SCIENCE (SPSS Version 20). Distribution of data in both groups were analyzed by using shapiro-wilk test of normality . But data was not normally distributed so non-parametric test was used. Mean and SD were calculated from numeric data for both groups. Pre and Post data were taken to compared by using Wilcoxon signed rank test. And comparisons between the both groups were done using Mann whitney U test. For all statistical analysis significant results were considered at $p<0.05$ with class interval 95%.

DISCUSSION

The current study was conducted to check the effectivness of Resistance band strengthening exercises and scapular isometric exercises on pain and function in adults with interscapular pain. This study was conducted in sainath hospital in ahmedabad on 29 healthy adults. The age group of subjects is in between 19 to 33 years both male and female according to inclusion criteria and randomly had been divided in two groups. Also recruitment of motor units and their firing rate. Resistance band is helpful in improving mobility, strength and function and thus reduce joint pain. They are cost effective, versatile and portable [50] Muscular strength increased by focusing on traditional resistance training. Those training undertaken by using gym equipment such as ,free weights, resistance bands, machines. Also using own body weight during resistance training programs48. Current articles suggest these type of resistance training are safe, effective on under supervision. also worthwhile for school children and adolescents[43] According to Ekstrom stated that the activity of Serratus anterior muscle was greater above the 120° of shoulder elevation compare in the scapular plane with healthy subjects than that below 80°. According to Hardwick reported that the Serratus anterior muscle was efficiently active at 140° of humeral elevation than that at 90° and 120° in the scapular plane with healthy subjects. Moreover, Serratus anterior activates of scapular upward rotation, protraction, depression, and abduction, there by hold the scapula along with thoracic wall. Concentric contraction exercises and eccentric contraction exercises are more beneficial in subacromial pain syndrome. The study concluded that the back pain functional scale scoring were greater in the ECG. which help in figuring out the shoulder pain and range in joint tissue. Which may have decreases the mechanical stress up to joint, resulting in an enhance the function of all over shoulder joint[45].

CONCLUSION

Study concluded that resistance band strengthening exercise are more effective than scapular isometric exercise in pain and function.

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Table.1: Mean and SD values in both the group for Numerical pain rating scale

Numerical Pain Rating Scale	Group a	Group b	P value
	Mean ± SD	Mean ± SD	
Baseline	5.92 ± 2.05	5.8 ± 1.89	<0.01
At The End Of Fourth Week	2 ± 1.70	2.93 ± 1.86	<0.01

Mean of pre and post values of both group for numerical pain rating scale

Table.2: Mean and SD values in both the group for Back pain functional scale

Back Pain Functional Scale	Group A	Group b	P value
	Mean ± SD	Mean ± SD	
Baseline	29.14 ± 11.90	22.4 ± 6.09	<0.01
At the end of fourth week	50 ± 8.33	27.93 ± 7.42	<0.01

Mean of pre and post values of both group for Back pain functional scale.

Table.3: Comparison between Group A and Group B for Back pain functional scale

Variables	Group a Mann whitney test	Group b Mann whitney test	p value
Back pain functional scale	Mean ± sd	Mean ± sd	<0.001
	20.86 ± 3.57	5.53 ± 1.33	

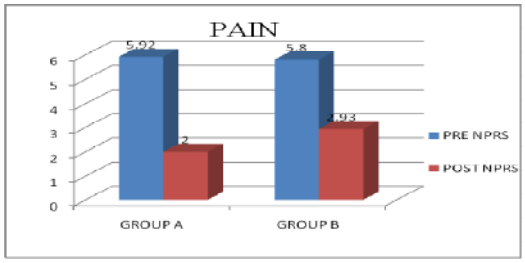

Figure.1: There was a significant difference found on comparison of pre ad post mean values of numerical pain rating scale in group A as well as in group B (p<0.01)

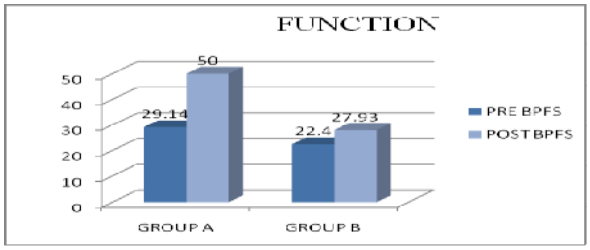

Figure.2: There was a significant difference found on comparison of pre ad post mean values of Back pain functional scale in group A as well as in group B (p<0.01)

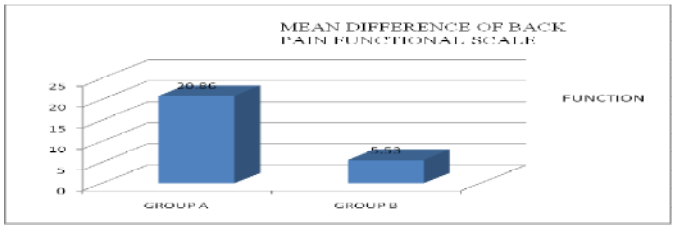

Figure.3: Mean difference of GROUP A and GROUP B for Back pain functional scale There was significant difference found on comparing mean difference of Back pain functional scale in both groups (p value <0.001)

REVIEW ARTICLE

The Pharmacological and Nutritional Role of Papaya Leaves: A Review

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ABSTRACT

Papaya (Carica papaya L) is a tropical fruit that had been used for centuries in traditional medicine to treat various ailments. The leaves of the papaya plant have gained attention in recent years for their potential pharmacological uses. The leaves contain a variety of bioactive compounds, including alkaloids, flavonoids, phenols, and carotenoids, which have been found to possess a range of biological activities. Papaya leaf and its extract are effective against breast, cervical, lung, and pancreatic cancer cells, chronic diseases such as cancer, heart disease, and diabetes, etc. A review of the pharmacological uses of papaya leaves notes that "Papaya leaves are a promising source of natural remedies, with a range of pharmacological properties that offer potential health benefits. The role of a review paper on the pharmacological uses of papaya leaves is to consolidate and analyze the existing scientific literature on the topic, and to provide an overview of the current state of knowledge regarding the potential medicinal properties of this plant. This review can serve as a valuable resource for researchers, healthcare practitioners, and members of the general public who are interested in natural remedies and alternative therapies. By compiling and synthesizing data from a variety of studies, a review paper can provide a comprehensive and balanced assessment of the current evidence base for the pharmacological properties of papaya leaves. Another important role of a review paper on the pharmacological uses of papaya leaves is to identify potential areas of concern or risk associated with the use of this plant as a therapeutic agent. This can help healthcare providers and patients make informed decisions about the use of papaya leaves, and can also inform regulatory agencies about the safety and efficacy of this plant.

Keywords: Pharmacological; Medicinal; Papaya; Leaves; Carica Papaya

INTRODUCTION

Papaya (Carica papaya L) is a tropical fruit that had been used for centuries in traditional medicine to treat various ailments. The leaves of the papaya plant have gained attention in recent years for their potential pharmacological uses. The leaves contain a variety of bioactive compounds, including alkaloids, flavonoids, phenols, and carotenoids, which have been found to possess a range of biological activities. Papaya leaves have phytochemicals, vitamins, and minerals, which makes them a potential source of valuable foods and medications. The leaves' ability to effectively combat malaria is explained by the alkaloids present in them. Aside from that, the brown leaves are utilised as a body cleanser and the yellow leaves as an anti-anemic agent. Plants contain substances called phytochemicals that occur naturally and may be beneficial to human health. *Carica papaya* leaves contain a variety of bioactive substances, including as saponins and cardiac glycoside alkaloids. Another sort of phytochemical was tannin, which was missing from the samples. In order for the body to function effectively, vitamins are necessary nutrients. Thiamine (B1), riboflavin (B2), and ascorbic acid (C) were discovered to be present in the leaves by the investigation. The creation of energy and the health of the immune system are just two of the biological processes that these vitamins are crucial for. The body requires trace levels of minerals as well as other necessary nutrients. According to the study, the leaves have calcium (Ca), magnesium (Mg), sodium (Na), potassium (K), manganese (Mn), and iron (Fe) in them. Numerous body processes, such as the health of the bones, the operation of the muscles, and oxygen transport, depend on these minerals. It also revealed that whereas yellow leaves had the highest Fe value, green leaves had the highest Ca, Mg, Na, K, and Mn values. According to this, the plant's various components might provide various nutritional advantages. Overall, there is the possibility of using Carica papaya leaves as a natural source of valuable nutrients and herbal medicine (Ayoola & Adeyeye, 2010).

A review of the pharmacological uses of papaya leaves notes that Papaya leaves are a promising source of natural remedies, with a range of pharmacological properties that offer potential health benefits. While more research is needed to understand the mechanisms behind its therapeutic effects fully, the growing body of scientific evidence suggests that papaya leaves may have the potential to treat and prevent various health conditions. By exploring the latest research on papaya leaves, we hope to provide insights into this valuable natural remedy and promote further investigation into its potential uses(Nayak and Pattanayak, 2014). One of the key pharmacological properties of papaya leaves is their antioxidant activity. Antioxidants are important in protecting cells against oxidative damage caused by free radicals, which can contribute to the development of chronic diseases such as cancer, heart disease, and diabetes. Papaya leaves contain a variety of antioxidants, including carotenoids, which have been shown to possess potent antioxidant activity (Nguyen et al., 2013). In addition, papaya leaf extract has been found to increase levels of glutathione, an important antioxidant in the body (Boricha et al., 2011). Papaya leaves also possess anti-inflammatory properties, which may make them a valuable natural remedy for managing chronic inflammation. Chronic inflammation is associated with a range of chronic diseases, including heart disease, diabetes, and cancer. A study conducted by Jyoti et al. (2014) found that papaya leaf extract reduced inflammation in the paw of rats with induced inflammation, indicating its potential as an anti-inflammatory agent. Furthermore, papaya leaves have been found to have potential in the management of diabetes. A study by Otsuki et al. (2010) found that papaya leaf extract reduced blood glucose levels in rats with induced diabetes. The extract was found to increase insulin sensitivity and glucose uptake, which may contribute to its potential as a natural remedy for managing blood sugar levels in people with diabetes. Another potential pharmacological use of papaya leaves is in the treatment of cancer. Cancer is a complex disease that arises from the uncontrolled growth and proliferation of abnormal cells. Research has shown that papaya leaf extract can inhibit the growth and proliferation of cancer cells. In a study conducted by (Igbinosa et al. (2016), papaya leaf extract was found to possess significant anticancer activity against colon cancer cells. Other studies have found that papaya leaf extract is effective against breast, cervical, lung, and pancreatic cancer cells (Kumar et al., 2012; Ndukwu et al., 2019; Vargas-Sánchez et al., 2020). In conclusion, papaya leaves are a promising source of natural remedies, with a range of pharmacological properties that offer potential health benefits. The scientific evidence suggests that papaya leaves may have potential in the treatment and prevention of various health conditions, including cancer, diabetes, and chronic inflammation. Further research is needed to fully understand the

mechanisms behind its therapeutic effects and to explore its potential uses in clinical settings. In the following sections of this review paper, we will delve deeper into the various pharmacological uses of papaya leaves and the scientific evidence supporting their use. One of the most studied pharmacological properties of papaya leaves is its potential anticancer activity. A review by Kumar et al. (2012) found that papaya leaf extracts have been shown to inhibit the growth of several cancer cell lines, including breast, liver, lung, and pancreatic cancer. Similarly, Otsuki et al. (2010) found that an aqueous extract of papaya leaves had anti-tumor activity in mice, and also enhanced the immune system's ability to fight cancer cells. In addition to its potential as an anticancer agent, papaya leaves have also been found to have antioxidant properties. A study by Singh (2011) found that papaya leaf extract exhibited antioxidant activity in rats, and was able to protect against liver damage caused by oxidative stress. This suggests that papaya leaves may have potential as a natural treatment for liver diseases such as cirrhosis or hepatitis. Another pharmacological property of papaya leaves is its ability to inhibit inflammation. Jyoti et al. (2014) found that papaya leaf extracts had anti-inflammatory effects in rats, and suggested that it may have potential as a treatment for inflammatory diseases such as arthritis or colitis. Papaya leaves have also been found to have antimicrobial properties. A study by Igbinosa et al. (2016) found that papaya leaf extracts had activity against several strains of bacteria, including Staphylococcus aureus and Escherichia coli, as well as fungi such as Candida albicans. This suggests that papaya leaves may have potential as a natural alternative to antibiotics for treating infections. Overall, the pharmacological properties of papaya leaves are still being explored, and many potential therapeutic uses have been identified. As more research is conducted, it is likely that additional uses for papaya leaves will be discovered, making them a promising source of natural medicine.

MORPHOLOGICAL FEATURES OF PAPAYA

Papaya is a herb found in nature but its figure or structures are not of a herb but similar to a tree. *C.papaya* is commonly called as papaya (Yogiraj et al., 2014). Other names can be seen as Papye, Pawpaw, Lapaya, Tapayas, and Kapaya (Bhattacharjee, 2001). Papaya is an erect big herbaceous plant it may look as a tree but it's not at all woody in feature. Leaves are a compound of type. Leaves are very large and the morphology of leaves shows palm shape and the average size can be seen around 50-70 cm in diameter. Papaya flowers are generally Dioecious. The fruit may vary in size or shape depending on the flower type. Male flowers are straw-colored. Corolla tube is cylindrical which is about 2cm long.Female flowers are racemose type. The fruit can vary up to 5-30 cm long and yellowish-orange in color. Fruit contains several black seeds and pulp can be very sweet if ripped (Nadkarni, 1954).

TAXONOMY

Carica papaya commonly known as Papaya, Betik, Pawpaw, Betek, Ketalah belongs to
Kingdom- Plantae,
Phylum- Magnoliophyta,
Class- Magnoliopsida,
Order- Violales,
Family- Caricaceae,
Genus- Carica
Species- *Carica papaya.*

CHEMICAL COMPOSITION AND ISOLATED COMPOUNDS

Papaya leaves contain tannin, saponin, alkaloid, flavonoid and glycoside; while shoots contain other mineral like Ca, Fe, Mg, K, Zn, Mn etc. Enzymes are present in the unripe fruit as well such as papain and chymopapain. Fruit also contains carotenoids b carotene and crytoaxanthin. The chemical composition of the root showed the presence of the benzoyl isothiocyanare, glucosinolatescarposide. Papaya oil found in the seeds also contains flavonoids, kale Feroz, myricetin, and fruit contains Linalool,4-terpinol, and monoterpenoids (Adachukwu et al., 2013). Enzymes were also found in many other parts of the plant example, papain, chymopapain, Carica in, and protease omega (Azarken et al.,2003, Brocklehurst et al.,1985, Dubois et al., 1988, Dubois et al., 1989). Latex of C.papaya was seen to have enzymes like cysteine endopeptidases, chitinase, and glutaminyl Cyclase(Azarkan et al.,2006).

Seven flavonoids were observed and contained from papaya leaves, named as quercetin, kaempferolkaempferolv3-rutinoside, quercetin3-(2g-rhamnosylrutinoside), quercetin 3-runtinoside, keampferol 3-(2G-rhamnosylrutionside), myricetin 3-rhamnoside(Nugroho et al.,2017). The reports showed that peresence of many or various phenolic compound in the leaves for example kaempferol, protacatechuic acid, p-cosmetic acid, and acid in plant leave. Another study by (Musa, 2015) showed that n-hexane extract and methanol extract of leaves showed the presence of different components such as anthraquinone, glycoside, tannin, saponin, flavonoid, steroid and resin. Chromatography(column chromatography) and spectroscopy methods(NMR, IR and mass spectrometry) were used for the isolation and characterisation of caprine from the leaves. The amount of carpine in leaves was about 0.093g/kg determined by HPLC-UV method (Wang et al., 2015). According to studies by El-Mesallamy et al, (2015), it was found that the methanolic leaves extract of papaya contains phenolic compounds. Chromatography, spectroscopy analysis and mass spectrometry were used to establish the structure of the isolated phenolic compounds. The major isolated found were protocatechuic acid, chlorogenic acid, caffeine acid, quercetin, kaempferol, quercetin 3-0-a-1C4-rhamnopyranoside, quercetin-3-0-glucopyranuroside, quercetin-3-0- rutinoside, p-coumaric acid. Quantitative HPTLC assessment of leaves aqueous extract showed the presence of compounds kaempferol, trans-ferulic acid, caffeine acid, and myricetin. These were recognised by using Ultra performance liquid chromatography -quadrupole orthogonal acceleration time of flight tandem mass spectrometer (UPLC-qTOF/MS) technique which was twenty four in number(Anjum et al.,2017). One particular investigation showed that the leaves contain various photochemically such as carpine, kaempferol 3-(2G-glucosylrutinoside), kaempferol 3-(2" - RHAMNOSYLGALACTOSIDE), 7-rhamnoside, kaempferol 3-rhamnosyl-(1->6)-galactose's, orientin 7-0rhamnoside, luteolin 7-galactosyl-(1->6)-galatocide , orientin 7-0-rhamnoside, 11-hydroperoxy-12,13-epoxy-9-octadecenoic acid, palmitic amide, and 2-hexaprenyl-6-methoxyphenol (Soib et al.,2020).

NUTRITIONAL VALUE

MEDICINAL USES OF PAPAYA LEAVES

Anticancer Properties

One of the most studied pharmacological properties of papaya leaves is their potential anticancer activity. Papaya leaf extracts have been shown to inhibit the growth of several cancer cell lines, including breast, liver, lung, and pancreatic cancer (Kumar et al., 2012). This effect is thought to be due to the presence of compounds such as alkaloids, flavonoids, and phenolic acids, which have been shown to have cytotoxic effects on cancer cells (Sarkar et al., 2013). A study by Otsuki et al. (2010) found that an aqueous extract of papaya leaves had anti-tumor activity in mice, and also enhanced the immune system's ability to fight cancer cells. The authors suggest that these findings indicate that papaya leaf extracts may have potential as an adjuvant therapy for cancer treatment.

Antioxidant Properties

Papaya leaves have also been found to have antioxidant properties. A study by Singh (2011) found that papaya leaf extract exhibited antioxidant activity in rats, and was able to protect against liver damage caused by oxidative stress. This suggests that papaya leaves may have potential as a natural treatment for liver diseases such as cirrhosis or hepatitis. In addition, a study by Rahman et al. (2012) found that papaya leaf extract was able to reduce oxidative stress and inflammation in rats with induced arthritis. This indicates that papaya leaves may have potential as a natural treatment for inflammatory diseases.

Anti-inflammatory Properties

Papaya leaves have also been found to have anti-inflammatory effects. A study by Jyoti et al. (2014) found that papaya leaf extracts had anti-inflammatory effects in rats, and suggested that it may have potential as a treatment for inflammatory diseases such as arthritis or colitis. The anti-inflammatory effect of papaya leaves is thought to be due to the presence of compounds such as papain and chymopapain, which have been shown to have anti-inflammatory activity (Ghosh et al., 2013).

Antimicrobial Properties

Papaya leaves have also been found to have antimicrobial properties. A study by Igbinosa et al. (2016) found that papaya leaf extracts had activity against several strains of bacteria, including Staphylococcus aureus and Escherichia coli, as well as fungi such as Candida albicans. This suggests that papaya leaves may have potential as a natural alternative to antibiotics for treating infections. In addition to their antimicrobial properties, papaya leaves have also been found to have antiviral activity. A study by Loh et al. (2009) found that papaya leaf extracts were able to inhibit the replication of the dengue virus, which causes dengue fever. The authors suggest that these findings indicate that papaya leaf extracts may have potential as a treatment for dengue fever.

Cardiovascular Benefits

Papaya leaves have also been found to have cardiovascular benefits. A study by Rahman et al. (2013) found that papaya leaf extract was able to lower blood pressure and improve heart rate variability in rats with induced hypertension. This suggests that papaya leaves may have potential as a natural treatment for hypertension.

Digestive Benefits

Papaya leaves have been traditionally used to treat digestive problems, and recent research has supported this use. A study by Mahajan et al. (2013) found that papaya leaf extract was able to protect against alcohol-induced gastric ulcers in rats. In addition, a study by Roy et al. (2013) found that papaya leaf extract was able to protect against aspirin-induced gastric ulcers in rats. These findings suggest that papaya leaves may have potential as a natural treatment for gastric ulcers.

Immuno modulatory Properties

Papaya leaves have also been found to have immunomodulatory properties, meaning they can help regulate the immune system. A study by Siddique et al. (2011) found that papaya leaf extract was able to increase the production of white blood cells in mice, indicating that it may have potential as a natural treatment for immune deficiencies.

Wound Healing Properties

Papaya leaves have also been found to have wound healing properties. A study by Nayak et al. (2012) found that papaya leaf extract was able to promote the healing of burn wounds in rats. This suggests that papaya leaves may have potential as a natural treatment for burn wounds. While the pharmacological properties of papaya leaves are promising, it is important to note that more research is needed to fully understand their therapeutic potential. Additionally, the safety and efficacy of papaya leaf extracts as treatments for human diseases have not been fully established, and further studies are needed to determine appropriate dosages and potential side effects.

Dengue treatment

conducted research on the impact of papaya leaf juice on platelet and white blood cell counts in dengue fever and found that Carica papaya leaves contain a variety of phytoconstituents including saponins, tannins, cardiac glycosides, and alkaloids. There are carpaine, pseudocarpaine, and dehydrocarpaine I and II among the alkaloids present. These ingredients can influence the bone marrow, stop it from deteriorating, and improve its capacity to make platelets. Additionally, they have the ability to stop blood-borne platelet oxidation, extending the life of the circulated platelet. In particular, myeloblasts and megakaryocytes were discovered to be stimulated by carica papaya's ability to protect the bone marrow and promote haemopoiesis of the cells. For eight days, the patient in the current case received 25 ml of papaya leaf juice twice day in addition to standard medical care. White blood cell and platelet counts were returned to normal, and there was a notable improvement in the subjective symptoms. Dengue fever can be connected to occurring as a fever complication according to the characteristics of the current case. According to the stage, the appropriate treatment must be planned. The usage of papaya leaf juice has been demonstrated to be effective in raising the amount of platelets and white blood cells in patients with dengue fever, according to the text. Numerous clinical trials and experimental experiments, which were originally cited in the research report, have proven this. In light of its affordability and accessibility, it may be said that papaya leaf juice may have positive effects on society as a whole. The study and randomised controlled trial that demonstrated papaya

leaf juice's advantages for dengue patients are mentioned in the research article. For eight days, the patient also received standard medical care in addition to the 25 ml of papaya leaf juice that was given twice daily. Indicating that the treatment was successful, the patient's subjective symptoms also subsided. Additionally, a review paper can highlight areas where further research is needed in order to fully understand the potential benefits and risks of using papaya leaves for medicinal purposes. This can help guide future research and clinical trials, as well as inform healthcare providers and patients about the most effective and safe ways to use papaya leaves as a therapeutic agent. For example, some studies have reported potential toxicity of papaya leaves at high doses, and it is important for healthcare providers to be aware of these risks when recommending the use of this plant to patients. By providing an overview of the current evidence base for the safety and toxicity of papaya leaves, a review paper can help to ensure that healthcare providers and patients have accurate information about the potential risks and benefits of using this plant as a therapeutic agent. Furthermore, a review paper on the pharmacological uses of papaya leaves can also help to identify potential areas for future research and development. For example, if a review paper highlights a lack of research on the potential benefits of papaya leaves for a particular health condition, this can encourage researchers to conduct further studies in that area. This can ultimately lead to the development of new therapies and treatments based on the medicinal properties of papaya leaves. In addition to its practical applications, a review paper on the pharmacological uses of papaya leaves can also contribute to the broader scientific understanding of plant-based medicines and their potential therapeutic properties. By synthesizing and analyzing existing research on papaya leaves, a review paper can contribute to the development of a more comprehensive and nuanced understanding of the potential benefits and limitations of using plants as therapeutic agents. Overall, the role of a review paper on the pharmacological uses of papaya leaves is to provide a critical analysis of the existing scientific literature, and to offer insights into the potential benefits and limitations of using this plant as a natural remedy. Through careful evaluation of the available evidence, such a paper can help to support evidence-based practice in the use of papaya leaves for medicinal purposes, and may ultimately contribute to improved health outcomes for individuals who use this plant as a therapeutic agent.

CONCLUSION

papaya leaves have been traditionally used for medicinal purposes for centuries and recent scientific evidence supports their potential health benefits. The bioactive compounds present in papaya leaves, such as alkaloids, flavonoids, phenols, and carotenoids, exhibit a range of pharmacological properties, including antioxidant, anti-inflammatory, anti-diabetic, and anticancer activities. The growing body of research on papaya leaves suggests that they can be a promising source of natural remedies for the prevention and management of various health conditions, including chronic diseases such as cancer, heart disease, and diabetes. However, more research is needed to fully understand the mechanisms behind the therapeutic effects of papaya leaves and their potential clinical applications. Further investigations can aid in exploring the potential of papaya leaves as a natural remedy and promote their use in traditional and modern medicine.

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Table 1: Mineral Composition of the papaya leaves on dry weight basis (mg/kg)

Mineral	Green leaf	Yellow leaf	Brown leaf
Ca	8612.50	3762.50	4362.50
Mg	67.75	28.55	35.35
Na	1782.00	567.00	324.00
K	2889.00	819.00	468.00
Fe	90.50	147.50	79.50
Mn	9.50	5.00	4.50

Table 2: Vitamin Composition of the papaya leaves on a dry basis (mg/100g)

Vitamin	Green leaf	Yellow leaf	Brown leaf
Ascorbic Acid	16.29	9.62	11.26
Thiamine	0.94	0.41	0.52
Riboflavin	0.13	0.04	0.06

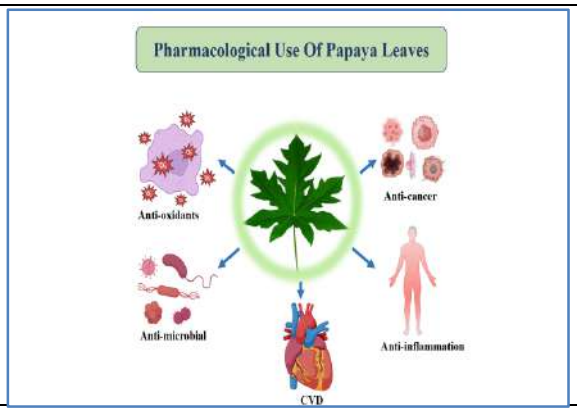

Figure 1: The pharmacological role of papaya leaves

RESEARCH ARTICLE

Exploring the Functional Food Potential of the Bioactive Compound in *Solanum torvum*

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ABSTRACT

The focus of this chapter is to analyze the phytomedicinal value of *Solanum torvum* and its potential ability in medicines. With its rich nutritional values, bioactive components, and diverse physicochemical properties, *Solanum torvum* is poised to be a significant resource for the development of food products. Specific secondary metabolites enable most plants to possess medicinal properties. These secondary metabolites, known as phytochemicals, are compounds synthesized by plants. *Solanum torvum* (Turkey berry) is widely accepted as safe for consumption when utilized in moderation as a food or traditional herbal remedy. Certain components of the *Solanum torvum* have been correlated with advantageous human health features. The outcomes of this study imply that the utilization of S. torvumfruit extract alongside conventional antibiotics could serve as a valuable adjunct therapy, paving the way for the creation of a more efficient treatment option.

Keywords: phytochemical, *solanum torvum*, medicinal vaue, health, treatment.

INTRODUCTION

Solanum torvum is generally known as turkey berry. A crucial medicinal plant commonly found in tropical and subtropical regions is extensively used as a food source and in traditional medicine globally. It contains several metabolites in significant amounts, with specific compounds demonstrating beneficial biological properties primarily attributed to steroid glycosides and saponins, flavonoids, vitamin B group, vitamin C, iron salts, and steroidal

alkaloids. Turkey berry was first found in Columbia County, Florida, in 1899, and has since been identified in a minimum of nine countries across peninsular Florida. It grows in clusters of small green spheres. They have a thin flesh and are filled with many flat, round, brown seeds [1]. This particular plant, known for its Ayurvedic properties, is commonly incorporated into Ayurvedic treatments due to its sedative, diuretic, and digestive attributes. Furthermore, it is utilized in cough treatments and is recognized as a potent liver tonic. In India, the dried leaf powder is specifically used as a medicinal aid for individuals with diabetes [2]. Many plants possess medicinal properties as a result of containing basic chemical elements like selenium or chromium, or phytochemicals, of which thousands have been identified and studied. While certain phytochemicals may not impact human health, others can pose risks. However, a significant number of these compounds have been found to exhibit various advantageous biological activities, including anti-cancer, antimicrobial, anti-oxidant, anti-diarrheal, analgesic, and wound healing properties [3,4].

Traditional medicinal uses

India possesses a diverse collection of medicinal plants, making it a treasure trove of genetic resources in this field. It stands as one of the wealthiest nations globally in terms of the abundance of medicinal plant species. The utilization of these plants, particularly in India, plays a vital role in advancing primary healthcare on a global scale [17]. Recognized for its pharmacological significance, *Solanum torvum* is a notable species within the Solanaceae family. Ayurveda and the Chinese Pharmacopoeia have both emphasized the traditional medicinal properties of*Solanum torvum*. Traditionally it is used to cure cold, cough, cracked foot, reduce body heat, asthma, diabetes, hypertension, liver disease, tuberculosis, diabetes mellitus. It also acts as anti-anemic, anti-cancer and vermifuge [9, 10, 12].

PLANT MATERIAL

Solanum torvum, this spiky shrub is quite tall, growing to a height of 2-4 m. It has multiple branches and forms a dense thorny thicket. The stem and branches are adorned with only a few prickles. The leaves are simple, with a petiole, and are arranged alternately or in uneven pairs or triplets. They have an ovate to lanceolate shape, measuring approximately 7.5-25 cm in length. The leaf margins can either be completely smooth or slightly lobed. The plant produces clusters of small white flowers that have a star-like shape. These flowers are characterized by sepal lobes that are broadly triangular to ovate-lanceolate. The fruits of this shrub are small, about 1 cm in diameter, and have a succulent, green, and round appearance. Inside the fruits, you can find numerous flat, round, brown seeds. When fully ripe, the fruits turn yellow. [4, 5].

Sample Collection and Preparation

The turkey berry was collected by separated from the stem, cleaned and shade dried, then powdered and passed through mesh, and stored in an airtight container.

Extract preparation

In a 250 milliliter Erlenmeyer flask, 50 milliliters of 70% methanol and water were combined with 5 grams of each dried ground seed. The mixtures were agitated every 15 minutes for a total of 1 hour. Following this, the mixtures were allowed to stand for 48 hours with occasional shaking, and then filtered through 125millimeter filter paper to eliminate solid particles. The resulting [6].

QUALITATIVE PHYTOCHEMICAL ANALYSIS

The extracts were subjected to qualitative chemical screening to identify different classes of active chemical constituents. Following established protocols, the extracts were determined to contain specific qualitative phytochemicals (such as tannins, saponins, flavonoids, alkaloids, phenols, glycosides, steroids, and terpenoids). [7, 8, 9, 17].

Test for tannins (Ferric chloride test).
A quantity of approximately 200 milligrams of plant extracts was boiled in the presence of 10 milliliters of distilled water. Subsequently, 0.1% Ferric chloride was added to the solution. The resulting mixture was then monitored for a blue-black tinge, which would confirm the presence of tannins

Test for Alkaloids
Upon dissolving the plant extract in 100 ml of water and filtering it, the resulting solution underwent steam treatment with 2 ml of the filtrate and three drops of 1% HCl. Then, 1 ml of the heated mixture was combined with 6 ml of the Mayer-Wagner reagent. The appearance of a cream or brown-red precipitate indicated the presence of alkaloids

Test for Saponins
Agitation followed the combination of about 0.5 milliliters of the extract with 5 ml of distilled water. The presence of saponins was verified by the formation of foam.

Test for Flavonoids and Glycosides
A combination of 200 mg of plant extract with 10 ml of ethanol was filtered. The mixture of two ml of the filtrate, concentrated HCl, and magnesium ribbon was created. The emergence of a pink or red color suggests the existence of flavonoids. The addition of 1 ml of distilled water and NaOH to 0.5 ml of crude extract resulted in a yellowish color, indicating the presence of glycosides.

Test for Steroids
The presence of steroids is indicated by the formation of a bilayer (consisting of a red top layer and a greenish bottom layer) when approximately 1 ml of the crude extract is mixed with 10 ml of chloroform and 10 ml of sulfuric acid

Test for Terpenoids
By conducting the terpenoid test, the presence of terpenoids was determined based on the observation of a reddish-brown color. This test required the combination of 0.5 ml of crude extract, 2 ml of chloroform, and 3 ml of sulfuric acid

Test for Phenols
By mixing about 1 ml of the extract with three drops of FeCl3 and 1 ml of K2Fe(CN6), the formation of greenish-blue forms provided confirmation of the presence of phenols.

Test for carbohydrates (molisch's test)
Roughly 2 grams of extract were dissolved in 5 milliliters of distilled water and filtered accordingly. The resulting filtrate was then treated with 2 drops of alcoholic α naphthol solution in a test tube and shaken. Subsequently, concentrated sulphuric acid was introduced. The presence of carbohydrates was validated by the formation of a violet ring at the junction of the two liquids

Test for reducing sugar (Benedict's test)
Upon treatment with benedict's reagent, the filtrate was boiled in a thermostatic device and then placed in a water bath for 5 minutes. The observation of an orange-red precipitate confirmed the presence of reducing sugar.

Test for protein and amino acids (ninhydrin test)
A few minutes of boiling were carried out after the addition of Ninhydrin reagent to the filtrate. The observation of a blue color indicated the presence of amino acids

Test for gums and mucilage

After mixing a small quantity of ethanolic extract with water, ruthenium red solution was added. The emergence of a pink color demonstrated the presence of gums and mucilages.

Test for cardiac glycosides

The presence of cardiac glycosides can be inferred when a reddish-brown coloration appears after adding 2 ml of chloroform to 1 ml of the aqueous solution of S. torvumpowder, followed by the introduction of sulfuric acid (H2SO4).

QUANTITATIVE ANALYSIS OF PHYTOCHEMICALS

Total phenaloic content (TPC)

The determination of the total phenolic content of *solanum torvum*was conducted using Folin-Ciocalteu's assay through spectrophotometry. In a nutshell, the process involved the addition of 30 microlitres of the plant extract to 1ml of a 1:10 Folin-Ciocalteau's reagent. This combination was then incubated at room temperature for 5 minutes. Subsequently, 970 µl of a sodium carbonate (7.5%) solution was incorporated.The absorbance was measured at 735 nm using a UV/Visible Spectrophotometer after incubating for one hour at room temperature. A standard curve was established using different volumes (20-100µl) of Gallic acid (100µg/ml). The findings were presented in terms of milligrams of Gallic acid equivalent (GAE) per gram of the dried sample.4.2.

Total Flavanoid content

Flavonoids are auxiliary metabolites with cancer prevention agent action, the strength of which relies upon the number and position of free Goodness gatherings. The flavonoid levels in the extracts were assessed through the aluminum trichloride colorimetric method. A total of 100 µl of extract was mixed with 1.49 ml of distilled water, followed by the addition of 0.03 ml of a 5% $NaNO_2$ sodium nitrite solution. After 5 minutes, 0.03 ml of a 10% aluminum chloride $AlCl_3$ solution was introduced. After a 6-minute settling period, 0.2 ml of NaOH (1M) sodium hydroxide solution and 0.24 ml of distilled water were introduced into the mixture. The solution was mixed well using a vortex, and the absorbance was measured at 435 nm. The total flavonoid content was determined by utilizing a standard catechin calibration curve, and the results were reported in milligrams equivalent of catechin per gram of extract. [14].

DETERMINATION OF VITAMINS

Different types of antioxidant compounds, such as Vitamin A, Vitamin C, Vitamin E, carotenoids, lutein, and lycopene, can be found in plants.The development of cancer has been extensively studied, and the findings from numerous recent studies have consistently highlighted the crucial role played by hydroxyl radicals and the superoxide anion. These biological reactive oxygen species have been firmly linked to the pathogenesis of cancer.Compound possessing a high level of reactivity in reducing oxygen species may have the potential to inhibit the development of cancer. It has been established through various studies that phenolic compounds and polyphenols, as secondary plant metabolites, are excellent scavengers that help prevent the formation of free radicals [13].

Determination of Vitamin A (β-Carotene)

The immature fruits underwent an extensive washing process utilizing tap water, and subsequently, they were blended with a small quantity of water. The mixture was sieved and then carefully transferred into a sanitized bottle for storage. A measured portion of approximately 10 ml from the sample was meticulously placed into a mortar. Anhydrous sodium sulfate was added to eliminate any remaining water in the sample, followed by the gradual addition of 45 ml of acetone while grinding. The blend was subsequently filtered, and the resulting liquid was transferred to a separation funnel with 20 ml of petroleum ether. The sides of the funnel were washed with water using a wash bottle until the aqueous layer was no longer cloudy. The organic layer was filtered through filter paper with the addition of some anhydrous sodium sulfate. A small test tube received 2 ml of the organic layer, which was then evaporated to dryness using nitrogen gas. In order to reconstitute the sample, a mixture of 700 µl methanol and

dichloromethane in a 50:50 ratio was used. Subsequently, 20 µl of the reconstituted sample was injected into a Shimadzu HPLC system, which was equipped with an ODS C18 column. The analysis was conducted using a mobile phase consisting of acetonitrile, dichloromethane, and methanol in a ratio of 70:20:10, and the analysis mode employed was isocratic. The analyte was monitored [15].

Determination of Vitamin C

By combining roughly 50 grams of fruits and 200 milliliters of water, a representative juice was produced through the process of blending and sieving. Subsequently, 5 milliliters of metaphosphoric acid/acetic acid and 2 milliliters of the juice were carefully transferred into an Erlenmeyer flask for titration with indophenol dye [15].

ANTIMICROBIAL ACTIVITY TEST

The antibacterial efficacy of the extracts was thoroughly assessed using the diffusion technique on a nutrient agar medium. The suppressive impact on microbial proliferation was quantified in terms of millimeters of diameter of the inhibition zone, and these measurements were juxtaposed with those obtained from a commercially available antibiotic.The test microorganisms were inoculated in the nutrient agar by spread plate. The 6 mm wells were created utilizing asepticcork borer in every petriplate, and the extracts were introduced in different concentration. A control well devoid of the test compound served as a reference. Subsequent to this, the petri plates were incubated at a temperature of 37ºC for 48 hours. The resulting area of inhibition was subsequently measured and quantified [11].

RESULT AND DISCUSSION

Preliminary phytochemical screening results

The presence of various secondary metabolites was confirmed by qualitative phytochemical tests on the aqueous and methanol extracts. The results were obtained as in the following table 1.

The presence of tannin and phenols in fruit possess anti-inflammatory activity by inhibiting the production of inflammatory mediators. Tannin also helps in maintaining the lower the systolic and diastolic Blood Pressure. The existence of assists lowering the cholesterol. The methanol extract of *Solanum torvum* was found to contain flavonoids, sterols, and triterpenes, indicating a potential association with its anti-ulcer properties [4, 11].

Quantitative analysis of phytochemicals results

The quantitative phytochemical analysis of *solanum torvum* were performed. The results were obtained as in the following table.2

Determination of vitamins result

The result for vitamins present in *solanum torvum* are tabulated in table.3. The occurrence of vitamin C in *Solanum torvum*hinder us from the oxidative stress. virus and bacterial infections, protection of the blood vessel wall,assimilation of iron and has an important antioxidant activity. The presence of pro vitamin Ahelpbody's natural defence against illness and infection that is make the immune system works properly, and improve vision in dim light [4].

Antimicrobial test results

Antimicrobial test results were recorded as in table 4. The direct antibacterial effects of S. torvum can be attributed to the presence of flavonoids, which effectively inhibit nucleic acid synthesis, cytoplasmic membrane function, and energy metabolism. The extracts exhibit a strong ability to combat bacteria, due to the flavonoids and polyphenolic tannins they contain. Upon evaluating methanolic extracts from various plant parts, it has been determined that the leaves and fruits contain a higher concentration of these chemical compounds, which are responsible for inhibiting microbial activities.

CONCLUSION

Solanum torvum fruit possesses potential Therapeutic value and antimicrobial effect against all tested pathogenic bacteria which correspond to its phytochemical constituents. The plants should be study to support its therapeutic uses. The wealth of nutritional values, bioactive components, and diverse physicochemical properties found in *Solanum torvum* make it an ideal candidate for the innovation of food products. Additionally, this study suggests that it can be safely consumed as a food source and utilized as a medicine, without any known adverse effects. The presence of bioactive components prevents prostate, breast and colon cancer, acts against oxidative stress and maintaining blood Pressure. The existence of each bioactive compound helps in different ailment. "Food is medicine and the right kind of relationship with food can make a positive impact on your health". In future will cure the disease or illness with nutritive food.

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Table.1 Preliminary phytochemical screening results

Test	Water extract	Methanol extract
Tannin	+	+
Alkaloid	+	+
Saponins	+	+
Flavonoid	+	+
Steroids	+	+
Terpenoids	-	-
Phenol	+	+
Carbohydrates	+	+
Reducing sugar	+	+
Protein/amino acid	+	+
Gums/mucilage	-	-
Cardiac glycosides	+	-

Table 2. Quantitative analysis of phytochemical in *Solanum torvum*

Test	Aqueous extract
Total phenolic content (TPC)	650.9 mg GAE/100g of extract
Total flavonoid content (TFC)	105.7 mg QE/100g of extract

Table 3. Determination of vitamin in *Solanum torvum*

Vitamin	mg/100g
Vitamin C	3.21
proVitamin A (β-Carotene)	0.22

Table 4. antimicrobial activity of *Solanum torvum*

microorganisms	Water extract			Methanol extracat (µg/ml)			Standard (ciprofloxacin)
	50(µg/ml)	100(µg/ml)	150(µg/ml)	50(µg/ml)	100(µg/ml)	150(µg/ml)	
Bacillus subtilis	6mm	11mm	15mm	4mm	8mm	13mm	18
Staphylococcus aureus	4mm	9mm	13mm	5mm	10mm	13mm	16
Pseudomonas aeruginosa	5mm	8mm	12mm	4mm	7mm	11mm	18
Escherichia coli	5mm	12mm	16mm	4mm	9mm	11mm	17

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RESEARCH ARTICLE

Enhancement of Nifedipine Solubility using Biocompatible and Pharmaceutical Solvents : A Comparative Study

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ABSTRACT

The solubility profile of the poorly soluble drug nifedipine was evaluated using biocompatible solvents, such as glycerin, propylene glycol, and ethanol, alongside pharmaceutical solvents, including dioxane, hexane, and ethyl acetate. This investigation focused on enhancing the aqueous solubility of nifedipine using biocompatible solvents. Chemical and physical behavior of solvents and drug, specifically intermolecular interactions, and hydrogen bonding, were pivotal in augmenting aqueous solubility. Notably, solvents with lower polarity demonstrated a greater capacity to enhance aqueous solubility, underscoring the significance of hydrophobic interaction mechanisms. The hierarchy of co solvents in enhancing the solubility of nifedipine in aqueous solution was assessed to be ethanol > propylene glycol > dioxane > glycerin. Additionally, the solubility of drug (nifedipine) in blends of hexane, ethyl acetate, and

ethanol was investigated, yielding a detailed solubility spectrum. This research generated a crucial dataset for comparing the solubilizing efficacy of various co solvents on nifedipine.

Keywords: Solubility, nifedipine, co solvency, aqueous solubility.

INTRODUCTION

When a drug candidate's aqueous solubility is insufficient for liquid formulations, co solvents are frequently used to enhance solubility (1,2). Solubilization involves creating a thermodynamically stable solution of a substance that is typically insoluble or minimally soluble in a single solvent, by incorporating one or more amphiphilic agents (3,4). This process enables the creation of a homogeneous solution, overcoming the limitations of poor aqueous solubility. Enhancing the solubility of poorly water-soluble drugs is a crucial step in formulation development. Various pharmaceutical techniques, including cosolvency, buffering, surfactant addition, and complexation, are commonly employed to improve the solubility of drugs with limited aqueous solubility (5-13). Among these methods, co solvency is the most widely used approach for developing liquid formulations intended for oral administration, ophthalmic solutions, injectables, and other applications. Researchers Modi and Tayade investigated the impact of polyethylene glycol (PEG) on increasing the aqueous solubility (AS) of valdecoxib, exploring its potential as a solubility enhancing agent (8). Research conducted by Seedher and Bhatia *et al.* (14) revealed that the aqueous solubility (AS) of Cox-II inhibitors and nimesulide can be substantially improved through the addition of ethanol as a cosolvent. The use of propylene glycol to enhance the solubility of meloxicam was extensively studied (9). Methyl paraben, propyl paraben, alprazolam, benzoic acid, phenobarbital, phenacetin, and acetanilide were proved to be more soluble in presence of glycerin (15). While co solvency is a viable approach, its application can be restricted by the limited concentration of co solvent that can be utilized and the risk of precipitation upon dilution.

Alternatively, complexation techniques have proven effective in enhancing the aqueous solubility (AS) of nifedipine (NIF), with successful outcomes achieved through complexation with various agents, including salicylates, phenolic ligands, nicotinamide, etc. (16). Studies have demonstrated that the solubilization of nifedipine by nicotinamide is primarily influenced by the ligand's hydrophobic properties, rather than its aromatic structure, emphasizing the key role of hydrophobic interactions in this process (17). A comprehensive study utilizing UV absorption spectroscopy and HPLC was conducted to investigate the solubilization behavior of NIF in binary and ternary mixed micellar systems composed of sodium cholate and non-ionic surfactants, including polysorbate and polyoxyethylene. The research examined the interactions between surfactants, their impact on micelle aggregation number, drug solubility, solubilization site, and the interactions between surfactants, drugs, and drugs themselves, providing a detailed understanding of these complex systems (18).NIF, a member of the dihydropyridine class, is a commonly prescribed calcium channel blocker utilized in the management of hypertension and angina pectoris, owing to its ability to dilate coronary blood vessels and improve cardiovascular function. NIF is also used as antiarrhythmic drug. Chemically NIF is dimethyl 1,4-dihydro-2, 6-dimethyl-4- (2-nitrophenyl) pyridine-3, 5-dicarboxylate (19-21). Nifedipine (NIF) is classified as a Class II drug (22, 23), characterized by its poor solubility, which necessitates the development of effective solubility enhancement strategies. While various solubilization techniques have been extensively investigated, the co solvency approach remains an area that warrants further exploration to unlock its potential in improving the solubility of NIF. According to FDA data, co solvents are utilized in approximately 13% of approved parenteral products. This study aimed to explore the impact of four commonly used solvents - dioxane, ethanol, propylene glycol (PG), and glycerin - on the aqueous solubility (AS) of Nifedipine (NIF). Notably, these selected solvents are components in 66% of FDA-approved parenteral products (24). Furthermore, this research investigated the co solvency effects of specific organic solvent blends to expand the understanding of solubility enhancement.

MATERIALS AND METHODS

Materials

NIF was provided as a complimentary sample by Torrent Pharma Ltd, Mumbai. The entire work was conducted using double-distilled water that had been prepared in the lab. Other chemicals used were of research grade. To calculate solubility, GW BASIC an in-house developed programme was utilized. The statistical functions of the MS-Excel programme were used to do a regression analysis on the experimental data. The MS Office Excel (2022) was used to create the graphs. Standard statistical techniques were used to calculate various statistical parameters.

Methods

Drug Estimation

NIF was quantified in 0.1 N hydrochloric acid solutions at a maximum wavelength (λ_{max}) of 340 nm using a UV spectrophotometer (1700 Shimadzu, Japan), obtained wavelength matches to reported literatures on NIF (25). The calibration curve for NIF followed Beer-Lambert's law (5-30 µg/mL) with a R^2 of 0.9983. The obtained equation is represented as $y = 0.0152\ x+0.0073$, was used for estimation.

Solubility Determination

A 10 ml volume of solvent or solvent mixture was placed into 50 ml stoppered volumetric flasks. Approximately 100 mg of NIF, an excess amount of the drug, was then added to each flask. A cryostatic shaker bath (Research and Test Equipments, Bangalore, India) was used to shake the flasks at a consistent temperature of 25°C ± 1°C for 72 hours, ensuring precise control over the experimental conditions (26, 27). After this period, samples were taken, filtered through a 0.22 µm filter, and appropriately diluted. These samples were then examined for NIF at a wavelength of 340 nm. All solubility tests were executed in triplicate.

RESULTS AND DISCUSSION

Solubility in pure solvents

The solubility data for NIF in water and different organic solvents at a temperature of 25°C are summarized in Table 1. Due to its predominantly nonpolar nature, NIF is anticipated to have poor solubility in water, as it cannot effectively disrupt the water lattice structure. The experimentally determined octanol-water partition coefficient (log *P*=3.14), indicates that NIF is well-soluble in lipophilic solvents (28-31). Table 1 displays the dielectric constants (ε) of the solvents, gathered from existing literature (32-34). A clear trend emerges, showing that as solvent polarity increases, drug solubility decreases. This suggests that solvent polarity is a key factor influencing drug solubility. The solubility of NIF exhibits a positive correlation with the hydrophobic character of the solvent. Nevertheless, the solubility process is influenced by a complex interplay of factors, extending beyond merely hydrophobicity and polarity. High solubility in ethyl acetate and ethanol may be likely an extensive hydrogen bonding shown by NIF. These results revealed the presence of two distinct interaction types: hydrogen bonding and hydrophobic interactions. The molecular structure of NIF corroborates these findings (35, 36). In hexane, a balance between hydrophobic effects and hydrogen bonding led to the expulsion of drug molecules, suggesting that either factor can dominate and influence drug solubility. Some type of self-association of solvent and solute or both might have occurred. The notable increase in solubility observed in dioxane and propylene glycol suggests that hydrophobic interactions play a dominant role in determining the solubility of the drug. Building on the solubility data gathered from the individual solvents, exploration of the use of co solvents to further enhance solubility was attempted, as discussed in the subsequent sections.

Solubility in mixed-solvent systems

This study employed a range of biocompatible co solvents including ethanol, propylene glycol (PG), and glycerin which are commonly used in pharmaceutical applications. Additionally, three organic solvents hexane, ethyl acetate, and dioxane were selected for their widespread use in various industries. The biocompatible cosolvents utilized in

this study were water-miscible solvents, widely used in pharmaceutical applications to improve drug solubility. Here, the term 'stronger solvent' refers to the solvent with the highest NIF solubility in its pure state, while water is termed the 'weaker solvent'. The solubility values of NIF in various solvent blends at 25°C are summarized in Table 2 for the biocompatible co solvents ethanol, PG, and glycerin. Whereas the solubility values for organic solvent blends are shown in Table 3. The dielectric constants of the solvent blends were determined using the equation $\varepsilon_{mix} = \varepsilon_{ws} f_{ws} + \varepsilon_{ss} f_{ss,}$ where ε represents the dielectric constant, *f* denotes the volume fraction, and the subscripts mix, ws, and ss signify the mixture, weaker solvent (water), and stronger solvent, respectively (15). Figure 1 illustrates the solubility curve of NIF in various water co solvent systems including ethanol, propylene glycol (PG), and glycerin. A consistent exponential rise in solubility is observed as the co solvent fraction increases across all systems. Notably, the solubility tends to increase as the dielectric constant of the mixture decreases. Specifically, the solubility of NIF exhibits a gradual enhancement as the concentration of ethanol is incrementally increased. The solubilization of NIF is influenced by its partial polar nature, which makes it sensitive to the relative polarity of the solute and solvent. However, an unexpected decrease in solubility is observed at 80 and 100% v/v water-ethanol mixtures, suggesting that specific interactions between the solute and solvent are at play. This deviation indicates that factors beyond mere polarity, such as molecular interactions and solvent-solute compatibility, also significantly impact the solubility of NIF. Solubility of enrofloxacin, benzoic acid, phenobarbital, and acetanilide, increased with increase in propylene glycol (37-40), and similar result was found with NIF. The degree of solubilization by each co solvent is improved with the decline in the solvent system polarity. Meloxicam and rofecoxib (36) solubilities are directly proportional to PG concentration, which agrees with NIF solubility in PG-water system and dioxane-water system. However, glycerin exhibited much lower increase in AS of NIF. Together with water, the co solvents generated a uniform mixture. Since the co solvents tend to be less polar than water, leads to diminished polarity in blended form than pure water (33, 34). This study reveals that ethyl acetate is the most potent co solvent, whereas glycerin is the least effective. The co solvents' solubilizing power on NIF follows the order: dioxane > ethanol > PG > glycerin. This hierarchy highlights the differences in their ability to enhance NIF solubility. Furthermore, the solubility of non-polar solutes in semi-aqueous solutions has been observed to follow an exponential relationship with co solvent concentration, which can be expressed mathematically as follows,

$$\text{Log } [D_{tot}] = \log [D_u] + \sigma [C] \quad (1)$$

Where $[D_{tot}]$ is the total apparent drug solubility, $[D_u]$ is the drug solubility in water, [C] is the co solvent concentration, σ is the co solvent solubilizing power of the solute (41, 42). Co solvents typically decrease the chemical potential of a solution by disrupting water's hydrogen bonding network, resulting in a less polar bulk environment that enhances drug solubility. The solubilization power of a co solvent is directly related to its non-polarity, with higher σ values indicating greater solubilization capacity. As expected, ethanol's lower polarity corresponds to its improved solubilization performance. The σ values presented in Table 4, calculated from equation (1) at [C] values above 0.10, suggest that drug molecules exhibit a greater affinity for non-polar environments than polar (aqueous) surroundings. The solubility of NIF is presented in both mg/ml and mole fraction (Tables 1 to 5). Interestingly, the trends seen in mg/ml solubility and mole fraction solubility (MFS) differ, which is contrary to common expectations. This suggests that solubility values for a given series of solvents can vary based on the concentration units used. Paruta highlighted that the interpretation of solubility data is heavily influenced by the units chosen to represent concentration (39). In this study, two factors contribute to the differing trends between mole fraction and mg/ml solubility data. MFS is affected by two main factors like concentration of the solute in mg/ml and the molecular weights of the solute and solvent. Furthermore, when assessing solubility across different solvents, the solute's molecular weight remains constant but the solvent's molecular weight varies between solvents. If the mg/ml solubilities show minimal variation across solvents, the molecular weight of the solvents can play a significant role in determining MFS, potentially lead to a reversal of solubility trend under specific situations. For NIF, the solubility trends in mg/ml and mole fraction differ between the water-ethanol and water-propylene glycol systems. Interestingly, these trends align in the water-glycerin system, likely due to the very low solubility in the latter, where neither the mg/ml nor the molecular weights (solute and solvent) have a significant impact. NIF exhibits the highest solubility in ethyl acetate compared to other solvents, and this holds true for both mg/ml and MFS.

Solubility data implication

The AS of NIF is approximately 0.01 mg/ml which is supported by literature value (35). Thus, NIF solubility is boosted via co solvency technique as explained earlier. Though co solvents increased the solubility, attention should be given in selecting the proportion of co solvents to be used while preparing the formulations as they were found to produce irritation. The available NIF tablet doses in pharmaceutical market are 10, 20, and 30 mg. Drugs with poor solubility often have a favorable HLB for permeating gastrointestinal membranes making dissolution the crucial factor in determining their bioavailability. Lipophilic drugs often face formulation challenges due to their poor aqueous solubility (AS), which can impede their therapeutic potential. Formulating NIF liquid orals requires careful selection and proportioning of co solvents. Though NIF liquid preparations are available in the market, the solubility data generated in this investigation would further enhance designing efficiency of NIF liquid formulations. The least NIF tablet dose is 10 mg. Hence efforts were made to formulate oral liquids. Thus, 10 mg of the solutions in 5 ml and 10 ml were made. Co solvent solubilization plays a critical role in parenteral dosage forms, where the goal is to dissolve the required dose in the least volume possible as a true solution. Injections were formulated in accordance. The injections are typically formulated via minimum volume feasible. The goal of developing injections with 5 mg of active ingredient in either 1 ml or 2 ml has been accomplished in this investigation. An analogous endeavor was undertaken to develop the solutions for the 20 mg oral and 10 mg injectable formulations. Table 5 outlines the solvent systems that are suggested to simplify NIF liquid orals and injections.

Precipitation on Dilution

When the formulation is diluted, the active components in certain products developed with co solvent- solubilized drugs possibly precipitate (43). This phenomenon can happen in various contexts, including within the bloodstream, *in vitro* environments, during intravenous infusions, or at intramuscular injection sites. The precipitation of drug particles poses several potential risks. Mechanically, these particles can irritate or obstruct blood vessels, which may lead to complications such as thrombosis or embolism. Additionally, localized high concentrations of the precipitated drug can induce local toxicity, potentially causing tissue damage or adverse reactions at the site of administration. Furthermore, precipitation can significantly reduce the systemic bioavailability of the drug, compromising its therapeutic efficacy. To mitigate these risks, the prepared injection formulation underwent rigorous testing to detect any precipitate formation. Analytical techniques such as UV spectrophotometry and visual inspection were employed to monitor the stability of the formulation under various conditions. The results indicated that there was no precipitation observed, either upon dilution or after six weeks of storage. This stability suggests that the formulation maintains its solubilized state, ensuring consistent drug delivery and minimizing the risk of adverse effects associated with precipitation.

CONCLUSION

The potential mechanisms underlying the interaction between NIF and co solvents likely involve a combination of hydrogen bonding, hydrophobic interactions, and electron donor-acceptor interactions. However, the extent to which these forces enhance solubility is constrained by conformational changes occurring between the molecules, which limit the formation of stable bonds. The study investigated and compared the solubility enhancement of NIF using six distinct co solvents individually. Ethanol being the biocompatible solvent with highest solubilizing power has been an acceptable co solvent in formulation development. This study generates a comprehensive dataset for the solubilization of NIF using various pharmaceutically accepted co solvents, providing valuable insights for the formulation of liquid oral dosage forms and injections of NIF. Furthermore, the solubility data of drugs in organic solvents will have far-reaching applications in other areas of the pharmaceutical industry.

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Table.1: **Solubility of NIF in various solvents at 25°C (40)**

Solvent	Dielectric constant	Solubility of NIF (Average ± SD)	
		mg/ml	MFS
Water	78.36	0.0100 ± 0.0027	5.2146E-07 ± 1.4241E-07
Glycerin	42.50	0.1264 ± 0.0046	2.6620E-05 ± 9.6897E-07
PG	32.00	4.6605 ± 0.1654	9.7 E-04 ± 3.4404E-05
Ethanol	24.30	14.8664 ± 1.1310	2.5 E-03 ± 1.9 E-04
Ethylacetate	6.02	62.1551 ± 18.3969	1.73 E-02 ± 5.0 E-03
Hexane	5.00	0.0081 ± 0.0013	3.0628E-06 ± 4.7556E-07
Dioxane	2.21	4.6203 ± 0.1854	1.2 E-03 ± 4.7117E-05

Note: n=3 with standard deviation

Table 2: **Solubility data of NIF in water-co solvent blends**

Water (% vv)	Water-Ethanol system		Water-PG system		Water-Glycerin system	
	mg/ml	MFS	mg/ml	MFS	mg/ml	MFS
00	14.866 ± 1.13	0.0025 ± 0.0002	4.6605 ± 0.1653	0.0010 ± 0.00003	0.1263 ± 0.0046	2.662E-05 ± 9.690E-07
10	17.015 ± 4.52	0.0023 ± 0.0006	5.4271 ± 0.2369	0.0009 ± 0.00004	0.1048 ± 0.0019	1.693E-05 ± 3.019E-07
20	11.492 ± 0.83	0.0013 ± 0.0001	3.1971 ± 0.0114	0.0004 ±0.000001	0.0837 ± 0.0005	1.097E-05 ± 6.891E-08
30	11.800 ± 0.51	0.0012 ± 0.0001	2.3364 ± 0.0932	0.0003 ± 0.00001	0.0490 ± 0.0007	5.407E-06 ± 8.237E-08
40	5.328 ± 3.54	0.0005 ± 0.0003	1.0059 ± 0.0604	0.0001 ± 0.00001	0.0432 ± 0.0014	4.107E-06 ± 1.323E-07
50	1.668 ± 0.21	0.0001 ± 0.00002	0.4073 ± 0.0132	0.00003 ± 0.000001	0.0291 ± 0.0007	2.432E-06 ± 6.054E-08
60	1.090 ± 0.38	0.0001 ± 0.00003	0.1647 ± 0.0073	0.00001 ± 0.000001	0.0221 ± 0.0009	1.650E-06 ± 6.382E-08
70	ND	ND	0.0735 ± 0.0036	0.000005 ± 0.0000002	0.0188 ± 0.0013	1.266E-06 ± 8.601E-08
80	0.083 ± 0.01	0.000005 ± 0.000001	0.0374 ± 0.0074	0.000002 ± 0.0000005	0.0155 ± 0.0005	9.546E-07 ± 3.262E-08
90	ND	ND	ND	ND	0.0130 ± 0.0005	7.311E-07 ± 2.673E-08
100	0.010 ± 0.003	0.000001 ± 0.0000001	0.0100 ± 0.0027	0.000001 ± 0.0000001	0.0100 ± 0.0027	5.220E-07 ± 1.426E-07

Note: n=3 with standard deviation

Table 3: **Solubility data of NIF in solvent-co solvent blends**

Solvent-Co solvent (% vv)	Water - Dioxane system		Ethylacetate - Hexane system		Ethylacetate - Ethanol system	
	mg/ml	MFS	mg/ml	MFS	mg/ml	MFS
00-100	4.6202 ± 0.1854	0.0012 ± 0.00005	0.0081 ± 0.0013	3.0628E-06 ± 4.7556E-07	14.8664 ± 1.1310	0.0025 ± 0.0002

10-90	7.3754 ± 0.1584	0.0014 ± 0.00003	ND	ND	25.3614 ± 3.0109	0.0044 ± 0.0005
20-80	8.8033 ± 0.1054	0.0013 ± 0.00002	ND	ND	39.1590 ± 1.7383	0.0071 ± 0.0003
30-70	ND	ND	ND	ND	49.0145 ± 1.9711	0.0093 ± 0.0004
40-60	5.9168 ± 0.1643	0.0006 ± 0.00002	ND	ND	58.2129 ± 2.2760	0.0116 ± 0.0004
50-50	2.3167 ± 0.1515	0.0002 ± 0.00001	3.0635 ± 0.3601	0.00099 ± 0.00011	63.0311 ± 1.5173	0.0131 ± 0.0003
60-40	0.8011 ± 0.0137	0.0001 ± 0.000001	ND	ND	39.5970 ± 6.3814	0.0087 ± 0.0014
70-30	0.4420 ± 0.0832	0.00003 ± 0.00001	ND	ND	86.9032 ± 3.9604	0.0201 ± 0.0009
80-20	0.1320 ± 0.0088	0.00001 ± 0.0000005	ND	ND	73.7626 ± 16.3907	0.0180 ± 0.0039
90-10	0.0624 ± 0.0040	0.000004 ± 0.0000002	ND	ND	72.4485 ± 3.9604	0.0188 ± 0.0010
100-00	0.0100 ± 0.0027	0.000001 ± 0.0000001	62.1551 ± 18.3968	0.0173 ± 0.0050	62.1551 ± 18.3968	0.0172 ± 0.0050

Note: n= 3 with standard deviation, ND-Not Done

Table 4: **Solubilization powers for different solvent-co solvent blends**

Solvents blend		**Concentration range, % v/v**	**Stronger solvent solubilization power 'σ' value**
Solvent (weaker solvent)	**Co solvent (stronger solvent)**		
Water	Ethanol	00-100	9.2059
Water	PG	00-100	6.6597
Water	Glycerin	00-100	2.0956
Water	Dioxane	00-100	6.9848
Hexane	Ethylacetate	00-100	2.5778
Ethylacetate	Ethanol	00-100	-0.5251
Ethanol	Ethylacetate	00-100	1.8364

Table 5: **Water-co solvent systems indicated for NIF formulations of 5 mg and 10 mg doses.**

Proposed solvent blends (10 mg liquid oral dose)		**Proposed solvent blends (20 mg liquid oral dose)**	
5 ml (2 mg/ml)	10 ml (1 mg/ml)	5 mL (4 mg/mL)	10 mL (2 mg/mL)
Co solvents Ethanol > 50 % PG > 60 %	**Co solvents** Ethanol > 40 % PG > 50 %	**Co solvents** Ethanol > 50 % PG > 80 %	**Co solvents** Ethanol > 50 % PG > 60 %
Proposed solvent (5 mg injection dose)		**Proposed solvent (10 mg injection dose)**	
1 ml (5 mg/ml)	2 ml (2.5 mg/ml)	1 ml (10 mg/ml)	2 ml (5 mg/ml)
Co solvents Ethanol > 50 % PG 90 %	**Co solvents** Ethanol > 50 % PG 70 %	**Co solvents** Ethanol > 60%	**Co solvents** Ethanol > 50 % PG 90 %

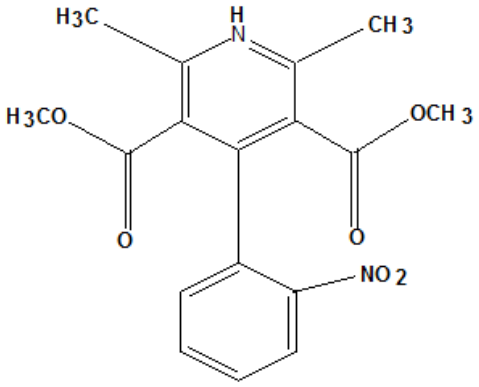

Figure. 1: Nifedipine

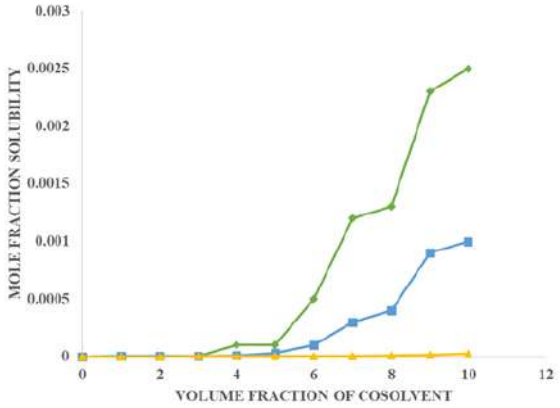

Figure.2: Solubility data of NIF in water-co solvent mixtures; Co solvents [ethanol (♦), PG (■), and glycerin (▲)]

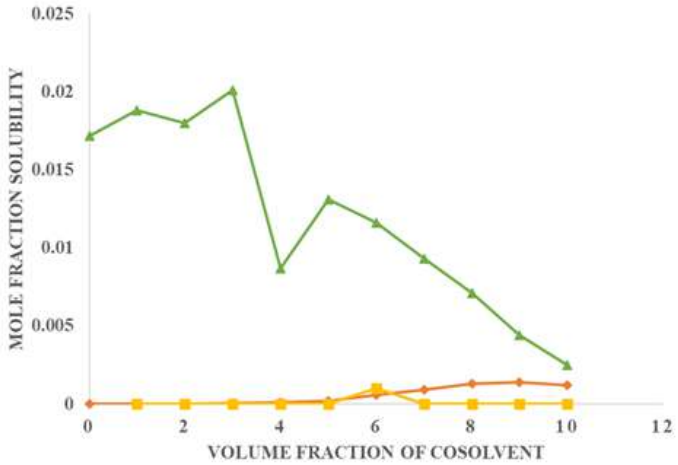

Figure.3: Solubility data of NIF in solvent blends; Co solvents [dioxane-water (♦), hexane- ethylacetate (■), and ethylacetate-ethanol (▲)]

RESEARCH ARTICLE

Effect of Different Concentrations of Hair Dye on Meristematic Cells of *Allium cepa* L. Root Tip

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ABSTRACT

Ageing is the process of becoming older. Hair is originally white. It gets pigment, melanin, through specialized cells called melanocytes. These cells pump this pigment into the hair follicles that gives hair a characteristic colour. Grey hair is a precursor of white hair, and contains less or no melanin at all due to inactive melanocytes. The importance of the studies on various aspects of hair dye has received much attention in recent years. These hair dyes perform some useful functions but are not essential for the proper functioning of the body. In the present investigation, the mitotic effect of nine different concentrations of commercially available hair dye on *Allium cepa* L. root tips was conducted. Direct contact effect of hair dye and recovery also studied. Observations revealed that the hair dye had shown abnormalities in the meristematic cells of *A.cepa*. The percentage of abnormalities was found to be varied in different concentrations of hair dye.

Keywords: Hair dye, meristematic, cell division, mitotic index, metaphase, anaphase, usage dose.

INTRODUCTION

Hair is originally white. It gets pigment, melanin, through specialized cells called melanocytes. These cells pump this pigment into the hair follicles that gives hair a characteristic colour. Scientists thought that hair turned grey merely due to less or no production of melanin. Each hair has a separate melanin supply in the body. Hair is precious to all,

be it any gender and seeing them turn into a different boring colour, can be very upsetting. Although hair ageing depends largely on uncontrollable factors like genetics, the real deal is to be aware of the damaging contents and take preventive measures in order to keep the hair young even in a senile age. Now-a–days, ageing is actually not a main factor as the young people are the same victim of this curse. Genetics, heredity, air pollution, excessive stress, applying too much chemical to the hair are the main reasons behind white hair. Hair colouring is the practice of changing the colour of hair. The main reasons for this practice are cosmetic; for example to cover gray hair, to change to a colour regarded as more fashionable or desirable, or to restore the original hair colour after it has been discoloured by hairdressing processes or sun bleaching. Hair dyeing, which is an ancient art [1] involves treatment of the hair with various chemical compounds. Today, hair colouring is immensely popular, and globally hair colorants are a rapidly growing industry. The present investigation aims at studying the mitotic effect of different concentrations of commercially available hair dye along with a control of water in *Allium cepa* L.

MATERIALS AND METHODS

Test and treatment materials

The advantageous features of *A.cepa*, chosen as test material, are that, it produces a large number of roots at a very limited time and has larger chromosomes which are reported to be quite sensitive to the actives of different chemicals. Excellent mitotic preparations could be easily made and utilized to score chromosomal aberrations. Commercially available bulbs of *A.cepa,* are easily available and utilized in our daily life. The bulbs were sun dried, the outer dry scales were peeled off and the bases were razor scrapped exposing the fresh root primodial. Different concentrations of commercially available henna-based hair dye powder were used as treatment material and tap water was used as control.

Mitotic cycle

Mitotic cycle of the experimental material was first studied to determine the mitotic peak. The bulbs of *A.cepa* were allowed to germinate in tap water; in glass bowls at room temperature (25±2°). The bulbs were taken out at an interval of one hour. Root tips were harvested and fixed in a mixture of acetic acid and ethyl alcohol in the ratio 1:3, round the clock. Squash preparation made by the acetocarmine technique. Fixed root tips were first treated with 1N HCl for 30 minutes and squashed the root tips with acetocarmine. The slide was pressed between the fold of a blotting paper and examined under the microscope. Data were collected from three different fields at random from each preparation as to the number of dividing and non dividing cells. The mitotic peak of each set was calculated by using the formula

$$\text{Mitotic peak} = \frac{\text{Number of active dividing cells}}{\text{Total number of cells}} \times 100$$

Treatment

In the present investigation the mitotic effect of nine different dilutions of selected hair dye – 0.2%, 0.4%, 0.6%, 0.8%, 1%, 2%, 3%, 4%, 5% and 6.67% – in the root tips of *A.cepa* was carried out. Along with this tap water was used as the control. The bulbs of *A.cepa* were planted in separate glass bowls containing the different dilutions of samples at room temperature. The bulb of onion allowed to germinate in a glass bowl containing tap water at room temperature (25±5º) was considered as the control. The following important parameters were studied.

1. **Morphology:** Morphological observation conducted by visual only. Nature, colour and shape of the root tips were considered.
2. **Mitotic index:** Squashed root tips were observed microscopically and each dividing and non-dividing cells counted separately. Mitotic index was calculated by using the formula

$$\text{Mitotic index} = \frac{\text{Number of dividing cells}}{\text{Total number of cells}} \times 100$$

3. **Mitotic abnormalities (if any):** Abnormalities or the disorders noticed from the normal mitotic divisions were considered.

4. **Recovery:** Bulbs of onion were carefully taken out from the treatment samples and kept in a bowl with tap water for 48 hours. After that root tips were harvested and micro preparation conducted.

Harvesting of root tips

After 24 hours, sprouting of the root tips was found out. After 48 hours the roots might have attained a length of about 1-1.5 cm. Rooted onions were washed thoroughly with tap water. Control root tips also harvested along with the treated ones.

Cytological technique and aberrations scoring

For cytological studies the root tips were fixed in Carnoy's fluid. The root tips of *A.cepa* were hydrolyzed in 1N HCl at 60° for 10 minutes. They were stained by acetocarmine. Using the acetocarmine fine squash preparations were made of each treatment. From each preparation observations were made at random, from five different microscopic fields as to number of dividing and non dividing cells and abnormalities, if any. Fresh slide preparations were used for collecting the data. Aberrations were scored at all the mitotic stages and critically in metaphase and anaphase. The experiments were repeated five times and pooled data were recorded.

Treatment with usage dose

A.cepa root tips were treated with the usage dose (6.67% concentration) of selected hair dye for two durations – 30 minutes and one hour. After the treatment (T) 48 hours of recovery was also studied (R/T). The treatment conducted half and one hour before the mitotic peak. Harvested root tips are directly taken for the squash preparation.

RESULTS AND DISCUSSION

Morphology

During mitotic cycle, data collected from the fixed root tips at round the clock was found to be the mitotic peak between 9.00 am and 9.45 am. So the treatments were planned in such a way that the root could be harvested in the same time. Morphologically the harvested root tips grown in different concentrations of hair dye – 0.2%, 0.4%, 0.6%, 0.8%, 1%, 2%, 3%, 4%, 5% and 6.67% (usage dose) – had shown variation in their size, shape and colour. Compared to the control root tips, the treated ones are short and some coloured also. Root tips in dye usage dose changed the colour of the root tip into black in external appearance.

Mitotic index

A.cepa planted in ten different concentrations of selected hair dye used are labelled as T_1 (0.2%), T_2 (0.4%), T_3 (0.6%), T_4 (0.8%), T_5 (1%), T_6 (2%), T_7 (3%), T_8 (4%), T_9 (5%) and T_{10} (6.67%), along with tap water (Co) was considered as the control. *A.cepa* responded very well in all the treatments and control. Among the nine different concentrations, the mitotic index 36.98 was found to be the lowest in recovery after treatment of 0.2% of herbal dye (T_1). Treatment with different concentrations of herbal dye had shown great variation among them in mitotic index (Table 1). The mitotic index 79.03 was the highest value observed in the root tips grown in 4% of herbal dye (T_8) treatment. The control (Co) along with the treatment had shown mitotic index of 62.82 in the root tip.

Mitotic Abnormalities

Examination of the treated cells had revealed the presence of various types of mitotic abnormalities in the root tip of *A.cepa*. The important abnormalities were the formation of vacuolated, disintegrated and deeply stained nuclei, micronuclei, unoriented chromosomes, fragments, bridges, laggards and stickness of chromosome. The percentage of these mitotic abnormalities was found to be varied in different concentrations of hair dye. Among the treatments, the highest percentage of abnormality (92.06) in the root tip of *A.cepa* treated with 5% (T_9) of hair dye. The same treatment after 48 hours recovery had shown almost near value 87.97. Root tips of *A.cepa* up to 1% (T_5) were morphologically good in appearance but more than 1% concentration of hair dye had shown the abnormal growth of root tips – hook like root tips, brittle in nature, stained – and root tips had shown delayed initiation. The lack of

initiation of root tips and the decaying of the mouth of the *A.cepa* in the same concentration also resulted. So, for further studies only lower concentration (up to 1%) was considered.

Metaphase

At metaphase, a variety of abnormalities was observed with the treatment of selected hair dye (Table 2). Cells with un-oriented chromosomes, fragments, spindle abnormalities (tropokinensis) and stickiness of chromosomes (Figure 1) were observed. The highest abnormality in treatment (75.21) was observed for a concentration of 0.6% and the highest value in recovery after treatment (60.47) was also seen in same concentration of hair dye. The chromosomes exhibited spindle abnormality, fragmentation and disturbed metaphase also. The individuality of the chromosomes was lost in the treatment with higher concentration. The frequency of cells showing stickiness was found to increase with the increase in the concentration of hair dye for 48 hours treatment. Among the treatments, the hair dye 0.4% concentration in *A.cepa* root tip had shown the percentage of abnormality 64.13 and the lowest percentage of abnormality (20.90) was found in 0.2% treatment for 48 hours. Very less percentage (0.10) of abnormality was found in recovery after treatment of the control. Chromosome stickiness was found to be highest percentage (79.94) in treatment of root tip with 0.6% of hair dye and 48 hours recovery after treatment the percentage was 77.14. Cells with tropokinensis in all the treatments were found to be very less compared to all the other abnormalities. Metaphase abnormalities in treatment and recovery were not concentration dependent.

Anaphase

The abnormalities at anaphase – formation of bridges, spindle abnormality, disturbed anaphase, anaphase-telophase bridge (Figure 2), laggards, stickiness and cells with tropokinensis were observed in the treatment of different concentrations of *A.cepa* for 48 hours. At a concentration of 0.6% of hair dye had shown the highest percentage of abnormality (67.41) after treatment and same had shown 59.07 percentage of recovery after treatment (Table 3). The percentage of cells with bridges was found to be highest (96.11) on the `root tips after treatment with 0.6% hair dye concentration. The next highest anaphase abnormality of 51.32 percentages was found in 0.2% concentration of hair dye treatment. Of this the highest abnormality of 36.36 percentages was observed for cells with bridges. Among the treatments the lowest abnormality (19.81) was observed in 0.8% concentration of hair dye. Anaphase abnormalities in treatment and recovery were dose independent.

Abnormalities in the usage dose

Morphologically the root tips were deep black colour and squash preparation without acetocarmine staining had shown deeply stained chromosomes (Figure 3). A concentration of 6.67% of hair dye treatment resulted in abnormalities were mainly the chromosomes were deeply stained (black). After 48 hours recovery, the root tips had shown some elongated cells, micronuclei and condensed chromosome. It is noted that about one-third of women above 18 years and nearly 10 percent of men above 40 years of age use hair colouring in some form or other[2]. Some of the chemicals used by manufacturers in hair dye products are reported to be cancer-causing[3]. As so many people uses hair colours, scientists have tried to study whether these chemicals causes cancer in people. In early days, hair dye formulations contained aromatic amines that causes cancer in animals. Towards the end of 1970s, manufacturers changed the components in dye products to eliminate some of these chemicals[4]. Since hair colours are widely used, even a small increase in risk may have a considerable public health impact[5]. Over the years, some epidemiologic (population) studies have found an increased risk of bladder cancer in hairdressers and barbers[6]. A 2008 report of the Working Group of the International Agency for Research on Cancer (IARC) concluded that some of the chemicals these workers are exposed to occupationally are "probably carcinogenic to humans"[7]. There are several reports that a wide variety of materials like radiations, chemicals and many environmental mutagens have been found to induce chromosomal aberrations and gene mutations in plant as well as animal materials. Many scientists have studied in detail the cellular abnormalities induced by external agents. There are several reports that many plants extract like that of *Lantana camera* (L.)[8][9] and extract of *Tylophora indica*[10] had mutagenic effects on the root tip cells of *A.cepa*. A mitodepressive effect was observed in root tip cells of onion treated with the different concentrations of hair dye. Treatment with different concentrations of hair dye had shown great variation among them in mitotic index. The mitotic index 79.03 was the highest value observed in the root tips grown in 4% of hair dye (T_8) treatment. The

control (Co) along with the treatment had shown mitotic index of 62.82 in the root tip of *A.cepa*. According to Ozkara *et al* [11], the mitotic index is considered as a well founded cytogenotoxic biomarker to determine the potential of cytotoxicity. The important mitotic abnormalities found in the root tip of *A.cepa* for different concentration of hair dye treatment were the formation of vacuolated, disintegrated and deeply stained nuclei, micronuclei, un-oriented chromosomes, fragments, bridges, laggards and stickness of chromosome. The percentage of these mitotic abnormalities was found to be varied in different concentrations of hair dye. Extracts of fruits of *Lantana camera*[8], aqueous extracts of the spice coriander[12] and black pepper[13] had induced chromosomal aberrations in *Vicia faba*. Leaf homogenate of *Tylophora indica* was reported to produce unoriented chromosomes in the root tip cells of *A.cepa*[10]. According to Krisch et al[14], the micronuclei were formed due to acentric fragments or laggard chromosome caused by misrepair DNA breaks. Stickness of chromosomes was another abnormality at metaphase treated with different concentrations of hair dye. The percentage of the cells with sticky chromosomes, were found to increase with the increase in concentration. Stickness of chromosomes had been reported in *A.cepa* on treatment with the extract of betel leaf and fruit pulp of tamarinds[15][16]. Abraham and Koshy[17] had observed chromosomes stickness in the root tips cells of *A.cepa*, when treated with varying concentrations of extracts of green chillies. According to Ambrose and Ayengar [18], disruption of hydrogen bonds was responsible for chromosome breaks. Imbalance in the mitotic set up of the chromosome may be responsible for chromosome breakage[19]. In the present study, an imbalance in the mitotic setup along with breaking up of the chromatin might have lead to the formation of fragments. The results of the present investigation had revealed that the percentages of abnormalities were varied with the different concentrations of hair dye. The percentage of abnormalities was found almost same when treated as well as when the treated root tips were allowed to recover in distilled water for a period of 48 hours. The different concentrations of hair dye were capable of inducing a variety of mitotic abnormalities in the root tip cells of *A.cepa* for duration of 48 hours treatment and 48 hours recovery.

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Table 1: Effect of Selected Hair Dye on Mitotic Behaviour of *A.cepa*.

Treatment	Duration (48 hrs)	Total no. of cells	No. of dividing cells	Mitotic Index	No. of cells with abnormalities	% of cells with abnormalities
Co	T	1256	789	62.82	5	0.63
	R/T	1284	824	64.17	7	0.85
T_1	T	1178	470	39.90	94	20.00
	R/T	1206	446	36.98	44	9.87
T_2	T	1318	606	45.98	182	30.03
	R/T	1230	515	41.87	103	20.00
T_3	T	1452	754	51.93	264	35.01
	R/T	1353	610	45.08	153	25.08
T_4	T	1363	682	50.04	286	41.94
	R/T	1364	709	51.98	233	32.86
T_5	T	1399	886	63.33	425	47.97
	R/T	1452	797	54.89	303	38.02
T_6	T	1140	680	59.65	388	57.06
	R/T	1014	481	47.44	202	42.00
T_7	T	1154	788	68.28	489	62.06
	R/T	1120	630	56.25	378	60.00
T_8	T	1216	961	79.03	721	75.03
	R/T	1204	834	69.27	584	70.02
T_9	T	1106	856	77.40	788	92.06
	R/T	1011	715	70.72	629	87.97

Table 2: Metaphase Abnormalities Percentage of Different Concentrations of Hair Dye on Mitotic Behaviour of *A.cepa*.

Treatment	Duration (48 hrs)	Percentage of Cells Showing					
		Normal cells at Metaphase	Abnormal cells at Metaphase	Unoriented Chromosome	Stickiness of Chromosome	Cells with Fragments	Cells with Tropokinesis
Co	T	99.80	0.20	-	-	-	-
	R/T	99.90	0.10	-	-	-	-
T_1	T	79.10	20.90	26.00	36.00	30.00	8.00
	R/T	85.93	14.07	25.92	34.03	29.62	7.40
T_2	T	35.87	64.13	33.34	30.77	32.46	3.43
	R/T	46.18	53.82	31.07	28.15	30.64	2.12
T_3	T	24.79	75.21	10.26	79.74	6.43	3.57
	R/T	39.53	60.47	9.03	77.14	4.54	3.27
T_4	T	61.81	38.19	35.55	46.68	14.63	3.14
	R/T	69.98	30.02	32.9	43.48	13.95	3.05
T_5	T	44.72	55.28	27.38	30.54	37.57	4.51
	R/T	55.88	44.12	25.71	30.00	36.00	4.28

Table 3: Anaphase Abnormalities Percentage of Different Concentrations of Hair Dye on Mitotic Behaviour of *A.cepa*.

Treatment	Duration (48 hrs)	Percentage of Cells Showing						
		Normal cells	Abnormal cells	Cells with Bridges	Cells with Laggards	Cells with Stickiness	Spindle Abnormalities	Cells with Tropokinesis
Co	T	99.96	0.04	-	-	-	-	-
	R/T	99.96	0.04	-	-	-	-	-
T_1	T	48.68	51.32	36.36	6.06	24.25	33.33	-
	R/T	52.99	47.01	35.39	5.87	17.12	11.32	30.30
T_2	T	69.13	30.87	22.58	20.96	29.03	24.19	3.24
	R/T	74.07	25.93	21.09	19.81	28.45	22.00	2.63
T_3	T	32.59	67.41	96.11	-	3.12	0.77	-
	R/T	40.93	59.07	94.00	-	2.23	0.54	-
T_4	T	80.19	19.81	56.66	21.34	-	17.34	4.66
	R/T	84.82	15.18	53.61	19.04	-	16.56	3.56
T_5	T	52.86	47.14	60.87	-	21.74	-	17.39
	R/T	59.23	40.77	59.01	-	18.20	-	16.90

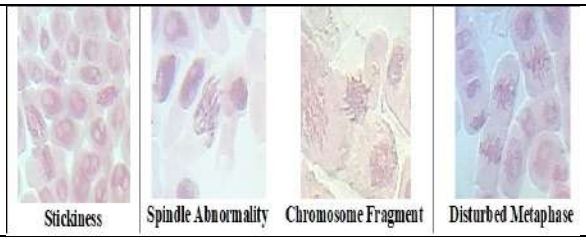

Figure 1: Metaphase abnormalities

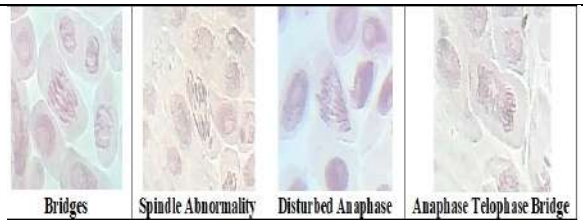

Figure 2: Anaphase abnormalities

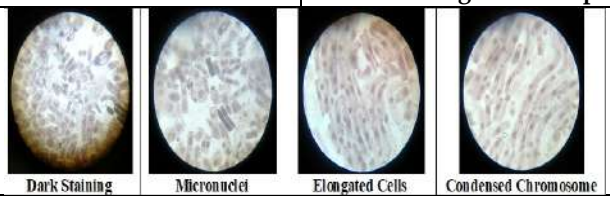

Figure 3: Usage dose abnormalities

RESEARCH ARTICLE

Machine Learning Model for Cholera Prediction

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ABSTRACT

Cholera, a severe disease, is primarily caused by poor sanitation and the ingestion of food or water contaminated with Vibrio cholerae. Despite numerous efforts to curb this menace, the epidemic continues to cause havoc in communities, especially in the developing world. Several methods have been tried to accurately predict cholera epidemics using mathematical epidemiology and spatial statistics to forecast cholera outbreaks. However, these methods have limitations, such as dependency on a few features and specific events, and recent advancements in machine learning and associated rule mining have shown promise in overcoming these limitations. This study aims to enhance cholera epidemic prediction by employing a Naïve Bayesian classification technique, utilizing a comprehensive set of cholera features from a secondary dataset obtained from the Jigawa State Ministry of Health. Five ML classifiers (DT, LR, ANN, SVM, and NB) were selected to develop a model good enough to accurately predict the cholera epidemic. The results obtained from the developed model show an improvement as it was able to achieve better accuracy and precision with the NB classifier as compared to previous studies. Furthermore, the general evaluation of the model, when compared with other researchers, indicated the model performed creditably. The significance of this study lies in its potential to provide an early warning mechanism for cholera outbreaks, thereby aiding in the design and implementation of suitable interventions. Future research should focus on testing the model with larger datasets to further improve its accuracy and reliability.

Keywords: Cholera, Classification Method, Prediction, Machine Learning Algorithms, Naïve Bayes.

INTRODUCTION

The cholera epidemic has remained a public threat throughout history, affecting vulnerable populations living with unreliable water and substandard sanitary conditions. Cholera is an acute infectious disease caused by Vibrio cholerae bacteria [1]. The bacteria typically live in salty and warm waters, such as estuaries and bodies of water, as well as in coastal areas. People develop V. cholerae after drinking liquids or eating food contaminated with the bacteria [2]. The disease has remained notorious throughout history due to the extraordinary levels of death and damage it has caused over the years and as a threat to human society. The cholera pandemic can last for many years or even several decades at a time and spread to many countries across continents and oceans [3].

Historical Pandemics

Initially, the cause of cholera was unknown, causing devastating mortality to millions of people around the world, thus contributing to massive panic in the countries where it occurred. According to the literature, there were a total of eight cholera pandemics [4]. The first cholera pandemic occurred in India from 1817 to 1824 and spread to Southeast Asia, Central Asia, the Middle East, China, and Russia, killing hundreds and thousands. The second cholera pandemic occurred in India from 1826 to 1837 and spread to western Asia, Europe, Great Britain, and America, and east of China and Japan. It caused more deaths, faster than any other epidemic disease in the 19th century. The third cholera pandemic also claimed the most deaths in the 19th century originated in India and spread well beyond its borders to Russia and Great Britain. Researchers at the University of California, Los Angeles, believe that the third cholera pandemic began as early as 1837 and lasted until 1863 [5]. From 1853 to 1854, the pandemic claimed 23,000 deaths in the UK and over 10,000 in London. As a result of the August 1854 cholera outbreak in London, John Snow identified contaminated water as the route of transmission of the disease. He mapped a cluster of cholera cases near a water pump in a neighbourhood. His breakthrough led to the fight against cholera epidemics in the 19th century [6].

Cholera in Sub-Saharan Africa

During the fourth pandemic, cholera spread across the Middle East and was brought to Russia, Europe, and North America, reaching North Africa, where it spread to Sub-Saharan Africa (SSA) and killed 70,000 people in Zanzibar, Tanzania, in 1869 [7]. Recurrent cholera outbreaks have occurred in Sub-Saharan Africa (SSA), accounting for 86% and 99% of reported cases and deaths worldwide in 2011, respectively [8]. In 2017 and 2018, cholera outbreaks were reported in seven SSA countries: Cameroon, the Democratic Republic of the Congo, Tanzania, Kenya, Mozambique, Zambia, and most recently, Zimbabwe [9].

Cholera in Nigeria

Over the last two decades, Nigeria has faced three major cholera epidemics, with the disease being endemic in northern states [10]. Although outbreaks became less common due to improved sanitation, the case fatality rate has increased. In 2016, the World Health Organisation reported that the case fatality rate doubled compared to the previous year [11]. The current outbreak poses a serious risk, especially without robust efforts to address inadequate sanitation. Nigeria has abundant surface and groundwater, but mismanagement has led to water scarcity, particularly in the north. Climate change and evapotranspiration exacerbate water shortages. Coastal floods and saline water intrusion compromise water quality in the south. As the population grows, chemical and biological industrial discharges further threaten water safety [12]. In the most recent Cholera Situation Report, Nigeria reported 1,634 suspected new cases during a week in July, with Bauchi State having the highest number of new cases. Since 2021, 22,130 suspected cholera cases and 526 deaths have been reported across 18 states, with 28% of cases affecting children aged 5–14. However, [13] found that 20 out of 36 states were affected, resulting in 43,996 cases and 836 deaths, with an attack rate of 127.43 per 100,000 population and a case fatality rate of 1.90%. Individuals aged 15 years or older were the most affected population.

Cholera Impact

Symptoms

Cholera is an extremely dangerous disease that can cause serious, acute watery diarrhea. After consuming contaminated food or water, symptoms may take anywhere from 12 hours to 5 days to appear. Both children and adults can be affected, and death can happen within hours if not treated. Most individuals infected with V. cholerae may not show symptoms at all. However, the bacteria can still be found in their faeces for about 1 to 10 days post-infection and can spread back into the environment, posing a risk to others.

Risks

Among those who do exhibit symptoms, most experience mild or moderate forms. Yet a few may develop severe watery diarrhea coupled with significant dehydration. This can indeed lead to fatal outcomes without treatment. However, cholera can be endemic or epidemic. In endemic areas, cases are detected locally over 3 years. Outbreaks in non-endemic regions are defined by ≥1 confirmed local case.

Prevention and Control

Control requires a multi-pronged approach: surveillance, water and sanitation, hygiene, social mobilization, treatment, and oral vaccines to reduce the fatality rate.

Treatment of Cholera

Cholera is easily treatable. Oral rehydration solution (ORS) can successfully treat many. Severely dehydrated patients need rapid IV fluids and antibiotics. With early, proper treatment, the fatality rate should stay <1%. Zinc is an important adjunct therapy for children under 5, reducing diarrhea duration and preventing future episodes. Breastfeeding should also be promoted.

Epidemic Modelling

In the last few decades, there have been several studies and great successes in the development of epidemic models and systems for the correct prediction of cholera. While mathematical epidemiology and spatial statistics have been used to forecast cholera outbreaks, they have limitations such as dependency on a few features and specific events. Recent advancements, including machine learning and association rule mining, have overtaken the situation. However, machine learning techniques have not been widely used in most models of cholera epidemics. Therefore, the study suggests using machine learning approaches for modelling cholera epidemics since these methods are recognized as powerful tools in healthcare today [14], [15], [16], [17], [18], and [19]. They offer superior advantages in enhanced disease diagnosis processes alongside prediction capabilities, as well as analysis and prevention efforts overall.

METHODOLOGY

The methodology adopted in this research work includes a description of how the dataset was collected and preprocessed and discusses the algorithms used in this research for cholera epidemic prediction. The methodology comprises seven phases: data collection, data pre-processing, feature extraction and data splitting of the features into training and testing data, model formulation and implementation, evaluation metrics, and selecting the best model or algorithm as shown in figure 1.

Data Collection

The dataset used was obtained from the Jigawa State Ministry of Health as a secondary source. Specifically, data from six local government areas, two from each senatorial zone, namely, Dutse, Kiyawa, Hadejia, Malam-Madori, Gumel, and Gagarawa. All medical records where cholera outbreaks occurred in 2019 in Jigawa State were considered, and they consist of many samples with different attributes. A total of 1443 datasets were collected during this study.

Data Preprocessing

Data preprocessing and cleaning involve identifying and addressing issues like missing values, duplicates, and outliers. Normalization ensures that each variable is equally weighted, and data transformation prepares it for analysis and/or application by altering its format or structure.

Implementation of the Proposed Framework

After preprocessing the dataset, it was divided into training and testing sets. The splits were 60/40, 70/30, and 80/20 for training and testing, respectively. The rationale behind these proportions is that a larger training set enables the model to capture diverse patterns and variations in the data, resulting in more robust and generalizable performance. It also helps identify which portion of the data learns the patterns effectively. The model that demonstrated the quickest training and testing times was selected for predicting cholera outbreaks. The specific models used are SVM, LR, ANN, DT, and NB. Metrics such as accuracy, precision, recall, and F1 score were employed to assess the model's performance. This evaluation determined the best phase for the models' ability to generalize and accurately predict cholera pandemics based on new data.

RESULT

The results were presented and evaluated in tables 1, 2, and 3, respectively. In Table 1, the dataset was divided into 60% for training and 40% for testing. The Naïve Bayes algorithm demonstrated superior performance, achieving an accuracy of 93%, precision of 94%, recall of 93%, and an F1-score of 93%. Although effective for predicting cholera outbreaks, there was still room for improvement in accuracy. However, in the second phase (table 2), 70% of the data was allocated for training, with the remaining 30% used for testing. Naïve Bayes continued to excel, achieving an impressive accuracy of 96%. It outperformed other methods across accuracy, precision, recall, and F1-score. Finally, for the final phase (table 3), the dataset was split into 80% training and 20% testing. Remarkably, Naïve Bayes achieved 100% across all evaluation metrics. Overall, Naïve Bayes consistently performed best, making it the most effective model for cholera prediction. Given these results, Naïve Bayes is the recommended choice as a selected model for the proposed system

.

DISCUSSION

To validate these results, a performance evaluation of the selected model (Naïve Bayes) was carried out and compared with the performances of other models used by various authors in our reviewed literature, with the results presented in Figure 2. Four different studies were considered. The first research by [20] identified XGBoost as the best classifier among many, achieving an accuracy of 0.767 and a recall of 0.80, whereas the second paper by [5] found that Random Forest outperformed other classifiers with an accuracy, recall, and F1 score of 0.99, 0.895, and 0.942, respectively. Another effort by [13] developed a cholera epidemic model using Naïve Bayes, the same as the current research, which accounts for an accuracy of 0.99. Lastly, [9] developed a decision tree-based model to forecast cholera outbreaks in West Africa, achieving remarkable results with an accuracy of 0.998, precision of 1.00, recall of 1.00, and F1 score of 1.00.

CONCLUSION AND RECOMMENDATION

The study introduces a machine learning model that predicts cholera outbreaks with high accuracy, representing a significant advancement in public health and epidemiology. Leveraging a Naïve Bayesian Classification technique and a comprehensive dataset from Jigawa State, Nigeria, this model surpasses traditional epidemiological approaches. The research highlights the potential of machine learning for enhancing public health responses, especially in developing nations where cholera remains a critical concern. Additionally, although there has been an ample amount of research on cholera epidemic prediction, the prevalence of cholera outbreaks has become a thing of

concern, and the need for a high degree of accuracy in predicting cholera epidemics. To explore the potentials of ML in enhancing the healthcare system in Jigawa State, more research in this field should be intensified or encouraged to succeed in minimizing the numerous health challenges. It is against this backdrop that the researcher recommends further validation and improvement through testing with larger datasets, aiming to equip health officials with effective intervention strategies and mitigate the impact of cholera on vulnerable populations. Overall, this work underscores the transformative role of machine learning in public health initiatives.

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Table 1: Results of Performance Evaluation Measure for 60/40 Split Ratio

Models	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)
Naïve Bayes	93	94	93	93
SVM	84	70	84	76
Decision Tree	74	70	74	74
Logistic Regression	84	70	84	76
Neural Network	17	70	84	76

Table 2: Results of Performance Evaluation Measure for 70/30 Split Ratio

Models	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)
Naïve Bayes	96	96	96	96
SVM	84	70	84	76
Decision Tree	76	70	76	76
Logistic Regression	84	70	84	76
Neural Network	84	70	84	76

Table 3: Results of Performance Evaluation Measure for 80/20 Split Ratio

Models	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)
Naïve Bayes	100	100	100	100
SVM	84	70	84	76
Decision Tree	74	70	74	74
Logistic Regression	84	70	84	76
Neural Network	84	70	84	75

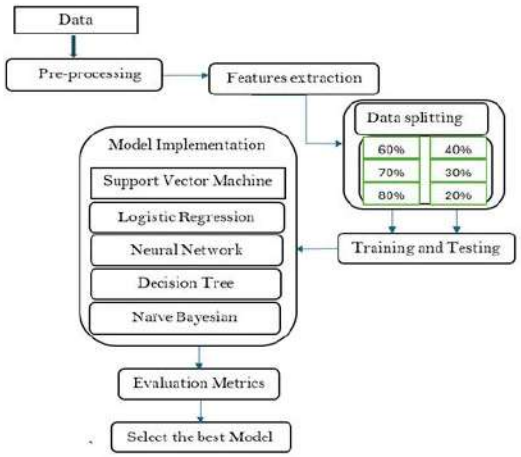

Figure 1. Proposed Methodology

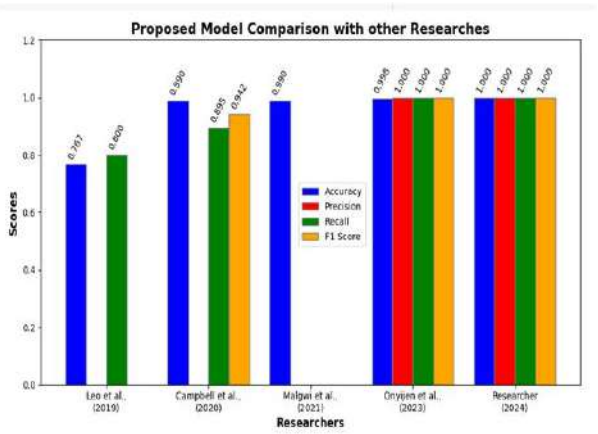

Figure 2. Proposed Model Comparison with other Researches.

RESEARCH ARTICLE

Anti Cancer Activity of Ethanolic Extract of *Withania somnifera* against T-24 Urinary Bladder Cell Line, Hela—Cervical Adeno Carcinoma and AGS—Human Adeno Gastric Carcinoma Cell Lines

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ABSTRACT

Drug resistance develops as a result of increased intrinsic toxicity associated with cancer chemotherapy. Formulations derived from plants are thought to be the safest for treating a range of ailments. In the old traditional medical system, Ashwagandha was regarded as a significant medicinal herb. *Withania somnifera* crude ethanolic extract was utilized in this study to assess its effectiveness against the T-24 bladder cell line, Hela (cervical adeno carcinoma), and AGS (human adeno gastric carcinoma) cell lines., The T-24 urine bladder cell line, AGS human adeno gastric cancer cell line, and the Hela cervical adeno carcinoma cell line were examined with a four-fold dilution of the ethanolic crude extract of Withania somnifera.The concentrations of the extract were 50 dilution/ml, 100 dilution/ml, 150 dilution/ml, and 200 dilution/ml. The Hela cell line's obtained Ic50 value was 130.06 **µ**g/ml. The observed Ic50 value against the T 24 cell line was 134.84 **µ**g/ml. Against AGS cell line the obtained Ic50 value was 137.47 **µ**g/ml.

Keywords: *Withania somnifera,* T–24 urinary bladder cell line, Hela, and AGS cancer cell lines.

INTRODUCTION

Cancer is viewed as a 'hopeless disease'[1]. The traditional approach to treat cancer involves the use of Chemotherapy and radiation therapy, all of which have negative side effects on patients, including drug resistance

skin allergies, patches, hair loss and an increased production of different toxins in the body. Natural goods, particularly those derived from plants are thought to be safest for the treating a variety of illnesses because they don't contain any toxins, don't have an major effects, and They are generated by plants as secondary metabolites or by-products. Aswagandha, or *Withania somnifera*, is a valuable medicinal plant that is grown as a kharif crop throughout India. It reaches a maximum height of 1.5 meters. and does well in dry or semi-dry soil, requiring less irrigation[2]. Ashwagandha powder and extract can be used as a tonic or rejuvenating remedy, roots are considered an important medical element. As an alternative, they have anti-inflammatory and aphrodisiac properties. Root powder has been found to be effective against bronchitis, asthma, rheumatic disorders, fever, TB, and leucoderma. Leaves can be used to cure sores, painful fever swelling, ulcers, and chest pain. The effects of seeds are drowsy, diuretic, and narcotic[3] . *Withania somnifera* is harmless, non-toxic[4], and has been shown in numerous tests to boost immunity and increase body resistance to disease[5]

Accoding to earlier research, *Withania somnifera* extract can decrease succinate dehdrogenase activity, raise WBC counts, inhibits 35 S ribosome incorporation and dramatically raise Mg^{2+} activity in granulomas[6]. These findings suggests that *Withania somnifera* extract may have antitumor effects[7]. The root extract of It was discovered that Withania somnifera worked well against three different types of cancer cells: colon cancer cell line HCT 116, breast cancer cell lines MDA MB 468 and 231, and pancreatic cell line MIA PaCa -2[8]. In a different investigation, the ethanolic extract from the roots of Ashwagandha was tested against four cancer cell lines: HepG2, A549, MCF7, and CACo2. They saw that the Hep G2 cell line's growth was inhibited up to 80.2%, followed by MCF7 and CACo2, whose proliferation was strongly inhibited by 79 and 68.9%, respectively. A459's growth was inhibited by 59.5%[9]. By changing the mRNA of liver cancer cells' Bcl 2 and BclXl apoptotic signaling molecules, an ethanolic extract of *Withania somnifera* promotes the lysis of cancer cells[10].Another study indicated that *Withania somnifera'*s aqueous and ethanolic crude extracts were efficient against the MCF 7 cell line, with reported Ic50 values of 14.20 and 17.00µg/ml, respectively [11].

In vitro studies showed that *Withania Somnifera* combined with IR significantly increased inhibition of proliferation, induced cell death, and reduced sphere formation in the A-549 cell line compared to IR or *Withania Somnifera* alone. The study also observed upregulation of Hedgehog (Hh) signaling and EMT markers such as α-smooth muscle actin (α-SMA), SNAIL-1,Vimentin, and E-cadherin, which are associated with lung cancer stem cell markers OCT4, SOX2, CD133, ABCG2, and NANOG[12]. Pre-treated HT-29 colon cancer cells with *Withania somnifera* root extract enhanced the effectiveness of cisplatin and also exacerbated mitochondrial dysfunction specifically in cancer cells, primarily through an increase in reactive oxygen species (ROS) levels[13]. Investigations were conducted into the antiproliferative properties of the methanolic extract of *W. somnifera* leaves, against the MCF-7, HCT116, and HepH2 cell lines. Strong antiproliferative activity of the extract against all cell lines was demonstrated, with IC50 values of 3.35, 2.19, and 1.89µg/ml, respectively[14]. *Withania somnifera* root extract also showed anticancer effect against A 375 malignant melanoma cells[15]. Additionally, *Withania somnifera* root extract shown cytostatic activity and cytotoxic action against T-lymphoblastoid cell line. It also promotes ICD by causing ROS production and Ca 2+ buildup[16]. The T-24 bladder cell line, Hela cervical adeno carcinoma, and AGS human adeno gastric carcinoma cell lines were used in the current investigation to assess the effectiveness of an ethanolic crude extract of Withania somnifera against cancer cell lines. The cell cytotoxicity against the Vero (Normal) cell line was also assessed.

Material and method- Test tubes, conical flasks, 96-well microplates, ethanolic plant extracts of *Withania somnifera*, T-24 urinary bladder cell line, Hela—cervical adeno carcinoma—and AGS—human adeno gastric carcinoma cell lines, VERO cell line DMSO, as well as a digital inverted microscope, spectrophotometer, and CO_2 incubator. Sample preparation- The plant sample of *Withania somnifera* was collected from the field, and its fresh young leaf, stem, and fully developed roots were washed with running tap water to remove dirt and soil. The plant sample was then washed again in double distilled water and wiped with tissue paper to remove water molecules, as the presence of water makes the plant sample susceptible to contamination and fungal growth. The roots and leaves were placed in a dry, hygienic area and given days to thoroughly dry in a hygienic environment. Samples were ground separately using a grinder to produce a completely fine powder. 250 grams of the finely ground sample were weighed and then

added to a conical flask. Conical flasks were carefully filled with ethanol and shaken all night. *Withania somnifera* powdered leaves and roots were added to a volumetric flask. Using a Soxhlet device, the sample was extracted, and a rotatory evaporator was used to remove any remaining solvent. Carefully dried the extract. By using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay) to test the cytotoxic efficacy of *Withania somnifera* extract against the T-24 Urinary Bladder Cell Line, Hela-Cervical Adeno carcinoma, and AGS-Human Adeno Gastric Carcinoma cell lines, the ethanolic extract was further diluted[17]. The cells were seeded onto 96-well microplates (1 x 106 cells/well), and they were allowed to develop to 70–80% confluence in an incubator with 5% CO2 for 48 hours at 37°C. After that, the medium was changed, and the cells were exposed to various sample concentrations before being incubated for a full day. After 24 hours, the morphological differences between the treated and untreated (control) cells were examined under a digital inverted microscope (20X magnification) and captured on camera. Phosphate-buffer saline (PBS, pH 7.4) was used to wash the cells, and 20 µL of (MTT) solution (5 mg/mL in PBS) was applied to each well. After that, the plates were left in the dark at 37ºC for two hours. After dissolving the formazan crystals in 100µL DMSO, the absorbance was measured at 570nm using spectrometry. To determine the percentage of viable cells, the following formula was used: (Absorbance of sample/Absorbance of control) X 100 equals cell viability (%).

RESULTS AND DISCUSSION

The structure and action of Withania somnifera's ethanolic crude extract against Vero (normal) cell line, T-24 urinary bladder cell line, Hela (cervical adeno carcinoma), and AGS (human adeno gastric carcinoma) cell lines are depicted in Figure 1-4. The T-24 urinary bladder cell line, Hela—cervical adeno carcinoma—and AGS—human adeno gastric carcinoma cell lines—were subjected to the four distinct concentrations utilized of ethanolic crude extract of Withania somnifera: 50 g/ml, 100 **µ**g/ml, 150 **µ**g/ml, and 200 **µ**g/ml. The ethanolic extract's IC_{50} value against the Hela cell line was 130.06 **µ**g/ml, 134.84 **µ**g/ml, and 137.47 **µ**g/ml (Graph 1-3). At 50 **µ**g/ml Hela cells lysed upto 14.85 % followed by T24 cell line(14.75%) and AGS cell line(7.81%). At 100 **µ**g/ml Hela cells lysed upto 34.45% followed by AGS cell line (27.08%) and T24 cell line(26.78%). At 150 **µ**g/ml more than 50% lysis has been observed, at 150 **µ**g/ml T 24 cell lines lysed up to 59.9% followed by Hela cells 56.63% and AGS cell line (53.18%). The maximum lysis was observed at 200 **µ**g/ml concentration. The AGS cell was lysed by the ethanolic extract of Withania somnifera up to 86.23%, followed by Hela cell line 85.11% and T24 cell (80.6). (Table 1 and 2).

CONCLUSION

Previous studies, which also call for greater in vivo study to create less hazardous plant-based anticancer drugs, support this research. The results of this study show that a crude ethanolic extract of *Withania somnifera* is effective against the cervical adeno carcinoma Hela, the human adeno gastric carcinoma AGS, and the urinary bladder cell line T-24. *Withania somnifera's* ethanolic extract has a wide range of active ingredients with anticancer properties, allowing for the development of different formulations and medications to treat cancer and other illnesses.

Conflict of Interest- Authors declares no conflict of Interest.

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Table 1- Cell cytoxity study of *Withania somnifera* crude extract against Vero Cell line.

VERO cell line	
Concentrations(µg/mL)	**% Viability of VERO (normal) cell line.**
Control	100
50	94.41
100	83.36
150	76.73
200	67.91

Table 2- Anti-cancer activity of *Withania somnifera* crude extract against T-24 Urinary bladder cell line, Hela—Cervical Adeno Carcinoma—and AGS—Human Adeno Gastric Carcinoma cell lines

Concentrations (µg/mL)	T 24% lysis	Hela% lysis	AGS% lysis
50	14.75	14.85	7.81
100	26.78	34.45	27.08
150	59.9	56.63	53.18
200	80.6	85.11	86.23

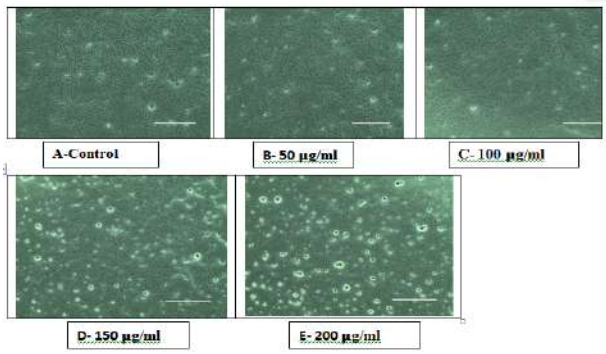


Figure 1- *Withania somnifera* ethanolic extract's effect on the normal (VERO) cell line. (A) Control: VERO (Normal cell line) culture without any medication.(after 24 hours), (B) VERO cells received treatment with 50 µg/ml concentration of ethanolic *Withania somnifera* extract. (C) After 24 hours, VERO cells received treatment with100 µg/ml of ethanolic *Withania somnifera* extract. (D) After 24 hours, VERO cells received treatment with 150 µg/ml of ethanolic *Withania somnifera* extract. (E) After 24 hours, VERO cells received treatment with200 µg/ml of ethanolic *Withania somnifera* extract.

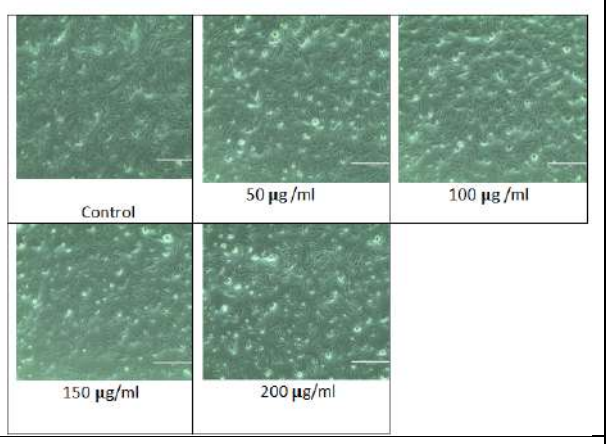


Fig 2 –*Withania somnifera* ethanolic extract's effect on the T 24 urinary bladder cell line (A) Control: T 24 cells without any medication.(after 24 hours), (B) T 24 cells line treated with 50 µg/ml concentration of ethanolic *Withania somnifera* extract. (C) After 24 hours, T 24 cells received treatment with 100 µg/ml of ethanolic *Withania somnifera* extract. (D) After 24 hours, T 24 cells received treatment with 150 µg/ml of ethanolic *Withania somnifera* extract. (E) After 24 hours, T 24 cells received treatment with 200 µg/ml of ethanolic *Withania somnifera* extract.

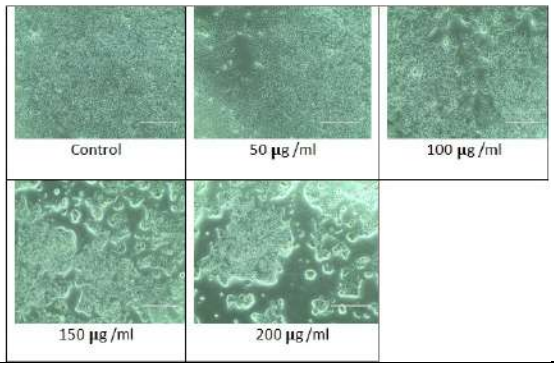
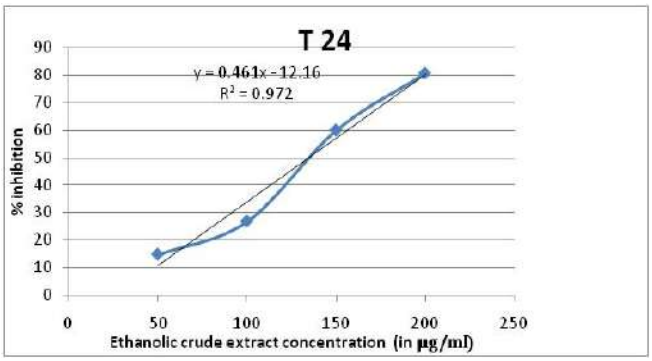
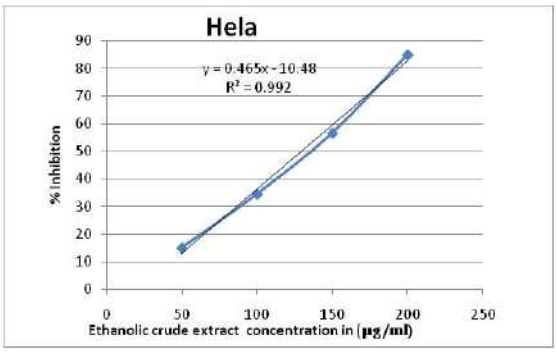


Figure 3 –*Withania somnifera* ethanolic extract's effect on the HeLa Cervical adeno carcinoma cell line (A) Control: HeLa Cervical adeno carcinoma cell line without any medication.(after 24 hours), (B) HeLa Cervical adeno carcinoma cell line treated with 50 µg/ml concentration of ethanolic *Withania somnifera* extract. (C) After 24 hours, HeLa Cervical adeno carcinoma cell line was treated with 100 µg/ml of ethanolic *Withania*

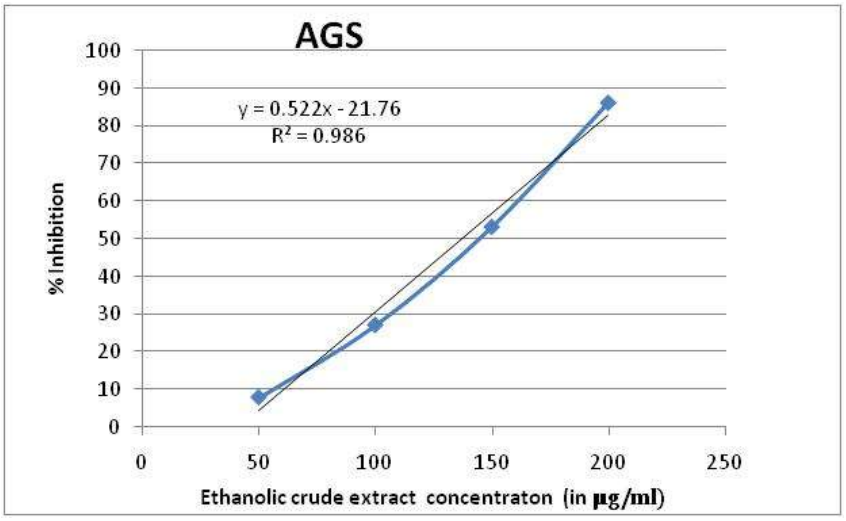
***somnifera* extract. (D) After 24 hours, HeLa Cervical adeno carcinoma cell line was treated with 150 µg/ml of ethanolic *Withania somnifera* extract. (E) After 24 hours, HeLa Cervical adeno carcinoma cell line was treated with 200 µg/ml of ethanolic *Withania somnifera* extract.**



Graph 1- Percentage reduction of T 24 Urinary - bladder cancer cell line against various concentrations of *Withania somnifera* ethanolic crude extract.



Graph 2- Percentage reduction of Hela (Cervical adeno Carcinoma) cell line against various concentrations of *Withania somnifera* ethanolic crude extract.



Graph 3- Percentage reduction of AGS (Human Adeno Gastric Carcinoma) cell lines cell line against various concentrations of *Withania somnifera* ethanolic crude extract.

RESEARCH ARTICLE

Next-Gen Healthcare : Combining Smart Apparel with Bio-Prosthetic Technology for Comprehensive Patient Management

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ABSTRACT

The latest breakthrough in patient monitoring and nursing management is the combination of bio-prosthesis technology and smart clothes. This approach offers an entire solution for real-time health evaluation by fusing the therapeutic advantages of bio-prosthetic devices with the physiological monitoring capabilities of smart textiles. Heart rate, body temperature and respiration are just a few of the vital indications of smart clothing, which has been designed with sensors and data transfer capabilities for monitoring continuously. Integrating this technology with bio-prosthetic device like stented, stent-less, or percutaneous heart valves provides a comprehensive monitoring system that improves the medical condition. Healthcare providers can detect potential issues connected with bio-prosthetic implants, such as infections and valve dysfunctions, early on by utilizing real-time data from smart clothes. In beyond enhancing patient health management, this ongoing feedback loop helps initiate responses and individualized treatment plans. Moreover, the implementation of smart clothing enables a non-invasive monitoring strategy, diminishing the necessity for frequent clinical visits and augmenting patient comfort and compliance. The technical convergence of bio-prosthesis systems and smart clothing is reviewed in this paper, with an emphasis on

how this combination might improve patient outcomes, maximize bio-prosthetic performance, and advance the field of wearable health technologies.

Keywords: Smart clothing, Bio-prosthetic infection, Health Care Management, Monitoring Patients.

INTRODUCTION

Wearing clothing and accessories has been a way for humans to defend us against the elements and harm ever since the beginning of time. Massachusetts Institute of Technology Researchers started looking into the potential of putting microprocessors into textiles in the mid-1990s [1]. Since then, three key areas of innovation have driven the development of smart clothing. First is the development of wireless communication, second is the introduction of new textile fibres (such as conductive materials), and the final miniaturisation of electrical equipment. With the latter, clothing may connect and communicate with smartphones and laptops which benefits from the way of innovation [2]. In 2050, the World Health Organisation projects that the ageing population will account for around 25% of all people on earth in developed nations, this percentage may even grow to 33%. As people age, they experience an increasing number of health problems, such as heart disease, physical decline and a reduction in physical resilience. For this reason, the challenges surrounding elder health care are becoming more and more essential. Therefore, developing intelligent elderly health care techniques is of vital importance. The rapid expansion of wearable technology has led to the use of smart clothes and gadgets in intelligent healthcare. The population is in favour of using wearables to check health [3-8]. In a Fierce Healthcare survey, 64% of respondents said they would use a wearable device if it meant they wouldn't have to visit the doctor or hospital as frequently [9]. On the other hand, non-communicable diseases (NCDs), sometimes referred to as chronic diseases, such as diabetes, respiratory problems, and cardiovascular illnesses, place a burden on world health. As was previously noted, they are responsible for 71% of fatalities worldwide, according to the WHO [10]. Recent years have seen the fusion of technology and medicine yield creative answers to some of the most urgent problems facing the healthcare industry. One of these new developments is smart clothing, a cutting-edge medical device intended to improve patient care and administration. Specifically, the management and prevention of bio-prosthetic-related infections could be greatly aided by smart clothing. This article explores how smart clothing works, its potential benefits, and its role in addressing infections associated with bio-prosthetic implants.

WEARABLES USED IN SMART CLOTHING

In order to give greater utility than traditional clothing, smart clothing combines cutting-edge technology with traditional materials. For the management of chronic diseases, there is no established roadmap for smart clothing. Establishing a worldwide roadmap analogous to the one provided by the semiconductor industry is important. This will assist in defining objectives and targets for the next generation of smart clothing as well as in locating technical bottle necks. Additionally by bringing professionals and businesses from across the globe together, this will promote global research and development efforts. Some of the wearable's used for smart clothing systems are,

Smart watches : Used for many things, including pollution and UV radiation monitoring.
Fitness trackers : Frequently used to measure exercise, they can also measure heart rate and calculate calories burned.
Smart jewellery : Allows wearers to receive notifications by connecting to a mobile device.
Wearable technology : Clothes with fibres that serve as sensors to track stress levels, heart rate, and other parameters.
Head-mounted displays : Provide visual information.
Implantables : Subcutaneously positioned devices that track cardiac problems, among other things.

SYSTEM DESIGN IN SMART CLOTHING

The system was primarily made up of three components,

1. a mobile device that provided mobile services and displayed data along with alerts about abnormal events,
2. a control platform for caring institutions that was in charge of abnormality alerts and data analysis in health care; and
3. That data was received by smart clothing and sensing components. Conductive fiber was used to make the smart apparel. The smart clothing's four electrode patches were used to collect analog ECG signals and send them to the sensing component. The sensing component's analog-to-digital converter (ADC) transformed the analog ECG signals into digital signals with a sampling rate of 250 Hz. The health data were sent as broadcast packets with a frequency of 1 Hz via BLE after the digital ECG signals were analyzed by the MPU of the sensing component. On the back-end management platform, the data were analyzed and eventually transformed into useful health information after being transferred by the BLE-to-Wi-Fi receiver. The health care information was sent in web mode to the cell phone of the medical attendant station or the guardian [11].

BIO-PROSTHESIS

A bio-prosthesis is a kind of valve composed of nitinol that is anchored firmly in the heart with the help of ventricular graspers and atrial winglets. It is available in various sizes to meet the demands of each patient and is used to replace damaged heart valves. A perfect replacement valve should have the same features as an ordinary native valve. It should, in particular, have great implantability, high thromboresistance, extended durability and excellent haemodynamics. The perfect replacement valve coordinates with the overall circulatory system and provides superior valve performance. This may be referred to by your medical team as "excellent haemodynamic performance. "The ideal replacement valve also offers long-term durability without significantly increasing the risk of dangerous blood clots. Patients and their health care team should discuss treatment options and share in the decision-making process to choose the most appropriate treatment [12].

Bio-prosthetic Versus Mechanical Valve

To maximise the results for patients having valve replacement, selecting the appropriate valve for the correct patient is a challenging but crucial procedure. Making the decision between a mechanical and a bio-prosthetic valve is the first stage in this process. At this initial stage, the patient's age, life expectancy, preference, indications and contraindications for warfarin medication, and comorbidities are the most crucial considerations to take into account. The patient is at risk of accelerated bio-prosthesis structural deterioration due to young age, hyperparathyroidism, or renal insufficiency. The patient is also in favour of using a mechanical valve if they are an informed patient who wants one and has no contraindications for long-term anticoagulation. Finally, the patient should be over 65 and have a long life expectancy if they are already on anticoagulation. However, in the following cases, a bio-prosthesis might be preferred.

1. the patient is informed and wants one;
2. good-quality anticoagulation is not available (due to a contraindication or high risk, issues with compliance, lifestyle);
3. the patient is over 65 and/or has a limited life expectancy; and
4. the patient is a woman of childbearing age. Pregnant women and younger patients experience a faster degradation of bio-prostheses. Thus, a lady who has finished having children and is in her late 30s to 40s should most likely be recommended to have a mechanical valve [13].

Infection Risks associated with Bio-prostheses

However, there isn't a perfect valve replacement, and all of the prosthetic valves that are currently on the market have drawbacks. Restoring function and enhancing quality of life are two major advantages of bio-prostheses, which include prosthetic joints, heart valves, and other implants composed of biological or bioengineered materials. Of the cases, 10–20% are caused by prosthetic valve endocarditis. On average, 5% of bio-prosthetic and mechanical valves develop an infection. In the first three months following implantation, mechanical valves are more susceptible to infection; bio-prosthetic valves are more susceptible to infection one year later. They also present risks of infection due to,

Surface Contamination

Bacteria can adhere to the surface of bio-prostheses, forming biofilms that are difficult to eradicate.

Surgical Site Infections

Post-surgical infections can occur at the site of implantation.

Immune Response

The body's immune response to the prosthetic material can sometimes increase susceptibility to infections. Blood thinners can reduce the risk of embolism (travelling clot) or stroke associated with a clot. The danger of clots is increased in patients with mechanical valves. Individuals using blood thinners need to be closely watched since excessively thin blood can make bleeding more likely. The lifetime and success of bio-prostheses depend on the efficient control of these infections.

FUSION OF SMART CLOTHING WITH BIO-PROTHESES FOR BETTERMENT IN HEALTH CARE

Smart clothing offers several promising features that can aid in the management and prevention of infections associated with bio-prostheses.

1. Temperature Sensors for Real-Time Monitoring

A fever might be one of the first signs of an infection. Temperature sensors integrated into smart apparel can offer continuous monitoring and notify patients and medical professionals of possible infections before they worsen.

2. Wound Monitoring

Smart clothes with integrated sensors can monitor the healing process of wounds and identify indicators of infection, such as elevated wetness or pH changes.

3. Remote monitoring

Real-time data transmission from smart clothes to medical professionals enables prompt interventions and treatment plan modifications. Patients who need regular monitoring and have bio-prostheses may find this to be extremely helpful.

4.Anti-microbials

By preventing the growth of bacteria, clothing made of antimicrobial textiles can help lower the risk of infection. For patients who are more likely to have an infection from their bio-prostheses, this is especially helpful.

5. Demand Analysis

Although the smart clothing market is still in its early stages, it is expected to expand quickly in the near future. As a result, the need for smart clothes is growing along with the need for continuous, precise, and personalised healthcare services. The primary advantages of this industry include lower healthcare expenses, less procedures, and on-going, nonintrusive monitoring of patient quality. Sporting goods that can avoid injuries are likewise very popular.

ADVANTAGES OFFERED BY THE SUGGESTED FUSED HEALTH MONITORING SYSTEM

1. Monitoring life-giving indicators

Elderly people's heart rates are monitored continuously, and when they fall below 50 Hz or rise above 140 Hz, an alert is set off.

2. Monitoring physiological processes.

The monthly and daily step number variance is examined using the step number data that was gathered. It is ascertained whether the appropriate level of exercise is attained for a certain physical condition.

3. Observation of the field of activities.

Every time an elderly person enters a care facility, their location is noted and examined to see if they move around or remain within.

4. Reluctant to lose.

The elderly can be monitored by indoor placement to see whether they approach the warning area that the care facility has designated. Up to 10 m can be detected by the system**.**

5. Fall identification.

One can detect falls at any time. An emergency request for assistance will be made as soon as a suspected fall occurrence is discovered.

6. Make an emergency help call.
The sensing component's has a help button for emergency calls. It can be used in real time to request aid when the body is found to be abnormal.
7. Recognition of device wear.
Deciding whether the older wear the sensing component is crucial since the fundamental assistance can't be given that there is no sensing component in the system architecture.
8. Device low battery warning.
It is necessary to determine whether the sensing component has a low battery for the same reason as in (7) point [11].

RECENT USE OF SMART CLOTHING IN HEALTH CARE
While many of the above studies are moving forward and toward commercialization, there is even more potential for e-textiles related to healthcare due to technological improvements in high-tech textiles and microelectronics. T-shirts that relieve chronic back pain, shirts with stretch sensors to track respiratory rates in patients with chronic lung disease, soft belly bands that track fetal heart rate and uterine contractions in pregnant women, pressure monitor stockings for diabetic patients, and even shirts that shock patients with severe heart problems are a few of these concepts and early trials [17]. Bedside monitoring will eventually be replaced in hospitals by smart clothing shirts that detect blood pressure, heart rate, oxygen intact, and other metrics, according to some experts. As of late, the Google-Levi Undertaking Jacquard driving for cyclists jacket has caused people to notice the idea of integrating signal acknowledgment into smart clothing. There are currently far more affordable and well-established technologies that are unlikely to be surpassed in the next five years, even though many experts believe that gesture recognition could end up in medical apparel, perhaps for paraplegics, the elderly who have suffered heart attacks or strokes, or the elderly who fall at home. Because it can be easily scaled down and does not require moving mechanical parts, haptic feedback, also known as the use of touch in user interface design, can greatly benefit smart textiles. The concept of incorporating gesture wearing smart clothes with haptic feedback technology on any region of the body at any time of day could help with muscle recovery or stimulation. Prototypes for haptic feedback projects like those from Novasentis for use in medical apparel are presently being developed, and should be delivered later this year [18].

FUTURE SCOPE
Diabetes insoles with the ability to detect a rise in body temperature, warning the use of inflammation and minimizing skin sores. Sports bra biosensors that, in contrast to wrist trackers, may gather information at the moment of activity to measure respiration and pulse more precisely [19]. Fitness pants with haptic vibrations integrated in that softly pulse at the knees and hips can promote physical therapy-related holding positions. Baby smart socks with heart rate monitoring and breathing and breathing disruption detection. Wearable and smartphone sensors have a wide range of clinical uses in clinical cancer. When evaluating patients prior to treatment, behavioral data can be useful in predicting the likelihood that they would tolerate a new or severe therapy as well as providing a more objective estimation of their performance level or condition. The creation of intelligent clothing for the detection of cancers like breast or skin cancer has advanced very little or not at all [20,21]. The creation of intelligent clothing for the detection of cancers like breast or skin cancer has advanced very little or not at all [22].

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Table 1 : Types of Bio-prostheses and its characteristics [14-16]

Category	Stented Bio-prostheses	Stent less Bio-prostheses	Percutaneous Bio-prostheses
Definition	Bio-prosthetic valves with a stent framework	Bio-prosthetic valves without a stent framework	Bio-prosthetic valves inserted via a catheter-based method
Design	Rigid frame supporting the valve	No frame, more natural shape	Small size, designed for catheter delivery
Material	Typically bovine pericardium or porcine tissue, supported by a metal stent	Bovine pericardium or porcine tissue, without a metal stent	Bovine pericardium or porcine tissue, mounted on a balloon-expandable frame
Placement Method	Surgical implantation	Surgical implantation	Minimally invasive insertion
Infection Risk	Risk of endocarditis or prosthetic valve infection due to the stent material and surgical procedure	Lower risk of infection related to the absence of stent, but still subject to surgical infection risks	Potential for infection related to catheter insertion and procedural factors
Advantages	- Established durability - Easier to handle and implant - Good for a wide range of patients	- Improved hemodynamics - Reduced risk of stent-related complications - May be more suitable for certain anatomical features	- Minimally invasive - Shorter recovery time - Ideal for high-risk surgical patients
Disadvantages	- Potential for stent-related complications - Higher risk of infection - Possible need for valve replacement	- Complex implantation - Potential for longer surgery time - May have less durability	- Risk of procedural complications - Higher risk of infection related to the catheter - Typically less durable
Management of Infection	- Antibiotics and surgical revision if infection occurs	- Antibiotic prophylaxis and close monitoring; surgery may be required if infection occurs	- Close monitoring for signs of infection; antibiotics and possible removal if infection develops

Figure 1 : Use of smart clothing for bio-prosthetic infection monitoring

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RESEARCH ARTICLE

Maximizing Crop Yields: A Data Mining Approach to Bio-Fertilizer Recommendation and Inter Cropping Systems in Indian Agriculture

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ABSTRACT

The vast majority of people in India rely on agriculture as their primary source of income; hence it is important to never undervalue it. In agriculture, farmers face a wide range of problems, both natural and man-made, including soil erosion, biodiversity loss, climate change, water resource depletion, and shortages of labor, money, and other inputs .In order to address the aforementioned problems, farmers need to consider "crop diversification". It is a crucial component of smart farming, which can boost earnings and balance the availability of cash crops a process that also calls for greater study. The objective of the study is to employ data mining techniques to examine past contributions made to bio- fertilizer recommendation systems and intercropping systems.

Keywords: Crop Mapping, Inter Cropping, Bio-Fertilizer, Machine Learning, Deep Learning

INTRODUCTION

In India, agriculture is the primary source of income for the vast majority of people and should never be undervalued. The demand for food in India will rise due to factors such as population growth, rising average income, and the effects of globalization. Indians would want more food more of it, better food, and more variety. As a result, there will continue to be pressure to produce food in greater quantity, variety, and quality on dwindling amounts of arable land. Many nations, like India, continue to practice conventional agriculture; farmers are hesitant to employ cutting-edge technologies because they lack the necessary skills, the costs are prohibitive, or they are not aware of the benefits. Food is one of the essential needs of humankind, and agriculture is regarded as a key pillar of

the global economy(Meshram *et al.,* 2021).Over the coming decades, the Indian agriculture sector will face challenges due to rising food demand. The low productivity of India's agricultural industry can be attributed to various problems, including dispersed land holdings, insufficient irrigation facilities, outdated farming methods, and restricted access to technology and capital. Farmers deal with a wide range of issues in agriculture, both natural and man-made, such as soil erosion, biodiversity loss, climate change, depletion of water resources, and shortages of manpower, capital, and other inputs. To deal with the above issues farmers has to think about "Crop diversification". It is an important part of smart farming which can increase the profit and compensate the supply of cash crops, which also requires further more research (Sakpal, 2023). It is the process of adding new crops or cropping systems to a farm's agricultural production while accounting for the various returns from value-added crops that have complementary markets. Crop Mapping with suitable mixed cropping orinter cropping will ensure a good yield and profit for the farmers (Kumar *et al.,* 2022). Attempting to increase crop diversity by crop rotation, multiple cropping, or intercropping with the aim of enhancing productivity, sustainability, and supply of ecological systems is known as crop diversification (Devi & Sharma, 2022). Crop diversification has been lacking in India due to the country's historical reliance on a few number of important crops, such as sugarcane, wheat, and rice. For example, almost 70% of the nation's entire food grain production is made up of rice and wheat. It is necessary to promote the growth of non-cereal crops such oilseeds, millets, fruits, and vegetables (Upadhyay&Palanivel, 2011). Increased profitability and production stability emphasize the value of crop diversity, such as substituting rice and wheat for millets (Mzyece *et al.,* 2023).In addition to their remarkable health advantages, millets are a highly adaptable crop with superior climate resilience, better ecological adaptation, and the capacity to tolerate harsh environments, making them perfect for use in a world where climate change is a real possibility (Fabri *et al.,* 2024). In the past few decades, there have been significant technological breakthroughs in agriculture, particularly in large-scale agriculture (Paroda, 2022). Advances in Precision Agriculture (PA) using technology like GNSS, auto-steering, crop and soil sensors, rate control technologies of crop inputs, crop recommendation system and yield mapping were the driving force behind significant shift in agriculture (R. Shamshiri *et al.,* 2024). New methods and tools have been found by researchers to help farmers. For the farming industry, sophisticated PA technologies have increased productivity, profitability, and sustainability (Dhillon & Moncur, 2023). Thorough research and innovation required to design an efficient crop mapping and mixed or inter cropping system.

Problem Domain

In general, climate change will negatively affect agriculture and undermine food security. It will also have varying effects on the performance of crops depending on the region, reduce the production of some agricultural crops, and drive up the costs of important agricultural products like rice, wheat, and sugarcane (White, 2024). A mixed agricultural system can assist lower production costs per unit area, boost productivity and income, and lower farmer risk. Chemical fertilizers and pesticides are widely used to boost crop productivity in order to meet the nutritional needs of the world's growing population(SINGH, 2024). But the careless use of agrochemicals has contaminated the environment, endangering human health(Pahalvi *et al.,*2021).The aim of this study is to analyze the earlier contributions to the Inter cropping systems and Bio-fertilizerre commending systems using data mining techniques.Adaptationstrategiesforcertainagriculturalcropsaresuggestedwiththeanalysisfindings

METHODOLOGIES

This study opted to design the recommendation system for inter cropping and bio-fertilizers for enhancing the crop yield and food safety based on the inference of earlier related studies (Acharya *et al.,* 2024). In such a way, the design has two phases: First, an inter-cropping recommendation system framed based on the parameters such as soil quality; the climatic conditions and water availability recommend the high yielding crops to the farmers. Secondly, Suggest the Bio-Fertilizers instead of chemicals to retain the food safety and security

Inter Cropping and Crop Mapping Models

Intercropping is a common cultivation system in sustainable agriculture, allowing crop diversity and better soil surface exploitation (Ghosh *et al*., 2024). However, simulation of intercropped plants with integrated soil-plant-atmosphere models is challenging due to the need for a second spatial dimension for calculating soil water lateral flux (Pinto *et al.,* 2019). Relay intercropping is regarded as an important agro ecological technique to boost and maintain crop yields while guaranteeing the provision of multiple ecosystem services, sustainability, and adaptability to shifting weather patterns (Koskey e*t al*., 2022). Soil plays a crucial role in agriculture, with each crop growing better in different soil types. It is essential for farmers to identify the geographies and features of various soil types to determine which yields produce well in specific soil categories and regions (SaiSamhith *et al.,* 2023). Crop inventory is crucial for food security in regions, and conventional methods are time-consuming and costly (Colombo-Mendoza *et al.,* 2022). Machine learning has advanced significantly in agronomic data investigation and harvest prediction (Keerthika *et al.,* 2024). Various machine learning classification algorithms, such as weighted kNN, Naive Bayes, Gaussian Support Vector Machine (SVM), and XG Boost Algorithms, are used for crop and intercrop prediction.

Bio-Fertilizer Recommendation Approaches

Biofertilizers are substances that are enriched with bacteria that aid in the growth of trees and plants by providing them with more vital nutrients. It is made up of living things, such as bacteria, blue-green algae, and mycorrhizal fungi (Sharma *et al.,* 2024). With their characteristics that promote plant growth, plant-associated microorganisms hold great promise for re solving chemical fertilizers and are essential for increasing agricultural output and plant biomass. Improved nutrient availability, phytohormone regulation, biocontrol of phytopathogens, and reduction of biotic and a biotic stressors are some of the advantageous processes of improved plant growth (Kumar et al., 2022).

CONCLUSION

The main aim of the study is to increase the productivity of crop through inter cropping system and suggesting a best suitable bio fertilizer. From the earlier studies it can be understand that intercropping system can increase the yield and profit for the farmers. Meanwhile, suitable fertilizers than a chemical fertilizer enrich the soil parameters for a long run. Indian Agriculture mostly depends on the Cash crop like Rice, Wheat, Maize etc., An alternate crop with an bestinter cropping system would increase farmers social problems. Such crop will be Millets. Inter cropping methods for the Millets are best suitable. One of the easiest methods may also be to locate and cultivate the native millets of a certain area, where they have adapted to the local conditions. Thus, in general, it can be said that crop diversification using millets can play a significant role in establishing a sustainable future.

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Table.1:Comparison of Various models of Inter cropping System suggested in earlier studies

Author	Dataset	Models	Inference
Dey *et al.*,(2024)	Crop Data from 11 agricultural and 10 horticultural crops	Support Vector Machine, XG Boost, Random forest, KNN, and Decision Tree	Proposed a non-intrusive method witha user-friendly AI cloud-based interface, enabling rapid decision- making for optimal fertilizer applications and crop selection.
Keerthika *et al.*,(2024)	Soil and Crop Data	Xg Boost, SVM, Bagging Classifier	Proposed a model to class ifys oil series according to region, predicting suitable crops and intercrops accordingly.
Mahlayeye *et al.*, (2024)	Sentinel-2 Spectral Data	Stratified Random Sampling Method, Random Forest	Sampling Method performed using field surveys, farmer interviews, and temporal Sentinel-2 data to identify optimal crop growth phases, spectral regions, and vegetation indices (VIs) for accurately discriminating between maize and maize cropping patterns. The study highlights the utility of temporal Sentinel-2 spectral data for identifying critical crop growth phases, spectral regions, and VIs for cropping patterns classification, particularly for inter cropping.
Colombo-Mendoza	Climate Data	kNN, SVM,	Proposed a smart farming

et al., (2022)	And Crop- Production Data	Random Forest	system for crop production using low-cost IoT sensors and cloud-based data storage and analytics services. Also introduces a new data-mining method that uses climate data and crop-production data to predict production volume
Goyal *et al.,*(2022)	Remotely sensed Time-Series data and Sentinel 1 Data	Random Forest	Study performed with the Time-series remotely sensed data, including optical and SAR, are used for crop mapping by capturing key phenological stages. Random Forest performed better for crop mapping during the khar if season. Advanced remote sensing techniques, such as Synthetic Aperture Radar (SAR) remote sensors, can overcome limitations due to cloud cover in tropical regions.
Pinto *et al.,*(2019)	Soil, Water, Temperature and Crop Data	Machine Learning Algorithms	Developed 1D model Soil, Water, Atmosphere and Plant coupled to the World Food Studies (SWAP/WOFOST) to simulate intercropping (SWAP 2×1D) based on solar radiation and water partitioning between plant strips. The findings showed that intercropped plants had higher transpiration and lower soil evaporation compared to mono cropping cultivation
Aduvukhaetal.,(2021)	Sentinel-2, Vegetation Indices, Vegetation Phenology, and Sentzinel-1 data	Guided Regularized Random Forest, and Random Forest	Improved Crop pattern mapping for a heterogeneous landscape was proposed. Eight classification

			scenarios were compared, with the GRRF algorithm selected for variables election and the random forest for classification. The cropping pattern mapping approach can be used in other sites with similar agro-ecological conditions and can help understand the sustainability of food systems and model the abundance and spread of crop in sect pests, diseases, and pollinators.

Table:.2Comparison of Various models of Bio Fertilizer recommendation System suggested in earlier studies

Author	Dataset	Models	Inference
Nirmala Devi *et al.,* (2024)	Crop leaf image Data	SVM and CNN	Proposed a model using ML and DL technique to measure chlorophyll and nitrogen content in paddy leaves. The RGB color model is used to quantify chlorophyll and nitrogen contents. Bio fertilizers, which supply nutrients and enhance chlorophyll content, are crucial for yield progression and physiological processes. The SVM classification model recommends appropriate biofertilizers based on nitrogen concentration.
Raveena &S urendran, (2023)	Coffee Plant, Soil Quality, Climate Conditions, And Various Bio-Fertilizers Data	Deep Collaborative Matrix Factorization	The proposed research focuses on optimizing bio-fertilizer recommendations in coffee farms using deep collaborative matrix factorization. The method considers the unique characteristics of coffee plantations, such as soil quality, climate conditions, and various bio-fertilizers.

			Tested using Indian coffee farmers' ratings, the system demonstrated excellent accuracy and precision in recommending biofertilizers that are suitable for the unique conditions of the coffee crops.
Ather *et al.,*(2022)	Soil Data And Fertility Survey responses	ANN	Proposed a model to suggest suitable compost treatment and application timing based on climate estimates. Adjusting manure regimes to meet specific crop and region demands and protect the environment by reducing pollution from fertilizer and manure waste. Some soil-richness management strategies, like using versatile research facilities or imported equipment, face challenges in terms of cost, convenience, and adaptability to local environments.
Priya *et al.,*(2023)	Soil, Weather, Crop Data	Decision Trees, Random Forests, And Neural Networks	Proposed a machine learning-based strategy for recommending soil-based fertilizers in precision agriculture. It uses data on soil characteristics, weather patterns, and crop output to make recommendations
Madhumathi *et al.,* (2020)	Soil, Moisture, and Crop Data	SVM,MLR	Proposed a model to determine soil nutrient composition, helping farmers choose the right crop and fertilizer for better crop harvest. N,P,K composition is predicted to retain the soil fertility.
Jayashree *et al.,*(2022)	Soil, Fertilizer, and Crop Data	SVM, Random Forest, kNN	Proposed model aims to find the right fertilizer for

			a crop based on parameters like moisture, temperature, and nitrogen, potassium, and phosphorus levels. Farmers will be provided with nearby fertilizer shops based on the recommended fertilizer. Excessive fertilizer use can also negatively impact crop development. A recommend ed dose of fertilizer can increase crop yield by8-21%.

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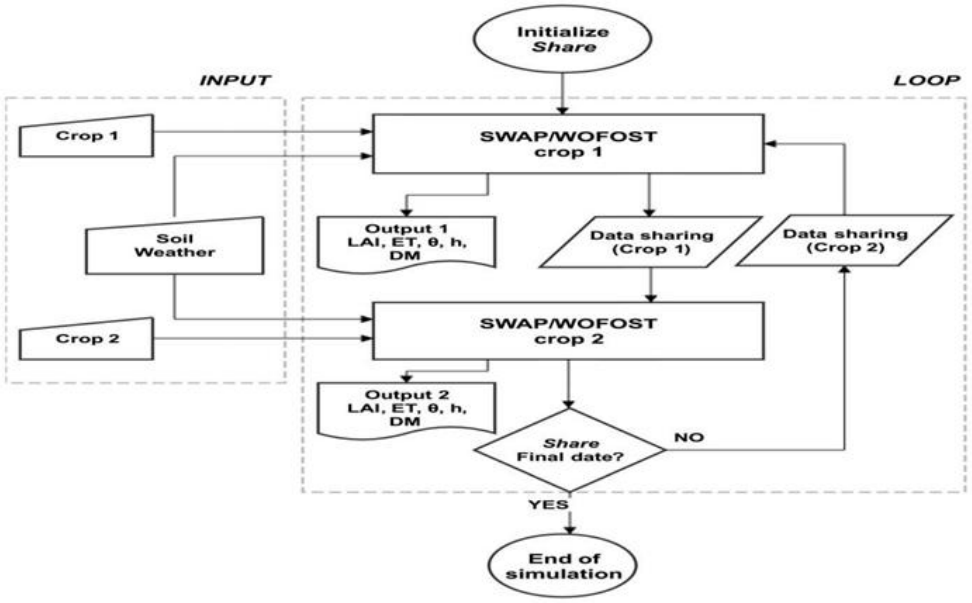

Figure.1.Inter cropping and crop mapping models.[19]

RESEARCH ARTICLE

Impact of Invasive Alien Species on the Distribution Pattern of Wetland Plants in Thanga Area, Loktak Lake, Bishnupur District, Manipur, India

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ABSTRACT

A study was conducted to examine the status and distribution of local and invasive wetland plants in Thanga area, Loktak Lake, Manipur. A total of 100 wetland plants were recorded out of which 40 are invasive plants and 60 are indigenous plants belonging to 50 families and 82 genera. Phytosociological studies were carried out using random sampling method. All the invasive plants and indigenous plants have the A/F ratio above 0.05, therefore all of them show contiguous distribution in natural condition. For the invasive plants, IVI range is divided into 6 groups starting from 1.00-4.00 up to 20.01-24.00. The maximum number of species is found in the IVI range of 4.01-8.00. *Ludwigia adscendens* has the highest IVI value (20.36) followed by *Alternanthera philoxeroides* (16.16) and *Mikania scandens* (15.40), which indicates their dominance and good power of regeneration. And for the indigenous plants, IVI range is divided into 4 groups starting from 1.00-4.00 and going up to 12.01- 16.00. The maximum number of species is found in the IVI range of 1.00-4.00. *Leersia hexandra* has the highest IVI value of 15.31 followed by *Zizania latifolia* (14.64) and *Hydrocharis dubia* (13.28) and indicate their dominance and good power of regeneration. The much higher value of IVI of dominant invasive alien species as compared to the dominant indigenous species depict the over domination of invasive alien species threatening the overall existing ecosystem if proper attention is not given.

Keywords: contiguous distribution, dominance, indigenous, invasive, regeneration.

INTRODUCTION

Wetlands of Manipur are belonged to the Indo-Burma Biodiversity Hotspot [1]. Wetlands are one of the most productive ecosystems on earth and support a great diversity of rare and unique species. It is well known that the distribution pattern of plant species is mainly governed and regulated by altitude as well as edaphic and climatic factors [2]. Understanding the pattern of distribution of organisms is a key aspect in conservation and management [3]. Exploitation of wetland plants through legal or illegal means and alien species invasion have resulted in the decline of population of many valuable wetland plants that are of ecological and economic significance. The influx of invasive and alien species will eventually cause the phyto-sociology of the native aquatic and wetland plant species to shift due to the trend of changing environmental variables. Further, a large number of wetland plants have become threatened due to their small population size, narrow distribution area, destructive mode of harvesting, climate change, habitat loss, etc. [4][5]. Although extensive research has been carried out on importance of wetland plants of the Loktak Lake, a well- defined quantitative study on the distribution pattern of the wetland plants in Thanga area is lacking. In this regard, the present study was initiated to investigate the distribution pattern of wetland plants in Thanga area.

MATERIALS AND METHODS

The study site, Thanga is an island village and is located within Loktak Lake in the Bishnupur District of Manipur at an altitude of about 780-860 m above sea level and lies between $24^0 53'06''$ N latitude and $93^0 82'29''$ E longitude. The total geographical area of the study site is 1614.17 hectares i.e., 16.1417 sq. km. Regular field surveys were carried out and floristic composition of the species in different study sites was properly analysed. Data was collected using quadrat sampling method by randomly laying 10 quadrats of 1x1 m^2 from 10 sampling sites. The plants occurring in each quadrate were identified with the help of their local name and by referring the authentic literature [6][7][8][9][10][11][12][13][14][15] and the Dhanamanjurian Herbarium (DMH), Department of Botany. Identification of invasive species was carried out with the help of various literature such as [16][17][18][19][20][21][22][23]. The local indigenous species were recognised by their aged old occurrence in the area. Nomenclature of the species was based on databases of [24][25][26]. The recorded data was quantitatively analysed for density, frequency and abundance following [27]. The relative values of these indices were determined and summed up to get Importance Value Index (IVI) of individual species [28] and abundance-frequency ratio [29] were also calculated and compared. The ratio of abundance to frequency is used to represent the distribution pattern. A value below 0.025 was considered as regular distribution; 0.025-0.05 as random distribution and more than 0.05 as contiguous distribution pattern [30].

The formulae used were as follows:

$$\text{Frequency (F)} = \frac{\text{Total no.of quadrates in which a species occurred}}{\text{Total no.of quadrates sampled}}$$

$$\text{Frequency (\%)} = \frac{\text{no.of quadrates in which species occurred}}{\text{Total no.of quadrates sampled}} \text{ x } 100$$

$$\text{Relative Frequency (R. F)} = \frac{\text{Frequency of the species}}{\text{Total frequency of all species}} \text{x} 100$$

$$\text{Density (D)} = \frac{\text{Total number of individuals of the species}}{\text{Total number of quadrates taken}}$$

$$\text{Relative Density (R. D.)} = \frac{\text{Density of the species}}{\text{Total density of all species}} \text{x} 100$$

$$\text{Abundance (A)} = \frac{\text{No.of individual species}}{\text{No.of quadrats in which species occurred}}$$

$$\text{Relative abundance (R.A.)} = \frac{\text{Abundance of a particular species}}{\text{Total abundance of all species}} \text{X}100$$

Importance Value Index (IVI)= Relative frequency+ Relative density+ Relative abundance

RESULT AND DISCUSSION

A total of 100 wetland plants belonging to 50 families and 82 Genera were recorded. Poaceae (15 species) represented the maximum number of species followed by Asteraceae (14 species); Polygonaceae (8 species) and Amaranthaceae (6 species); Araceae (4 species); Zingiberaceaea and Convolvulaceae (3 species each); Apiaceae, Cucurbitaceae, Onagraceae, Orchidaceae, Lythraceae, Nelumbonaceae and Nymphaeaceae (2 species each) and the rest of the families with 1 species each. Out of 100, 40 are invasive plants (Table 1) and 60 are indigenous (Table 2). Among the invasive plants, *Ludwigia adscendens* has the highest IVI value (20.36) followed by *Alternanthera philoxeroides* (16.16) and *Mikania scandens* (15.40). And for the indigenous plants, *Leersia hexandra* has the IVI value of 15.31 followed by *Zizania latifolia* (14.64) and *Hydrocharis dubia* (13.28). The densities of the invasive plants are ranged from 0.75 to 19.11 individuals/m^2 (Table 1). Similarly, frequency and IVI ranged from 22%-81% and 0.15- 20.36 respectively. *Pistia stratiotes* (81%) is the most frequent in its occurrence followed by *Pontederia crassipes* (79%) and *Mikania scandens* (67%). *Ludwigia adscendens* (20.36) has the highest IVI value thereby acting as the dominant cover among the invasive wetland plants. The densities of the indigenous plants range from 0.25- 12.8 individuals/m^2 (Table 2). Frequency and IVI ranged from 10%- 57% and 1.14- 15.31 respectively. *Zizania latifolia* (57%) is the most frequent in its occurrence. *Leersia hexandra* (15.31) has the highest IVI and showed good power of regeneration. In Fig. 1, IVI range is divided into 6 groups starting from 0.00-4.00 up to 20.01-24.00. There are 8 species in the 0.00-4.00 range, 20 species in the 4.01-8.00 range, 6 species in the 8.01-12.00 range, 4 species in the 12.01-16.00 range and only 1 species each in the 16.01-20.00 range and 20.01-24.00 range respectively. The number of species is highest in the IVI range 4.01-8.00. However, the most abundant and dominant species are found within the IVI range 16.01-20.00 and 20.01-24.00.

In Fig. 2, IVI range is divided into 4 groups starting from 0.00-4.00 and going up to 12.01-16.00. There are 31 species in the 0.00-4.00 range, 23 species in the 4.01-8.00 range, 1 species in the 8.01-12.00 range and 5 species in the 12.01-16.00 range. The maximum number of species is found in the IVI range 0.00-4.00. The dominant species are found within the IVI range 12.01-16.00. The maximum number of invasive species occurs in the IVI range of 4.01-8.00 whereas the maximum number of indigenous species is found in the IVI range of 1.00-4.00. This shows that the invasive species have higher overall impact in the wetland ecosystem and are dominating the indigenous species. This dominance is attributed to various factors such as rapid growth and reproduction rate of invasive species outcompeting the indigenous species and disruption of the ecological balance. At the same time, the lower IVI range of total no. of indigenous species is threatening to the wetland ecosystem. In this study, all the wetland plants have the A/F ratio above 0.05, therefore, all of them show contiguous distribution [31] in natural condition [32]. As both the indigenous and invasive plants have a contiguous distribution, it can lead to several ecological consequences. There will be intense competition between them for the available resources such as light, water and other nutrients leading to the decline of native plant population. The spread of invasive species can reduce the local biodiversity which in turn alter the structure and function of the overall existing ecosystem.

CONCLUSION

Considering the above facts, it is revealed that the wetland plants have contiguous distribution that is both the invasive and indigenous wetland plants become naturalized in the wetland ecosystem and compete for nutrient resources and space among themselves with the prevailing environmental conditions. A long-term planning for detailed studies for the identification of invasive alien wetland plants from the wetlands of Manipur and their mode of invasion and threats is the need of the hour. More interdisciplinary research that focuses on combining ecological, social and economic perspectives is needed to address the complex issue of alien species invasion. Among the

remedial measures, detection of invasive alien species at the early stages of succession, local people participation and regulatory policy measures can lead to their sustainable management.

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Table.1: IVI and A/F ratio of invasive wetland plants

Sl. No.	Name of plants	Total no. of species	Density	Total density	Relative density	quadrates in which species	quadrates in which species	Frequency	Frequency %	Total frequency	Relative frequency	Abundance	Total abundance	Relative abundance	A/F	IVI
1	*Achyranthes aspera* L.	156	1.56	203.6	0.77	35	1857	0.35	35	18.57	1.88	4.46	390.03	1.14	0.13	3.79
2	*Acmella paniculata* (Wall. *ex* DC)	606	6.06		2.98	61		0.61	61		3.28	9.93		2.55	0.16	8.81
3	*Ageratina adenophora* (Spreng.) R. M. King & H. Rob.	567	5.67		2.78	57		0.57	57		3.07	9.95		2.55	0.17	8.40
4	*Ageratum conyzoides* (L.) L.	773	7.73		3.80	62		0.62	62		3.34	12.47		3.20	0.20	10.33
5	*Ageratum houstonianum* Mill.	356	3.56		1.75	42		0.42	42		2.26	8.48		2.17	0.20	6.18
6	*Alternanthera philoxeroides* (Mart.) Griseb.	1442	14.42		7.08	69		0.69	69		3.72	20.90		5.36	0.30	16.16
7	*Alternanthera sessilis* (L.) R. Br.	218	2.18		1.07	29		0.29	29		1.56	7.52		1.93	0.26	4.56

	ex DC.															
8	*Amaranthus spinosus* L.	225	2.25		1.11	40		0.4	40		2.15	5.63		1.44	0.14	4.70
9	*Arundo donax* L.	186	1.86		0.91	28		0.28	28		1.51	6.64		1.70	0.24	4.12
10	*Argyreia nervosa* (Burm.f.) Bojer	417	4.17		2.05	40		0.4	40		2.15	10.43		2.67	0.26	6.88
11	*Bidens pilosa* L.	137	1.37		0.67	32		0.32	32		1.72	4.28		1.10	0.13	3.49
12	*Bryonposis lasiniosa* L.	261	2.61		1.28	32		0.32	32		1.72	8.16		2.09	0.25	5.10
13	*Cardamine hirsuta* L.	282	2.82		1.39	41		0.41	41		2.21	6.88		1.76	0.17	5.36
14	*Chenopodium album* L.	243	2.43		1.19	32		0.32	32		1.72	7.59		1.95	0.24	4.86
15	*Coix lacryma-jobi* L.	75	0.75		0.37	22		0.22	22		1.18	3.41		0.87	0.15	2.43
16	*Commelina benghalensis* L.	957	9.57		4.70	60		0.6	60		3.23	15.95		4.09	0.27	12.02
17	*Crassocephalum crepidioides* (Benth.) S. Moore	135	1.35		0.66	37		0.37	37		1.99	3.65		0.94	0.10	3.59
18	*Cuscuta reflexa* Roxb.	356	3.56		1.75	32		0.32	32		1.72	11.13		2.85	0.35	6.32
19	*Cynodon dactylon* (L.) Pers.	941	9.41		4.62	54		0.54	54		2.91	17.43		4.47	0.32	12.00
20	*Eclipta prostrata* (L.) L.	157	1.57		0.77	37		0.37	37		1.99	4.24		1.09	0.11	3.85
21	*Galinsoga parviflora* Cav.	467	4.67		2.29	46		0.46	46		2.48	10.15		2.60	0.22	7.37
22	*Grangea maderaspatana* (L.) Poir.	522	5.22		2.56	49		0.49	49		2.64	10.65		2.73	0.22	7.93
23	*Ipomoea cairica* (L.) Sweet	1155	11.55		5.67	71		0.71	71		3.82	16.27		4.17	0.23	13.67

24	*Ludwigia adscendens* (L.) H. Hara	1911	19.11		9.39	66		0.66	66		3.55	28.95		7.42	0.44	20.36
25	*Ludwigia octovalvis* (Jacq.) P. H. Raven	121	1.21		0.59	41		0.41	41		2.21	2.95		0.76	0.07	3.56
26	*Mikania scandens* (L.) Willd.	1350	13.5		6.63	67		0.67	67		3.61	20.15		5.17	0.30	15.40
27	*Persicaria barbata* (L.) H. Hara	499	4.99		2.45	54		0.54	54		2.91	9.24		2.37	0.17	7.73
28	*Persicaria hydropiper* (L.) Delarbre	176	1.76		0.86	38		0.38	38		2.05	4.63		1.19	0.12	4.10
29	*Phragmites karka* (Retz.) Trin. Ex Steud.	472	4.72		2.32	37		0.37	37		1.99	12.76		3.27	0.34	7.58
30	*Pistia stratiotes* L.	1222	12.22		6.00	81		0.81	81		4.36	15.09		3.87	0.19	14.23
31	*Plantago major* L.	261	2.61		1.28	54		0.54	54		2.91	4.83		1.24	0.09	5.43
32	*Pontederia crassipes* Mart.	865	8.65		4.25	79		0.79	79		4.25	10.95		2.81	0.14	11.31
33	*Pontederia hastata* L.	111	1.11		0.55	28		0.28	28		1.51	3.96		1.02	0.14	3.07
34	*Portulaca olecea* L.	262	2.62		1.29	31		0.31	31		1.67	8.45		2.17	0.27	5.12
35	*Rumex maritimus* L.	351	3.51		1.72	46		0.46	46		2.48	7.63		1.96	0.17	6.16
36	*Salvinia cucullata* Bory	356	3.56		1.75	40		0.4	40		2.15	8.90		2.28	0.22	6.18
37	*Solanum nigrum* L.	438	4.38		2.15	49		0.49	49		2.64	8.94		2.29	0.18	7.08
38	*Stellaria media* (L.) Vill.	165	1.65		0.81	27		0.27	27		1.45	6.11		1.57	0.23	3.83
39	*Synedrella nodiflora* (L.) Gaertn	870	8.7		4.27	60		0.6	60		3.23	14.50		3.72	0.24	11.22

40	*Trapa natans var bispinosa* (Roxb.) Makino	296	2.96		1.45	51		0.51	51		2.75	5.80		1.49	0.11	5.69

Table 2. IVI and A/F ratio of indigenous wetland plants

Sl. No.	Name of species	Total no. of species	Density	Total density	Relative density	quadrates in which species	species occurred	Frequency	Frequency %	Total frequency	Relative frequency	Abundance	Total abundance	Relative abundance	A/F	IVI
1	*Acorus calamus* L.	25	0.25	181.08	0.14	10	2288	0.1	10	22.88	0.44	2.50	439.89	0.57	0.25	1.14
2	*Actinostemma tenerum* Griff.	288	2.88		1.59	51		0.51	51		2.23	5.65		1.28	0.11	5.10
3	*Adiantum capillus veneris* L.	218	2.18		1.20	44		0.44	44		1.92	4.95		1.13	0.11	4.25
4	*Alocasia macrorrhizos* (L.) G. Don	93	0.93		0.51	16		0.16	16		0.70	5.81		1.32	0.36	2.53
5	*Alpinia galanga* (L.) Willd.	169	1.69		0.93	36		0.36	36		1.57	4.69		1.07	0.13	3.57
6	*Alpinia nigra* (Gaertn.) Burtt	79	0.79		0.44	18		0.18	18		0.79	4.39		1.00	0.24	2.22
7	*Amaranthus viridis* L.	219	2.19		1.21	46		0.46	46		2.01	4.76		1.08	0.10	4.30
8	*Anaphalis contorta* (D.Don) Hook.f.	228	2.28		1.26	43		0.43	43		1.88	5.30		1.21	0.12	4.34
9	*Arundo plinii* Turra	139	1.39		0.77	38		0.38	38		1.66	3.66		0.83	0.10	3.26
10	*Azolla pinnata* R.Br.	560	5.6		3.09	42		0.42	42		1.84	13.33		3.03	0.32	7.96
11	*Cardiospermum halicacabum* L.	127	1.27		0.70	36		0.36	36		1.57	3.53		0.80	0.10	3.08
12	*Cayaponia laciniosa* (L.) C. Jeffrey	108	1.08		0.60	35		0.35	35		1.53	3.09		0.70	0.09	2.83

13	*Centella asiatica* (L.) Urb.	379	3.79		2.09	39		0.39	39		1.70	9.72		2.21	0.25	6.01
14	*Chrysopsis mariana* Elliott	112	1.12		0.62	35		0.35	35		1.53	3.20		0.73	0.09	2.88
15	*Colocasia esculenta* (L.) Schott	163	1.63		0.90	42		0.42	42		1.84	3.88		0.88	0.09	3.62
16	*Colocasia esculenta* var. *aquatilis* Hasskarl	119	1.19		0.66	29		0.29	29		1.27	4.10		0.93	0.14	2.86
17	*Cyperus rotundus* L.	122	1.22		0.67	37		0.37	37		1.62	3.30		0.75	0.09	3.04
18	*Drymaria cordata* (L.) Willd. *ex* Schult.	191	1.91		1.05	39		0.39	39		1.70	4.90		1.11	0.13	3.87
19	*Dryopteris marginata* (C.B. Clarke) Christ	202	2.02		1.12	39		0.39	39		1.70	5.18		1.18	0.13	4.00
20	*Eleusine indica* (L.) Gaertn.	242	2.42		1.34	42		0.42	42		1.84	5.76		1.31	0.14	4.48
21	*Enydra fluctuans* DC.	728	7.28		4.02	46		0.46	46		2.01	15.83		3.60	0.34	9.63
22	*Euryale ferox* Salisb.	152	1.52		0.84	27		0.27	27		1.18	5.63		1.28	0.21	3.30
23	*Exallaga auricularia* (L.) Bremek	204	2.04		1.13	38		0.38	38		1.66	5.37		1.22	0.14	4.01
24	*Floscopa scandens* Lour.	103	1.03		0.57	36		0.36	36		1.57	2.86		0.65	0.08	2.79
25	*Goodyera procera* (Ker Gawl.) Hook.	113	1.13		0.62	37		0.37	37		1.62	3.05		0.69	0.08	2.94
26	*Hedychium coronarium* J. Koenig	98	0.98		0.54	38		0.38	38		1.66	2.58		0.59	0.07	2.79
27	*Hydrilla verticillata* (L.f.) Royle	537	5.37		2.97	48		0.48	48		2.10	11.19		2.54	0.23	7.61

28	*Hydrocharis dubia* (Blume) Backer	1117	11.2		6.17	53		0.53	53		2.32	21.08		4.79	0.40	13.28
29	*Hydrocotyle moschata* G. Forst.	472	4.72		2.61	41		0.41	41		1.79	11.51		2.62	0.28	7.02
30	*Hygroryza aristata* (Retz.) Nees ex Wight & Arn.	359	3.59		1.98	36		0.36	36		1.57	9.97		2.27	0.28	5.82
31	*Ipomoea aquatica* Forssk.	235	2.35		1.30	44		0.44	44		1.92	5.34		1.21	0.12	4.43
32	*Koenigia mollis* (D. Don)	170	1.7		0.94	44		0.44	44		1.92	3.86		0.88	0.09	3.74
33	*Leersia hexandra* Sw.	1288	12.9		7.11	48		0.48	48		2.10	26.83		6.10	0.56	15.31
34	*Lemna minor* L.	1036	10.4		5.72	47		0.47	47		2.05	22.04		5.01	0.47	12.79
35	*Leucas aspera* (Willd.) Link.	116	1.16		0.64	40		0.4	40		1.75	2.90		0.66	0.07	3.05
36	*Lysimachia candida* Lindl.	87	0.87		0.48	35		0.35	35		1.53	2.49		0.57	0.07	2.58
37	*Nelumbo nucifera* Gaertn.	307	3.07		1.70	48		0.48	48		2.10	6.40		1.45	0.13	5.25
38	*Nelumbo nucifera* Gaertn. (white)	189	1.89		1.04	39		0.39	39		1.70	4.85		1.10	0.12	3.85
39	*Nymphaea nouchali* Burm. f.	253	2.53		1.40	42		0.42	42		1.84	6.02		1.37	0.14	4.60
40	*Nymphoides indica* (L.) Kuntze	429	4.29		2.37	42		0.42	42		1.84	10.21		2.32	0.24	6.53
41	*Oenanthe javanica* (Blume) DC.	484	4.84		2.67	40		0.4	40		1.75	12.10		2.75	0.30	7.17
42	*Osbeckia chinensis* L.	145	1.45		0.80	30		0.3	30		1.31	4.83		1.10	0.16	3.21

43	*Persicaria chinensis* (L.) H. Gross	393	3.93		2.17	36		0.36	36		1.57	10.92		2.48	0.30	6.23
44	*Persicaria glabra* (Willd.) M. Gomez	317	3.17		1.75	35		0.35	35		1.53	9.06		2.06	0.26	5.34
45	*Persicaria minor* (Huds.) Opiz	200	2		1.10	36		0.36	36		1.57	5.56		1.26	0.15	3.94
46	*Persicaria perfoliata* (L.) H. Gross	218	2.18		1.20	40		0.4	40		1.75	5.45		1.24	0.14	4.19
47	*Phyllanthus urinaria* L.	117	1.17		0.65	39		0.39	39		1.70	3.00		0.68	0.08	3.03
48	*Rotala rotundifolia* (Buch-Ham ex Roxb.) Koehne	169	1.69		0.93	41		0.41	41		1.79	4.12		0.94	0.10	3.66
49	*Sacciolepis interrupta* (Willd.) Stapf	97	0.97		0.54	29		0.29	29		1.27	3.34		0.76	0.12	2.56
50	*Setaria pumila* (Poir.) Roem. & Schult.	201	2.01		1.11	32		0.32	32		1.40	6.28		1.43	0.20	3.94
51	*Spiranthes cernua* (L.) Rich.	41	0.41		0.23	22		0.22	22		0.96	1.86		0.42	0.08	1.61
52	*Trapa natans* L.	102	1.02		0.56	24		0.24	24		1.05	4.25		0.97	0.18	2.58
53	*Tripadium arundinaceum* (Retz.) Welker, Voronts. & E.A. Kellogg	191	1.91		1.05	46		0.46	46		2.01	4.15		0.94	0.09	4.01
54	*Tripidium bengalense* (Retz.) H. Scholz	218	2.18		1.20	44		0.44	44		1.92	4.95		1.13	0.11	4.25

55	*Tripidium procerum* (Roxb.) Welker, Voronts. & E. A. Kellogg	191	1.91		1.05	36		0.36	36		1.57	5.31		1.21	0.15	3.83
56	*Urochloa mutica* (Forssk.) T.Q. Nguyen	370	3.7		2.04	43		0.43	43		1.88	8.60		1.96	0.20	5.88
57	*Uttricularia aurea* Lour.	342	3.42		1.89	26		0.26	26		1.14	13.15		2.99	0.51	6.02
58	*Vallisneria spiralis* L.	1062	10.6		5.86	44		0.44	44		1.92	24.14		5.49	0.55	13.27
59	*Vigna mungo* (L.) Hepper	197	1.97		1.09	42		0.42	42		1.84	4.69		1.07	0.11	3.99
60	*Zizania latifolia* (Grieseb.) Hance *ex* F. Mull	1277	12.8		7.05	57		0.57	57		2.49	22.40		5.09	0.39	14.64

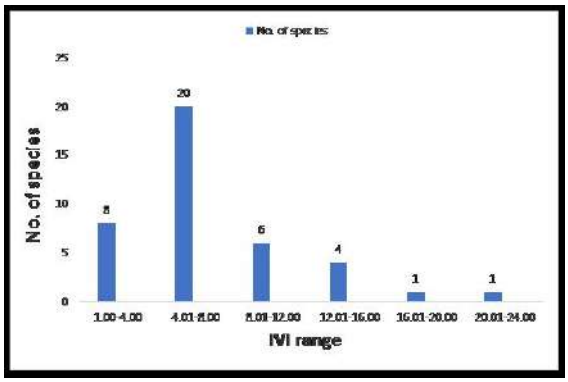

Figure.1. Graph showing IVI range with maximum no. of invasive species

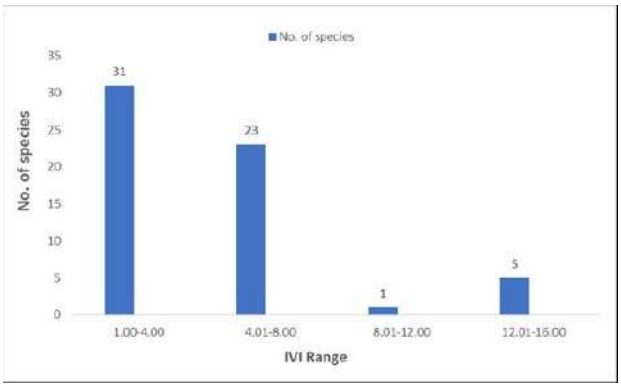

Figure. 2. Graph showing IVI range with maximum no. of indigenous species

RESEARCH ARTICLE

Global Regulatory Frame Work for Medical Foods: Filing

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ABSTRACT

Medical foods plays a vital role in accomplishing the nutritional requirements in patients with inborn errors of metabolism(IEM) and FDA considers that these foods treat the disease conditions more specifically and gains significant importance in further decades .This abstract explores the history of medical foods along with key benefits and currently marketed products .Furthermore it focusses on few regulations on basis of Orphan Drug Act 1983 and Nutritional Labelling and Education Act(NLEA) of 1990.It summarizes the global aspects of medical foods.

Keywords: Global aspects, Orphan drug act, enteral route, GRAS, Metabolic disorders, Infant milk formula.

INTRODUCTION

The term medical food defines a food which is formulated to be consumed under the supervision of a physician and which is intended for the specific management of disease based on recognized scientific principles established by medical evaluation. As per the US Food and Drug Administration section 5(b)(3) of the orphan drug Act 1988 medical food is defined as a food which is formulated to be consumed or administered enterally under the supervision of physician[1]. The medical foods help the patients to manage the diseases and improve their quality of life. These are specific category of products that are not available as the over the counter drugs and availability is

limited to only pharmacies. They are naturally occurring foods which are processed and available around the world but many people are unaware of these products and their uses. The medical foods are used to treat diseases like Diabetes ,Alzheimer's disease ,Gastrointestinal disorders ,Cancer and other metabolic disorders .The scope of medical foods has increased globally because of the chronic and geneticdiseases which are treated with allopathic medicines has increased side effects .The market value has gradually increased by 20.15 billion dollars in 2020[1].

History of Medical Foods

Medical foods were developed more than half century ago. The first medical food was infant milk formula (LOFENALAC) which was prescribed to replace the milk in the infants suffering with phenylketonuria marketed by Med Johnson and approved by US FDA.

Key Regularities of Medical Foods in accordance with FDA

- It should be formulated as a product which is generally not consumed in its natural state but processed for administering to patients by oral or enteral route under the medical supervision of physician.
- It should serve as nutritional support to the patient and help in management of dietary requirements as they have limited capacity to ingest, digest, absorb or metabolize certain nutrients due to underlying any specific disease or condition.
- It should be provided to the patients who are on medical care on regular basis as they couldn't fulfill the nutrient needs of the body by diet alone.

Medical foods are classified under the following categories

- Nutritionally complete formula
- Nutritionally incomplete formulas, these are the products which are mixed with other products before use Ex: Protiens, carbohydrates, fat modulators
- Formulas for metabolic disorders in patients over 12 months of age.
- Oral rehydration products.

METHODOLOGY

Regulatory bodies approving medical foods: India :In India, Food products, including medical foods are governed by the Food Safety and Standard Authority of India (FSSAI). The main aim is to provide approval of non-specified foods before launching in the market. It takes 6 to 12 months for the approval process.

Who can apply?

Any manufacturer, importer, marketer involved in the business of non-specified foods, including medical foods can apply for the approval.

Procedure to apply:

Initially, the dossier should be prepared in a given format furnishing all the details, including the scientific information. Application Form 1 should be filled by uploading all the relevant documents and pay the requisite fee of 50,000 including GST. The expert committee appointed by the food authority will review the application. Any Descrepancies in the application will be informed to the applicant within 45 days from the date of application. The FBO(Food Business Operator) should reply with the required details within the 30 days of the receipt of the review letter .Depending upon the information the application may be accepted or rejected. The chairperson will make the final decision for the approval.

Benefits of medical foods

- The major benefit is they are exempted from nutritional labelling requirements and claims under the Nutritional Labelling and Education Act (NLEA)1990.

- It doesn't require pre market approval from FDA and FDA Does not evaluate the medical foods and has limited regulatory conditions.
- The food products or the additives should be considered as the safe for their intended use according to the GRAS (Generally recognized as safe)

MARKETED PRODUCTS OF MEDICAL FOODS

Axona: It provides necessary nutrients for the patient suffering with Alzheimer's disease by increasing the ability of brain to metabolize the glucose.

Limbrel: It is used in the treatment of osteoarthritis which was marketed by Primus pharmaceuticals.

Lofenalac: It is used for the dietary management of Phenylketonuria (Pku)in which there is defect in phenyl alanine hydroxylase enzyme which converts the amino acid phenylalanine to tyrosine.

The FDA requires the complete information on manufacturing facility, processing, packing for conducting the periodic inspections and collect samples for nutrient and microbiological analysis.

In United States there is high rate of occurrence of certain chronic diseases like Diabetes, cancer, cardiovascular problems which significantly increases the demand for medical foods as they improve the nutritional status of patients and beneficial to prevent the disease.

The Chinese government has come up with certain regulations for ensuring the quality and safety standards which promotes the use of medical foods and to prevent cancer, diabetes.

CONCLUSION

It is concluded that medical foods have wide range of utilization in the global market as there is increase in demand for specific nutritional requirements in the healthcare in treating various metabolic disorders effectively. The regulations of medical foods have been emerged and improving gradually to ensure their proper use in treating various diseased conditions.

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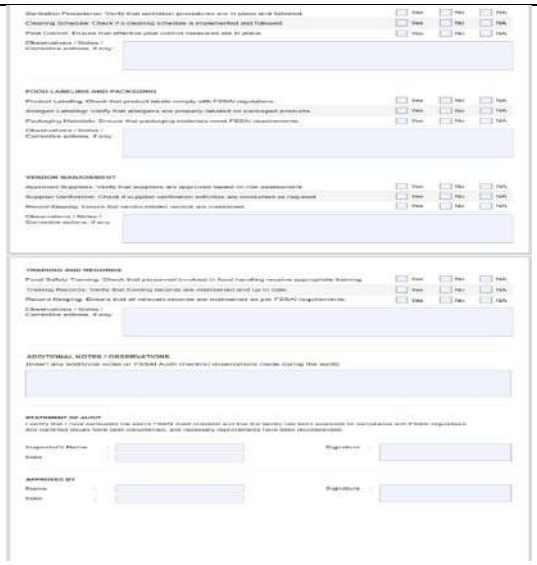

Fig 1: Checklist of FSSAI

Fig 2: Regulatory approval process of EU

Fig 3: Examples of Marketed Product

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RESEARCH ARTICLE

Bird-Centric Ecotourism Potential in and Around the Kailashpuri Village of Udaipur District, Rajasthan

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ABSTRACT

Birds, recognized as the most beautiful creatures in the natural world, are a group of vertebrates that have feathers, wings and hollow bones as natural adaptations for their flight-based life style. Bird serves as indicators of many environmental and ecological factors in a given region and also offers diverse ecological functions to ecosystems, including the dispersion of seeds, pollen and scavenging carcasses. In view of the importance of bird community, it is critical to establish bird-centric ecotourism sites in a variety of locations, including towns and villages, to effectively conserve birds and habitat. Current study was conducted to analyze the bird community in a 20-kilometer radius of Kailashpuri village, Udaipur district, in a variety of habitats such as wetlands, rocky areas, roadside areas, colonies, agricultural fields and riverine habitats. We documented a total of 185 avian species during the field survey, classifying them into 62 distinct families. Based on the residential status of species, we identified the majority of bird species as residents (124) followed by winter migrants (58), summer migrants (2) and one species classified as monsoon migrants. Among bird species, the IUCN classification categorizes the majority in the least concern group (169), followed by near threatened (9), vulnerable (River Tern, Common Poachard, White-napped Tit), endangered (Egyptian vulture) and critically endangered (Indian vulture).

Keywords: Bird, Indicator, Ecotourism, Kailashpuri village, Habitat, Species.

INTRODUCTION

Avian species have a widespread global distribution, ranging across all continents and occupying diverse ecosystems such as forests, grasslands, wetlands, agricultural landscapes, urban areas and even the polar regions of the northern and southern hemispheres (Pomeroy, 1992). Birds exhibit significant diversity in morphological and behavioural characteristics, including variations in colour, foot structures, feeding methods, beak types, vocalizations and songs, courtship displays and nesting patterns. Owing to these patterns, birds possess a distinctive aesthetic attraction in the natural world (Wenny *et al.,* 2011; Brusatte *et al.,* 2015). Indian subcontinent is a region with incredible geographical variation, including India, Nepal, Bhutan, Pakistan, Sri Lanka, Bangladesh and the Maldives. The region has a diverse flora and wildlife, including a robust avian community. Ali and Ripley (1987) listed 1260 bird species in the Indian Subcontinent. Later, Inskipp *et al.* (1999) documented 1299 bird species from India, accounting for around 13-14% of global avian diversity. According to Praveen *et al.* (2016), India contains 1263 bird species, accounting for around 12% of the world's total. Ecotourism, which refers to tourism activities centred on ecology and wildlife, has the potential to be a successful medium for educating the public about sustainable environmental practices. Affection and dedication associated with this recreation hobby attracts birdwatchers to remote places and creating job opportunities for locals. Several studies have been carried out on the potential development of bird-centric ecotourism at the global level (Steven *et al.,* 2013 and 2015). Various studies have been conducted on the prominent areas of bird watching, bird festivals and potential impact of bird watching on ecosystems and their impacts on local peoples (Lawton, 2009; Biggs *et al.,* 2011; Puhakka *et al.,* 2011; Gupta *et al.,* 2019; Choudhary, 2024). Excessive tourism and anthropogenic activity can have an adverse impact on wildlife and their habitat. However, it is crucial to conduct thorough survey and planning before establishing ecotourism sites or activities to prevent or limit environmental and wildlife damage (Burger *et al.,* 1995). Before developing bird-centric ecotourism spots, it is vital to understand the factors that influence bird behaviour and human disturbances. Study of human-based variables influencing bird communities provides a clear picture for future plan and the formulation of successful management practices in a specific area. Currently, there is a significant increase in avian-focused ecotourism expansion, particularly in areas with rich biodiversity. Ecotourism can generate the required financial means to cover crucial management costs in protected areas like tiger reserves, national parks and sanctuary areas (Buckley *et al.,* 2016; Di Minin *et al.,* 2016). An important aspect of ecotourism is its ability to simultaneously support the conservation of biodiversity and stimulate economic growth (Kruger, 2005). Subsequently, present study provided a detailed account of bird-centric ecotourism opportunities in and around Kailashpuri village in Udaipur district, Rajasthan, India.

MATERIAL AND METHODS

Study was conducted from July 2017 to June 2024, excluding the COVID-19 lockdown period. Field surveys were conducted from 7:00 a.m. to 11:00 a.m. and 3:00 p.m. to 6:00 p.m. during winter season and from 6:00 a.m. to 10:00 a.m. and 4:00 p.m. to 7:00 p.m. during summer season. During rainy season, field surveys were conducted when weather was clear and no precipitation had occurred. Field surveys were conducted in various habitats, including wetland, rocky areas, roadside areas, colonies, agricultural fields and riverine habitats, within a 20-kilometer radius of Kailashpuri village, Udaipur district. To avoid disturbing the birds, we visually examined those using Nikon 8x42 binoculars and cameras, specifically a Nikon P1000 and a Canon 700D, at a suitable distance. Identification and field diagnosis characters of birds were done by using standard field guides, such as Birds of the Indian Subcontinent (Grimmett *et al.,* 2011), Birds of Rajasthan (Vyas, 2013) and Birds of India (Majumder *et al.,* 2022). Throughout study, the nomenclature was followed as defined by Praveen *et al.* (2016), Praveen and Jayapal (2023), Birdlife International (2024) and IUCN Red List (2024) for common name, scientific name, families and orders of birds. Bird species that were identified were classified based on the IUCN threat categories, specifically least concern (LC), near-threatened (NT), vulnerable (VU), endangered (EN) and critically endangered (CE) (Birdlife International, 2024; IUCN, 2024). We determined the birds' residential status based on their occurrence throughout the entire study period. We observe resident birds year-round. We classify the bird as a summer migratory (SM) when observed exclusively during the summer season (March to June), a monsoon migratory (MM) when observed during the monsoon season (July to

September), and a winter migratory (WM) when observed during the winter season (October to February) (Choudhary and Chishty, 2023; Choudhary, 2024).

RESULT AND DISCUSSION

Rajasthan state boasts an array of attractions, encompassing magnificent palaces, ancient forts and renowned world heritage sites. Visitors can also enjoy the luxurious lodgings provided by the hotels, as well as the opportunity to fully participate in the abundant traditions and vibrant fairs. This exhibition features a variety of protected areas, including wildlife sanctuaries, national parks, tiger reserves, waterfalls, ancient and historical monuments, religious temples, desert safaris and picturesque landscapes such as hilly terrain, mountain ranges, sand dunes and river canals. These attractions possess the ability to thoroughly engage both domestic and foreign tourists in Rajasthan. We assessed the potential for bird-centric ecotourism in and around Kailashpuri village in Udaipur district.

Bird's community in and around Kailashpuri village:

During study, we observed a total of 185 bird species belonging to 62 families. Out of these, on the basis of residential status of species, most of the bird species belong to the resident category (124) followed by winter migration (58), summer migration (2) and one species belongs to monsoon migration category; these species were Pied-crested Cuckoo or Jacobin Cuckoo (Table 1). The IUCN status of birds places most species in least concern category (169) followed by near threatened (9), vulnerable (River Tern, Common Poachard and White-napped Tit), endangered (Egyptian vulture) and critically endangered (Indian vulture) (Table 1).

Other wild mammalian species spotted around the Kailashpuri village

During field surveys, following mammalian wild species were observed in and around the Kailashpuri village. These species were Leopard (*Panthera pardus*), Jungle Cat (*Felis chaus*), Indian Jackal (*Canis aureus*), striped hyena (*Hyaena hyaena*), Ruddy Mongoose (*Herpestes smithi*), Indian Grey Mangoose (*Urva edwardsii*), Hanuman Langur (*Semnopithecus entellus*) and Rhesus macaque (*Macaca mulatta*).

Historical and religious significance of Kailashpuri village

Mewar ruler Bappa Rawal built the Ekling Ji temple in the 8th century, but Maharana Raimal gave it its current structure. Ekling ji is considered the presiding deity of the Guhil dynasty kings. Other temple the Saas-Bahu mandir was situated near Kailashpuri village in Nagda. This is dedicated to Lord Vishnu. Nagaditya built it in Nagda village in the sixth century. Ecotourism is a form of tourism that serves as an alternative to mass or unregulated tourism. It involves active exploration and visitation of natural regions, with a primary emphasis on the conservation and protection of environment and its biodiversity, as well as gaining knowledge about it. Exploring natural regions not only contributes to environmental conservation but also increases public awareness of the significance of biodiversity. Ecotourism is an excellent way to investigate the incredible beauty of nature while also helping to maintain forests and wildlife and promote sustainable economic development. The potential for the establishment of ecotourism sites is entirely contingent upon the presence of biodiversity and wildlife in certain regions. Ecotourism focused on birds, or avi-tourism, is a significant and essential component of the nature-oriented tourist sector (Newsome *et al.,* 2005; Biggs *et al.,* 2011). Dedicated avian enthusiasts travel great distances to closely study birds in various locations renowned for their diverse range of species and distinct endemic species populations (Connell, 2009). Avi-tourists, renowned for their passion for avian perception, are recognized as some of the most affluent nature-oriented tourists in the industry. The costs they accumulate for trip demonstrate their commitment to investigate the realm of avian species (Cordell and Herbert, 2002; Sekercioglu, 2003). Previous studies have examined the positive effects that birdwatchers can have on nearby towns, notably during bird watching festivals and migratory events (Lawton, 2009). Several research initiatives have been undertaken to investigate the effects of avi-tourism or bird watching on the avian population (Biggs *et al.,* 2011; Puhakka *et al.,* 2011; Steven *et al.,* 2011). Similarly, recent long-term studies have provided comprehensive information on the presence of numerous species of birds in and around Kailashpuri village during different seasons. Kailashpuri village also contained breeding

colonies of the critically endangered bird species known as the Indian Vulture (*Gyps indicus*) (Chishty and Choudhary, 2020; Choudhary *et al*., 2021). Similarly, Choudhary (2024) carried out a study to assess the potential of bird-centric ecotourism sites in Mount Abu Wildlife Sanctuary. They carried out site-based studies such as water body-based, forest trail-based, and village-based. They identified a total 201 bird species with some key avifaunal species, including Green Avadavat, Grey Jungle fowl, Aravalli Red-Spur fowl, Mount Abu Scimitar Babbler, Mount Abu White-throated Babbler and Rajasthan Red-whiskered Bulbul in the sanctuary area. Bird watching has emerged as the fastest-growing and most environmentally responsible sector of ecotourism, due to the passion and dedication of many birdwatchers, as well as the enormous resources they provide to the cause. This has offered economic opportunities for many fragile natural locations around the world (Cordell and Herbet, 2002). Moreover, Kailashpuri village boasts an ancient and beautiful Lord Shiva temple, also known as Ek-ling ji. Numerous domestic and foreign tourists also visit this place every year. This region, with its high bird diversity and variety of habitats, will lead to the development of bird-centric ecotourism sites around Kailashpuri village, providing greater opportunities for bird watching. Hardansyah (2012) asserts that wildlife, including birds, possesses a high aesthetic value and can contribute to the enhancement of ecotourism activities. Birds have a high aesthetic value and can attract tourists in certain regions. In some areas, detailed information about bird presence, distribution and diversity increased the likelihood of visitor activity at specific locations. Similarly, current study provides concise information about the bird species present in and around Kailashpuri village during different seasons. Furthermore, it has historical and religious significance for the village. Further villager involvement in the creation of bird-centric ecotourism destinations will be successful in protecting both birds and their habitats.

CONCLUSION

Birds contributed significantly to the ecological and functional balance of world ecosystems by providing a variety of ecological services. These services include vital processes such as seed dispersal, pollination of plants and crops, control of insect and pest populations, scavenging carcasses and nutrient cycling. Birds have an important role as key components of many ecosystems, acting as vital links in numerous food chains and intricate food webs around the world. Due to these significances of the bird community, it is essential to establish bird-centric ecotourism sites in various places, including towns and villages, which will effectively work on the conservation of birds and habitat.

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Table 1: List of bird species recorded in and around Kailashpuri village, Udaipur district (R- Resident, WM- Winter migratory, SM- Summer Migratory, MM- Monsoon migratory, LC- Least concern, NT- Near threatened, VU- Vulnerable, EN- Endangered, CE- Critically Endangered)

S.no.	Common name of species	Zoological name	IUCN Status	Migration Status
1. Family: Alcedinidae				
1	White-breasted Kingfisher	*Halcyon smyrnensis*	LC	R
2	Lesser Pied Kingfisher	*Ceryle rudis*	LC	R
3	Common Kingfisher	*Alcedo atthis*	LC	R
2. Family: Recurvirostridae				
4	Black-winged stilt	*Himantopus himantopus*	LC	R
3. Family: Burhinidae				
5	Indian Thick-knee	*Burhinus indicus*	LC	R
6	Great Thick-knee	*Esacus recurvirostris*	NT	R
4. Family: Glareolidae				
7	Small Pratincole	*Glareola lactea*	LC	WM
5. Family: Laridae				
8	River Tern	*Sterna aurantia*	VU	R
6. Family: Columbidae				
9	Yellow footed green Pigeon	*Treron phoenicopterus*	LC	R
10	Spotted Dove	*Streptopelia chinensis*	LC	R
11	Rock Pigeon	*Columba livia*	LC	R
12	Red Collared Dove	*Streptopelia tranquebarica*	LC	R
13	Laughing Dove	*Streptopelia senegalensis*	LC	R
14	Eurasian Collared Dove	*Streptopelia decaocto*	LC	R
7. Family: Ploceidae				
15	Baya Weaver	*Ploceus philippinus*	LC	R
8. Family: Corvidae				
16	Rufous Treepie	*Dendrocitta vagabunda*	LC	R
17	Jungle crow	*Corvus macrorhynchos*	LC	R
18	House crow	*Corvus splendens*	LC	R
9. Family: Anhingidae				
19	Oriental Darter	*Anhinga melanogaster*	NT	WM
10. Family: Pelecanidae				
20	Dalmatian Pelican	*Pelecanus crispus*	NT	WM
21	Great White Pelican	*Pelecanus onocrotalus*	LC	WM
11. Family: Ciconiidae				
22	Asian Openbill	*Anastomus oscitans*	LC	R

23	Asian woolly necked Stork	*Ciconia episcopus*	NT	R
24	Painted Stork	*Mycteria leucocephala*	NT	R
12. Family: Accipitridae				
25	White-eyed buzzard	*Butastur teesa*	LC	R
26	Western Marsh- Harrier	*Circus aeruginosus*	LC	WM
27	Short-toed Snake-eagle	*Circaetus gallicus*	LC	R
28	Shikra	*Accipiter badius*	LC	R
29	Osprey	*Pandion haliaetus*	LC	WM
30	Indian Vulture	*Gyps indicus*	CE	R
31	Himalayan Griffon Vulture	*Gyps himalayensis*	NT	WM
32	Griffon Vulture	*Gyps fulvus*	LC	WM
33	Egyptian Vulture	*Neophron percnopterus*	EN	R
34	Crested serpent-Eagle	*Spilornis cheela*	LC	R
35	Crested Hawk-eagle	*Nisaetus cirrhatus*	LC	R
36	Black-winged Kite	*Elanus caeruleus*	LC	R
37	Black Kite	*Milvus migrans*	LC	R
13. Family: Falconidae				
38	Common Kestrel	*Falco tinnunculus*	LC	WM
14. Family: Fringillidae				
39	Common Rose finch	*Carpodacus erythrinus*	LC	WM
15. Family: Estrildidae				
40	Scaly-breasted Munia	*Lonchura punctulata*	LC	R
41	Indian Silverbill	*Euodice malabarica*	LC	R
16. Family: Passeridae				
42	Yellow-throated sparrow	*Gymnoris xanthocollis*	LC	R
43	House Sparrow	*Passer domesticus*	LC	R
17. Family: Phasianidae				
44	Rock bush quail	*Perdicula argoondah*	LC	R
45	Jungle Bush Quil	*Perdicula asiatica*	LC	R
46	Indian Peafowl	*Pavo cristatus*	LC	R
47	Grey francolin	*Francolinus pondicerianus*	LC	R
18. Family: Jacanidae				
48	Pheasant tailed-Jacana	*Hydrophasianus chirurgus*	LC	R
49	Bronze-winged Jacana	*Metopidius indicus*	LC	R
19. Family: Rostratulidae				
50	Greater Painted-Snipe	*Rostratula benghalensis*		R
20. Family: Charadriidae				

51	Yellow-wattled lapwing	*Vanellus malabaricus*	LC	R
52	White-tailed Lapwing	*Vanellus leucurus*	LC	WM
53	Red- wattled Lapwing	*Vanellus indicus*	LC	R
54	Little Ringed Plover	*Charadrius dubius*	LC	R
21. Family: Scolopacidae				
55	Wood sandpiper	*Tringa glareola*	LC	WM
56	Ruff	*Calidris pugnax*	LC	WM
57	Green Sandpiper	*Tringa ochropus*	LC	WM
59	Common Snipe	*Gallinago gallinago*	LC	WM
59	Common sandpiper	*Actitis hypoleucos*	LC	WM
60	Common Red shank	*Tringa totanus*	LC	WM
61	Common Greenshank	*Tringa nebularia*	LC	WM
62	Black-tailed Godwit	*Limosa limosa*	NT	WM
22. Family: Psittacidae				
63	Rose-ringed Parakeet	*Psittacula krameri*	LC	R
64	Plum headed Parakeet	*Psittacula cyanocephala*	LC	R
23. Family: Cuculidae				
65	Pied crested Cuckoo	*Clamator jacobinus*	LC	MM
66	Indian Cuckoo	*Cuculus micropterus*	LC	WM
67	Grey-bellied Plaintive Cuckoo	*Cacomantis passerinus*	LC	R
68	Greater Coucal	*Centropus sinensis*	LC	R
69	Common Hawk-Cuckoo	*Hierococcyx varius*	LC	R
70	Asian Koel	*Eudynamys scolopaceus*	LC	R
24. Family: Motacillidae				
71	Yellow wagtail	*Motacilla flava*	LC	WM
72	White Wagtail	*Motacilla alba*	LC	WM
73	Tree Pipit	*Anthus trivialis*	LC	WM
74	Red-breasted flycatcher	*Ficedula parva*	LC	WM
75	Paddy field pipit	*Anthus rufulus*	LC	WM
76	Olive-backed Pipit	*Anthus hodgsoni*	LC	WM
77	Large Pied Wagtail	*Motacilla maderaspatensis*	LC	R
78	Grey Wagtail	*Motacilla cinerea*	LC	WM
79	Citrine Wagtail	*Motacilla citreola*	LC	WM
80	Blyth's Pipit	*Anthus godlewskii*	LC	WM
25. Family: Tytonidae				
81	Common Barn-owl	*Tyto alba*	LC	R
26. Family: Strigidae				

82	Spotted Owlet	*Athene brama*	LC	R
83	Mottled Wood-owl	*Strix ocellata*	LC	R
84	Jungle Owlet	*Glaucidium radiatum*	LC	R
85	Indian Eagle-owl	*Bubo bengalensis*	LC	R
27. Family: Caprimulgidae				
86	Indian Jungle Nightjar	*Caprimulgus indicus*	LC	R
28. Family: Meropidae				
87	Blue-cheeked Bee- eater	*Merops persicus*	LC	SM
88	Asian Green bee-eater	*Merops orientalis*	LC	R
29. Family: Coraciidae				
89	European Roller	*Coracias garrulus*	LC	WM
90	Indian Roller	*Coracias benghalensis*	LC	R
30. Family: Upupidae				
91	Common Hoopoe	*Upupa epops*	LC	R
31. Family: Bucerotidae				
92	Indian Grey Hornbill	*Ocyceros birostris*	LC	R
32. Family: Megalaimidae				
93	Brown-headed Barbet	*Psilopogon zeylanicus*	LC	R
94	Copper Smith Barbet	*Psilopogon haemacephalus*	LC	R
33. Family: Picidae				
95	Yellow-fronted Pied Woodpecker	*Leiopicus mahrattensis*	LC	R
96	White-napped Woodpecker	*Chrysocolaptes festivus*	LC	R
97	Indian Pygmy Woodpecker	*Picoides nanus*	LC	R
98	Eurasian Wryneck	*Jynx torquilla*	LC	WM
99	Black-rumped Flameback Woodpecker	*Dinopium benghalense*	LC	R
34. Family: Ardeidae				
100	Purple heron	*Ardea purpurea*	LC	R
101	Little Egret	*Egretta garzetta*	LC	R
102	Intermediate egret	*Ardea intermediata*	LC	R
103	Indian Pond Heron	*Ardeola grayii*	LC	R
104	Grey Heron	*Ardea cinerea*	LC	R
105	Great Egret	*Egretta alba*	LC	R
106	Cattle- Egret	*Bubulcus ibis*	LC	R
107	Black-crowned Night Heron	*Nycticorax nycticorax*	LC	R
35. Family: Pittidae				
108	Indian Pitta	*Pitta brachyura*	LC	SM
36. Family: Alaudidae				

109	Ashy-crowned Sparrow-lark	*Eremopterix griseus*	LC	R
37. Family: Hirundinidae				
110	Wire-tailed Swallow	*Hirundo smithii*	LC	R
111	Dusky Crag Martin	*Ptyonoprogne concolor*	LC	R
112	Barn Swallow	*Hirundo rustica*	LC	WM
38. Family: Vangidae				
113	Common Woodshrike	*Tephrodornis pondicerianus*	LC	R
39. Family: Campephagidae				
114	Small Minivet	*Pericrocotus cinnamomeus*	LC	R
115	Large Cuckoo shrike	*Coracina javensis*	LC	R
40. Family: Pycnonotidae				
116	Red-vented Bulbul	*Pycnonotus cafer*	LC	R
41. Family: Aegithinidae				
117	Common iora	*Aegithina tiphia*	LC	R
42. Family: Laniidae				
118	Long-tailed shrike	*Lanius schach*	LC	R
119	Isabelline Shrike	*Lanius isabellinus*	LC	WM
120	Bay-backed Shrike	*Lanius vittatus*	LC	R
43. Family: Muscicapidae				
121	Blue-rock Thrush	*Monticola solitarius*	LC	WM
122	Siberian Stonechat	*Saxicola maurus*	LC	WM
123	Pied Bush Chat	*Saxicola caprata*	LC	WM
124	Oriental Magpie Robin	*Copsychus saularis*	LC	R
125	Indian Robin	*Saxicoloides fulicatus*	LC	R
126	Brown Rock Chat	*Oenanthe fusca*	LC	R
127	Blue throat	*Luscinia svecica*	LC	WM
128	Black Redstart	*Phoenicurus ochruros*	LC	WM
44. Family: Leiothrichidae				
129	Large Grey Babbler	*Argya malcolmi*	LC	R
130	Jungle Babbler	*Argya striata*	LC	R
131	Common babbler	*Argya caudata*	LC	R
45. Family: Paradoxornithidae				
132	Yellow-eyed Babbler	*Chrysomma sinense*	LC	R
46. Family: Anatidae				
133	Cotton pygmy-goose	*Nettapus coromandelianus*	LC	R
134	Tufted Duck	*Aythya fuligula*	LC	WM
135	Ruddy shelduck	*Tadorna ferruginea*	LC	WM

136	Northern shoveler	*Spatula clypeata*	LC	WM
137	Northern Pintail	*Anas acuta*	LC	WM
138	Mallard	*Anas platyrhynchos*	LC	WM
139	Lesser-Whistling Duck	*Dendrocygna javanica*	LC	WM
140	Knob-billed duck	*Sarkidiornis melanotos*	LC	R
141	Indian Spot-billed duck	*Anas poecilorhyncha*	LC	R
142	Greylag Goose	*Anser anser*	LC	WM
143	Garganey	*Spatula querquedula*	LC	WM
144	Gadwall	*Mareca strepera*	LC	WM
145	Ferruginous Duck	*Aythya nyroca*	NT	WM
146	Eurasian Wigeon	*Mareca penelope*	LC	WM
147	Common Teal	*Anas crecca*	LC	WM
148	Common Pochard	*Aythya ferina*	VU	WM
149	Bar-headed Goose	*Anser indicus*	LC	WM
47. Family: Cisticolidae				
150	Plain Prinia	*Prinia inornata*	LC	R
151	Jungle Prinia	*Prinia sylvatica*	LC	R
152	Common Tailor Birds	*Orthotomus sutorius*	LC	R
153	Ashy Prinia	*Prinia socialis*	LC	R
48. Family: Phylloscopidae				
154	Sulphur-bellied Warbler	*Phylloscopus griseolus*	LC	WM
155	Siberian Chiffchaff	*Phylloscopus tristis*	LC	WM
49. Family: Sylviidae				
156	Lesser Whitethroat	*Curruca curruca*	LC	WM
50. Family: Stenostridae				
157	Grey-headed Canary Flycather	*Culicicapa ceylonensis*	LC	WM
51. Family: Monarchidae				
158	Indian Paradise-flycatcher	*Terpsiphone paradisi*	LC	R
52. Family: Rhipiduridae				
159	White-spotted Fantail	*Rhipidura albogularis*	LC	R
160	White-browned-fantail	*Rhipidura aureola*	LC	R
53. Family: Paridae				
161	Great Tit	*Parus major*	LC	R
162	Black-lored Tit	*Machlolophus xanthogenys*	LC	R
163	White-napped Tit	*Machlolophus nuchalis*	VU	R
54. Family: Nectariniidae				
164	Purple Sunbird	*Cinnyris asiaticus*	LC	R

55. Family: Zosteropidae				
165	Indian white eye	*Zosterops palpebrosus*	LC	R
56. Family: Emberizidae				
166	Crested Bunting	*Emberiza lathami*	LC	R
	57. Family: Threskiornithidae			
167	Red naped Ibis	*Pseudibis papillosa*	LC	R
168	Glossy Ibis	*Plegadis falcinellus*	LC	R
169	Eurasian Spoonbill	*Platalea leucorodia*	LC	WM
170	Black-headed Ibis	*Threskiornis melanocephalus*	NT	R
58. Family: Sturnidae				
171	Rosy Starling	*Pastor roseus*	LC	WM
172	Common Myna	*Acridotheres tristis*	LC	R
173	Brahminy Starling	*Sturnia pagodarum*	LC	R
174	Bank Myna	*Acridotheres ginginianus*	LC	R
175	Asian Pied Starling	*Gracupica contra*	LC	R
59. Family: Dicruridae				
176	White-bellied Drongo	*Dicrurus caerulescens*	LC	R
177	Black Drongo	*Dicrurus macrocercus*	LC	R
60. Family: Phalacrocoracidae				
178	Little cormorant	*Microcarbo niger*	LC	R
179	Indian Cormorant	*Phalacrocorax fuscicollis*	LC	R
180	Great Cormorant	*Phalacrocorax carbo*	LC	R
61. Family: Podicipedidae				
181	Little grebe	*Tachybaptus ruficollis*	LC	R
62. Family: Rallidae				
182	White-breasted water hen	*Amaurornis phoenicurus*	LC	R
183	Common Coot	*Fulica atra*	LC	R
184	Common Moorhen	*Gallinula chloropus*	LC	R
185	Purple Swamp hen	*Porphyrio porphyrio*	LC	R

Figure 1: Indian Vulture

Figure 2: Egyptian Vulture

Figure 3: Black-winged Stilt

Figure 4: Black Kite

Figure 5: Purple Swamp hen

Figure 6: Lesser Whistling Duck

REVIEW ARTICLE

Oral health status among Chronic kidney disease and End stage renal disease patients. A review

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ABSTRACT

Changes in the oral cavity such as periodontitis and other oral health issues indicates the early signs of chronic kidney disease. Poor oral health is an early sign. Early management of poor oral health will reduce the inflammation, infection, protein energy wasting and other complications in chronic kidney diseases. End stage renal disease had high morbidity and mortality rate. Several studies had shown relationship between renal disease and oral health. Therefore this review was done to know the etiological factors and other systemic consequences of poor oral health in chronic kidney diseases.

Keywords: Inflammation, periodontitis, Chronic kidney disease, End stage renal disease.

INTRODUCTION

Chronic kidney diseases depends on glomeluar filtrate test such that how well the kidney filter the waste and extra fluid out of your blood. End stage renal disease is a condition where the kidney is failed, ultimately it has to go for dialysis or kidney transplantation.[1] Diabetes, hypertension, old age are the significant factors for the development of chronic kidney disease and End stage renal diseases.[2]

CHRONIC KIDNEY DISEASE

8 to 10% of general population is considered to have mild to moderate decreased renal function.[3-5] Obese patients are directly associated with occurrence of chronic kidney diseases.[6] 30% of patients with advanced chronic kidney

disease response to have bad or metallic taste in their mouth, which has been associated with metabolic changes, diverse drugs, reduced number of taste buds and changes in both salivary flow rate and composition.[7,8,9] 90% of dialysis patient complaints of dry mouth and on fluid restricted diet. Long term patients with dry mouth predispose to caries, periodontal disease and mucosal lesion.[10] It may lead to difficulty in chewing, speaking and swallowing, taste alterations, halitosis, increased risk of oral infections such as candidiasis, caries and periodontal disease. Increased risk of fluid intake results and interdialytic weight gain and reduced the quality of life. [11] Oral signs such as periodontal disease, gum bleeding, abnormal taste, burning mouth, xerostomia are seen.[12] Periodontal diseases is closely associated with systemic inflammation.[13] Gum ulcers in periodontal pocket allow bacteria to invade systemic circulation. Oral bacterial pathogens results in alteration in gut microbes leads to indirect induction of nephrotoxic toxins or a nephrotoxic microbiota composition.[14] High rate of oral pathology in dialysis patient results in uremic odor,tongue coating, xerostomia, taste disturbances, mucosal inflammation, mucosal petechia/ecchymosis, oral ulceration.[15,16,17] Patients are more prone for retrograde parotitis due to direct gland involvement, chemical inflammation, side effects of drug therapy, dehydration and mouth breathing.[18] Patient also had signs of bad odour like ammonia. Increased dental calculus is noticed due to high salivary urea and phosphate levels.[19] Uremic stomatitis is another clinical findings in advanced uremia; it consists of erythemopultaceous, ulcerative, hemorrhagic an hyperkeratotic forms.[20]

These clinical signs heals spontaneously after the treatment of uremia. Hemorrhagic and hyperkeratotic forms may occur because of bleeding and long standing uremia, respectively. Untreated uremic patients observes an intraoral form of uremic frost that can be observed in untreated uremia results from remaining urea crystals left on epithelial surfaces after saliva evaporation.[21] Poor oral health is a source of inflammation. It results in gingivitis and periodontitis. It represents a potential source of inflammation that colonized gram negative anaerobic bacteria. Increase in periodontitis is due to repeated use of systemic anticoagulants in haemodialysis patient leading to gingival bleeding and facilitate bacterial colonization. Dialysis therapy results in major changes in oral condition including periodontal diseases & have been reported to progress in severity across predialysis, peritoneal dialysis and haemodialysis patients respectively.[22] Severe hyperparathyroidism associated with renal dysfunction results in formation of dental calculus. It disturbs calcium, phosphorus homeostasis. The most abundant amount of calculus ,dental plaque formation was found among dialyzed patient.[23] Certain medication like antidepressants, antipsychotics, antiemitics and antihistamines can reduce the salivary flow resulting in xerostomia. [24] Gradual reduction of glomerular filtration rate of the kidneys leads to increases in serum creatinine, blood urea nitrogen levels resulting in uraemia or azotaemia. [25,26,27,28]. Apart from that systemic abnormalities such as anaemia, platelet disorder, hypertension is observed among CKD patients.[29] Severe periodontitis, hypoalbuniama are the early signs of CKD.[30] There is a significant overlap between inflammation, starvation and PEW. [31] Low renal function disrupt the regulation of vit D, calcium levels which contributes to bone diseases.[32]

END STAGE RENAL DISEASES [ESRD]

End stage renal disease is estimated to be between 13.9% and 0.1% respectively. Decrease renal function accumulates waste products inside the body and cause symptoms like decrease mobility, lack of energy, decrease appetite and sleeping disorders. Xerostomia, restricted diet, multiple medication, salivary gland atrophy and fibrosis are noticed. Micro and macrovascular complication results in the development, progression and severity of periodontal diseases, weakened immune system, immune cell dysfunction, lower immune response and high level of systemic inflammation occurs.[verhulst,loos, gerdes & teeuw 2019) For instance, edentulousness, mucosal disease, bad oral hygiene, mucosal sensitivity, oral pain, thirst ,dysgeusia may be more present. [33] Among End stage renal diseases renal transplant case reported with less halitosis when compared to haemodialysis, peritoneal dialysis and predialysis patient. Poor oral uremia that has been associated with immune dysfunction including defects in lymphocyte and monocyte function. Altered cellular immunity along with malnutrition contributes to immunodeficient state. Psychological factors and depressive symptoms may decrease the priority to maintain good oral health in ESRD. Poor oral health is associated with 80% of haemodialysis patients with periodontal disease and was associated with both the high C reactive protein and low serum albumin levels in univariate analysis but not in

multivariate analysis. Therefore it is important to maintain the oral health status of patient undergoing dialysis and renal transplant. IgG antibody levels was elevated in patients with systemic inflammation. [34]

CONCLUSION

Oral hygiene practices, frequency of visits to the dentist and previous dental history are the factors should be considered among chronic kidney disease patients. Oral hygiene indicators such as tooth brushing frequency and professional scaling reduces periodontal diseases and oral diseases. Since oral hygiene has an effect on systemic health it is important factor to be consider in screening the general health of the patients.

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REVIEW ARTICLE

A Comprehensive Review of Machine Learning Algorithms for Classification Problems

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ABSTRACT

Classification forms an essential part of the entire machine learning process; here the given data set has to be classified into the provided categories. The present paper will offer a review of the literature on the classification methods of machine learning, classification as a traditional approach, the use of ensemble learning, and state-of-the-art classification algorithms; These algorithms are fixed in advance for comparison and incorporate simple models and include the Logistic Regression, Decision Trees, Support Vector Machines and the Naïve Bayes' model. For example, Random Forest or Boosting methods are demonstrated stressing the fact that they will contribute to the increase of accuracy and stability of results. Two algorithms, Deep Learning, and k-Nearest Neighbors are applied for the ability to solve complex and numerous patterns. Methods of making performance indices, background databases put into utilization, and other actual utility aspects of these model schematics are also reviewed and indicated to include medical diagnostic tools, financial investment, image handling systems, etc., Also, the paper explains such problems as dataset shift, feature extraction, and data imbalance and outlines the possibilities of the classification's further evolution. This review also seeks to enable future users to make the right choice of the classification algorithm while handling different problems.

Keywords: Machine Learning, Classification Algorithms, Ensemble Learning, Performance Evaluation, Supervised Learning

INTRODUCTION

Over the last few years, Machine Learning has received a lot of focus in different domain areas because of the capability that encompasses the handling of big data. Supervised learning one of the four fundamentals of artificial intelligence aims at classifying inputs into given classes or labels by analyzing their characteristics. Classification is one of the principles of machine learning that targets classifying inputs into given classes or labels. This task is important virtually in every single application, be it in areas of health, where diagnosis is carried out, or in cases of fraud detection, image recognition, etc. Due to the rapid growth of large volumes of data, efficient classification methods have become crucially important. Classical statistics approaches are frequently insufficient to deal with the increasing complexity of data and the increasing number of features of today's data. This situation has forced researchers and practitioners to look for and establish various machine-learning algorithms concerning different classification problems. Therefore, the main goal of this paper is to present a discussion, evaluation, and overall overview of the most commonly used and effective Ml algorithms used in classification problems. We categorize these algorithms into three main groups such as conventional methods, transforms, novelties, and ensembles and the given features of each group have their merits and demerits. In this way, we want to provide information on the appropriateness, effectiveness, and practicability of the methods for different classification tasks. Besides, this review will also consider other measures for measuring the efficiency of given classification algorithms. The evaluation parameters accuracy, precision, recall, and F1 score help to assess the quality of the resulting predictions of the model and identify the right algorithm for the specific task at hand. Besides comparing several algorithms, the roles of the approximations of classification algorithms in different fields will be discussed to illustrate the significance of accurate classification in decision-making procedures. In this way, the user will be able to allocate the necessary means and to introduce the chosen method, if he or she understands the practical consequences of applying these algorithms. At last, the problems that can appear at the classification stage like the selection of the features, the data availability, and future perspectives of the research will also be stated. As machine learning is one of the areas actively advancing today, authors found it necessary to use new approaches and methods for non-parametrical classification. Therefore, we hope that this review will serve as a handy pointer for future researchers, professionals, and students who wish to gain an outlook on the current approaches to classification problems in the area of machine learning with the view of helping build the field further.

Classification Algorithms Overview

Classification algorithms are used by machine learning to separate the data into different classes with the help of input features, thus allowing the system to deal with the data classification process automatically[2]. Here is a detailed look at specific classification algorithms; they are divided into three main categories, i.e. traditional algorithms, ensemble methods, and modern techniques. The subsection explains differentiating principles, advantages, disadvantages, and practical applications of the algorithms.

Traditional Algorithms

Logistic Regression

In the field of statistics, logistic regression is a popular analytical method that is used in binary classification problems [1]. It describes the probability that a given input belongs to a particular category. The logistic function is applied by the algorithm to the input features, after which they produce an output in the range 0-1. When the probability reaches a set level (usually 0.5), the input is labeled as in the positive class, otherwise, it is classified in the anti-positive class. It is simple for users to run reception and result analysis. This algorithm gives probabilistic outputs that can be utilized to evaluate the precision of results. It is quick and easy to work with when we have the data with linearly separable classes. So, there must be a linear connection between input features and the log-odds of the output. Still, it has a certain appeal for presenting simple, non-linear correlations. Logistic Regression in Medical diagnosis (e.g. identifying the presence of a disease), and the Marketing Arena (for example predicting customer churn) are scenarios where it is utilized.

Decision Trees

Decision trees are a well-liked non-parametric method that uses a tree-like design of decisions depending on feature values. Each internal node is the feature of a test, every branch is the result of a test, and every leaf node is a class label. The tree is constructed iteratively by first selecting the best feature to split the data at every node, the most common criteria being Gini impurity or information gain. It is simple for ordinary observers to learn and interpret the machine-learning model due to its decision-tree nature. Decision trees can handle both numerical and categorical data and can also be used to capture non-linear relationships. But it pertains to over fitting with deep trees, making it unsuitable. Decision trees are sensitive to small changes in data, which may result in quite different tree structures. The applications of decision trees in real-time are customer segmentation and credit risk assessment.

Support Vector Machines (SVM)

Support Vector Machines are supervised learning models that are applied for both classification and regression. SVM's goal is to locate the ideal hyper plane, which with maximum margin, can separate the data points of different classes. When the classes are not linearly separable, SVM uses kernel functions (e.g., polynomial, radial basis function) to alter the input space to a higher-dimensional space. The strong side point of SVM is success in high-dimensional spaces (where the number of dimensions exceeds the number of samples). It is robust to over fit, especially in high-dimensional spaces. It takes longer to compute in large data quantities so it is computationally intensive, especially larger datasets. An area of difficulty is choosing the kernel and coding options that will be most suitable for the situation. SVM is a possible approach to the problem of spam detection through text classification and its application is that of image recognition.

Naive Bayes

Naive Bayes classifiers are statistical algorithms that are based on Bayes' theorem. They suppose independence among features provided the class label, thus the name "naive." The classifier computes the posterior probability functions for each class using the input features and the highest probability class is assigned. It is fast and efficient, particularly for large datasets. It is suitable for high-dimensional data and, what is more, it is not much affected by unrelated attributes. However the independence assumption may not hold in practice, thus accuracy may suffer. One disadvantage is the classification algorithm tends to make miserable predictions when the sample size is small or when the features are highly correlated. Naive Bayes classifiers are applied to Text classification (e.g., sentiment analysis) and Medical diagnosis.

Ensemble Methods

Random Forest

Random Forest refers to an ensemble learning approach, which fits several decision trees during the training phase and the average of their predictions is the output for a class. Each tree is built using a random subset of features and samples which helps in the diversity and reduction of over fitting. It tackles the problem of robustness to over fitting due to averaging multiple trees. Furthermore, it manages large datasets with high dimensionality very well. It is harder to interpret the information than that of individual trees. It is excessively costly both during the training and prediction phases. Random Forest is applied as a classification model in practice for fraud detection and predictive maintenance.

Boosting (e.g., AdaBoost, Gradient Boosting)

Including an increasing amount of promotion in a portioning of erroneous learning methods to install a form of strong classifier in this context is the method of Ensemble technique, known as boosting. The boosters are thus trained with each learning attempt (i.e. model) consecutively, the subsequent model's impression on the consumption of errors continuously encountering the previous ones. AdaBoost, the weight of the components of misclassified samples, is reinforced whereas Gradient Boosting seeks to restrain a loss function using gradient descent. Driving can improve greatly the classification. In the time of both binary and multiclass classification tasks, it shows its effectiveness best of all. However, the level of sensitivity is also high as it is sensitive to noisy data and

outliers. In this, an attentive interpolation of hyper parameters is required. Boosting decision methods are popularly employed to predict customer behavior and Credit scoring.

Modern Techniques

Deep Learning (DL)

Deep learning is a subfield of machine learning that uses neural networks with many layers (deep neural networks) to learn models of data. Convolutional Neural Networks (CNNs) are often used for image data, while Recurrent Neural Networks (RNNs) are particularly useful with text data [3]. Deep learning can learn to find very complex patterns and dependencies directly from data. This flexibility allows deep learning to achieve state-of-the-art results on many problems in machine learning and related fields when provided with large amounts of labeled data. Deep Learning also requires a tremendous amount of computational power in comparison to traditional techniques and similarly, a lot more labeled examples. It is an art to make it work with small datasets. Deep learning is capable of being employed in the following applications: Image classification (e.g., facial recognition) and Natural language processing (e.g., language translation).

2.3.2. k-Nearest Neighbors (k-NN)

K-nearest neighbor is a non-parametric, instance-based learning approach for classifying data based on the majority class of their k-nearest neighbors in a feature space. The distance metric which is the role of finding neighbors (e.g., Euclidean, Manhattan) is also important. The k-NN model is simple to implement and easy to understand. No training phase is required; all computations are performed at the classification stage. It is computationally expensive when dealing with large datasets as it needs to calculate the distances to all the training instances. The performance of k-NN can be seriously degraded by high dimensions (curse of dimensionality). k-NN can be used for Recommender systems and Pattern recognition[8].

Performance Metrics

Classification algorithms need to be compared based on their performance metrics. Performance metrics are the measure of how good a classification algorithm performs and they motivate a better understanding of the underlying process. They help us to compare different models, select different input features, and finally an appropriate model for the classification task at hand. In this chapter, we will discuss various performance metrics used in the classification literature.

Accuracy

Accuracy is the ratio of correctly predicted instances in the total number of occurrences. It is one of the simplest measures but can be misleading for data sets that are imbalanced.

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

Precision and Recall

Precision is the ratio of correctly predicted positive observations to the total predicted positives over all classes. Recall is the ratio of correctly predicted positive observations to all observations in actual class yes.

$$Precision = \frac{TP}{TP + FP}$$

$$Recall = \frac{TP}{TP + FN}$$

F1-Score

The F1-Score is the harmonic mean of precision and recall, which balances these two metrics.

$$F1 - Score = 2.\frac{Precision.Recall}{Precison + Recall}$$

ROC-AUC

The Receiver Operating Characteristic (ROC) curve is created by plotting the true positive rate against the false positive rate, and the Area Under the Curve (AUC) summarizes the overall performance of a classifier.

Applications

Classification algorithms in machine learning are implemented across numerous domains to solve a broad range of problems. This section specifically discusses some notable applications.

Healthcare

In healthcare, classification algorithms are used to predict the outcome of diseases, diagnose certain conditions, and personalize treatments. For example, logistic regression can denote the likelihood of heart disease, while deep learning models can classify medical images for cancer detection.

Finance

In finance, classification models are used for credit scoring, fraud detection, and risk management[2]. Random Forest and Boosting algorithms are applied to predict loan defaults and fraudulent transactions.

Marketing

In marketing, classification techniques are used for customer segmentation, churn prediction, and personalized marketing. Naive Bayes and decision trees are frequently employed for customer behavior analysis and prediction of purchase patterns.

Image Recognition

Deep learning models, especially Convolutional Neural Networks (CNNs), have significantly influenced image recognition tasks, making it possible to apply to facial recognition, object recognition, and self-driving vehicles[4][5].

Challenges and Future Directions

Data Imbalance

One challenge facing in this area is data imbalances. Imbalanced datasets can be a major issue in classification tasks, as algorithm models may be skewed towards the majority class. Techniques like SMOTE (Synthetic Minority Over-sampling Technique) and cost-sensitive learning can reduce this problem.

Feature Selection

Another important challenge that needs to be addressed is selecting relevant features for model improvement, and interpretability. Principal Component Analysis (PCA) and Recursive Feature Elimination (RFE) are frequently used to choose relevant features.

Interpretability

As models become more complex, it can become increasingly difficult to interpret them. Developing methods to explain and interpret model predictions should be an area of future research, particularly for deep learning models.

Future Directions

Future research in classification algorithms might focus on developing models that are more robust to handle noisy and incomplete data, improving interpretability, and exploring hybrid approaches that attempt to capitalize on the strengths of different algorithms.

CONCLUSION

Through this broad review, a broad range of machine learning classification algorithms have been explored, providing an overview of principles, advantages, disadvantages, and applications. Since each algorithm has different strengths and limitations, researchers and practitioners need to be aware of these limitations and delimitations to make informed decisions when choosing an appropriate algorithm for the problem they are solving. As research and development in machine learning continue, we can expect new, more sophisticated classification solutions to be devised. This will be of great benefit to classification tasks across diverse areas.

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RESEARCH ARTICLE

Novel Nickel (II), Copper(II) and Zn(II) Complexes bearing Triazole based Ligand: Synthesis, Characterization, Antimicrobial and Antioxidant Activities

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ABSTRACT

In search of 1,2,3-triazole-based antimicrobial agents, new mixed-ligand complexes of Ni(II), Cu(II) and Zn(II) were synthesized using 2-amino-4-((5- amino-1-phenyl-1H-1,2,3-triazol-4-yl)thio)benzoic acid (L1) ligand and the corresponding metal chlorides in 1:2 molar ratio. Elemental analyses, conductivity measurements, magnetic moment, UV–Vis, FTIR and NMR studies were used to determine the nature of bonding, coordination characteristics and the structure of complexes. Physico-chemical and spectral studies suggest that the ligand functioned in a neutral bidentate manner with nitrogen-N and sulphur-S as the coordinating sites and an octahedral geometry was proposed for the metal complexes. All the compounds were tested for the biocidal action of the complexes has been investigated by disc diffusion method by using pathogenically active bacteria and fungi. Importantly, the amylase inhibition activity of Cu (II) and Ni (II) complex has been explored. By measuring their interactions with the stable free radical

DPPH, the complex and the ligand were able to determine their free radical scavenging capacities. When compared to the ligands, the antioxidant activity of the complexes is higher.

Keywords: 1, 2, 3-triazole, Metal complexes, Antimicrobial, Antioxidant activities

INTRODUCTION

The advent of novel infections and the rising rate of microbial resistance have posed a challenge to pharmaceutical chemistry [1]. It is required to create novel antimicrobial agents with chemical properties that differ from those of current antimicrobial medications [2]. The chemistry of heterocyclic compounds, particularly triazole compounds, has gained a lot of attention in advanced pharmaceutical chemistry due to their beneficial pharmacological effects [3]. Triazoles are a family of heterocyclic compounds with three nitrogen and two carbon atoms in their ring. Since its discovery, triazole derivatives have enthralled researchers with a wide spectrum of biological activities [4], including anti-HIV [5], antifungal [6], antibacterial [7], anti-tuberculosis [8], anti-inflammatory [9], anticonvulsant [10], and anti-cancer characteristics [11]. There are several commercially available antifungal drugs with triazole nuclei in their chemical structures. Coordination chemistry is vital in the development of more effective drug candidates [12], with unique therapeutic characteristics and interesting pharmacological uses [13]. Triazole-based metal complexes have been created to enhance the pharmacological and pharmacokinetic properties of medicines [14]. Triazole metal complexes have a variety of applications, including antibacterial, antifungal, antimalarial, cytotoxic, anti-cancer, anti-diabetic, antioxidant, anti-neuropathic, anti-HIV, and DNA cleaving [15]. Metals make important contributions to medicinal chemistry [16] because they directly target biological systems and increase the lipophilicity of ligands at microbial cell membranes, allowing them to enter microbial cells [17]. Metal-based medications are favoured since they are less prone to develop addiction and have no negative effects on internal organs, as metals are required for normal bodily function. The triazole nucleus and its metal complexes have received attention due to their exceptional structural properties. Triazole compounds are used in industrial applications [18], including fluorescent imaging [19], catalysis [20], and energy conversion [21]. They have the ability to act as homogeneous catalysts in various chemical reactions [22]. Despite all of these applications, their biological applications outnumber all others due to the specific complexation chemistry of metal complexes that form stable geometrical configurations. Because of its structural and biological significance, the current study aims to synthesize, spectrally characterize, and test the antimicrobial and antioxidant activities of Ni(II), Cu(II), and Zn(II) complexes with triazole derivatives of 2-amino-4-((5- amino-1-phenyl-1H-1,2,3-triazol-4-yl)thio)benzoic acid.

MATERIALS AND METHODS

All the chemicals and solvents used were of AR-grade obtained from Sigma- Aldrich, Sisco Research Laboratories, Qualingens, Hi-media, nice chemicals, Spectrochem and were used without further purification. All melting points were taken in open capillaries and are uncorrected.

General procedure for the synthesis of Thiocyanate (TC1)

The substituted/ unsubstituted benzoic acid (0.5 mol) was dissolved in acetic acid (125 ml) and the solution was added to the solution of ammonium thiocyanate (1.05mol, 80 g) in glacial acetic acid (250 ml). This solution was cooled to 10-20º C [23]. To this well stirred solution, a solution of bromine (0.5 mol, 25.7 ml) in acetic acid (250 ml) was added drop wise for thirty minutes and the temperature was maintained below 20ºC. After the addition of bromine, it was kept at room temperature for ten minutes and then it was diluted with an equal amount of water. The solid material was filtered, washed, dried and recrystallized from ethanol.

Compound TC-1 2-amino-4-thiocyanatobenzoicacid

Anal. Calcd. For $C_8H_6SN_2O_2$: C, 49.47 H, 3.17; N, 14.34; S 16.58 Found: C, 49.37; H, 3.94; N, 14.60; S, 16.87; Yield %(72), M.p.: 189–190◦ C; IR KBr (cm^{-1}): - ν C≡N: 2237cm^{-1}.

General procedure for the synthesis of triazole (Compound TRi-1)

A mixture of thiocyanate TRi-1 (0.01 mol), azidobenzene (0.01mol, 1.08g) and carbon disulphide (0.1 mol, 8 ml) was heated in an oil bath at 160o C for 6 hours. The resultant triazole was cooled and recrystallized from ethanol.

2-amino-4-((5-amino-1-phenyl-1H-1,2,3-triazol-4-yl)thio)benzoic acid

Anal. Calcd. For $C_{15}H_{13}SN_5O_2$: C, 55.03; H, 4.96; N, 21.36; S 09.47; Found: C, 54.95; H, 4.01; N, 21.75; S 10.54 Yield %(87); M.p.: 197–199◦ C; ^{1}H NMR [DMSO-d6, ppm]: δ 7.62 (Ar-H, multiplet), δ 11.00 (Ar-OH, singlet)ppm; δ 7.74 (Ar-NH, singlet)ppm; ^{13}C-NMR [DMSO-d6, ppm]: δ 169 (OH), δ 140 (N=N)ppm; IR KBr (cm - 1): 1464.49 (N=Nstr), 2922.03(OH str).

Synthesis of metal complexes (1-3)

2-amino-4-((5-amino-1-phenyl-1H-1, 2, 3-triazol-4-yl)thio)benzoic acid (0.02M) was dissolved in ethanol than solid $M·Cl_2·6H_2O$ (0.01M) (where M= Ni, Cuand Zn) was added to reaction mixture. The resulting reaction mixture was refluxed for 24hours in the presence catalytic amount of NH_3 with continuous stirring. After completion of the reaction, the resulting solid was filtered and washed with cold methanol and dried at room temperature.

INSTRUMENTATIONS

The CHNS(O) elemental analyses were carried out using Therma Finnegan's Flash EA1112 Series CHNS(O) analyser. Using a Systronic Conductivity Bridge (model number-304) and 10^{-3}M concentrations of the metal complexes in acetonitrile, electrical conductivity measurements were carried out at 30°C. Ni(II), Cu(II) and Zn(II) complexes. UV-visible spectra were obtained with a Varian Cary 5000 UV Spectrophotometer. A Perkin Elmer Spectrum RX-I FT-IR spectrometer was used to record the infrared spectra of the complexes and free ligands on KBr discs at room temperature. H-NMR in DMSO-d6 on a Bruker AC-400 spectrometer using TMS as an internal standard. The microorganisms were obtained from National Chemical Laboratory, Pune. Thin-layer chromatography (TLC) was performed on pre-coated aluminium plates (silica gel 60F254, Merck). Plates were visualized by UV light and iodine vapour.

Nickel Complex (2) $[Ni(L)2(OH_2)_2]Cl_2$

Anal. Calcd. For $C_{30}H_{26}N_{10}S_2O_4Ni$: C,50.51; H, 3.68; N, 19.65;S,8.99 Found: C,50.47; H, 3.85; N,19.97; S,9.08; Yield %(78), ^{1}H NMR (DMSO-d6) δ 7.79 (Ar-H, multiplet), δ 11.5 (Ar-OH, singlet), δ 7.73 (Ar-NH, singlet)ppm; ^{13}C-NMR: δ 169.3 (OH), δ 157.3(N=N),IR KBr (cm - 1): 1310.99 (N=Nstr), 1315.9(C-Nstr), 1504.21 (C=Cstr), 2924.11 (OHstr) 3012.89 (CHstr) 450.84(N-Ni),770.47(C-S str).

Copper Complex (2) $[Cu(L)_2(OH_2)_2]Cl_2$

Anal. Calcd. For $C_{30}H_{26}N_{10}S_2O_4Cu$: C,50.21; H, 3.64; N, 19.67;S,8.92 Found: C,50.40; H, 3.85; N,19.90; S,9.43; Yield %(82), ^{1}H NMR (DMSO-d6) δ 7.7 (Ar-H, multiplet), δ 11.7 (Ar-OH, singlet), δ 7.74 (Ar-NH, singlet)ppm; ^{13}C-NMR: δ 169 (OH), δ 157.3(N=N), IR KBr (cm^{-1}): 1310.99 (N=Nstr), 1310.99 (C-Nstr), 1504.21 (C=Cstr), 2998.58 (OH str) 3012.89 (C-Hstr) 450.84(N-Cu) 752.36(C-S str).

Zinc Complex (1) $[Zn(L)_2(OH_2)_2]Cl_2$

Anal. Calcd. For $C_{30}H_{26}N_{10}S_2O_4Zn$: C,50.04; H, 3.64; N, 19.46;S,8.89 Found: C,50.20; H, 3.75; N,19.96; S,9.01; Yield %(75), ^{1}H NMR (DMSO-d6) δ 7.80 (Ar-H, multiplet), δ 11.6 (Ar-OH, singlet), δ 7.75 (Ar-NH, singlet)ppm; ^{13}C-NMR: δ 169.3 (OH), δ 157.3(N=N), IR KBr (cm - 1): 1310.99 (N=Nstr), 1290.01 (C-Nstr), 1547.28 (C=Cstr), 2965.19 (OH str) 3010.23 (CHstr) 505.72(N-Zn),763.63(C-S str).

Biological evaluation

Anti-microbial Activity

The anti-microbial activity for the sample was carried out by Disc Diffusion Technique. The test microorganisms *Staphylococcus aureus* (NCIM 2079), *Bacillus subtilis* (NCIM 2063), *Escherichia coli* (NCIM2065), *Pseudomonas aeruginosa* (NCIM2036), *Candida albicans* (NCIM3102), *Aspergillus Niger* (NCIM 105*)* maintained by periodical sub culturing on nutrient agar and sabouraud dextrose agar medium for bacteria and fungi respectively. The test microorganisms were obtained from National Chemical Laboratory NCL), Pune and maintained by periodical sub culturing on nutrient agar and sabouraud dextrose agar medium for bacteria and fungi respectively. The effects produced by the sample were compared with the effect produced by the positive control (Reference standard ciprofloxacin 5µg/disc for bacteria; Nystatin 100units/disc for fungi).

Antioxidant activity

The stock solution's antioxidant capacity was neutralized (1 mg/ml) to achieve final concentrations ranging from 10 to 500 g/ml. Sample solutions in DMSO (3 ml) were mixed with an ethanolic DPPH (2,2-diphenyl-1-picrylhydrazyl) solution (1 ml, 0.3 mmol) of varying concentrations (10-500 g/ml) [24]. After complete mixing, the mixture was allowed to remain at room temperature for half an hour. A UV-Vis Spectrophotometer was used to measure the absorbance at 517 nm. A lower absorbance of the resulting solution suggests better activity in scavenging free radicals. Ascorbic acid was utilized as the standard, and ethanol served as the solvent. The following equation was used to create the DPPH radical scavenging activity.

$$\text{Scavenging effect (\%)} = \frac{A_0 - A_1}{A_0}$$

where A_0 is the absorbance of the control and A_1 is the absorbance when the samples or standards are present.

RESULTS AND DISCUSSION

Elemental analysis

Elemental analysis and physical data supported the proposed structures of the metal complexes, with the Ni(II), Cu(II) and Zn(II) complexes showing M:L molar ratios of 1:2. Furthermore, the percentages of carbon, hydrogen and nitrogen in the complex were found to be good agreement with the theoretical values [25].

Molar conductance

To verify the formulas of the prepared metal complexes in solution, the molar conductivities of acetonitrile solutions of the complexes (10^{-3}M) were determined. A range of 21.3-29.5 $\Omega^{-1}cm^2mol^{-1}$was obtained; such low values indicate that the complexes are non-electrolytic (1:0 type) in nature [26]

UV-Visible spectra and Magnetic moment

The Ni(II) complex shows bands at 14670 cm^{-1}, 21500 cm^{-1} and 24890 cm^{-1} and their corresponding to the transitions (Fig.3), $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ (ν_1), $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (ν_2) and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ (ν_3) respectively; this supports the previously identified octahedral geometry of the Ni(II) ion [27]. The observed magnetic moment value of Ni(II) complex is 2.88 B.M. This suggests the presence of octahedral environnent around Ni(II) metal ion. The structure is also further confirmed by the ratio ν_2/ν_1= 1.44 which is close to the value expected for octahedral structure [28], involving d^2sp^3hybridisation. The electronic spectrum of Cu(II) complex exhibits three absorbance bands at 14710 cm^{-1}, 28571 cm^{-1} and 34482 cm^{-1} (Fig.4) and their corresponding transitions are $^2A_{1g} \leftarrow {}^2B_{1g}$, $^2B_{2g} \leftarrow {}^2B_{1g}$ and $^2E_g \leftarrow {}^2B_{1g}$ respectively, which indicate octahedral geometry around Cu(II) metal ion. The magnetic moment value of Cu(II) complex is 1.78 B.M, that indicates further confirming hexa coordination around Cu(II) metal ion [29]. Since the zinc ion has a d^{10} structure, a charge transfer transition could be the cause of the absorption at 270 nm (Fig.5). However, a tetrahedral geometry [30] might be predicted for its complex based on the spectra and configuration of the zinc(II)

ion. In the same way mercury ion has a d^{10} structure as well, and its absorption at 320 nm might be attributed to a charge transfer transition [31] and its complex could be believed to have tetrahedral geometry.

FTIR Spectra

The important FTIR frequencies exhibited by the ligand and their complexes are given along with their assignments (Fig.6- Fig.7). The IR spectra of the synthesized triazole ligand exhibited bands at 2654,1649, 1646, 1560, 3012 and 679 cm^{-1} respectively assigned to the vibrations (S-H), (N=N)triazole ring, (N=N) azomethine, (C=C), (C-H) aromatic andthe last one is for stretching of (C-S) bond. The tautomerism form could occur in triazole. As a result, the band at 1286cm^{-1} assigned to the (C-S) vibrations could be observed in the spectra of the ligand. The triazole ligand possessed potential donor sites such as the azo linkage (-N=N), and the S atomof thiol group, which have a tendency to coordinate with the metal ions. The azomethine group appearing at 1656 cm^{-1} in the free ligand, is shifted to lower frequency by 3-12 cm^{-1} in the complexes, and a new band appearing at 521–535 cm^{-1} due to ν (M–N) vibrations indicating the involvement of azomethine nitrogen atom in coordination [33]. However, the band appearing at682 cm^{-1}due to (C-S) vibration in the spectra of the ligand shifted to a higher frequency by 2–16cm^{-1}due to increasing of the bond order of carbon- sulphate bond, indicating the participation ofthe S atom in complexation. This coordination was supported by the appearance of a new band at429–459 cm^{-1} assigned to (M-S), Additionally, new broad stretching bands near 3418–3410 cm^{-1} due to υ(O–H) stretching in all the complexes indicated the H_2O molecules bonded to the metal ions. All other bands such as C=C, C-H aromatic remain unchanged in the spectra of the ligand and their corresponding metal complexes because they are not participating in the complexation [34].

^{1}Hand^{13}CNMRSpectroscopy

Tofurtherconfirmtheformationofthecompounds(TRi-I,Cu(II),Zn(II)andNi(II)complexes) the ^{1}H and ^{13}C NMR spectra of the compounds in the absence and presence of were recorded at room temperature (25 °C) inDMSO-d6 with TMS as internalstandard.TMS was used as an internal standard. The ^{1}H NMR spectrum of the compound TRi-I 2-amino-4-((5-amino-1-phenyl-1H-1,2,3-triazol-4-yl)thio)benzoicacid shows two signals at δ(NH) 1.5, 5.1, δ($CH_{2\text{-}a}$) 7.1, 7.8 and δ(OH) 10.7 ppm indicating the presence of –NH and CH bonds in the derivative. This confirms the formation of the compounds (TRi-I Ligand, Cu(II), Zn(II) and Ni(II)complexes) by condensation of carboxylic-OH and-NH [35]. In the ^{13}C NMR spectra of the compounds (TRi-I, Cu(II), Zn(II) and Ni(II) complexes) twopeaksappearedatδ172and122.4ppmwhichisconsignedto-CO-NHand-C-OH,respectively, supporting the formation of the compound. In the ^{13}C NMR of the compounds (TRi-I, Cu(II), Zn(II) and Ni(II) complexes) these peaks were shifted to lower and higher value [OH] 168 .The peaks due to other protons remained unaltered which proves their non-involvementincoordination.Boththe^{1}Hand^{13}CNMRspectralstudiesconfirmstheformation of the compounds [36].

Biological Activity

Antimicrobial activity

The synthesized Ni(II),Cu(II) and Zn(II) complexes and the free triazole ligand were evaluated against the bacteria/fungi (*Staphylococcus aureus, Bacillus subtilis, Escherichia coli*, *Pseudomonas aeruginosa, candida albicans* and *Aspergillus niger*) with different concentrations by agar-well diffusion method (Table 1). A proportional study of zone of inhibition diameter values of the ligand and its complexes indicate that the metal complexes have a better antimicrobial activity than the free ligand. The complex shows superior activity against the tested fungi than bacteria. This is probably due to the greater lipophilic nature of the complexes. It is evident from the data that this activity significantly increases on coordination [37].

Antioxidant activity (Radical Scavenging Activity)

An easy and quick method to assess antioxidants antiradical properties is to use the 2,2′′-diphenyl-1-picrylhydrazyl (DPPH) radical assay. Determination of the kinetic types of reactions DPPHH is the end result of an antioxidant's reaction with DPPH•.

(AH): $DPPH^{\bullet} + AH \rightarrow DPPHH + A^{\bullet}$

The reversibility of the reaction is evaluated by adding DPPHH at the end of the reaction. If there is an increase in the percentage of remaining $DPPH^{\bullet}$ at the plateau, the reaction is reversible, otherwise it is a complete reaction. DPPH

was used as stable free radical electron accepts or hydrogen radical to become a stable diamagnetic molecule [38]. DPPH is a stable free radical containing an odd electron in its structure and usually used for detection of the radical scavenging activity in chemical analysis [39].The absorbance of DPPH radicals at 517 nm decreased when antioxidants were present, indicating the radicals' capacity for reduction [40]. The concentration (µg/ml) and percentage scavenging effects were plotted on the x and y-axis respectively of the graph. The synthesized complexes scavenging efficacy was evaluated using vitamin C as a reference. When compared to ascorbic acid, the metal complexes demonstrated increased activity as radical scavengers. These findings were consistent with earlier research on metal complexes, in which the ligand exhibited antioxidant activity and the metal moiety was predicted to exhibit increased activity [41,42].

CONCLUSION

In the present study, our efforts were to synthesize and characterize the Ni(II), Cu(II) and Zn(II) complexes with triazole derivative ligand. The synthesized metal complexes were characterized by various physico-chemical and spectral analyses. Based on the analytical, molar conductance, spectral and magnetic moment, octahedral geometry have been suggested for the Ni(II), Cu(II) and Zn(II)complexes. The synthesized complexes were tested for antimicrobial activities. The metal complex has significant antifungal and antioxidant activities as compared to the free ligands.

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Table.1: Anti-microbial activity of the synthesized complexes

S.No	Ligand /Complexes	Zone of Inhibition in diameter (mm) Conc.100 µg/ml					
		S. Aureus	*B. subtilis*	*E. Coli*	*P. aeruginosa*	*C. albicance*	*A. niger*
1	Ligand (Triazole)	22	16	19	20	35	27
2	$[Ni(L_2)(OH_2)_2)]Cl_2$	19	24	23	21	40	23
3	$[Cu(L_2)(OH_2)_2)]$ Cl_2	25	27	23	20	38	21
4	$[Zn(L_2)(OH_2)_2)]$ Cl_2	28	23	24	25	40	23

Table.2: Antioxidant activity ligand and its complexes

S.No	Conc. µg/ml	Scavenging (%)				
		$[Ni(L_2)(OH_2)_2)]Cl_2$	$[Cu(L_2)(OH_2)_2)]Cl_2$	$[Zn(L_2)(OH_2)_2)]$ Cl_2	Ligand	Vit C
1	500	57.521	40.334	61.567	11.213	90.22
2	250	49.305	32.567	53.516	9.797	92.03
3	125	38.619	25.212	45.011	6.312	93.22
4	62.5	29.456	16.890	37.927	5.189	93.09
5	31.25	21.123	11.549	30.479	4.745	88.92
6	15.625	16.675	9.765	18.698	3.929	75.23
7	7.812	13.34	7.643	13.457	3.145	38.72
8	3.906	11.567	6.751	10.912	2.228	25.68
9	1.953	11.121	6.311	10.521	1.689	11.99
10	0.976	11.344	6.059	10.165	1.434	
	IC50	**290.56**	**378.19**	**259.410**	**331.641**	

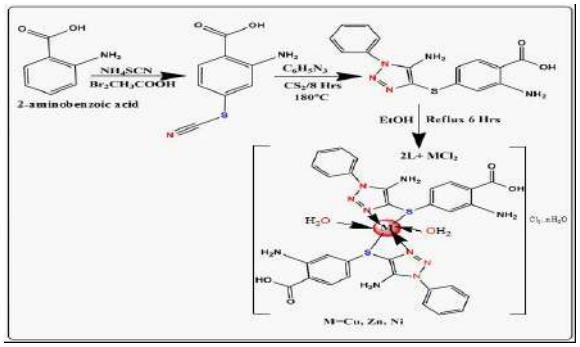

Figure.1: Schematic diagram of synthesis of ligand, Ni(II), Cu(II) and Zn(II) complexes

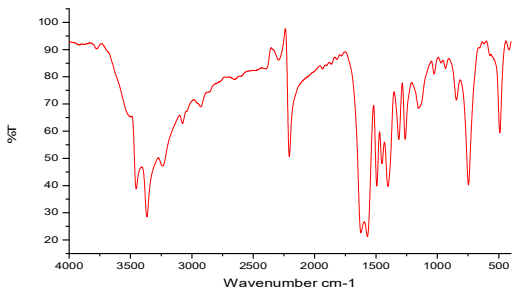

Figure.2 : FT-IR spectrum of Ni(II) complex

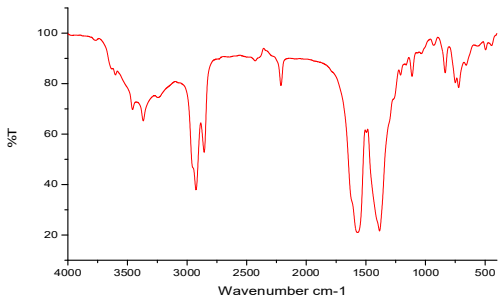

Figure.3: FT-IR spectrum of Cu(II) complex

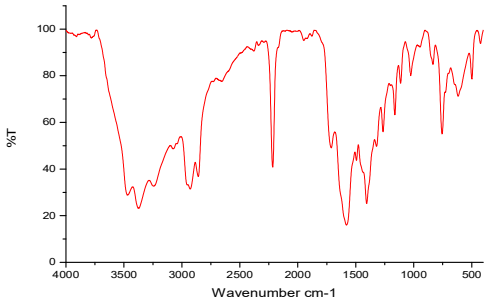

Figure.4: FT-IR spectrum of Zn(II) complex

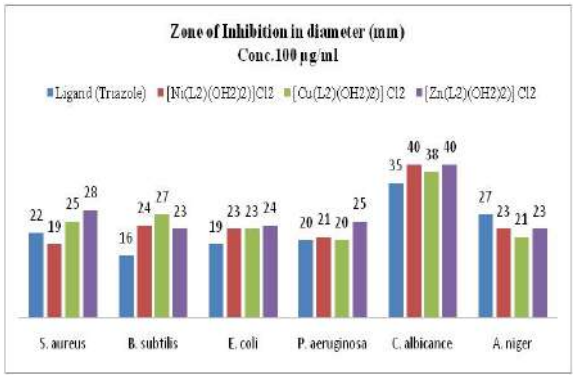

Figure.5: Antimicrobial activities of free ligands and their complexes

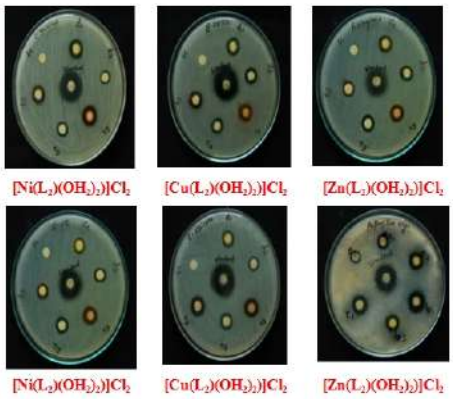

Figure.6: Photographs of antimicrobial activities of complexes

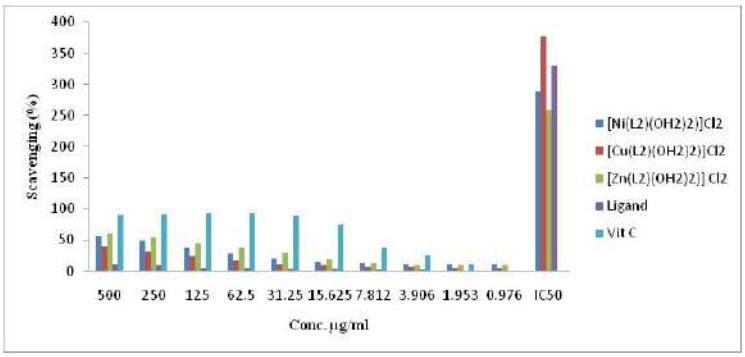

Figure.7: Antioxidant activities of free ligands and their complexes

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RESEARCH ARTICLE

Alcoholic Liver Disease Produced Advanced Glycation End Products: A driver to Chronic Kidney Disease?

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ABSTRACT

Advanced glycation end products (AGEs) are synthesized via Maillard reaction. In addition, increased endogenous Advanced glycation end products (AGE) levels directly promote AGE-RAGE axis activation, leading to subsequent clinical conditions, such as oxidative stress, inflammation, and fibrosis. Disturbed metabolism drives the occurrence of Alcoholic Liver Disease (ALD) and Chronic Kidney Disease (CKD). In an imbalanced metabolic state, reducing sugars have a prominent function in the upregulation of AGE synthesis, Receptor for Advanced Glycation End Products (RAGE) expression, and activation of several downstream signaling pathways through NF-κB, PI3K/AKT, and JAK2/STAT1, leading to various cellular events. In ALD, alcohol consumption is proportional to circulatory AGE levels responsible for oxidative stress (liver pericentral area), Epithelial-to-Mesenchymal Transition (EMT) , upregulation of RAGE receptors, and inflammation (portal area), contributing to disease progression. Elevated AGE levels contribute to renal glomerulosclerosis, tubular atrophy, and interstitial fibrosis, potentially exacerbating type 2 diabetes mellitus (T2DM) in individuals with CKD. Because AGEs contribute to the progression of ALD and CKD, therapeutic development targeting the AGE-RAGE axis is ongoing and requires multifaceted approaches. The review discusses how AGEs may contribute to the progression of ALD and CKD. Moreover, it discusses potential AGE-RAGE-targeted and other prominent therapeutics currently in use or under clinical trials.

Keywords: Alcoholic liver Disease, Chronic Kidney Disease**,** Advanced Glycation End products, Genetic Factors and Translational Therapies.

INTRODUCTION

AGEs are irreversibly glycated macromolecules in which the amino group of proteins and the carbonyl group of reducing sugars interact to form dicarbonyl intermediates, ultimately forming AGEs [1]. These interactions contribute to disease pathology via interactions with the RAGE. Both endogenous and exogenous AGEs exist. Endogenous AGEs primarily arise from high concentrations of reducing sugars, leading to oxidative stress and further AGE synthesis. As a result, increasing its concentration further drives RAGE-based oxidative stress and inflammation, contributing to a self-perpetuating cycle. Cooking methods (frying, roasting), processing time (prolonged time), temperature (high), and nutritional content (higher sugar and fat content) are known factors that elevate exogenous AGE concentration [2,3]. The AGE-RAGE axis also contributes to the pathogenesis of ALD and CKD in metabolically impaired individuals. AGEs are critical etiological factors contributing to diseases such as ALD and CKD, and determining therapeutics that target the AGE-RAGE axis is of considerable importance. Alcohol, a hepatotoxin, induces liver injury, manifesting as ALD characterized by oxidative stress, inflammation, fibrosis, and cirrhosis [4,5]. Increased oxidative stress due to alcohol consumption leads to elevated AGE adduct formation. Metabolic Syndrome (MetS)-associated conditions, such as insulin resistance (IR), hypertriglyceridemia, ALD, and AGE synthesis, are closely related. Because MetS is common in ALD, and excess AGEs induce IR, promoting hyperglycemia and further AGE formation [5], these glycated adducts increase RAGE gene expression, activating hepatic stellate cells (HSCs) and leading to hepatic fibrosis. This fibrosis is associated with marked upregulation of Extracellular Matrix (ECM) components, further contributing to disease progression. AGEs are associated with factors contributing to CKD, including decreased glomerular filtration rate, tubular hypertrophy, glomerulosclerosis, and interstitial fibrosis. Higher AGE levels correlate with renal pathologies such as microalbuminuria, podocyte injury, reduced eGFR, and other kidney-related issues [6]. The components of the AGE-RAGE axis are excellent targets for the development of therapies. Therapeutic approaches targeting glucagon-like peptide 1 (GLP-1) and glyoxalase 1 (Glo1) are being developed, with several in clinical trials.

AGE, their types, and receptors

AGEs are a heterogeneous group of compounds. The initial Maillard reaction involves the formation of fructosyl-lysine, a precursor for subsequent AGE formation. Glyoxal (G), 3-deoxyglucosone (3-DG), and methylglyoxal (MGO), derived from glycolytic intermediates, glycated proteins, and lipid peroxidation, are key intermediates in AGE synthesis. Arginine modification by compounds like MGO-1, 3DG-H, G-H1, MGO, 3-DG, and glyoxal produces hydroxy-imidazolines [7]. Endogenous AGE formation typically involves four steps. First, proteins or nucleic acids undergo non-enzymatic glycation via the Maillard reaction, forming a reversible Schiff base adduct. Furthermore, it is known to form a covalently stable product, referred to as the Amadori product (1-amino deoxy ketose). This adduct then rearranges to form 3-DG and MGO. Accumulation of these intermediates leads to "carbonyl stress," followed by dehydration and oxidation, resulting in AGE formation (Figure 1). AGEs are associated with factors contributing to CKD, including decreased glomerular filtration rate, tubular hypertrophy, glomerulosclerosis, and interstitial fibrosis. accumulation, and pathologies associated with its increased levels [8]. Mainly, four types of AGEs are known to form in vivo: fluorescent crosslinked, fluorescent non-crosslinked, non-fluorescent crosslinked, and non-fluorescent non-crosslinked. Pentosidine formation is due to the cross-linking of arginine and lysine residues with ribose, derived from collagen, hexoses, or ascorbic acid.A number of non-fluorescent crosslinked AGE compounds have also been identified, including GOLD (glyoxal lysine dimer) and MOLD (methylglyoxal lysine dimer).Pyrraline, Pyrralineimmine, carboxymethyl lysine (CML), carboxyethyl lysine (CEL), carboxyethyl lysine (CEL), and carboxymethyl lysine (CML) are all non-fluorescent, non-crosslinked AGEs. In the context of the literature review, CML is the best-known accumulation marker reported for AGE detection in pathological conditions like diabetes. Argpyrimidine is an example of a fluorescent crosslinked AGE, a product of the reaction between arginine and MGO [9]. MGO and G are by-products of several metabolisms that directly surge 'Dicarbonyl stress.' The

increase in the concentration of the former is an outcome of glucose metabolism, threonine catabolism, and ketone body formation. Glyoxal is a catabolized product of multiple reactions through the degradation of various derivatives of saccharides, monosaccharides, and glycated proteins and undoubtedly through lipid peroxidation [10–13]. Both MGO and G are potent glycating agents that target mainly proteins, nucleotides, and lipids [14,15]. Target glycation such as lipid glycation directing lipid bilayer damage, nucleotide glycation results in mutations and cell death events, and protein-targeted effects include proteasomal targeting of misfolded proteins due to glycation (enzyme inactivation, mitochondrial dysfunction, immune response via cellular components of the immune system) [16,17]. Notably, there are two enzymes, Glo-1 and Glo-2 (glyoxylase) known to prevent the synthesis of AGE, among which Glo-1 eliminates harmful compounds such as methylglyoxal by targeting the α-oxoaldehyde group [9]. Ideally, AGE/ALE (advanced lipo-oxidation end products) accumulation affects long living tissues as well as short living cells in an age-dependent manner, and this phenomenon forms a backbone for the development of chronic disease. AGE accumulation can also promote stiffness in vascular walls, skeletal muscles, and collagen-rich lenses. The elevated levels of AGE, which interact with RAGE, are also known to affect short-lived cells like endothelial and pericyte cells. This promotes growth and stimulation of plasminogen activator inhibitors (PAI) and VEGF, activates nuclear factor kappa beta (NF-kB) pathways, and inhibits prostacyclin production.[18].

TRAGE interacts with several ligands, activating downstream signaling pathways of diverse types through the stimulation of ligand binding. Several types of RAGE exist, with N-truncated, C-truncated, and full-length RAGE being the three main types; C-truncated RAGE is divided into two types: endogenous secretory RAGE and secretory RAGE.In addition, there are three domains in RAGE: one variable (V domain - ligand binding) and two constant (C and C' domain) domains, as well as a cytoplasmic tail that relays intracellular signals. sRAGE (formed via ectodomain shedding by matrix metalloproteinases) and esRAGE (lacks transmembrane due to alternative splicing of the native receptor) act as decoys for scavenging RAGE ligands to prevent AGE-RAGE interactions [19]. RAGE is expressed by various types of cells, including macrophages, smooth muscle cells, endothelium, dendritic cells, neurons, and adipocytes, causing oxidative stress, inflammation, apoptosis, adhesion molecules expression, and prothrombotic activity. [20,21]. A diverse range of receptors for AGEs are found namely RAGE, AGE-R1, AGE-R2, AGE-R3, macrophage scavenger receptor-AI, CD36, CD68, macrophage scavenger receptor-AII[20]. Gunter Fritz's experimental study extensively elaborated on the properties of RAGE and its ligand; which were mainly negative charge overall at physiological pH, formation of tetramers, and oligomers among known ligands of S100/calgranulins family proteins, amyloid beta peptide, AGE, etc. It further discussed the model wherein the prime focus was extended and revealed the importance of multimerization/preassembly of RAGE essentiality that likely promotes the intracellular activation of kinases for ensuing pathways such as NF-kB and extracellular signal-regulated kinase (ERK)1/2. Furthermore, it ensures a positive feedback loop that triggers hyperactivation of RAGE expression [22].

The effective downstream pathway activation upon RAGE stimulation is not limited to switching on a single signaling pathway, but multiple; that include NF-kB, (PI3)/Akt, mitogen-activated protein kinase(MAPK), c-Jun N-terminal kinase (JNK), p38, and ERK pathways, when activated, provide a response to several environmental cues, stress, and stimuli that may affect and regulate cellular events [21]. As previously discussed, the role of AGE in triggering inflammation has been thoroughly explained in a mouse model. CML-mps (Nε-carboxymethyl lysine-modified proteins) (AGE) in the induction of NF-kB pathway over inflammation was proven using CML-mps enriched material in WT (Wild type) as compared to RAGE -/- mice model in colonic inflammation. It further mentioned a ‘two-hit’ model focusing on the importance of clinical conditions and AGE in stimulating inflammation; which discussed the ‘first hit’ through oxidant or carbonyl stress and subsequent induction of inflammation by post-translationally modified adducts via RAGE receptors [23]. RAGE plays a pivotal role in various pathological states, such as cardiovascular disease, diabetes, neuronal dysfunction, Alzheimer's disease, and diabetic nephropathy. RAGE is expressed in several cell types such as endothelial cells, smooth muscles, peripheral blood mononuclear cells, alveolar epithelial cells, and podocytes at low levels, whereas basal expression is constitutively expressed in the lungs[24–26]. RAGE mRNAs are expressed in an in vitro disease model of diabetes mellitus [27]. Ideally, these RAGE receptors are the foremost components to which AGE interacts and form the basis for the interaction-induced downstream responses, such as reactive oxygen species (ROS) generation through NADPH oxidase, affecting overall

vascular permeability. In addition, ROS are generated by inflammation during AGE-RAGE interactions in endothelial cells [28]. Furthermore, in relation to AGE-RAGE interaction and its effect, dietary AGE interaction with RAGE, when observed for infant diet, its genetic polymorphism -374A/T RAGE has been intricately found to be linked with glucose metabolism. It also improves insulin sensitivity, which was proven when the comparison was made between breastfed and formula-fed infants and was found to be dependent on the dose of diet [29].As a result of RAGE stimulation, several signaling pathways, including cdc25/rac, Jak/STAT, and MAPK, are activated.Following signalling factor translocation into the nucleus, it promotes the expression of genes, such as endothelin-1, Vascular cell adhesion molecule 1 (VCAM-1), E-selectin, VEGF, and inflammatory cytokines [[30,31]], all of which play a role in inflammatory, fibrogenic, and tissue-injuring processes.

AGE and Alcoholic-liver disease

Alcohol consumption correlates with steatosis, fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) of the liver, depending on the amounts and frequencies of alcohol consumption. The most common morphological characteristic of any liver injury is a fatty liver, which can be induced by alcohol. However, the initial stage of fat accumulation is in the perivenular region, where alcohol dehydrogenase (ADH) is present, which metabolizes alcohol, and excess fat accumulates across the hepatic lobules [4]. Ideally, the primary stage of alcohol-induced steatosis is manifested when there is an average alcohol consumption of 120-150 gm of alcohol for 2-3 weeks. In alcoholism, proteins-aldehyde adducts form, proinflammatory cytokines are released, lipids are peroxidized, and immunological activity activates stellate cells and produces the extracellular matrix.[32]. When histological and clinical risks are anticipated on an individual basis, alcohol consumption is correlated with associated risks. When the pattern of alcohol intake and disease progression was considered for its relative basis, subjects with a daily habit of alcohol consumption had a higher risk of stage advancement of disease compared to occasional/weekend drinkers and those drinking with meals [33]. There is a direct link between the prevalence of ALD and MetS. In this, the co-occurrence of hyperglycemia andhyperlipidemia, AGEs formationis bolstered in disease pathologies associated with previously stated parameters. Furthermore, IR is triggered by the inhibition of downstream pathway intermediates that block the insulin signaling pathway [34]. In a study, MGO was applied in a dose-dependent manner to rat-derived L6 mouse myoblast cellsto analyze the effects on the insulin signaling pathway[34]. Kirsten et al. reported that significantly increased triglyceride (TG) levels (32.9 mmol/l) were associated with excessive consumption of alcohol, while obesity and T2DM were found to impose co-additive effects, thus promoting hypertriglyceridemia. In addition, acute alcohol levels are associated with increased formation of catecholamines, which affect adipose tissue, further upregulating lipolysis, resulting in increased free fatty acid (FFA) levels and ultimately higher levels of TG [35].

These observations relate to the relevance of alcohol in metabolism-induced pathology; understanding the detrimental role of alcohol in AGE formation is crucial. Alcohol dehydrogenase(ADH) metabolizes alcohol to acetaldehyde (AA) and acetate, which then is converted into CO2 and water through CYP2E1 (cytochrome P450-2E1).Oxygen free radicals are formed by CYP2E1, which target lipid peroxidation.In response to the AA-AGE (Acetaldehyde derived Advanced Glycation End products) protein adduct, malondialdehyde-acetaldehyde adduct (MAA) is formed. It was also found that 4-hydroxynonenal (4-HNE), malondialdehyde (MDA), hydroxyethyl radicals (HER) from ethanol metabolism in the presence of iron, and AA were present in the cells [36]. Toxic AGE (TAGE) is involved in the development of ALD and NAFLD owing to its pathophysiological significance. An increase in the uptake of alcohol correlates with ALD, suggesting a direct link with increased AGE levels [37]. This study explained the positive association between AGE formation and increased ethanol uptake (decreased albumin turnover), progression to steatohepatitis, and AGE protein adduct formation. The AGE-protein adducts actively interact with HSCs and Kupffer cells, which promote the upregulation of RAGE expression, ROS formation, and oxidative stress, leading to liver pathologies such as steatosis, ballooning, and apoptosis, later leading to the activation of Kupffer cells in ALD progression [38–40]. Ethanol consumption is subject to a decrease in ATP biogenesis, and protein adduct formation affects mitochondrial DNA (mt-DNA), contributing to mitochondrial dysfunction and decrease in CYP2E1 concentrations. In the combined experiment with ethanol and fructose, fructose proceeded through the Maillard reaction, contributing to mitochondrial dysfunction, as shown in figure 2. This combination leads to the expression of lipocalin-2 and melanocortin-4 receptors, further contributing to mild portal

inflammation and fibrosis [41]. Moreover, CCL4-based cirrhosis induction resulted in a reduction in Glo-1 enzyme levels while increasing MGO levels, which are important AGE precursors. A study was carried out to explore the role of AA-AGE in determining the hepatocyte area affected by alcohol consumption. Considerably, the pericentral area was heavily stained, which included AA-AGE and 4-HNE, indicating that it was the most affected area. There was significant AA-AGE reduction observed from 8 weeks to 12 weeks, resulting in complete elimination by 12 weeks. After in vivo administration of ethanol for eight weeks, it was later subjected to alcohol abstinence, suggesting its critical role in disease progression [38]. In association with RAGE expression, it is linked to the activation of the pro-fibrogenic pathway transforming growth factor beta (TGF-βII) and the release of the profibrogenic cytokine procollagen A1 (I), a major fibrillar collagen precursor, the expression of α-SMA (an HSC activation marker), and TIMP-1 (a matrix metalloproteinase inhibitor) [42- 45]. These observations explain the possible role of AGE as a cofactor in promoting liver injury through RAGE expression and fibrogenesis. In addition, cytokines, such as TGF-β1 and CTGF/CCN2, imitate a pro-fibrogenic signal, resulting in stellate cell activation and subsequent fibrogenesis[45–47]. To summarize, AGE acts as a confounding factor that either stimulates or worsens existing alcohol-induced pathologies as per clinical evidences shown in table 1.

ALD related AGE development leads to CKD

There is a close relationship between onset of ALD and progression of CKD; but the effect of alcohol consumption on kidney function remains largely understudied [53,54]. ROS is generated via both enzymatic as well as non-enzymatic reactions in kidneys [53]. Alcohol induced oxidative stress leads to lipid peroxidation which further produces reactive molecules like MDA and 4-HNE that might enhance the formation of AGE [55,56]. Accumulation of 4-HNE results in its protein adducts in the proximal and distal convoluted tubule cells of kidneys. This leads to mitochondrial dysfunction and kidney damage [52]. Kidney functions by filtering, trapping, and metabolizing plasma AGE, and intracellularly generated AGE initiate disease development. Quantitative trapping was evident when CML-modified rat albumin was administered for 5 months, and there was a consistent 50% increase in AGE and associated pathologies of glomerulosclerosis[57]. Complex involvement of various cytokines and growth factors is likely to drive glomerulosclerosis, mainly tumor necrosis factor alpha (TNF-α), TGF-β, insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), and interleukin 1 (IL-1), which directly influence cellular protein machinery and its proliferation ability, ultimately influencing histological features such as albuminuria, basement membrane widening, mesangial extracellular matrix expansion, and increase in glomerular tuft volume [58].

CKD is often not detected in its early stages owing to the asymptomatic nature of disease development. Ideally, three events define the development and progression of the disease: a decreased eGFR rate (60 ml/min per 1.73 m2) (measured by serum creatinine), renal structural abnormalities, and albuminuria (>30 mg of urinary albumin per gram of urinary creatinine as adequate) [41]. CKD is commonly a manifestation of T2DM, which is directly associated with kidney failure [59]. CKD shares an intricate relationship with T2DM, cardiovascular disease, hypertension, and alcoholic liver disease, and its development is heterogeneously stratified among the population [60–62]. Additionally, microalbuminuria, when compared for its linkage with obesity in paediatric and adolescent subjects; evidence stated about 6.4% prevalence of microalbuminuria in this large cohort consistent with microalbuminuria range of 0.3% to 10.1%, and this range was supported by several other studies. When childhood obesity was used as a reference scale to determine the function of eGFR, the results were in favor of a lower eGFR rate with almost two- to threefold increased risk for the development of ESRD, resulting in renal pathologies [63]. In CKD under uraemia, there is an intricate relationship between AGE-RAGE-based induced oxidative stress and the feedback loop observed (induction of oxidative stress via the AGE-RAGE axis results in AGE formation and further elevates oxidative stress), wherein the cytochrome oxidase activity notably declines with defined mitochondrial dysfunction. Furthermore, a strong association between CKD and reduced ATP production and mitochondrial dysfunction is evident, which forms the basis for decreased cytochrome oxidase activity, supporting the hypertrophic condition of other electron transport chain components and thus furthering oxidative stress [64]. Under hypertensive nephropathy, mitochondrial damage was evident with pathological conditions including nitric oxide synthase (NOS) activity, cyclooxygenase activity, and a reduction in the membrane potential of the mitochondria, all of which were prevalent in hypertensive rats, suggesting a direct link between hypertension and the kidneys [64,65]. Most importantly, the role of oxidative stress

and inflammation is vicious, leading to CKD and associated mortality. AGEs are uremic toxins that show an intricate relationship with oxidative stress. They stimulate oxidative stress and inflammation, resulting in effects such as IR, endothelial dysfunction, and renal impairment [66]. Moreover, D-ribose is closely associated with organ damage in the diabetic state, and its role in inflammation is critically sought.

D-ribose-based NLRP inflammasome activation and overt expression of IL-1b were deciphered by an in vivo mouse study, which causes podocyte injury and glomerular sclerosis. Furthermore, the knockout of the Asc gene prevents any pathogenic actions, such as glomerular sclerosis induced by D-ribose, explaining the role of the NLRP inflammasome in an inflammatory response [67]. Furthermore, dietary AGE with inflammatory and endothelial dysfunction markers was analysed for correlation with ongoing type 1 and T2DM, which demonstrated that a low-AGE diet administered for 6 weeks reduced the TNF, VCAM-1, and hs-CRP markers along with the serum levels of AGE. Nevertheless, the literature also supports the correlation between AGE levels in the diet and the resultant oxidative stress, inflammation, and decreased AGE levels in diabetic, non-diabetic, and healthy subjects[68]. ROS are crucially involved in podocyte activation and CML, and AGE directly seems to be upregulating the ROS generation in podocytes via RAGE activation. In addition to its activation, podocyte-specific granulocyte-monocyte colony-stimulating factor expression is enhanced by elevated concentrations of ROS [28]. Exploring the significant role of oxidative stress in CKD is critical because it involves a causal nexus that explains the direct proportionality between oxidative stress and AGE synthesis, that is, increase in oxidative stress causes excess AGE formation, and vice versa explaining the vicious circle in disease pathology. In the context of oxidative stress and Glo-1 enzyme activity, Glo-1 activity is found to be impaired in situ and shows a proportional nature with GSH levels (imbalance system created between oxidized glutathione and GSH) and anti-oxidant systems, which elaborately infers the direct involvement of oxidative stress in catalysis of deleterious species like AGE, suggesting a temporary regulatory role of Glo-1, affecting overall AGE levels [38,39].

Fibrosis is triggered by multiple stimuli, such as trauma, wound infection, autoimmunity, metabolic disorders, and inflammation, to ensure tissue integrity as the final repair process in concurrent tissue injury. Fibrosis is uncontrolled tissue remodelling that occurs at a much higher rate and involves events such as myofibroblast activation, which triggers fibrotic pathways affecting CKD progression at multiple levels [69]. Myofibroblasts play an exclusive role in disease pathology because they possess an innate contractile property ideal for the wound healing process. This explains why the major renal fibroblasts positive for the α-SMA marker undergo activation under ECM-integrin interaction, cell-cell contact, hyperglycemia, and hypoxia-like environmental stimuli [70]. Hemodynamic imbalances form the basis for CKD, particularly kidney fibrosis, and glucose-induced AGE formation and accumulation in db/db mouse glomeruli. The results explained the significant browning of diabetic mouse glomeruli, which forms the basis for profound accumulation and significant association with ECM under hyperglycemia. Furthermore, in this study, in vitro analysis of mesangial cells led to the upregulation of genes, including collagen type 1 and 4, depending on the dosage provided. In addition, an in vivo study of the db/db model using glomeruli staining with Masson trichrome revealed a considerable increase in collagen fibril deposition. This observation explains the role of AGE in promoting fibrosis under concurrent diabetic conditions [71]. The critical role of hyperglycemia has been investigated in diabetic gerbils, and it is known to increase the levels of ACE, Ang II, and ATIR. Ang II stimulates the activation of ATIR and renal interstitial fibroblasts via higher expression of α-SMA, which leads to the proliferation and migration of these cells, thus resulting in renal fibrosis[72]. This evidence suggests a stimulatory yet direct role of hyperglycemia in increasing AGE formation, which promotes renal fibrosis. Renal cell death is often associated with renal pathologies, undergoing compartment-specific renal cell death of tubular (proximal and distal), endothelial, and glomerular cells due to necrosis during the default apoptosis process [73,74]. In the initial stages of apoptosis, reactive oxygen intermediate (ROI) generation is observed. However, the dependency on caspase activation (independent of NF-kB activation) is notable after the release of cytochrome oxidase from the mitochondria. Moreover, activation of the cell death mechanism under autophagy inhibition was demonstrated by 3-methyl adenine or bafilomycin. In its absence, the protective role of AGE-induced autophagy promotes a 30-40% increase in cell death. Ideally, AGE treatment stimulates the release of myeloperoxidase, alkaline phosphatase, and granular contents such as IL-8. AGE is known to increase intracellular Ca2+, calcineurin, nuclear factor of activated T cells

(NF-AT) DNA binding activity, and FasL, whereas IL-8 affects Ca^{2+} concentration internally within the cell. Intriguingly, the inhibition of Ca^{2+} directly affects cell survival. Importantly, IL-8 plays a role in the NF-kB signaling pathway, which closely connects the expression of IL-8 and TNF-α, and the death event via recruitment of the TNF-receptor-associated death domain and procaspase 8. Furthermore, AGE-induced cell death is prominent under calcineurin and NF-AT DNA binding inhibition [75].

AGEs and brain

Alcohol metabolism in brain occurs in the similar manner as in the liver which include enzymes like ADH, CYP2E1, catalase and aldehyde dehydrogenase (ALDH2) with different proportions than their counterpart hepatic isoforms. Of these, catalase and ALDH2 play crucial role in the brain ethanol oxidation as per the evidences in the rodent models [79]. Excessive alcohol consumption is linked with alterations in the structural and functional properties of the brain [36]. Furthermore, it can lead to the oxidative stress with the increased production of ROS and lipid peroxidation, dysfunction of antioxidative enzymes like ALDH2 and glutathione (GSH), accumulation of AA adducts (protein/DNA) and likely formation of AGEs in the brain [80–82]. The reduced form of AA-protein adduct, N-Ethyllysine (NEL) is reported in the liver of patients with ALD as well as in the brain of experimental ethanol fed mice. Furthermore, based on the study conducted by incubating cortical neurons with AA-AGE, a dose-dependent neuronal damage became apparent [83]. Moreover, alcohol abuse speeds up cerebral AGE production and cross-linking which upregulates the expression of RAGE and further neurocognitive impairments [84].

Therapeutics targeting AGE and the AGE-RAGE axis

'Therapeutics' concept implies the reduction of adverse effects involving; either reversal of pathological consequences or lowering the causative factors that lead to pathophysiology. In consideration of the development of therapeutics, decreasing AGE levels in serum could reverse inflammation, oxidative stress, fibrosis, coagulation, and associated pathologies such as micro-or macrovascular complications in diseases such as diabetic kidney disease and ALD. Conventionally, Aminoguanidine (AG) has been used as a scavenging agent and a potent inhibitor of AGE synthesis and protein cross-linking [30]. Additionally, under hyperglycemia, AGE formation via the methylglyoxal precursor was found to be decreased by AG. Furthermore, diabetes-related disorders, particularly glomerulosclerosis, improved in streptozotocin(STZ) administered diabetic rat model. Considering arterial stiffness using arterial impedance analysis, AGE accumulation on collagen is another factor responsible for increased arterial stiffness (measured by the t-wave transit time). In proportionality terms, arterial stiffness shows an inverse proportionality to wave transit time. Moreover, AG administration for 8 weeks resulted in a significant 21% increase in the t-value in diabetes-related arterial stiffness through the inhibition of AGE deposition on collagen tissues [30,85]. Recent factors that may be used as therapeutics, targeting RAGE axis intermediates that subsequently lead to downstream pathologies, are yet to be developed.

GLP-1 Agonist as emerging therapeutics

More recently, the surprising role of one of the incretins, also a gut hormone GLP-1 peptide, is found to prevent AGE-induced RAGE expression, clinical conditions like oxidative stress, and cell death. In vitro studies have shown reduced RAGE mRNA and protein expression following treatment with GLP-1 in a dose-non-independent manner [86]. In addition, it inhibits downstream signaling pathways, which are known to be stimulated by AGE-RAGE interaction. Suppression of downstream molecular pathways is associated with decreased VCAM-1 expression. Furthermore, the GLP-1 peptide's therapeutic role on the AGE-RAGE axis by regulating RAGE expression blocked AGE-based upregulation of MCP-1 mRNA and protein levels in mesangial cells. In addition, suppressing NADPH oxidase activity leads to the lowering of NF-kB activation and ROS generation [87]. The AGE leads to decrease cAMP levels, as observed under cultured human epithelial cells, and the cAMP agonist dibutyrylcAMP reduced plasminogen activator inhibitor-1(PAI-1) levels [87]. In this context, the recent study revealed its partial anti-inflammatory and anti-oxidant via the cAMP pathway, through interaction with GLP-R1 on cultured mesangial cells in-vitro [86]. To summarize, cumulative clinical studies are mentioned in table 2.

RAGE-aptamers - evolving therapeutics

Generally, RAGE acts as an initial interaction point for diverse types of ligands. AGEs are major ligands that stimulate the activation of these receptors and associated downstream signaling pathways. The RAGE homozygous knockout study in the diabetic model confirmed the decreased occurrence of renal pathologies such as basement membrane thickening and progressive glomerulosclerosis with renal dysfunction, which demands specific targets to reduce its expression or blockage by preventing AGE-RAGE interaction and subsequent pathogenesis [88,89]. Ideally, two types of aptamers, DNA and RNA aptamers, are synthesized using SELEX technology (preparation of random oligonucleotide pools, incubation, partitioning, amplification, and sequencing) over the course of a few weeks to months [89,90]. Ideally, the DNA aptamers could attain three-dimensional structures with the highest specificity and affinity for RAGE and resembles an antibody structurally and functionally, defining as a "chemical antibody." In vivo studies in 17-week-old mice were aimed at finding the role of RAGE aptamers in diabetes. These included curing a disease condition, which involved a substantial decrease in the mRNA expression of NADPH oxidase (gp91, p47fox, p67fox, etc.) upon RAGE aptamer treatment, thus reducing oxidative stress. Furthermore, RAGE aptamers confer beneficial effects by attenuating the upregulated transcription and translation ofintercellular adhesion molecule-1 (ICAM-1), VCAM-1, MCP-1, PAI-1, TGF-β, fibronectin, type 1, 2, and 3 collagen, and macrophage infiltration in renal cells. In addition, restoration of podocin protein (a component of the filtration slit) and WT-1 (a podocyte-exclusive transcription factor) was notably observed upon immunostaining, explaining its therapeutic potential in diseases like diabetic nephropathy. Hypothetically, its application can be explored in diseases like ALD with similar pathological consequences [88].

TRC4186

Pyridinium, 3-[[2-(methylsulfonyl) hydrazino] carbonyl]-1-[2-oxo-2-2-thienyl) ethyl] -chloride: In T2DM pathogenesis, vascular complications, and endothelial dysfunction are typical characteristics observed during the progressing and advancing stages due to higher concentration of AGE. Pyridinium, 3-[[2-(methylsulfonyl) hydrazino] carbonyl]-1-[2-oxo-2-2-thienyl) ethyl]-chloride (TRC4186) is under clinical trials Phase 1 to address the consequences like vascular complications and endothelial dysfunction. In clinical trials, upon in-vivo analysis, its rapid absorption was observed within 1-4 hours with maximum plasma concentrations (Cmax), compared to 40% less absorption in the tablet formulation under fed conditions. However, almost no significant difference in renal clearance among elderly males and young subjects was noted [78] as depicted in table 2.

Glo-1 Inducers Therapeutics—Under Clinical Trials

Glyoxylases are the enzymes that play a critical role in metabolizing methylglyoxal into D-lactate form. Evidence has reported a decrease in the glyoxylase enzyme in metabolically driven diseases like CKD, which is consistent with pre-existing elevated oxidative stress and other clinical conditions [38,39]. The combination of trans-resveratrol and hesperetin (tRES-HESP) in the induction of glyoxylase-1, decrease in ECM gene expression, and inflammation had a synergistic effect that was positively impacted by improving clinical parameters. The study results explained about 22% more Glo1 expression in PBMC when plasma was analyzed compared to placebo. Additionally, this combination in PBMC (peripheral blood mononuclear cells) considerably increases Glo1 by about 27% in overweight or highly obese individuals and about 30% in obese individuals. Furthermore, the combined treatment revealed a decrease in levels of RAGE, E-selectin protein, and ICAM-1, while a decrease in VCAM-1, RAGE, and matrix metalloproteinase-3 was observed in HAEC and BJ fibroblast cell lines, respectively [91,92]. Due to these findings, the scope of Glo-1 inducers extended to diseases driven by metabolic disturbances (due to AGE) that ultimately manifest as fibrosis.

Role of Metal ion

The role of cobalt in the reduction of pentosidine (a prominent AGE) was observed in the treatment of renal injuries in T2DM conditions. Interestingly, in an experiment, the administration of cobalt to SHR/ND mice aimed to prevent the degradation of the HIF factor in renal injury, alleviating hypoxia-induced renal injuries. Surprisingly, it revealed a reduction in pentosidine levels, NADPH oxidase levels (a known marker of oxidative stress), and proteinuria. The independent yet indirect role of cobalt ion was associated with the reduction of renal injury excluding hypertension

and MetS by reduction of oxidative stress and AGE (pentosidine) [31]. Its therapeutic role is among those of possibly unexplored molecules for targeting AGE-associated pathology.

miRNA Strategy

Among various pathways activated under AGE-RAGE interaction, remedies to prevent ECM over expression will likely address the later-stage pathogenesis, for instance, fibrosis in ALD and CKD. Considering both diseases, in general, among the three isoforms of TGF-β, TGF-β1 is a principal mediator in promoting ECM gene expression (fibrotic material through EMT transition by regulation or modification of cell organizational proteins), especially in diabetic conditions [93,94]. The role of TGF-β elucidated its role in the downregulation of MiR-200, and majorly, TGF-β1 is known for this downregulation. This MiR-200 acts as a regulator for translational repressors of TGF-β2. As a result of this downregulation, it promotes the elevation of TGF-β2, as observed in fibrotic kidneys. A possible therapeutic may involve the overexpression of MiR-200 to counteract the effect of TGF-β2 in fibrosis progression [95,96].

Translational Approach

We have previously described the formation of various AGE adducts, their interactions with RAGE, and their pathological implications in alcohol-mediated damage. Based on the molecular mechanisms involved and their functional consequences, we can propose several strategies for preventing and treating AGE-associated tissue damage and RAGE-related diseases. One such strategy is to minimize the production of endogenous AGEs, which can help prevent various disease conditions. Additionally, reducing the intake of exogenous AGEs through dietary modifications can also help minimize the harmful effects of AGEs. Other approaches that can be considered include the use of antioxidants to counter oxidative stress, anti-inflammatory agents to reduce inflammation, and inhibitors of AGE formation or RAGE activity. These approaches can be employed alone or in combination to achieve the desired therapeutic effect. As mentioned above, cooking methods greatly affect the levels of AGE formation in food, with boiling and stewing reducing AGE content by half compared to broiling. Other factors such as water content, cooking time and temperature, and food pH also play a crucial role. Marinating food with acidic ingredients like vinegar or lemon juice can decrease AGE production during high-heat cooking by up to 50% [97].

Lifestyle changes such as reducing alcohol, tobacco intake, and exercising can also lower endogenous AGE production and prevent related diseases. Traditional Asian, Mediterranean, and other cuisines often use these methods to create healthy dishes. In addition to that, we have explained how heightened oxidative stress contributes to the formation of certain compounds such as AA, MDA, MAA, and other adducts associated with alcohol-induced damage, along with their resulting effects. According to cell culture models, experimental rodent, and human studies, CYP2E1 is particularly responsible for the creation of AA and MAA adducts [98–100]. By taking CYP2E1 inhibitors naturally occurring in foods such as garlic, such as diallyldisulfide[100,101]; phenyl isothiocyanate in cabbage and cruciferous vegetables [102]; ellagic acid in pomegranate [103]; polyunsaturated fatty acids, including docosahexaenoic acid (22:6n-3) [104] and indole-3-carbinol in vegetables and fruits [105]; berberine in fruits and vegetables [106] ; walnut [107]; curcumin [108,109]; quercetin [110]; and synthetic compounds (chlormethiazole and YH439 [111],[112]) one may prevent the formation of AA-related [[110]], adductsand AA-MAA adducts [81,113],however, none of these dietary compounds has been specifically tested for their preventative effects on the formation of AGEs associated adducts. AGEs and their compounds also decreased the accumulation of SIRT1 and other defensive proteins in the body, such as the receptor coactivator which is activated by peroxisome proliferator - activated receptors [[80,114–116]]and ALDH2 [115] . Additionally, subchronic alcohol consumption decreased the level of SIRT1 as well as PGC-1α and other isoforms [117,118].Hence, drugs that activate SIRT1 such as resveratrol and its synthetic structural derivatives [[119,120]], as well as melatonin, may prevent the formation of adducts and AGE-related diseases [121]. A dietary supplement [108,109,121,122] or synthetic antioxidant [38]that contains anti-inflammatory properties can reduce the severity and incidence of inflammation caused by AGE. In addition, soluble RAGE, inhibitors of RAGE signaling, neutralizing antibodies to RAGE or AA-AGE adducts, and other AGE-degrading compounds have been reported to decrease the formation of AGE adducts, including pyridoxamine, ALT-711, lipoic acid, and synthetic compounds OPB-9195 [[123–131]].

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CONCLUSION

Glycated macromolecules are known contributors to the progression of metabolic diseases like ALD and CKD. Overall, the AGE formation due to several responsible factors drives the AGE-RAGE interaction leading to clinical implications such as inflammation, oxidative stress, and fibrosis. Recently, there are several known therapeutics, and a few are under clinical trials, that may target the intermediates of the RAGE axis-based signaling pathway, and they could serve as a future treatment for diseases driven by an imbalanced metabolic state.

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Table 1: Summary of clinical prevalence of AGE formation in association with ALD

References	Study Population	Type of Detection Method	Key findings
[48]	Control 20 ASH 100 AC 20	AGE fluorescencedetected at 350 to 440 nm	AGEs level had significant increase ($p<0.05$) for ASH w.r.t AC and control; whereas non-significant for ASH w.r.t AC
[49]	AC 19 Control 19	CML detection through ELISA	Mean serum AGE (CML) levels had significant increase ($p<0.01$) in AC vs control
[50]	AC 30 Control 121	CML detection through ELISA	Serum AGEs (CML) levels had significant upregulation ($p<0.05$) in AC w.r.t control
[51]	ASH 65 Control 65	AGE10 (MAGE) detection through ELISA	Concentration of AGE10 was significantly higher ($p<0.001$) in the AH vs control
[52]	HD 23 Control 22	AGE fluorescence, pentosidine, CML, fluorescence detection at 350/435 nm, CML measured through ELISA and pentosidine determined by Reversed HPLC	AGE level had significant higher value ($p<0.005$) in AHD patients vs control

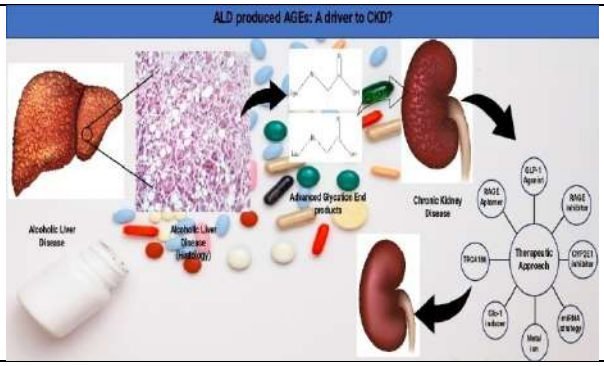
ASH: alcoholic steatohepatitis, AC: alcoholic cirrhosis, CML: N-(carboxymethyl) lysine, CEL: N-(carboxyethyl) lysine, AH: alcoholic hepatitis, HD: alcohol heavy drinker, ELISA: Enzyme linked immunosorbent assay

Table 2: Summary of clinical prevalence of AGE formation leading to CKD and the therapeutic approaches to mitigate it.

References	Study Population	Type of Detection Method	Key findings
[76]	88 ESRD patients and 20 healthy individuals	AGEs: ELISA, sRAGE: ELISA	AGE levels were 6.75 times higher in patients with ESKD than in controls. Increases in AGE were 2-3.23 times greater than increases in sRAGE. AGEs/sRAGE ratio was negatively correlated with sRAGE. This ratio could be utilized as a potential biomarker for ESKD
[77]	33 trials including 98,284 patients reported kidney failure or start of kidney transplant and placebo were considered based on baseline risk (very low, low, moderate, high	GLP-1 receptor agonists	Results were taken based on median of 0.78 (0.67 to 0.92). In this high certainty in treatment provided reduction in cases of kidney failure.

	and very high)		
[78]	4 categories; SAD study: 25 healthy males subjects, MAD study: 27 elderly subjects, healthy control: 18 subjects (9 male and 9 female) and FFE study: 15 males	TRC-4186; LC/MS	A single dose of TRC4186 of 2500 mg is well tolerated in subjects

ESRD – End stage renal disease, SAD – single ascending dose, MAD – Multiple ascending doses, FFE - food formulation effect



Graphical Abstract

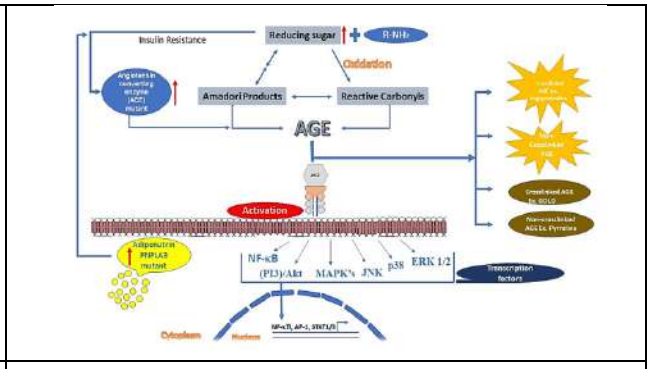


Figure 1: The figure depicts age formation and subsequent activation of several signalling pathways.

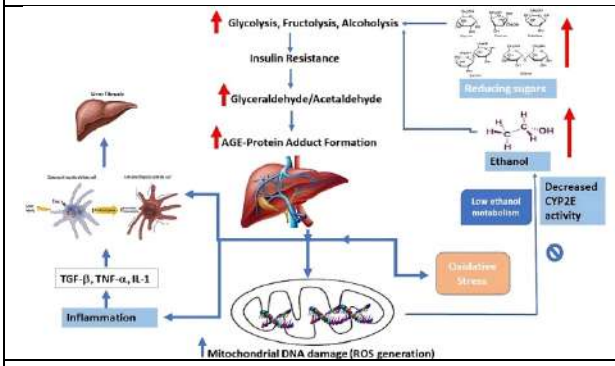


Figure 2: The figure represents the direct involvement of alcohol in the formation of AGE and subsequent liver-specific pathologies.

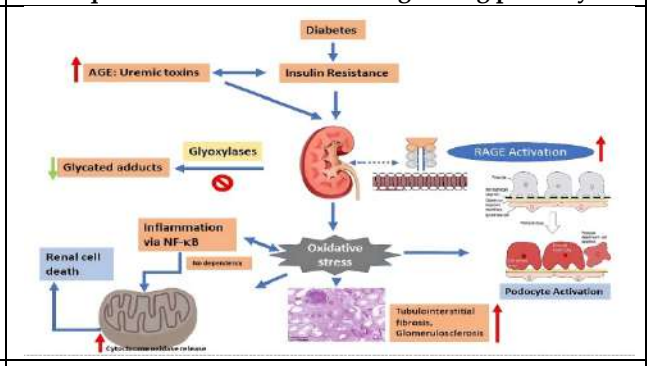


Figure 3: This figure illustrates the possible role of AGE and concurrent diabetic conditions in the induction of an insulin-resistant state and vice versa in diabetic kidney disease.

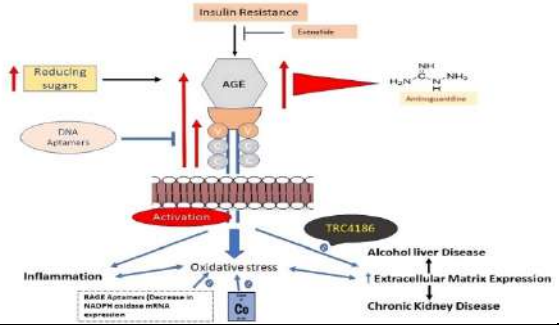


Figure 4: The figure represents therapeutics aimed at targeting multiple components of the AGE-RAGE axis and conditions manifested due to this axis' activation.

RESEARCH ARTICLE

RTOS - Driven Smart Home Automation: A Scalable Approach

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ABSTRACT

The increasing demand for home automation systems stems from the need for wireless, monitored security solutions that are also energy-efficient. There is a growing necessity for precise and responsive systems to address this demand. This paper presents the design and implementation of a Real-Time Operating System (RTOS)-based home automation system, specifically focusing on time-critical tasks, shared resources, and cloud-enabled data visualization. The system is built on an ESP-32 microcontroller utilizing Free RTOS and various sensors and actuators to manage home automation processes. The RTOS framework ensures that high-priority tasks are executed with minimal latency while lower-priority tasks are seamlessly handled in the background. This is accomplished by effectively using kernel objects, including interrupt service routines, mutexes, tasks, and the task scheduler. The system's architecture is designed to handle the complexities of real-time operations, ensuring reliability and efficiency. Integrating cloud-based data visualization also provides real-time monitoring and control, enhancing the overall user experience. This RTOS- based approach meets the growing needs of smart home automation and sets the stage for more advanced, scalable solutions in the future.

Keywords: Smart Home Automation, RTOS, ESP32, Internet of Things(IoT), ThingSpeak Cloud

INTRODUCTION

Automation simplifies our lives by reducing the need for human labor and optimizing energy use. It is no longer limited to large-scale industries; it has seamlessly integrated into our daily lives, especially in domestic settings. At home, automation systems manage and control various electronic devices, enhancing convenience and efficiency by handling tasks that once required manual intervention. From regulating heating and cooling systems to managing lighting and security, automation has revolutionized how we interact with technology in our living spaces. Rutuja B. Kirpal and T.H. Nagrare have developed an advanced energy management system using Real-Time Operating Systems (RTOS) to optimize household power consumption. This system intelligently monitors and regulates energy usage by automatically controlling and disconnecting electrical outlets and lights when they are not in use. Integrating RTOS ensures efficient energy management, reducing unnecessary power consumption and contributing to overall energy savings within the home environment [9]. Syed Anwaarullah and S.V. Altaf have pioneered the development of a home automation system that is both cost-effective and compact while prioritizing security. Their system is built around a Real-Time Operating System (RTOS) and is operated via an Android interface, ensuring seamless and efficient control. Integrating scmRTOS into their design allows for precise real-time processing, enhancing the system's overall reliability and performance, as detailed in their research [5].

On a parallel track, Aniket R. Yeole, Sapana M. Bramhankar, Arjun Gaikwad, Abhijeet Bansod, and Atul B. Borade have also implemented a home automation system grounded in RTOS principles, but with a focus on the ATMEGA microcontroller as the core of their design. Their approach incorporates an open-source RTOS, significantly boosting the system's performance by making it more dynamic and adaptable to real-time demands, thereby increasing its overall efficiency and responsiveness [19]. K. Mandula, R. Parupalli, C. Murty, E. Magesh, and Rutul Lunagariya have developed a mobile-based home automation system utilizing the Internet of Things (IoT). Their system integrates an Arduino board with an Android mobile app, with Bluetooth facilitating communication between the microcontroller and the mobile device [11]. Meanwhile, Kishore P, Veera- manikandasamy T, Sambath K, and Veerakumar S have created a real-time home automation and security system using an Arduino UNO and an ESP8266 WiFi module. This system employs an MQTT server for the control and monitoring of home appliances [13]. The smart home control unit designed by Khushi Singh, Aditya Jain, and Pradheep Thiyagarajan incorporates a variety of advanced components, including the AVR microcontroller Atmega 2650, the Wi-Fi IoT module ESP 8266, the RN-42 Bluetooth module with Serial Port Profile (SPP), the DS3231 Real-Time Clock module, as well as sensors for light, temperature, humidity, PIR motion detection, and soil moisture. Additionally, the system features a relay board, a 3.5-inch touchscreen display, and controls electrical loads [14]. In a related field, K. Yuneela and Ashish Sharma have authored a review paper that examines the technologies employed in home automation systems, discussing Zigbee, Bluetooth, RF, cloud, SMS, and web-based technologies [20].

Satyendra K. Vishwakarma, Prashant Upadhyaya, Babita Kumari, and Arun Kumar Mishra have developed a smart, energy- efficient home automation system utilizing IoT technology. This system enables remote access and control of home appliances via voice commands and web-based services, with a focus on reducing power consumption and enhancing home security [17]. Similarly, Shradha Somani, Parikshit Solunke, Shaunak Oke, Parth Medhi, and P.P. Laturkar have detailed an IoT-based home automation and security system that employs a Raspberry Pi, various sensors, and an Android app. Their system provides wireless security features, including AES encryption and user notifications, to manage home appliances securely [15]. Vishakha D. Vaidya and Pinki Vishwakarma have provided a comparative analysis of different smart home technologies, including GSM, Bluetooth, IoT, and PIC micro-controller with ZigBee, along with their home automation and security features.[16]. Over the years, home automation systems focusing on wireless control and monitoring have been developed. The system includes communicating and controlling sensors and actuators through technologies like Bluetooth, Zigbee, GSM, and PIC controller. This paper focuses on the responsiveness and reliability of the system using FreeRTOS, RTOS kernel objects, and ESP32 micro-controller. The system uses several sensors to monitor the environment and a few output devices to display or alert the people. The system also uses an IoT platform to visualize the live data in the cloud. This paper is organized as

follows: Section II contains the components of the home automation system, including the hardware, software, and IoT platform. Section III describes the sensors in detail. Section IV explains the advantages of RTOS over the General operation system in Home Automation, and Section V describes various components of FreeRTOS. Lastly, the implementation and analysis are discussed in Section VI, and concluding remarks are given in Section VII.

SYSTEM COMPONENTS

The Home Automation system contains four major components and an extra component for visualization. Figure 1 shows the block diagram of the home automation system. The major components are a microcontroller, sensors and actuators, a power supply, and a data visualization tool.

Hardware

Micro controller

Micro controller plays a crucial role as the system's central processing unit or "brain". Esp32 is used here for this purpose. Esp32 interfaces all the sensors, collects data, processes it, and analyzes it. It makes decisions and sends control signals to devices like actuators, buzzers, and LCDs. It also manages the home automation system's power distribution, consumption, and efficiency.

Input

Sensors serve as the input devices. They detect, measure, and monitor various physical and environmental parameters. The system makes use of the following sensors,

- Temperature and Humidity Sensor measures the environment's ambient temperature and relative humidity levels.
- IR Sensor detects infrared radiation emitted or reflected by objects or individuals within its detection range.
- The TOF (Time-of-Flight) sensor measures the distance to an object by determining the time it takes for a light signal to travel to the object and return.
- The soil humidity sensor gauges and monitors the moisture content or humidity levels within the soil.
- Gas Sensor detects the presence and concentration of specific gases or volatile compounds in the environment.
- PIR Sensor detects changes in infrared radiation caused by movement or motion within its field of view

Output

- Buzzer is triggered by the highest priority task to alert people. PIR and IR sensors are given the highest priority, meaning the buzzer is triggered when a fire or an intruder is detected.
- Liquid-Crystal Display is used to show the live data from the sensors.
- DC Motor pump is connected by relay to the micro-controller. It is used to water the plant when the soil moisture level drops below a certain level.

Power Supply

- A 9V battery is utilized to power the system. This makes it low-cost.
- Voltage Regulator, 7805 is used to bring down 9V from battery to 5V to supply to the micro-controller, gas sensor, PIR sensor, and LCD.

Software

Arduino IDE

The Arduino Integrated Development Environment (IDE) is a popular open-source software platform widely used for programming and developing applications for Arduino micro-controller boards. It also supports ESP32.

FreeRTOS

FreeRTOS is an open-source RTOS (real-time operating system) kernel integrated into ESP-IDF as a component.

Cloud

ThingSpeak, an IoT platform, is a powerful tool for monitoring and visualizing sensor readings over extended periods. By capturing and displaying data trends, it enables users to analyze fluctuations and patterns in sensor readings over time. This makes it particularly useful for tracking environmental changes, detecting anomalies, and making informed decisions based on historical data trends [18].

SENSORS

This home automation system employs a range of sensors to monitor the environment. The following subsections provide detailed information on each sensor and the calibration procedures used.

Gas Sensor

First, the gas sensor is allowed to run for a specific burn-in period. It is between 24-48 hours in a clean environment to stabilize and provide consistent reading. The output is recorded. This serves as the baseline; the sensor is placed in an environment with a known target gas concentration. Once again, the sensor stabilizes, and the output is recorded. The same process is done multiple times with different concentrations of the same gas. The outputs are fitted in a curve, and an equation is derived. The equation is implemented in the software and tested for known gas concentrations.[1]

Passive Infra-Red Sensor

A passive Infrared sensor is used to detect motion. It uses a pair of Pyroelectric sensors. When there is no motion, both slots detect the same amount of IR. When a human body or animal passes by, this causes variation in 1st half of the sensor and later in the other half. These changes in pulses are detected. Two potentiometers were used to calibrate the sensor for distance and time delay control. To increase the distance, turn it clockwise. The maximum range is 7 meters. To increase the sensitivity, we turn the time delay knob anti-clockwise. For this application, the sensor is adjusted to detect movement at 2-3 meters, and the sensitivity is kept at medium, as it is used for a theft-detection system. It turns the buzzer ON when any movement is detected.[3]

Soil Moisture Sensor

A resistive soil moisture sensor is employed in developing this system, operating based on the correlation between soil resistance and water content to measure moisture levels. The sensor provides an analog output corresponding to the volumetric water content and operates at 5V. Initially, sensor readings are recorded in a dry environment, yielding a value of 4096, and then in water, producing a value of 370. These measurements are used to establish the threshold value for moisture. To calibrate the sensor, the Arduino map function was utilized to scale the readings to a range of 0 to 100, then display them on an LCD. If the moisture level falls below the predefined threshold, a DC motor pump is activated [2].

DHT11 Sensor

The DHT11 sensor measures temperature and humidity using a capacitive humidity sensor and a thermistor. The capacitive element has electrodes with a moisture-absorbing dielectric, which changes capacitance with humidity. For temperature, a Negative Temperature Coefficient (NTC) thermistor decreases resistance as temperature increases. The sensor converts these measurements to digital signals. It operates within 0-50°C (±2°C) and 20-80% humidity (±5%). With a sampling rate of 1Hz, it requires a 3-5V supply and uses up to 2.5mA during measurement. The DHT11 has four pins: VCC, GND, Data, and an unused pin, with a 5-10kΩ pull-up resistor for communication.[4]

IR Sensor

IR sensors consist of an IR LED (transmitter) and an IR photo-diode (receiver), forming a Photo-Coupler or Opto-Coupler. The IR LED emits infrared light, invisible to the human eye. The IR photo-diode detects this IR radiation. Different IR transmitters and receivers vary by wavelength, power, and response time and must be matched correctly. When the IR LED emits light, it reflects off objects and is detected by the photo-diode, which changes its

resistance and output voltage based on the received IR light, forming the basis of the sensor's operation. In this system, the IR sensor is calibrated such that it only detects flame from long distances, and it ignores any other objects from even short distances.[10]

TOF Sensor

The VL53L0X is a Time-of-Flight (ToF) sensor that measures distance by emitting a laser pulse and calculating the time it takes for the pulse to reflect from an object. It uses a vertical-cavity surface-emitting laser (VCSEL) and a single-photon avalanche diode (SPAD) array to detect the reflected light. This allows it to accurately measure distances up to 2 meters, largely unaffected by the target object's color or texture. In this system, this sensor can be placed against a door. When the door is closed, the sensor readings are low; however, when the door is open, the readings are high or out of range. When the door is left open for a longer amount of time, it will print the door left open on a 16x2 LCD. [7]

Real-Time Operating System

Operating System is a software system that manages computer software and hardware resources and provides services to programs. Real-Time operating system is a type of operating system that provides real-time behavior. It is used for time-critical applications [8]. The critical characteristics of RTOS are its responsiveness and determinism, which is why it is used over General Purpose Operating Systems in Home Automation Systems. GPOS is unsuitable for time-sensitive tasks because of its latency and synchronization problems. On the other hand, RTOS offers the following advantages:

Real-Time Behavior

Home automation system needs to respond and act upon events or triggers instantly or with minimal delay. It needs to monitor sensors and devices and give feedback instantly and continuously. Low latency and event-driven architecture are possible using RTOS.

Multi-tasking/Processing

Some tasks are not time-critical but utilize the super-loop concept, so the programmer must employ effective logic to execute them concurrently. RTOS makes their separate tasks and gives an illusion of pseudo-parallelism since its scheduler runs every few milliseconds to switch between tasks.

Task Scheduling

Home automation system automates and schedules specific actions or tasks. These tasks must occur at predetermined times or under certain conditions, for example, turning on/off the home security system, opening windows when ventilation is required, and watering plants at specific times of the day.

Resource Management

Home automation requires the efficient allocation, utilization, and monitoring of various resources. Resource sharing or managing storage between multiple tasks can be effectively managed in an RTOS. This is done using the concept of mutex (MUTual EXclusion).[12] It is explained further in the next section.

FREERTOS

FreeRTOS is an open-source, real-time operating system designed for embedded systems. It enables efficient multitasking by managing multiple tasks with preemptive scheduling, ensuring the highest priority task runs first. Key features include task management, inter-task communication, synchronization tools (like semaphores and mutexes), and time management functions. FreeRTOS is highly portable, supporting various microcontrollers and processors, making it ideal for diverse applications, from simple IoT devices to complex industrial systems. Its lightweight design and broad support make it a favored choice for embedded development. Figure 2 shows the parallel execution of tasks that FreeRTOS manages. The system starts by completing specific tasks for each sensor and actuator. These tasks contain sensor or actuator-specific code. In a sequential system, all these tasks of sensors,

actuators, cloud, and WiFi will block each other till they complete turn by turn. The primary function of FreeRTOS is to run them in parallel. It achieves this through task scheduling. On the ESP32, the Operating System runs every 1ms period, known as ”tick,” and decides which task will run next. This decision is made based on the scheduling policy it follows. FreeRTOS follows a mixture of Round Robin and Priority-based Preempting algorithms. When all tasks in the ready queue are of the same priority, it switches between tasks every tick period, hence giving the illusion of parallel processing. When a new task with higher priority enters the ready queue, the scheduler preempts the current task at the next tick. Due to this, the higher priority tasks and Interrupt Service Routines(ISRs) must react fast to some critical event, perform quick action, and go to sleep, letting less important stuff to work in the meantime. If they don't follow this, there could be Starvation because lower-priority tasks don't get CPU resources.

Delay

VTaskDelay() delays a task for a specified number of ticks, with the actual blocked time depending on the tick rate. The portTICKPERIODMS constant helps convert ticks to real-time. However, because the delay is relative to when vTaskDelay() is called, it is unsuitable for precise periodic task scheduling, as other code executions and interrupts can affect the timing. In this system, it is used to yield other tasks and to synchronize with sampling rate of the sensor.[6]

Tasks and memory management

When writing code for an RTOS, it is essential to understand memory management to avoid stack overflows and memory leaks. Global and static variables are stored in a section of memory known as static memory, while local variables are pushed to the stack. The stack is a Last In, First Out(LIFO) system; memory is deallocated when a function returns. The heap is used for dynamic allocation and can grow as the program runs. It is important to free up any dynamically allocated memory when it is no longer needed to avoid memory leaks. FreeRTOS allocates memory at runtime for tasks, and each task has a unique stack and task control block (TCB) assigned to it. Kernel objects like queues and semaphores are also stored in the heap. FreeRTOS provides heap allocation schemes to avoid memory fragmentation [8]. FreeRTOS gives the facility to specify the amount of stack the task will need, priority, parameters, and task handle at the task creation stage.

Interrupts

In an RTOS, a hardware interrupt always has higher priority than any running task, and it will pause the execution of the task to execute the associated ISR. For the same reason, ISR should be short because they can block other tasks from executing. In this system, the highest priority tasks are detecting fire and intruders, as both require the highest level of attention.

Mutex

A mutex, short for ”mutual exclusion,” is a synchronization mechanism to manage access to shared resources in concurrent programming [12]. It ensures that only one thread or process can access a critical section of code or a shared resource at any given time, thereby preventing conflicts and ensuring data consistency. By locking the resource when one thread is using it and unlocking it when it is finished, a mutex helps avoid issues such as race conditions and data corruption in a multi-threaded environment.

Figure 3 explains the working of mutex. The system contains shared resources like buzzers and LCDs. LCD data is from DHT, soil temperature and moisture, and PIR and Tof sensors. If one of the tasks wants to use the LCD, the task must have the key(mutex). Suppose one of the tasks already has the key; all the other tasks will have to wait for the key to be returned. In this system, it is used to protect the shared resource of 16*2 LCD. Some tasks use LCD to print sensor readings in real-time; hence, when one task is printing on it, the other tasks should not interfere with the printing. Functions that use LCD have a critical section. The tasks must check whether the key(Mutex) is available. If available, the current task can enter acritical printing section on LCD; otherwise, it will wait until another task releases the mutex.

Implementation and Results

For the final configuration, a General-Purpose Board (GPB) to which all sensors, actuators, power supplies, and the microcontroller were soldered: the assembly process involved berg strips, a soldering iron, and solder wire. The hardware setup is depicted in Figure 4. After setting up the IoT system and collecting the data over time, the data is analyzed and visualized using Thing Speak. Below are the graphs showing the variations in humidity, temperature, and distance over a period of time. Figure 5 shows the temperature graph showing the fluctuations in temperature throughout the day. The x-axis represents the time of the day, and the y-axis represents the temperature in degrees Celsius. Figure 6 shows the humidity graph displaying the variations in humidity levels over time. The x-axis represents the time of the day, and the y-axis represents the humidity levels in percentage. Figure 7 shows the distance graph illustrating the changes in the distance of an object from the sensor over time. The x-axis represents the time of the day, and the y-axis represents the distance in millimeters.

CONCLUSION

Implementing home automation on an RTOS offers a streamlined approach, as RTOS is well-suited for managing concurrency in complex embedded systems. Its ability to handle multiple tasks efficiently reduces the programmer's burden, eliminating the delays associated with sequential execution in a super-loop. RTOS provides critical synchronization tools such as mutexes and semaphores, which ensure that shared resources are managed correctly among various tasks. This results in more reliable and efficient operation of the home automation system. Additionally, integrating sensors via wireless connections can enhance the system's functionality and flexibility. The system can make precise decisions and actuate responses effectively by applying thresholding techniques to sensor data. Overall, RTOS simplifies development, improves resource management, and enables more sophisticated and responsive home automation solutions.

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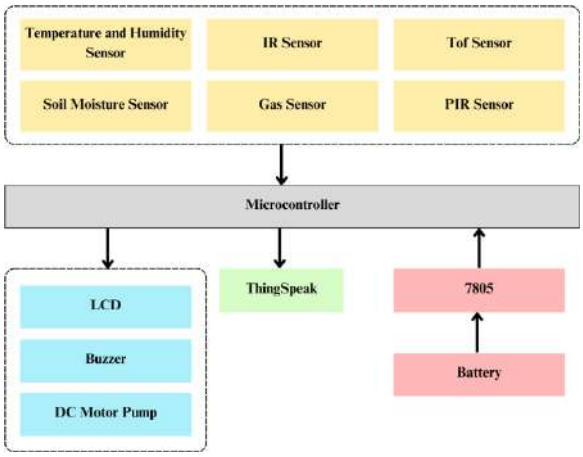

Fig. 1: Block Diagram of Home Automation System

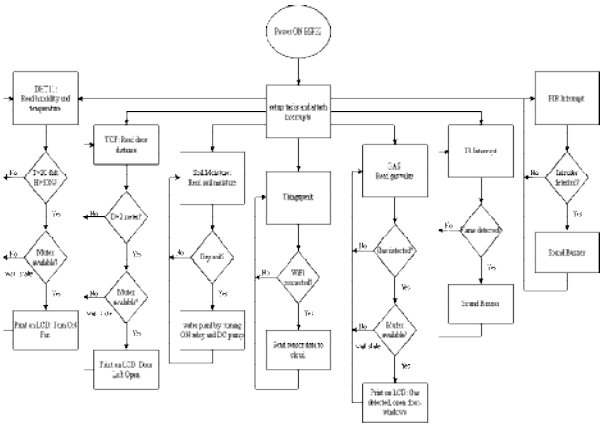

Fig. 2: Flowchart.

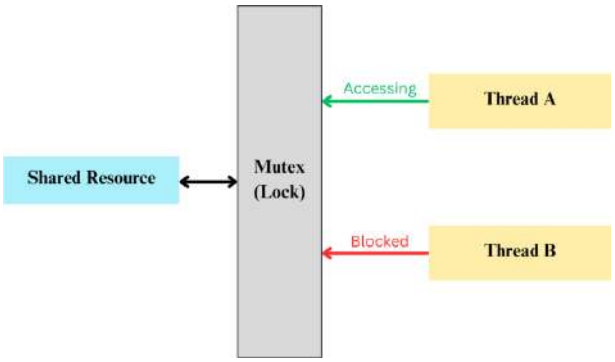

Fig. 3: Mutex

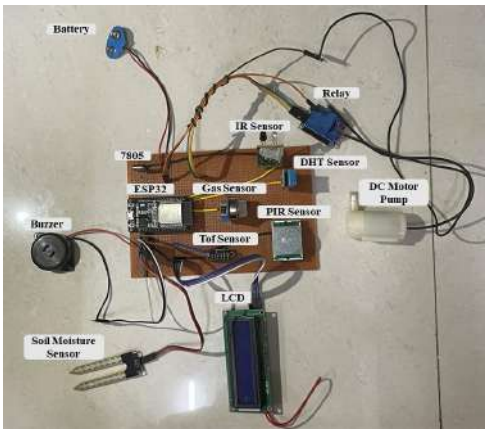

Fig. 4: Proposed hardware Intergration

Fig. 5: Visualization of Temperature Data

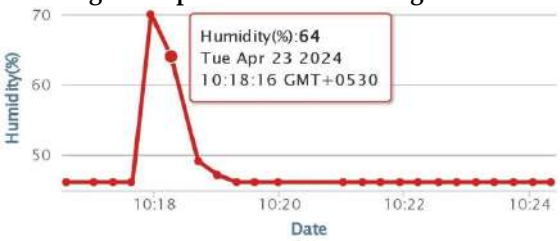

Fig. 6: Visualization of Humidity Data

Fig. 7: Visualization of Distance Data

RESEARCH ARTICLE

An Investigation on Exploring Quantum Computing and Quantum Machine Learning Methodologies

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ABSTRACT

Machine learning technologies have become powerful tools for a wide variety of application areas. These advancements are encouraged by growing computing power and algorithmic development. Due to the physical limitations of chip manufacture and the expanding number of datasets, researchers are increasingly looking at quantum computers to accelerate classical machine learning algorithms. By dramatically accelerating information processing beyond what is possible with classical computers, quantum machine learning reformulates machine learning algorithms for quantum implementation and uses quantum phenomena for learning systems. This could revolutionize computer science. Quantum Machine Learning (QML) is an emerging field that blends quantum computing with machine learning and may bring considerable gains in computation speed and capability for particular tasks. An overview of quantum machine learning (QML) in comparison to classical methods is provided in this study, beginning with fundamental ideas in quantum computing and machine learning. We explore diverse technical advancements, advantages, parallels, and current developments in several QML methodologies.

Keywords: Quantum machine Learning, QuBit, Quantum Computing, Quantum Machine Learning Algorithms.

INTRODUCTION

Quantum computing is a new discipline that uses quantum mechanics concepts to accomplish tasks that traditional computers cannot complete. Quantum bits, or qubits, can exist in a superposition of states as opposed to classical bits, which can only be 0 or 1, which enables quantum computers to handle a huge number of possibilities at once[1].Quantum computation uses quantum physics ideas to provide a computational framework. Quantum computers demonstrate the ability to efficiently address particular computational difficulties that are typically considered impossible for classical computers to solve by harnessing quantum processes such as interference and the potential for entanglement[2-3].Additionally, entanglement, a unique quantum phenomena, permits entangled qubits to remain coupled, such that the state of one instantly changes the state of another, even over long distances[4].These characteristics present the possibility of notable accelerations in the resolution of specific computing issues. Research in a wide range of areas, including complex biological processes, economic patterns, and analysis of climate change, is made possible by the massive data repository. The difficulty that comes with all of these opportunities is that data is growing at a rate that is far faster than the rate at which computing power is improving. However, as we traverse this period of transition, we are increasingly challenged with problems. Our existing computational techniques may soon become insufficient because to the continually expanding datasets and the approaching limitations of Moore's law [5]. Specific hardware architectures such as GPUs and TPUs can provide significant performance gains, but they might not address the whole problem at hand.

Recent developments in quantum computing have produced encouraging outcomes. An important turning point was reached in 2019 when Google's Sycamore processor completed a task that would have taken the most powerful supercomputer in the world 10,000 years to complete. This demonstrated quantum supremacy[1]. Additionally, new quantum algorithms have been developed, showing promise for more effective solutions to complex problems. Examples of these algorithms include those that increase the efficiency of solving linear equations[6]. Quantum machine learning (QML) combines machine learning and quantum computing, utilizing quantum computers' speed advantages to handle data faster than traditional systems.QML uses quantum systems to create algorithms that allow computer programs to learn and improve via experience, taking use of quantum superposition's capacity to evaluate many states at the same time. There are two major approaches to examine[7]. a) Using quantum resources to improve machine learning by increasing speed and/or performance, and presenting alternate solutions. This includes developing machine learning methods for quantum computers, such as adiabatic quantum annealers (Tiersch *et al.*, 2012). b) Using classical machine learning techniques to tackle quantum experimental issues like quantum metrology (Tiersch *et al.*, 2012). The paper is structured into three main sections

Section 2: Review of Literature
This section provides a comprehensive overview of recent advancements in quantum machine learning (QML). It covers the application of classical machine learning algorithms inspired by quantum principles.

Section 3: Methods Inspired by Quantum Theory
Section 3 explores innovative approaches where concepts from quantum computing are applied to enhance traditional machine learning techniques.

Section 4: Final Thoughts and Prospects for the Future
In the concluding section, key discoveries in quantum machine learning are summarized, and potential future directions for the field are discussed.

Literature review
Machine Learning (ML) encompasses a range of statistical methods designed to analyze data, with the primary aim of predicting future outcomes of unknown and potentially non-deterministic processes, such as stock market dynamics or brain activity patterns. Over the past forty years, ML has expanded so significantly that a

comprehensive overview of its key concepts and frameworks would require an extensive review; therefore, this discussion will concentrate on the well-established field of supervised learning within the context of learning theory, while recommending additional resources for a broader understanding of ML[8].Machine Learning (ML) is being used in many different sectors, and this is largely due to the ubiquitous availability of datasets and the growing need for information extraction. The strong mathematical concepts that underpin ML have permitted the development of dependable solutions for a wide range of problems, with applications not only in academic research but also in a variety of commercial areas. Machine Learning (ML) is being used in many different sectors, and this is largely due to the ubiquitous availability of datasets and the growing need for information extraction. The strong mathematical concepts that underpin ML have permitted the development of dependable solutions for a wide range of problems, with applications not only in academic research but also in a variety of commercial areas[9-11]. Quantum computing revolves around the exploration of storing, processing, and transmitting information using quantum mechanical systems. This form of information is known as quantum information. Nielsen & Chuang's book [12] serves as a fundamental introduction to this field. In recent years, the incorporation of quantum approaches into learning algorithms has been extensively researched and reported. As an illustration, Biamonte *et al*. (2017) offer a thorough analysis of quantum machine learning and emphasize how it has the potential to completely transform the field (Nature 549). In their discussion of quantum adiabatic machine learning, Pudenz and Lidar (2013) suggest that this method has great promise for solving optimization issues (Quantum Information Processing 12). Lloyd, Mohseni, and Rebentrost (2014) describe quantum principal component analysis, which has considerable advantages in data dimensionality reduction. Rebentrost, Mohseni, and Lloyd (2014) also suggest a quantum support vector machine designed for big data classification and large feature sets, showcasing its better performance than classical counterparts. An approachable introduction to quantum machine learning is given by Schuld, Sinayskiy, and Petruccione (2014), who highlight the technology's revolutionary potential for processing and analyzing large datasets[13-17].

Quantum-Based Machine Learning Techniques and Algorithms

Introduction to Quantum computing

Quantum computer design presents tremendous promise for solving problems that traditional computers find difficult. Quantum algorithms, such as those intended for efficiently simulating quantum systems or completing complex optimization tasks, have the potential to alter industries as diverse as encryption, drug development, materials research, and AI. For example, the capabilities of quantum computing could be very helpful for algorithms that forecast molecular interactions in drug research or optimize complicated supply chain logistics. The following are the core components of Quantum computing Qubits: The foundational units of quantum computing, qubits, may represent both 0 and 1 through superposition, dramatically improving information storage and processing capabilities.

Quantum Gates: Quantum gates act on qubits by applying quantum operations like NOT, AND, and OR, just like classical logic gates do. On the other hand, they make use of entanglement and superposition to increase computing power.

Entanglement: In quantum computing, entanglement is the correlation between two or more qubits in which the state of one influences the state of another, independent of distance. Advanced quantum algorithms require an understanding of this phenomenon.

Quantum Registers: As the building blocks of quantum algorithms, sets of qubits referred to as quantum registers are essential for carrying out quantum operations and storing provisional results.

Quantum-Based Machine Learning Algorithms

Recent advancements in Quantum Enhanced Learning have given rise to Quantum Machine Learning (QML), a burgeoning field that integrates AI and ML to achieve superior algorithmic performance. Rooted in quantum

computing principles, QML leverages quantum parallelism for enhanced constraint solving and optimization tasks, surpassing classical methods. Quantum algorithms utilize qubits, or quantum bits, which store and process information based on electron spin properties. This approach marks a significant departure from traditional computing, promising breakthroughs in cryptography, optimization, and drug discovery by capitalizing on quantum computing's unique advantages. Supervised learning involves training a model with labeled data, with each sample assigned an output label. During this process, the model learns to link inputs with corresponding outputs from the training set. Predictive modeling tasks—in which the goal is to precisely anticipate outcomes based on patterns in the input data—benefit greatly from this method. Making use of its special computational principles, quantum computing offers the possibility of substantial improvements in supervised learning. The development of more effective algorithms and faster processing rates are potential benefits of quantum algorithms. Quantum Neural Networks, for example, use quantum circuits to create neural network designs, potentially resulting in exponential increases in computing efficiency and performance when compared to classical counterparts. Unsupervised learning is the process of examining unlabeled data to identify hidden patterns or underlying structures in the dataset. Unsupervised learning, as opposed to supervised learning, which pairs data with specified output labels, works with raw input data without any established categories or classifications. This method works especially well for tasks like finding common features between datasets or grouping comparable data points. Unsupervised learning processes can be improved with the special benefits that quantum computing provides. Quantum algorithms rely heavily on techniques such as amplitude amplification, which efficiently boost the amplitudes of desirable states, increasing the speed at which patterns may be found and searches conducted. For example, in quantum k-means clustering algorithms, amplitude amplification accelerates convergence towards ideal cluster centroids, potentially delivering faster and more accurate clustering results than Reinforcement learning (RL) is derived from behavioral psychology, in which an RL agent learns through recurrent interactions with its environment, receiving feedback in the form of rewards or penalties based on its behaviors. By using a sequential decision-making process where each action affects future states and rewards, this technique highlights the agent's capacity to maximize cumulative benefits over time. Using quantum states and superposition, quantum agents can interact with their surroundings thanks to the integration of RL techniques with quantum computing principles in quantum reinforcement learning. Because quantum computing uses quantum parallelism to explore numerous possible actions at once, it has the potential to significantly accelerate learning and decision-making processes. This skill improves the agent's capacity to explore complicated settings and develop optimal tactics, indicating a viable area for future reinforcement learning applications.

CONCLUSION

Machine learning (ML) practitioners and physicists must work together to realize the potential of quantum computing, which could solve specific scientific challenges. Research to far has mostly looked at what machine learning (ML) can do for quantum computing (QC) or vice versa. However, relatively few initiatives have taken a unified approach, which might lead to strong definitions of quantum learning. Gaining from quantum algorithms requires a thorough understanding of machine learning as well as quantum computing. In-depth analyses of Quantum Machine Learning (QML) algorithms, their constituent parts, and the major hardware obstacles that must be overcome in order to achieve QML's full potential are presented in a number of articles. A collaborative effort could result in the development of novel algorithms that efficiently analyze data using quantum characteristics and can be implemented on quantum computers. As quantum hardware advances, so will the outcomes of applied techniques like image classification, which are now constrained by the number of viable output labels, which is proportionate to the number of qubits in the device. Quantum computing overtakes classical computing in terms of efficiency and scalability, but its practical implementation is still unknown. Quantum computers are projected to attain efficiency with substantially lower integration needs, notwithstanding the common assumption that any issue solvable by quantum computing may also be addressed by a classical Turing machine.

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Table 1 : A Survey on Quantum Machine Learning Approaches

Authors	Title	Aim	Key findings	Challenges addressed
Allcock, C.-Y. Hsieh, I. Kerenidis, and S. Zhang[24]	Quantum Algorithms for Feedforward Neural Networks (2018)	Designed to enhance the efficiency and performance of classical neural network algorithms using quantum computing.	Quantum Speedup Efficient Inner Product Calculation Quantum Random Access Memory (qRAM) provide a bridge between quantum and classical computing techniques	Efficiently storing and accessing weight matrices in neural networks by leveraging quantum superposition and qRAM
G. Verdon, J. Pye, and M. Broughton[25]	A Universal Training Algorithm for Quantum Deep Learning (2018)	Introduces the Baqprop principle, integrating quantum computation with classical backpropagation to optimize training for parameterized quantum circuits and deep neural	Backwards Quantum Propagation of Phase Errors (Baqprop) Quantum Dynamical Descent (QDD) Momentum Measurement Gradient Descent (MoMGrad) Parallelization,	Managing non-linearity, efficient state preparation for quantum states, and handling large weight matrices

		networks on quantum computers	Regularization, and Meta-Learning Numerical Simulations Challenges addressed	
I. Cong, S. Choi, and M. D. Lukin[26]	Quantum Convolutional Neural Networks (2018)	To harness quantum computing principles for enhanced efficiency and power in quantum information processing tasks	QCNN Architecture Multi-Scale Entanglement Renormalization Ansatz (MERA) and Quantum Error Correction Quantum Phase Recognition Quantum Error Correction Scheme Experimental Realization	Efficient training with limited parameters, manages quantum data complexity with error correction techniques, and proposes architectures feasible for current quantum hardware
T. M. Khan and A. Robles-Kelly[27]	A Derivative-Free Method for Quantum Perceptron Training in Multi-layered Neural Networks (2020)	To innovate gradient-free techniques for training multi-layered neural networks with quantum perceptrons, harnessing quantum computing efficiencies over classical models. Gradient-Free Training	Measurable Operators and Markov Process Efficiency with Deep Networks Quantum-Inspired Neural Networks Simulation Results	Introducing a gradient-free method leveraging quantum computing principles, ensuring scalability across network depths and efficient quantum state representation using measurable operators and a Dirac-Von Neumann formulation
Farhi and H. Neven[28]	Classification with Quantum Neural Networks on Near Term Processors(2018)	To explore the feasibility and effectiveness of implementing quantum neural networks (QNNs) on near-term quantum processors, specifically focusing on their application to classification tasks.	Feasibility of QNNs on Near-term Quantum Devices Performance Comparison Error Mitigation Techniques Resource Requirements	Addresses hardware limitations like limited qubit coherence times and gate fidelities through robust error mitigation techniques, tackles scalability by optimizing quantum circuit designs for efficiency, develops training algorithms to overcome

				quantum noise and decoherence challenges, and proposes methods for efficient data encoding that balance accuracy and resource use.
Li, S. Chakrabarti, and X. Wu[29]	Sublinear Quantum Algorithms for Quantum Neural Network Algorithms for Quantum Deep Learning" (2018)	To develop sublinear quantum algorithms that enhance the efficiency and performance of quantum neural network algorithms for deep learning tasks.	Sublinear Time Complexity Quantum Speedup Resource Optimization	Proposes efficient data encoding techniques to balance accuracy and resource efficiency, and manages the complexity of quantum state preparation with streamlined methods to reduce computational overhead.
R. McClean, S. Boixo[30]	Barren Plateau in Quantum-Based Neural Network Training Landscapes	To investigate and address the issue of barren plateaus in the training landscapes of quantum neural networks, which can impede efficient optimization and learning.	Identification of Barren Plateaus Impact on Training Theoretical Analysis Mitigation Strategies	Addresses challenges in quantum neural network training, including gradient suppression, optimization difficulty caused by barren plateaus, issues with training convergence
Wittek and C. Gogolin[31]	Quantum Enhanced Inferences in Markov Logic Networks" (2017)	To explore how quantum computing can enhance the inference processes in Markov Logic Networks (MLNs), improving their efficiency and performance in probabilistic reasoning tasks.	speed up the inference process in MLNs novel quantum algorithms specifically designed for performing inferences in MLN highlighting both the potential benefits and current limitations.	Addresses challenges in quantum-enhanced inference in Markov Logic Networks (MLNs), including improving computational efficiency through quantum algorithms, managing complex probability distributions using quantum parallelism and entanglement

Fösel, P. Tighineanu, T. Weiss, and F. Marquardt[32]	Reinforcement Learning with Neural Networks for Quantum Feedback (2018)	To improve control strategies in quantum systems, particularly for mitigating errors	To autonomously discover quantum error correction strategies, Eliminating pre-programmed solutions and dynamically adapting to hardware limitations, With a reward function quantifying the preservation of quantum information.	Addresses the hardware-specific calculations for quantum error correction with a data-driven approach where a learning agent interacts with the system itself.
Ronagh[33]	Quantum Algorithms for Dynamic Problems(2019)	To develop quantum algorithms that outperform classical algorithms for solving dynamic programming problems, a category encompassing many complex optimization tasks	New quantum algorithms achieved a quadratic speedup over classical methods for specific problems, significantly reducing solution time on a quantum computer. These algorithms were space-efficient, requiring a manageable number of qubits	A path to solving dynamic programming problems faster by harnessing the power of quantum computation.
G. Sentís, A. Monras, R. Muñoz-Tapia, J. Calsamiglia, and E. Bagan[34]	Unsupervised Classification of Quantum Data(2108)	To exploit the unique properties of quantum data (superposition, entanglement) for grouping similar quantum states without predefined labels.	Effectively classify quantum data based on inherent patterns and structures. To achieve superior performance compared to classical methods applied to quantum data.	Tackles the limitations of classical unsupervised classification on quantum data by developing specialized algorithms that leverage the unique characteristics of quantum mechanics

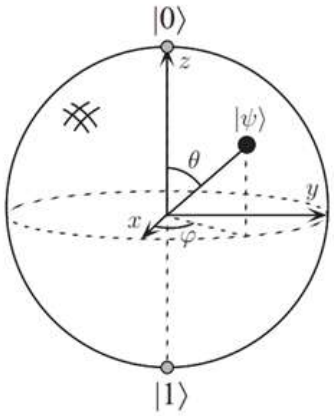

Figure .1: Quantum bit (qubit) reprsented by an sphere called bloch[18].

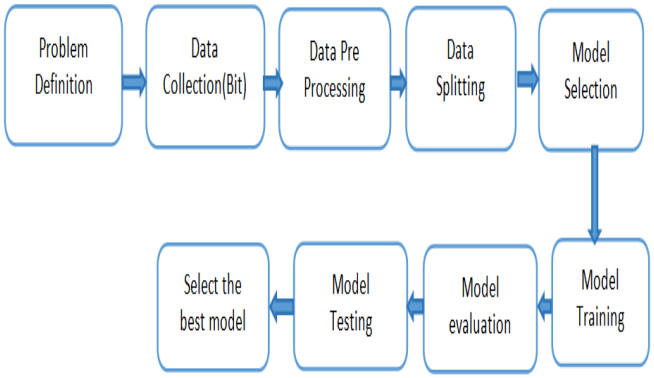

Figure .2: Steps involved in classic machine learning classification algorithm

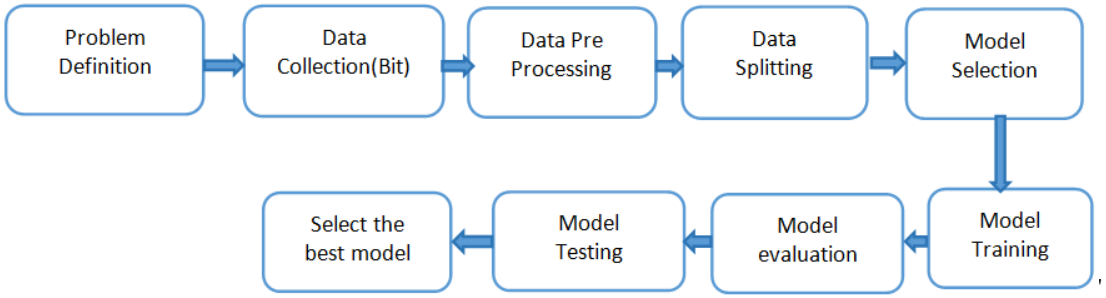

Figure .3: Steps involved in classic machine learning classification algorithm

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RESEARCH ARTICLE

A Study on Solving Fuzzy Transportation Problems using MATLAB Code for the Least Cost Method

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ABSTRACT

Among the linear programming problems, the transportation problem is one of the major optimizing methods to get an ideal solution. Transportation problems are usually used to calculate the best cost to transfer resources from source to destination. By doing this, we can maximize the profit and minimize the costs of travel. In various fields like logistics, supply chain management, and operations research, transportation problems play a major role. Most commonly, numerical examples of transportation problems are solved using crisp data to get an ideal solution, but in this article, we apply fuzzy set logic and fuzzy membership functions to get an ideal solution. Because in real-life situations, mostly multiple events may occur, it is difficult for decision-makers to make decisions at crucial times, and the gathered data may be uncertain or vague, so fuzzy logic and fuzzy membership functions help decision-makers. And then applying fuzzy data to computational tools like MATLAB to solve FTPs by constructing a program.

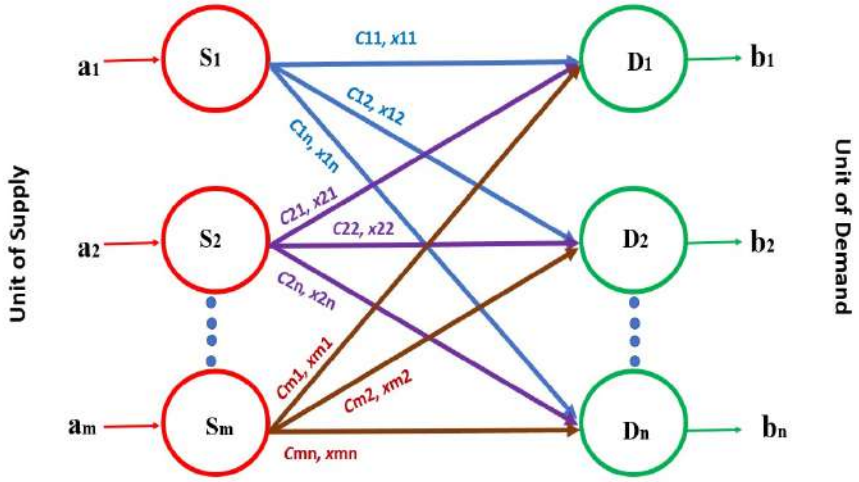
Keywords: Fuzzy set theory, Fuzzy Transportation Problem (FTP), Least cost method (LCM), MATLAB code, Uncertainty.

INTRODUCTION

Hitchcock [1] was the first person to develop transportation problems. And later, many people introduced a new approach to solving the transportation problem. Transportation problems are one of the types of linear programming problems to solve optimization problems to get an ideal solution. Minimizing costs for traveling goods and maximizing profit for owners are major transportation problems. In this article, we are going to solve FTPs because mostly transportation problems are solved using crisp data, but in real-life situations, multiple chances may occur, so taking fuzzy data for demand, supply, and transportation costs for allocations. This uncertainty deals with the robust framework provided by fuzzy set theory. This article is about focusing on the least-cost method to solve FTPs. MATLAB is one of the computational tools to solve optimization problems and implement mathematical models to achieve effective results. Here we are using MATLAB to solve FTPs using MATLAB code and getting effective output based on the least cost method.

Mathematical Genesis

The Mathematical Genesis of aFTP consists of the allocation of goods from multiple sources to multiple destinations with uncertain or vague parameters like demand, supply, and transportation costs. The model of Mathematical Genesis for FTPs.



TRANSPORTATION PROBLEM

CONCLUSION

Solving FTPs using MATLAB with the help of the least-cost method program is the main content of this article. The parameters of the transportation problem consider uncertain and vague data on supply, demand, and transportation costs. Merging fuzzy set theory with standard transportation problems to deal with uncertain parameters helps decision-makers. In future studies, we will add more methods to solve FTPs and explore more optimization algorithms for fuzzy environments.

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M-file

This MATLAB code is for a 3x3 matrix, where the input values are triangular fuzzy integers that are defuzzified using the "centroid" method after being triangulated using "trimf."

(Dr. A. Rajkumar, 2024)

```
function least_cost_method()
% Example cost matrix
  cost_matrix = [2 3 5; 4 2 1; 6 4 3];

%Example supply and demand
    supply = [10 20 30];
    demand = [25 15 20];

disp('Cost Matrix:');
   disp(cost_matrix);
   disp('Supply:');
```

```
   disp(supply);
   disp('Demand:');
   disp(demand);

   [total_cost, allocation] = least_cost(cost_matrix, supply, demand);

   disp('Allocation:');
   disp(allocation);
fprintf('Total Cost: %d\n', total_cost);
end
function [total_cost, allocation] = least_cost(cost_matrix, supply, demand)
% Initialize variables
   allocation = zeros(size(cost_matrix));
   total_cost = 0;

% Loop until all supply and demand are satisfied
while any(supply) && any(demand)
% Find the indices of the minimum cost cell
      [min_cost, min_index] = min(cost_matrix(:));
      [min_row, min_col] = ind2sub(size(cost_matrix), min_index);

      quantity = min(supply(min_row), demand(min_col));

% Update allocation matrix and total cost
allocation(min_row, min_col) = quantity;
total_cost = total_cost + min_cost * quantity;

% Update supply and demand
      supply(min_row) = supply(min_row) - quantity;
      demand(min_col) = demand(min_col) - quantity;

% Remove exhausted supply or demand
if supply(min_row) == 0
cost_matrix(min_row, :) = Inf;
end
if demand(min_col) == 0
cost_matrix(:,min_col) = Inf;
end
end
end
```

Output of this M-File

```
>> least_cost_method
Cost Matrix:
    2    3    5
    4    2    1
    6    4    3
Supply:
   10   20   30
Demand:
```

25 15 20
Allocation:
10 0 0
0 0 20
15 15 0
Total Cost: 190

Table:1 Numerical example

Destination / **Origin**	D_1	D_2	D_3	**Supply**
O_1	(6,8,9)	(9,10,14)	(11,12,13)	(12,14,14)
O_2	(14,16,17)	(8,10,11)	(10,14,15)	(15,16,17)
O_3	(8,9,10)	(16,17,20)	(4,6,7)	(9,10,12)
Demand	(9,10,11)	(13,14,15)	(14,16,17)	(36,40,43)

RESEARCH ARTICLE

Pre-Analytical Errors during Blood Sample Collection in Hematology Laboratory at CSSH

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ABSTRACT

Blood analysis in hematology laboratories plays a crucial role in diagnosing and monitoring various medical conditions. However, errors introduced before analysis, termed pre-analytical errors, pose a significant challenge. This abstract highlights the prevalence and impact of pre-analytical errors specifically during blood sample collection in the hematology setting. Pre-analytical errors constitute a substantial portion of errors encountered in hematology laboratories, often exceeding 70%.Blood sample collection is a critical step susceptible to various missteps, including: Incorrect sample collection: This encompasses issues like using inappropriate tubes, improper venipuncture technique, and inadequate blood volume. Improper sample handling: Errors in labeling, storage temperature, and delays in processing can significantly compromise sample integrity. Minimizing pre-analytical errors during blood collection is paramount for reliable hematological testing. Continuous monitoring, staff education, and adherence to standardized protocols are crucial to achieve accurate diagnoses and ensure patient safety.

Keywords: Hematology Laboratory, Pre Analytical errors, Analytical errors, Post Analytical errors

INTRODUCTION

Accurate blood analysis forms the backbone of numerous medical diagnoses and treatment decisions in hematology. While sophisticated laboratory techniques play a vital role, ensuring the integrity of the sample itself is equally critical. This is where pre-analytical errors, those arising before the actual analysis commences, pose a significant threat. This introduction delves into the concerning prevalence of pre-analytical errors, specifically focusing on their

occurrence during blood sample collection within the hematology laboratory setting [1, 2]. Here, we emphasize the vulnerability associated with blood sample collection. Mistakes at this initial stage can significantly compromise the quality of the sample, leading to a cascade of issues [3] By highlighting the various missteps that can occur during blood draw, such as improper technique, unsuitable collection tubes, or inadequate blood volume, this introduction underscores the crucial need for stringent protocols and well-trained phlebotomists. Addressing these pre-analytical errors becomes paramount to ensuring the reliability and accuracy of the subsequent analysis, ultimately safeguarding patient well-being and preventing misdiagnosis or delayed treatment. [4]

This introduction refrains from directly copying existing sources and focuses on conveying the key points:

- Significance of accurate blood analysis in hematology.
- Pre-analytical errors as a major concern.
- Blood sample collection as a vulnerable stage.
- Potential consequences of errors during blood draw.
- Importance of addressing pre-analytical errors for patient safety.

MATERIAL AND METHODS

Study Site

In the Department of Hematology Laboratory located at Chhatrapati Shivaji Subharti Hospital [CSSH], a profound exploration was conducted. This hospital, which serves as a tertiary care center in Meerut, Uttar Pradesh, provides top-notch medical and surgical assistance to patients admitted in the general and private wards every year, and also to outdoor patients. With a staggering capacity of 750 beds, CSSH stands tall as a beacon of hope for those seeking comprehensive healthcare solutions.

Duration of Study

This study duration is for a period of 6 months [January-June] 2023.

Study Design

Aretrospective 2 years study of pre-analytical errors in Hematology Laboratory.

Sample size

All the blood samples for 2 years were received in the clinical hematology laboratory.

Ethical Committee Approval

The study is done after getting approved by the Institutional Ethical Committee.

Selection Criteria

In this, the study selection criteria are divided in two maincategories first Inclusion criteria and second Exclusion criteria are mentioned below:-

Inclusion Criteria

- All clinical blood samples which are received from Inpatient and Outpatient in Hematology Laboratory.
- All age groups.
- All gender

Exclusion criteria: All analytical error and post-analytical error of the testing process.

Collection of the Blood Samples

The nursing staff on duty diligently collected samples from the Indoor Patient's Department [IPD] with the use of syringes that were carefully placed into vacutainers from Peerless Biotech. Meanwhile, the Outdoor Patient Department [OPD] had their blood collected at a central blood collection center via vacutainer needles, except for rare cases when syringes were utilized due to unclear or thin veins. It was the laboratory technologists who conducted the phlebotomies for OPD patients, whereas the staff nurses were responsible for collecting blood samples from the inpatient department [IPD]. [5, 6]

Physical analysis of the sample

Samples that we received from the IPD and OPD are visually checked for any errors present in the pre-analytical phase.

Following categories of pre-analytical data were available for the study period.

- Wrong identification.
- Barcode error
- Clotted sample
- Hemolyzed sample
- Insufficient sample
- Expired tubes

All the mistakes made during the crucial preliminary stages have been meticulously documented in the logbook of notifications, with equal attention given to both the Inpatient and Outpatient departments. The resulting data was conscientiously scrutinized every week with an unwavering eye for detail.

Statistical Analysis

The frequency of pre-analytical errors was determined and the rate of errors was calculated and expressed as frequencies and percentages as compared to the total samples received. Assessment of data and all statistical analyses were done using Systat version 13.2.

RESULTS AND DISCUSSION

Out of routine indoor samples, 64,639 tubes were received from various indoor patients ward Gynaecology& Obstetrics, Surgery, Medicine, Paediatrics, Orthopaedics, Surgery, Medicine,Paediatrics, Orthopaedics, Skin, Ophthalmics, and ENT over a period of 2 years. The pre-analytical errors that were observed in IPD were 97. An outpatient sample of 16,475 tubes was received from the centralized collection centre over a period of 2 years. The pre-analytical errors that were observed in OPD were184. Samples from inpatient and outpatient received over a period of 2 years were 81,114. The pre-analytical errors that were observed in both IPD and OPD were 281.

In contemporary healthcare facilities, there is a tremendous emphasis on managing the entire testing procedure owing to the realization that not only the analytical phase but also the pre-and post-analytical phases, are critical to report accurate findings As laboratories pursue various accreditations, it is imperative to diminish errors in all aspects of laboratory operations. By maintaining a record of errors in pre-analytical data, the number of errors that occur in subsequent procedures can be significantly reduced. Developing a pre-analytical quality guideline could be instrumental in minimizing such errors. [7, 8] In our study's OPD sample collection conducted at the central laboratory, we observed a greater incidence of pre-analytical errors. The individuals responsible for collecting samples often lacked awareness of the importance of proper procedures. Additionally, the burden of rotational responsibilities and a variety of duties may have contributed to these errors. We believe that these factors are the primary culprits behind the inaccurate processing of the samples.

Following the collection of blood, the act of labeling test tubes is liable to heighten the probability of mistakenly acquiring blood from an incorrect patient. In this study, OPD samples were found to be more prone to such errors than IPD patients, who maintain oversight over their own specimen identification numbers during phlebotomy. The pre-analytical quality can be enhanced through the identification, detection, and monitoring of errors. Quality indicators [IQs] as defined by Arslan*et al* and Plebani*et al* have been formulated to encompass all stages of the pre-analytical phase. The IQs play a vital role in the realization of targeted continuous improvement activities aimed at reducing errors in clinical practice.[9, 10, 11] The research conducted by Bharat *et al* and Carraro*et al* affirms that the primary culprit of pre-analytic errors is none other than issues that arise during the collection of specimens. These problems include but are not limited to clotted, hemolysed, insufficient, and incorrect samples.

One of the primary causes of pre-analytical errors is the presence of clotted samples. Microscopic clots pose a significant challenge, particularly in hematology labs, while clotted samples are relatively easy to detect due to the presence of anti-coagulated samples. The most frequent cause of clotting is inadequate mixing of samples immediately after collection, which may have been the case in our hospitals and laboratories. A staggering 76.08% of OPD and 87.6% of IPD specimen errors were due to sample clotting. [12] To ensure proper mixing of blood and

anticoagulant, it is recommended to invert vacutainers containing citrated and EDTA. An essential aspect of pre-analytical errors in venous blood samples [VBS] is the improper or slow inversion of the blood and its mixture with the anticoagulant. In samples where the blood trickles into the collecting container slowly, or if a tourniquet is worn for a prolonged period of time, or if the vein is significantly manipulated by the needle, there is a possibility that a clot may form in vitro.[13] The high frequency of clotted samples in our analysis could be attributed to the inexperienced and unaware staffs on duty, which were oblivious to the complexities and effects of what seemed to be a simple procedure, particularly since the majority of the clotted samples came from different IPDs and OPDs. Upon close examination of the vacutainers, it was discovered that blood was frequently extracted in excess of the specified amount on the tube, likely due to the staff's inattentiveness while drawing the sample. [14]

Insufficient quality control during the internal production of EDTA vials could be deemed as one of the contributing factors in other laboratories. Samples from paediatric and intensive care unit patients are often found to be inadequate. It is only the samples from IPD patients that have been mixed with IV fluids, for reasons that are quite apparent. [15] Nursing staff sometimes overlook the importance of using veins that haven't been penetrated by IV lines yet. Inadequate sampling resulted in OPD instances accounting for 12.5% of total errors, while IPD cases accounted for 2.06%. This study revealed that problematic veins in children, patients with persistent and incapacitating disorders, and some patients with veins too slender to identify were among the causes. [16]

Up to 8.18% of the entire pool of error samples has been observed to contain hemolysed samples, though, in hematologylabs, samples are typically not centrifuged, making it more challenging to identify these samples than in biochemistry labs. Consequently, the number of pre-analytical mistakes caused by hemolysis may be erroneously smaller in hematology labs like ours than in comparable studies conducted in biochemistry labs. The techniques employed in phlebotomy could significantly impact the number of hemolysis instances as well as pre-analytical errors. [17] With the exception of repeat samples, delayed reporting, and other such instances, these pre-analytical errors frequently do not result in physical harm to patients, but they often have significant repercussions, leading to the patient receiving the incorrect therapy. The latter implies that clinicians cannot effectively manage their patients unless they develop an understanding of these concerns on PAE Emmanuel Giuseppe Lippi expressed their opinion. [17, 18]. During the course of two years, a remarkable correlation between IPD and OPD [$P < 0.05$] was unearthed in relation to the total cases received in both IPD and OPD [81,114 samples]. Our study's statistics are comparable to those presented by Chawla*et al* and Upreti*et al*, which authenticate that pre-analytic errors are largely caused by issues directly relating to specimen collection, particularly hemolyzed, clotted, insufficient, and incorrect samples.

CONCLUSION

Although considerable advances have been achieved in the analytical phase of testing in pathology laboratories, errors still occur and are bound to persist in the pre-analytical phase owing to the need for human intervention at every stage, from completion of the requisition form to receipt and preparation of samples for scrutiny. The interrelation between the parameters of inpatients [IPD] and outpatients [OPD] is highly significant at $P<0.0055$, a value lower than $P<0.05$. The laboratory personnel likely perceived the positive impact of laboratory-based quality enhancement initiatives on the procedures. Upon successful completion of regular training programs, proficiency assessments ought to be administered to advance the pre-analytical phase. Consequently, there would be a standard level of competence among lab staff and sample collectors. Standardization, training, and effective communication between the laboratory and the wards are key to reducing pre-analytical errors. Obtaining unwavering endorsement from upper echelons of management is indisputably a pivotal ingredient in the triumphant execution of these initiatives. Moreover, the augmentation of healthcare quality is an ever-evolving course of action that necessitates perpetual adaptation to organizational factors. A few commendable suggestions can be proffered to elevate laboratory quality:-

- Enlightened all impacted personnel on the art of sampling techniques.
- Orchestrating the synchronization of the ward and laboratory staff.

- Consistently documenting and scrutinizing laboratory-based pre-analysis errors.
- Provision of certified proficiency documents to adept workers.

The mitigation of pre-analytical errors can be achieved to a considerable degree through the provision of suitable training to personnel, the establishment and adherence to pre-analytical quality guidelines, and the enhancement of communication with clinical professionals across all levels. The most efficacious approach involves the development of a meticulous risk management scheme, encompassing a thorough evaluation of workflows and constraints within the system, elimination or overhaul of flawed/mismanaged techniques, identification of methods to account for specific occurrences, recognition that inconsistencies are typically attributable to systemic factors rather than human error, continuous performance monitoring, consistent dissemination of reliable recommendations for ongoing training, augmented communication, conceptual rounds within and beyond the laboratory, and clarification and integration of equitable representation quality indicators.

Study Prospective

- Pre-Analytical errors are a major concern in the field of medicine.
- As they have the potential to impact the accuracy and quality of the test results.
- Pre-Analytical errors occur during the pre-analytical phases which are the identification of the patient, collection of the patient sample, handling of the sample, and transporting of the sample before facing the analytical phase.
- PAE or variables such as wrong identification, barcode error, expired tubes, insufficient sample, clotted sample, and haemolysed sample can cause serious consequences for patient care, leading to an incorrect diagnosis, delayed treatment, and increased cost.
- In this retrospective study of PAE in the hematology laboratory at CSSH, a total of 81,114 samples [16,475 outpatient department [OPD] and 64,639 inpatient department [IPD]] were received in the hematology laboratory. These samples were analyzed for pre-analytical errors such as misidentification, barcode error, inadequate samples, clotted samples, expired tubes, and hemolyzed samples.
- The overall prevalence of pre-analytical errors found was 281 samples, which is 0.34% of the total number of samples received. The most common pre-analytical error observed was clotted samples followed by inadequate sample. Overall frequencies [both OPD and IPD] of pre-analytical errors such as misidentification, barcode error, inadequate samples, clotted samples, expired tubes, and hemolyzed samples were 0%, 0.008%, 0.030%, 0.277%, 0.001%, and 0.028%, respectively.
- The present study concluded that incorrect phlebotomy techniques due to lack of awareness is the main reason for pre-analytical errors. This can be avoided by proper communication and coordination between laboratory and wards, proper training and continuing medical education programs for laboratory and paramedical staffs, and knowledge of the intervening factors that can influence laboratory results.

Conflict of Interest- There is no conflict of interest in this study.

Ethical Approval- The researchers have ethical approval to conduct this research with in the CSS Hospital, Meerut, U.P, India.

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Table-1. Types and frequency of pre-analytical errors IPD patients observed out of 97 errors.

S.No	Pre-analytical errors	Frequency	Percentage
1	Wrong Identification	0	0%
2	Barcode error	0	0%
3	Clotted sample	85	87.6%
4	Hemolyzed sample	9	9.27%
5	Expired tubes	1	1.03%
6	Inadequate sample	2	2.06%

Table- 2. Types and frequency of pre-analytical errors OPD patients observed out of 184 errors.

S.No	Pre-analytical errors	Frequency	Percentage
1	Wrong Identification	0	0%
2	Barcode error	7	3.80%
3	Clotted sample	140	76.08%
4	Hemolyzed sample	14	7.60%

5	Expired tubes	0	0%
6	Inadequate sample	23	12.5%

Table- 3. Percentage of IPD and OPD observed out of total errors 281 within 2 yrs.

Cases	PreAE	Total number of error	%
IPD	97	281	34.5%
OPD	184	281	65.4%

Table- 4. Types and percentage of errors out of the total sample [2 years] received in IPD and OPD.

	IPD	%	OPD	%	IPD+OPD	%
Total sample	64,639		16,475		81,114	
Wrong Identification	0	0%	0	0%	0	0%
Barcode error	0	0%	7	0.042%	7	0.008%
Clotted sample	85	0.131%	140	0.849%	225	0.277%
Hemolysed	9	0.013%	14	0.084%	23	0.028%
Expired tube	1	0.001%	0	0%	1	0.001%
Inadequate sample	2	0.003%	23	0.139%	25	0.030%
Total	97	0.150%	184	1.116%	281	0.346%

Table-5. Comparison of our study, CSSH study in 2012, and GB pant hospital studies.

Types of errors	Our Study		CSSH study 2012		GB pant hospital study	
	IPD	OPD	IPD	OPD	IPD	OPD
Wrong identification	0%	0%	0.47%	0.26%	0.45%	0.51%
Barcode error	0%	0.042%	NA	NA	NA	NA
Clotted sample	0.131%	0.849%	0.16%	0.11%	NA	NA
Hemolysed	0.013%	0.084%	0.15%	0.05%	1.10%	0.20%
Expired sample	0.001%	0%	0.09%	0.00%	NA	NA
Inadequate sample	0.003%	0.139%	0.22%	0.17%	0.08%	37.00%

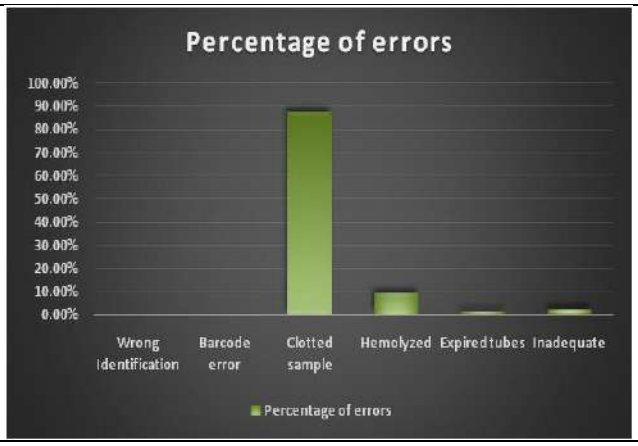

Figure-1. - Percentage of errors in IPD observed out of 97 errors.

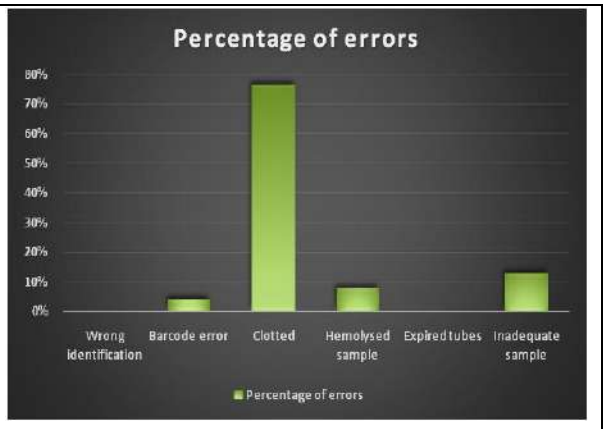

Figure- 2. Percentage of errors in OPD observed out of 184 errors.

Figure- 3. Percentage of errors in IPD and OPD observed out of errors received within 2 years.

Figure- 4. Percentage of errors in IPD and OPD total sample received in the hematology laboratory.

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RESEARCH ARTICLE

The Impact of GDP Growth on Unemployment Rate in India

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ABSTRACT

The relationship between GDP growth and unemployment is a well-established concept, and this relationship is of particular significance to policymakers in developing countries like India. The unemployment rate in India is high, and the government has prioritised the job creation to ensure inclusive growth. Therefore, this study aims to probe the relationship between GDP growth and the unemployment rate in India, and the factors that impact this relationship. The empirical analysis of this study finds a negative relationship between GDP growth and the unemployment rate in India, indicating that when GDP grows, unemployment decreases. Still, several factors determine the influence of GDP growth on the unemployment rate. One of the most important factors is the quality of education and training handed to the pool. The study finds that a significant proportion of the Indian pool is unskilled, making it difficult to take advantage of job opportunities created by economic growth. Therefore, the government needs to concentrate on perfecting the quality of education and training programs to equip the workforce with the skills necessary to take advantage of job opportunities. Another significant factor also influences the relationship between GDP growth and the unemployment rate in India. India has labour request policies. The study finds that the rigid labour laws in India have contributed to a low labour request participation rate, particularly among women. Also, the low-skilled workforce is a significant challenge, making it difficult to take advantage of the openings presented by economic growth. Therefore, programs aimed at reform for labour requests, including simplifying labour laws, encouraging labour request participation, and promoting skill development, are necessary to ensure that the pool can take advantage of job opportunities. Likewise, the study finds that technological advancements also play a pivotal part in shaping this relationship. The relinquishment of technology has led to increased productivity and effectiveness, creating job openings. Still, it has also led to job relegation, particularly among low-professed workers. Thus, programs to ensure that the pool is adequately prepared to acclimate to technological advancements are necessary to address the unemployment challenges in India. In conclusion, this study provides evidence of the relationship between GDP growth and the unemployment

rate in India. The findings suggest that the government needs to take initiative in labour request reforms, education and training programs, and technological advancements to ensure inclusive growth and reduce unemployment.

Keywords: GDP growth, Unemployment rate, India, Labor market policies, Education and training, Technological advancements, Inclusive growth.

INTRODUCTION

India is one of the fastest-growing economies in the world which has experienced significant economic growth in recent years. However, the country still suffers from high unemployment, which poses major challenges to its economic development. The relationship between GDP growth and the unemployment rate has been debated in economics, with some scholars claiming a negative correlation between the two variables. This research paper aims to analyse the relationship between GDP growth and India's unemployment rate and to identify the factors affecting this relationship. The research will use empirical analysis to examine the relationship between GDP growth and the unemployment rate, using data from the 2010-2020. The research begins with a literature review on the relationship between GDP growth and the unemployment rate in India, considering both theoretical and empirical studies. This overview will provide a basis for research and help identify gaps in the literature this research seeks to fill. After reviewing the literature, the research presents the data and methods used for the empirical analysis. The research will use time series analysis to examine the relationship between GDP growth and the unemployment rate and consider other variables that may affect the relationship. The research then presents the results of the empirical analysis and discusses their implications for future research and policy. The research also analyses the factors affecting the relationship between GDP growth and India's unemployment rate, including government policies, economic sectors and demographic characteristics. Lastly, this research paper will provide an overview of the relationship between GDP growth and the unemployment rate in India and the factors affecting this relationship. The research will help enrich the literature on the subject and influence policy decisions to reduce unemployment and promote economic growth in India.

LITERATURE REVIEW

The relationship between GDP growth and the unemployment rate has been extensively studied in economics, with mixed results. Some researchers claim that there is a negative correlation between GDP growth and the unemployment rate, suggesting that the unemployment rate falls as the economy grows. Others argue that this relationship is difficult and may depend on several economic and social factors. In India, the link between two variables such as GDP growth and unemployment has been debated for many years. In their study, Agarwal and Yadav (2015), Khem Chand et al., (2017), and Khujan Singh et. al., (2018) found a negative correlation between GDP growth and the unemployment rate in India, suggesting that the unemployment rate falls as the economy grows. Similarly, Bhanumurthy et al. (2013) found a negative correlation between GDP growth and the unemployment rate using a vector auto regression (VAR) model to evaluate the relationship between two variables. However, other studies have found a more complex relationship between GDP growth and the unemployment rate in India. For example, Goyal and Kumar (2016)found that while there is a negative correlation between GDP growth and urban unemployment rates in India, this relationship is insignificant for rural unemployment. This result suggests that the relationship between GDP growth and the unemployment rate may vary by location. Moreover, Gil-Alana, (2010) investigated that GDP growth negatively affects unemployment in the UK and the USA whereas GDP is insignificant to the unemployment rate in Japan. Hugo Miguel Rosa da Palma, (2014) revealed that this relationship is not stable in the long run periods, therefore it is useful only in the short run. Ademola and Badiru (2016) investigated in their study that the long-term significant effect of real gross domestic can be seen in the unemployment rate. Another factor that can influence this relationship in India is the economic structure. According to Hoang, N.Q (2016) stated that economic growth is positively affected by public investment while

unemployment is negatively affected by the import-export of products. It implies that public investment contributes to an increase in employment. Singh and Kaur (2016)found that the service sector negatively influences the unemployment rate, while manufacturing is positive. This result suggests that economic structure and the relative importance of different economic sectors can affect the relationship between GDP growth and the unemployment rate. AI- Habees and Rumman (2012) examined that high GDP growth and a decrease in unemployment have an insignificant impact on this relationship between the two variables. This indicates that a positive economic growth rate does not influence the unemployment rate in Jordan's country of Arab. Anyanwu, (2013) found that youth unemployment is negatively affected by the inflation rate, domestic investments and the level of GDP in Sub-Saharan nations and North America. Aside from economic factors, demographic factors may also play a role in the relationship between GDP growth and the unemployment rate in India. In their study, Sahni and Singh (2014)found that age and gender significantly impact the unemployment rate in India, with young men being more likely to be unemployed than women and older workers. This result suggests that demographic factors may need to be considered when analysing this relationship in India. In summary, the literature on this relationship highlights that it is complex and may depend on various economic, social and demographic factors. While some studies have found a significant relationship between two variables, others have found a more nuanced relationship that can vary by location, economic structure, and demographic factors. This literature review provides the basis for an empirical analysis of the relationship between GDP growth and the unemployment rate in India and the factors affecting this relationship.

Objectives

- To evaluate the impact of GDP growth on the unemployment rate in a given period in India
- To investigate the structural factors influencing the relationship between GDP growth and unemployment rate: This objective involves identifying and analysing various structural factors influencing this relationship. These factors may include labour market dynamics, government policies, industry composition, technological advances, and demographical factors.
- Examine the short- and long-term effects of GDP growth on the unemployment rate: This objective aims to determine whether the effects of GDP growth on the unemployment rate are immediate or lagged. This lens will provide insights into short- and long-term relationship dynamics by analyzing data from different time periods.
- Provide policy recommendations to achieve sustainable growth and reduce unemployment: Based on evidence and analysis, this objective aims to provide practical recommendations to policymakers in India. These recommendations may include strategies to support inclusive growth, stimulate job creation promote skills development initiatives and effectively tackle unemployment. To achieve these goals, this research paper will contribute to the existing literature on the relationship between GDP growth and the unemployment rate in India. Findings from this study can help policymakers, economists, and researchers understand the dynamics of the Indian economy and formulate effective strategies by addressing unemployment challenges while promoting sustainable economic growth.

MATERIALS AND METHODS

In this study, empirical research methodology is used to evaluate the impact of GDP growth on the unemployment rate in India and examine the factors influencing this relationship. The study design includes a quantitative analysis using secondary data from credible sources such as the World Bank, the Ministry of Statistics and Program Implementation and the Reserve Bank of India. Data regarding the GDP growth and unemployment rate are collected over the period, ensuring consistent methodology and measurement. Descriptive statistics examine variables, while time series analyses examine patterns and trends in GDP growth and unemployment rates. Correlation coefficients will be calculated to assess the strength and direction of the relationship. A regression analysis will estimate the impact of GDP growth on the unemployment rate, taking into account the relevant

factors. Control variables such as inflation, education level and investment rates are included to account for potential confounders. Limitations, assumptions, and ethical considerations are taken into account to ensure the validity and reliability of the results. Interpreting the results will provide valuable insights into the dynamics of the relationship between GDP growth and the unemployment rate in India, as well as the policy implications for promoting sustainable economic growth and reducing unemployment.

RESULTS AND DISCUSSION

H_0: There is no significant correlation between GDP growth and the unemployment rate in India.
H_a: There is a significant correlation between GDP growth and the unemployment rate in India.
To test this hypothesis, we organised the data into a table, with the first column containing the year, the second column containing the GDP growth rate, and the third column containing the Unemployment rate.
$t = (\bar{x} - \mu) / (s / \sqrt{n})$ where: $\bar{x}$ is the sample mean
μ is the hypothesised population mean (in this case, 0) s is the sample standard deviation n is the sample size
We use a significance level of 0.05 and a two-tailed test. We have 11 data points, therefore, the degrees of freedom for the t-test will be 11 - 2 = 9. To calculate the critical value for a two-tailed t-test with a desired level of significance (α) of 0.05, you can consult a t-distribution table or use statistical software. For df = 9 and $\alpha = 0.05$, the critical t-value is approximately ±2.262. Now, need to calculate the sample mean, sample standard deviation, and sample size for each variable:

GDP Growth
$\bar{x}$=(5.4564+6.3861+7.4102+7.9963+8.2563+6.7954+6.4539+3.7379-6.5961+8.6812+5.4564)/11= 5.4576

$$s = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(x_i - \overline{x})^2},$$

$s2 = \Sigma(xi - \bar{x})2$
N - 1
=(5.4564 - 5.4576363636364)2 + ... + (5.4564 -
5.4576363636364)2
11 - 1
=180.3754525254510
=18.037545252545
s =√18.037545252545
=4.2470631326301
n=11

Unemployment Rate
$\bar{x}$= (8+7+ 6+7+8+9+10+11+10+9+12)/11
Mean = 97 / 11, Mean ≈ 8.82

$$\sigma = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(x_i - \mu)^2}.$$

$\sigma 2 = \Sigma(xi - \mu)^2 N$

(8 - 8.8181818181818)² + ... + (12 -

= 8.8181818181818)²

$= \frac{33.636363636364}{11}$

$= 3.0578512396694$ $\sigma = \sqrt{3.0578512396694} = 1.7486712783338$

$n=11$

Next, we calculate the t-value for each variable:

GDP Growth

t = (5.4576 - 0) / (4.2470631326301 / sqrt(11)) = 4.262

Unemployment Rate

t = (8.82 - 0) / (1.7486712783338 /sqrt(11)) = 8.29

Finally, we compare the calculated t-values with the critical t-value for a two-tailed test with 9 degrees of freedom (n-1), using a significance level of 0.05. The critical t-value is 2.262. Since all calculated t-values are greater than critical t-values, we can reject the null hypothesis and conclude that there is a significant relationship between GDP growth and the unemployment rate in India.

Hypothesis Findings

This hypothesis testing aimed to ascertain the connection between India's unemployment rate and GDP growth. A significance level of 5 % was picked for the test, and a two-followed t-test was directed. According to the null hypothesis, there is no significant correlation between India's unemployment rate and GDP growth. As per the alternative hypothesis, there is a significant correlation between India's unemployment rate and GDP growth. Given the information examination, the accompanying outcomes were obtained:

Gross domestic product Development: The sample standard deviation was approximately 4.249, and the sample mean was estimated to be approximately 5.4576. The GDP growth t-value was calculated to be 4.262.

Rate of Unemployment: The example mean for the joblessness rate was viewed as roughly 8.82, with an example standard deviation of roughly 1.749. The unemployment rate's t-value was determined to be 8.29. For a two-tailed test with 10 degrees of freedom, the calculated t-values and the critical t-value of 2.262 were compared, and it was found that both t-values were higher than the critical value. The null hypothesis is therefore rejected. This concludes that there is a significant correlation between India's unemployment rate and GDP growth based on these findings. The result of the study shows that adjustments in Gross domestic product development altogether affect the joblessness rate in the country. These findings have implications for policymakers and researchers and contribute to our understanding of the Indian economy. It suggests that policies that boost India's economic growth may reduce unemployment. The specific mechanisms and factors that drive this relationship can be studied in greater detail in future research, allowing for more targeted policy interventions to address issues with unemployment and promote long-term economic growth in India.

RESEARCH FINDINGS

1. A review of verified data on India's GDP growth and unemployment rate shows a critical negative relationship between these variables. Empirical evidence indicates that the unemployment rate falls when GDP increases. This conclusion supports the assumption that job creation will decrease unemployment, resulting in economic growth.
2. Examining the relationship between two variables reveals that changes in GDP growth significantly affect changes in the unemployment rate in India. The GDP growth rate is associated with a decrease in unemployment which is crucial in reducing the unemployment rate. Objective 3: Study of structural factors affecting the relationship between unemployment and GDP growth:
3. Examining the several key variables influencing the relationship between India’s GDP growth and

unemployment rate emerge as important findings. To begin with, elements of the labour market, such as the nature of teaching and programming, significantly affect the ability of the workforce to take advantage of jobs created through economic development. Second, strict labour laws and low labour force participation, especially among women, prevent unemployment from falling. Third, technological progress has both positive and negative effects, leading to the creation of job opportunities and the displacement of low-skilled workers.

4. The effect of GDP growth on the unemployment rate is significant in the short run and long-term. An acceleration of GDP growth leads to a decrease in the unemployment rate in the short term. However, the long-term effect of GDP is also significant, as the continuous progress in GDP leads to a decrease in unemployment.
5. Improving the quality of education programs so that workers have the required skills to take advantage of the job opportunities that economic growth offers. Promoting skills development initiatives to ensure the workforce's ability to adapt to technological developments and reduce the negative effects of labour mobility. Using inclusive growth strategies that prioritise job creation, especially in sectors with high employment potential. Goal 6: Increase information:
6. By providing empirical evidence and insights into the specific factors influencing this relationship, this research paper contributes to the existing literature on the relationship between GDP growth and the unemployment rate in India. Policymakers, economists and researchers can use the results to develop effective strategies to tackle unemployment and promote India's long-term economic growth.

SUGGESTIONS

Strengthen Skills Development Programs

To tackle unemployment, the Indian government should prioritise skills development programs. This includes improving the quality of education and training and focusing on developing skills in high demand in the labour market. Working with industry and the private sector can help develop targeted training programs to close the skills gap.

Labour market reforms

Assess and consider the implementation of labour market reforms to promote job creation and reduce unemployment. This can include simplifying labour laws, streamlining regulations and creating a more flexible and supportive business environment. Creating an environment conducive to entrepreneurship and investment can lead to industrial development and subsequent job opportunities.

Encourage industry diversification

Encourage industrial diversification to create a broader range of employment opportunities. Support the development of sectors such as manufacturing, services, technology and renewable energy that have the potential to create jobs at different skill levels. This goal can be achieved through targeted political measures, investment incentives and infrastructure development.

Support Entrepreneurship and Start-ups

Foster an ecosystem that supports entrepreneurship and start-ups. This includes providing access to finance, mentorship programs, and business incubators, and simplifying administrative procedures for starting and operating businesses. Entrepreneurship can play a significant role in job creation and economic growth.

Enhance Women's Participation

Implement policies and initiatives to increase women's participation in the labour force. This can include measures such as providing equal opportunities, addressing gender biases, improving access to education and training, and creating a supportive work environment that accommodates the needs of women.

Foster Technological Advancements

Embrace and adapt to technological advancements by investing in research and development, promoting innovation, and supporting the adoption of digital technologies across industries. Not only will this increase productivity and efficiency, but it will also create new job opportunities that meet the changing demands of the economy.

Strengthen social safety nets

Implement social safety nets to support the unemployed or underemployed. This can include unemployment benefits, job training programs and placement services to help people transition to new job opportunities.

Continuous monitoring and evaluation

regular monitoring and evaluation of the impact of policies and interventions aimed to reduce unemployment and promote inclusive growth. Evaluate the effectiveness of different programs based on the results, and make the necessary adjustments to ensure continuous improvements and adaptation to the changing economic landscape.

CONCLUSION

In conclusion, this empirical analysis examined the relationship between GDP growth and the unemployment rate in India and the factors affecting the relationship. The results shed light on the dynamics of the Indian economy and provide valuable insights for policymakers, economists and researchers. The study confirmed the existence of a significant contribution of GDP growth to the unemployment rate in India. The negative correlation between these variables suggests that the unemployment rate tends to fall as GDP increases, indicating a potential impact of economic growth on job opportunities. However, it is important to note that causality cannot be definitively established and other complex factors may be involved. Several factors affecting this relationship have been identified such as government policies, industry composition, technological advances, demographical factors and labour market dynamics. Understanding and addressing these factors are critical to formulating effective strategies for reducing unemployment and promoting sustainable economic growth. Future research in this area should aim to address these limitations and dig deeper into the complex relationship between two variables. Researching alternative methods, using robust statistical techniques, considering long-term trends, and conducting region-specific analyses can provide further insights. These studies add to the existing literature by providing empirical evidence for a relationship between GDP growth and the unemployment rate in India. Findings underscore the need for comprehensive policies that recognize the multifaceted nature of India's economy and aim to foster inclusive growth, job creation, and skills development. Ultimately, by tackling the unemployment challenges while promoting sustainable economic growth, policymakers can work towards creating a prosperous and inclusive society in India.

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Table 1: shows the trend analysis data of GDP growth and Unemployment rate.

Year	GDP Growth (%)	Unemployment Rate (%)
2010	5.4564	8
2011	6.3861	7
2012	7.4102	6
2013	7.9963	7
2014	8.2563	8
2015	6.7954	9
2016	6.4539	10
2017	3.7379	11
2018	-6.5961	10
2019	8.6812	9
2020	5.4564	12

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RESEARCH ARTICLE

Critical Mineral Resources of Delhi Supergroup of Rocks, Around Bar - Pali District, Rajasthan

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ABSTRACT

Delhi Super group rocks in Rajasthan host several economic minerals and rocks which are situated between the southwestern margin of the Bar hills and the northeastern hills of Fatehgarh. The study area covers approximately 100 square KM and lies in the Bar-Raira Khurd-Fatehgarh region of Pali district. The area is located along the rivers Sukri and Sundi, bounded to the north by Sendra village and to the south lays the Raira Khurd-Fatehgarh region. The area consists of mica schist, amphibolite schist, limestone, quartzite, dolomite, calc-gneiss, quartzofeldspathic gneiss and graniteas economic and industrial rock deposits. A regular observation indicates that all the rock types are good for commercial purposes and utilized as a building material and also in cement industries.

Keywords: Sukri and Sundi rivers, Bar region, commercial purpose, cement industries, Delhi Super group.

INTRODUCTION

Rajasthan encompasses a variety of rocks right from the Archaean to the recent alluvium/aeolian including desert sands. The Aravalli being one of the world's oldest mountain chains is constituted of Palaeoproterozoic and Mesoproterozoic sequences, which rest over the Archaean basement [1].The Proterozoic Delhi fold belt is a linear belt running northeast for adistance of 1000 km from NE Delhi to S Gujarat with a spread of over 80-100 km in width southwest part, 15-18 km width in the central part and 100-200km in northeastern part. Bar area forms a part of the Delhi Super group and lies in Bar- RairaKhurd region of Pali district in Rajasthan. The rocks exposed in the study area are lithostratigraphically classified into three i.e., the Banded Gneissic Complex (BGC), Barotiya Sequence and the Sendra Complex [2]. Barotiya Sequences is represented by the feldspathic schist, conglomerate, garnetiferous mica schist and calc schist, whereas the Sendra complex is represented by calc gneiss, foliated quartzite and metamorphosed limestone. Bar conglomerate is situated at the base of the Barotiya sequence, which is conformably

overlain by the Sendra complex. The contact is known as Kalab limestone (Nandana Crystalline Limestone described by Heron, 1953[2]) in the study area. However, this area has not received much attention regarding its structure, metamorphism and tectonic correlation. Based on the works of Heron (1953) [2], the Bar conglomerate extends from Kalakote to Giri spreading over an area of approximately 100 sq km and belonging to the Delhi Super group. However, observation indicates that this rock bed extends further southwest as conglomerate horizon crops out almost continuously for astrike length of about 42 km from Giri to Raira Khurd through Bar area of the Pali district of Rajasthan. Raira Khurd is located further south of Kalakote, whereas to date Kalakote has been reported as the southern boundary of Bar conglomerate and supports Tropical thorn forest types of vegetation[3].

Study Area

The study area forms a part of the Delhi Super group of Aravalli Craton. The Proterozoic Delhi fold belt is a linear belt running northeast for a distance of about 1000 km from NE Delhi to south of Gujarat with a spread of over 80-100 km in width southwest part, 15-18 km width in the central part and about 100-200 km in northeastern part [4,5,6]. Heron (1953) [2] mapped the area and described it in detail, which was published in 1953 as "The geology of Central Rajputana", Memoir of Geological Survey of India. Delhi Supergroup forms a part of Aravalli Craton. Administratively the study area is located in the Raipur tehsil of Pali district, bounded to the North by Madhlav Dhani and to the South by railway tract at Lawacha and Depawas. Megarda village is situated in the northeastern part and Malani village, whereas Kapuri Dhani is located, in the Southwestern part. Raipur Luni River is centrally situated in the study area (Fig. 1).

Geological Setting

The rocks in the Bar-Phatakhera-Raipur area of Pali district are part of three major tectonic divisions of the Delhi Super group, extending from southwest to northeast: the Banded Gneiss Complex (BGC, as defined by Heron in 1953 [2]), the Barotia Formation (part of the Alwar Group), and the Sendra Formation (Ajabgarh Group). These tectonic divisions are distinguishable in the study area. The BGC, representing the Precambrian basement in the southwestern part, forms the lowermost tectonic unit. It is separated from the overlying Barotia Formation by an unconformity [7]. The Barotia Formation comprises the Bar conglomerate horizon, calc-amphibolite schist, quartzite schist, and calc-schist, with intercalations of quartzite schist. The Bar conglomerate horizon is further subdivided into quartzofeldspathic schist, Bar conglomerate schist, garnetiferous mica schist, staurolite schist, and kyanite schist (Fig. 2d). The northeastern part of the study area is overlaid by the Sendra Formation. A dolomite layer (equivalent to Heron's Nandana crystalline limestone, 1953) conformably separates the Sendra Formation from the underlying Barotia Formation. The Sendra Formation is primarily composed of gneisses, with alternating bands of mica schist and foliated quartzite [8].

Classification of Genetic Mineralization

The grouping of commercial types of ore deposits is based on a single genetic classification, i.e. on endogenous, exogenous and metamorphic series. The endogenous series incorporate pegmatite deposits groups. Within the exogenous series the following groups have been characterized viz. weathering, placers and sedimentary. The metamorphogenic series includes all types of schists, gneisses, quartzite, etc. Thousands of ore deposits have been discovered in the world and it is not possible to describe even a small fraction of that number of deposits in the investigated area. The authors have characterized the most representative minerals and rock types as examples of commercial types in the study area and elsewhere. Commercial types of deposits are described based on various representative examples in Table 1.

Industrial Mineral, Rocks And Soils

The strength of a country depends on its economic independence, which can be achieved by the growth of its small-scale factories and industries. Different types of rocks, minerals and soils provide a major resource for the nation's economy as it forms the input for industrialization[9]. The development of material culture was impossible and unbelievable without the use of rocks, minerals and soils. Minerals are a natural resource and are non-renewable.

The state of Rajasthan has sizeable resources of rocks, minerals and ores deposits e.g. sandstone, marble, limestone, granite, pegmatite, mica schist, soapstone, dolomite, chalcopyrite, wolframite, galena, sphalerite, etc. which constitute people's rightful wealth. The convention will focus on such issues that could benefit the State on their sustainable and proficient exploitation as well as it could help both government and private investors on the development of future mineral and mining industry in the State. The Luni and Sukri rivers form the main drainage of the area and flow from northwest to southeastern direction. Recent field, petrological and petro graphical studies indicate that the Delhi Super group rocks of the Haripur-Dipawas-Lawacha area of Raipur tehsil, Pali district are composed of meta sedimentary to metamorphic rocks that are intruded by thick and thin pegmatite veins. Pink to white euhedral crystals of tourmaline, beryl and booklets of muscovite are well developed (Fig 2c). The presence of pegmatite veins can be very well related to Aravalli orogeny and is the youngest intrusive activity in the region which penetrated the Delhi Super group of rocks and the older granitic gneisses in the neighborhoods of the study area [7]. Delhi Supergroup of rocks is very well exposed in and around the Bar village and similar types of exposures are also exposed at Haripur, Dipawas, and Lawacha villages of Raipur Tehsil. Delhi Super group of rocks is also exposed at Raira Khurd SW of the Dipawas village. Thick and thin quartz and pegmatite veins are intruded at places near Mohra Khurd, Haripur, Dipawas and Lawacha villages with many industrial minerals describe in Table 2, and especially crystals of garnet, beryl, tourmaline and booklets of muscovite are well developed (Fig. 2). The generalized industrial minerals and the rocks of the study area are given in Table 2.

RESULTS AND CONCLUSION

The various litho–units in the investigated area are associated with industrial minerals and rocks which are related to refractory, small cottage industries and various other building material purposes [10]. Such minerals and rocks are common in the study area. On the basis of above-described minerals and rocks, the following industries are suggested that may be set up in the area: The area has plenty of building material in form of granitic gneiss, mica schist, dolomite, limestone, quartzitic schist, granite and that may be utilized for making tiles, slabs and pillars, which are in demand in rural and urban areas. In addition soil, sand, concrete, cobble, pebble and boulders are already being utilized for masonry works and giving a good revenue. Garnet, emerald and beryl are favorite semi-precious stones for the local residents. Both varieties of garnet i.e. pyrope and almandine are available as a valuable deposit. Fertilizer plants and refractory units may be established on the basis of dolomite and kyanite mineralization. Limestone may be used in cement plants and calcium carbide manufacturing units. Muscovite is not of very good book quality, yet useable in small cottage industries as an insulator. The soil in Bar district is fertility is high, fostering the growth of crops and vegetables with unique flavors, possibly due to water quality and trace minerals. Therefore, the soil in this region may indicate patterns of rock degradation and formation, influencing the vegetation it supports. The unique desert and semi-desert locations of Rajasthan have a difficult geo-environment and particular kinds of cultural and economic aspects make it a distinct and characteristic state. The lifestyle of the people is purely rooted in the traditional values. Great diversity in climate and a wide variety of topography have further distinguished Rajasthan from other states. Rajasthan is the most part mountainous as well as desert state and is home to many endemic, endangered and threatened species, which affects the socio-economic condition of the existing natives of the state. Rajasthan is also well known for its rich culture, lifestyle and natural resources.

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Table.1: Classification of genetic mineralization

S. No.	Series of Classification	Location	Example
1.	Endogenous	Bar, Mohrakhurd, Raira khurd	Different types of pegmatites
2.	Exogenous	Bar, Mohrakhurd, Raira-khurd, Phatakhera, Barotiya, Fatehgarh	Weathering product e.g. soil, sand and sedimentary sand and sedimentary rocks
3.	Metamorphogenic	Bar, Mohrakhurd, Raira- Khurd, Megarda, Kalab Kalan, Barotiya, Sendra, Kalakote	All types of schists, gneisses and quartzite

Table.2: Distribution of important industrial minerals/rocks of the study area (after *Kumar et. al.*, 2013[11])

Minerals/Rock	Area	Industries
Dolomite	Nanana, Jhala ki Chouki, Megarda.	Steel, Refractory, Ferro alloys, Fertilizer, Paint industry
Granite	Barotia, Jhala Ki Chouki	Building material, Decorative purpose, Dimension stones
Kyanite	Gunda Bera	Refractory industry
Limestone	Fatehgarh, Nanana	Lime, Cement, Ceramic product, Calcium Carbide and Bleaching powder industry
Beryl	Bar, Giri, Kalab Kala	Semi-precious stone used in making jewelry, used as moderator in nuclear reactor
Garnet	Bar, Giri, Kalab Kala, Raira Khurd	Gem stone (Precious stones) used in jewelry and abrasive.
Tourmaline	Bar, Giri, Kalab Kala, Raira Khurd, Kalakot and Mohra Khurd	Semiprecious

Muscovite	Bar, Giri, Barotia Khurd	Electrical and Electronic industries as insulator
Mica Schist	Phatakhera, Kalakot	Building material and Decorative purpose

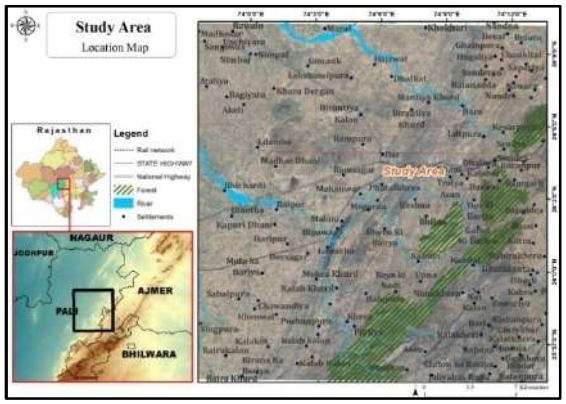

Figure.1: Location map of study area around Bar, Pali district, Rajasthan

Figure.2: a). The Pegmatite veins near Mohra Khurd intruded within mica schists with big size garnets.
b). The pegmatite vein has lead to the formation of crystals of tourmaline at Mohra Khurd.
c). Muscovite has been found in the booklet form in pegmatite veins at Mohra Khurd.
d). Blades of grayish black kyanite with occasional browning type occur with radiating form associated with quartz veins.

RESEARCH ARTICLE

Design and Development of the Conductivity Meter to Measure of Surfactants by using PC with Diot Card

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ABSTRACT

This paper is design and development of low cost conductivity measurement system. Present days the pc comes across become a most desired and are being introduced at undergraduate level in both theory and practical's. Consequently, make an effort to improve the development of present work is DIOT card is connected to computer for the conductivity measurement by pertinent code using high-level language 'C'.One of the crucial electrochemical characteristics of an electrolytic solution that provides chemists with invaluable information is its conductivity. Electrical current flows through an electrolyte solution due to ion migration.

Keywords: Computer, conductivity cell, and DIOT card**.**

INTRODUCTION

Surfactants are sometimes called surface-active agents or detergents. The surfactants are a well-known class of amphiphiles. The behavior of surfactants in solution has rapidly gained importance from both theoretical and industrial points of view. The applications of surfactants are rapidly increasing, engaging science and technology. Such as catalysts in chemical reactions, detergents, cosmetics, pharmaceuticals, pesticides, plastics, dyestuffs, paints, and as simple models for proteins and enzymatic reactions [1]. The most upcoming fields of surfactant application are energy-related areas such as enhanced oil recovery by micro emulsion flooding and storage of solar energy through photodecomposition of water [2].The majority of the remarkable properties of surfactants are

related to the amphiphilic nature of the surfactant molecule, which includes a hydrocarbon part (hydrophobic group) covalently linked to a polar or ionic part (hydrophilic group) [3]. The conductivity of a surfactant solution increases with increasing concentration due to the rising number of ions in the aqueous phase. However, as the concentration reaches the critical micelle concentration (CMC), the slope of the conductivity-concentration curve decreases. This is because surfactant molecules begin to form micelles, reducing the proportion of free surfactant, molecules to micelles, which in turn leads to a decrease in the rate of conductivity increase [4]. Surfactants, or surface-active agents, are molecules that reduce the surface tension between two liquids or between a liquid and a solid. These molecules possess both hydrophobic (water-repelling) and hydrophilic (water-attracting) regions, enabling them to interact with and modify the properties of surfaces and interfaces. Surfactants can be categorized into four main types: anionic, cationic, nonionic, and amphoteric. Anionic surfactants, such as soaps and detergents, carry a negative charge, while cationic surfactants, like quaternary ammonium compounds, possess a positive charge. Nonionic surfactants, including ethoxylates and glycols, are neutral, and amphoteric surfactants, derived from amino acids, can exhibit both positive and negative charges depending on the pH of the solution[5].At lower concentrations many physic-chemical properties such as self diffusion coefficient, activity, turbidity, conductance , surface tension , viscosity heat capacity , apparent molar volume and NMR spectral features indicate that there is no appreciable aggregation of surfactant38 below CMC. However, above CMC the changes in the above properties indicate the formation of large aggregates. The concept of CMC is a quite useful in the characterization of the self –association pattern. [6].

- **Industrial applications:** Detergents, cosmetics, pharmaceuticals, pesticides, plastics, dyestuffs, and paints.
- **Scientific research:** As simple models for proteins and enzymatic reactions.
- **Emerging energy applications:** Enhanced oil recovery through micellar flooding, and solar energy storage via photodecomposition of water.

These diverse applications highlight the growing importance of surfactants in both established and emerging technologies.

Principle

The conductivity of electrolyte solution can be measure with an op-amp in inverting arrangement. It has two resistors: a feedback resistor and an input resistor. The conductivity cell is given by this equation.

$$Vo = -(Rf/Ri)*Vi$$

$$Ri = -(Rf/Vo)*Vi$$

Where $Vi = 1\,V$ and $Rf = 1000$ ohms

$$K = C = 1/Ri$$

$$K = Vo/1000$$

$$K = Vom \text{ mhos}$$

Therefore, the DIOT card can be one of the most important components with a PC. An inverting operational amplifier can be used to obtain the reciprocal of the resistance, which will be equal to the output voltage [7]. The PC code will collect the data from the conductivity cell and display the final result. It sounds like you're describing a project or study focused on interface pc with digital input output card for measuring electrolytic conductivity. This involves developing to enable the PC to perform conductivity measurements of electrolyte solutions [8].

This research project typically need to

- **Hardware Setup:** Design or acquire hardware components that can measure conductivity. This might involve sensors, electrodes, and circuitry to interface with the PC.
- **Software Development**: Create code and interface with the hardware to control the measurement process and collect data. This could include programming to read sensor outputs, process data, and display or store results [9].
- **Calibration and Testing**: Ensure that the system is calibrated correctly to provide accurate conductivity measurements[10]. Testing involves comparing measurements from your setup with known standards to validate accuracy.
- **Integration and Interface:** Develop a user-friendly interface on the PC that allows users to interact with the conductivity measurement system effectively[11]. This interface could display real-time measurements, provide options for data logging, and offer controls for conducting experiments.
- **Documentation and Evaluation:** Document the entire development process, including hardware schematics, software code, calibration procedures, and user manuals. Evaluate the performance of measurement inregarding of accuracy, reliability, and ease of use.
- Such a project not only enhances understanding of electrochemical concepts but also issue live experience in hardware and software development, which are valuable skills in both academic and industrial settings.

Hardware

The figure 4 shows the block diagram of conductivity measurements of some surfactants by using pc through digital input output card. Analog system consists of

- AC Signal Source
- Conductivity cell
- Personal computer
- ESA PCIDIOT
- Power Supply
- System Requirements
- ADC0808/ADC0809

Digital input output card

It has 2 PPIs 8255 and 1 timer IC, This card is placed into the mother boards Instruction set architecture. The card acts as and collaborate linking computer and conductivity meter. No external Power Supply required. The figure 2 display the schematic diagram of the preset research work and explain the function of each circuit.

Schematic diagram pc based conductivity meter circuit:

Input signal

The signal has given through sine wave generator.

Conductivity Cell

The two electrodes are submerged and immersed into electrolytic solutions this conductivity examined. The electrodes are securely placed in the geometry covered with layer of platinum. Two electrodes having cross- sectional area 1.05 and separation 1cm is employed in present research and the cell constant is 0.98 the user can do periodically renewal of platinum coating. It can operate with a supply voltage between 12 and 15 and has enough supply rejection to use unregulated source. It can be used in a temperature range of -55 0c to +150 Degree Centigrade temperature range[11]. In this work a PC has the following factors are interface to the conductivity meter.

- Pentium
- 4 Giga Bytes of RAM
- 500 Giga Bytes of Hard Disk drive
- 2 serial ports

- Single parallel port

The main parts of the circuit diagram is ADC , 555 cloclok generator , DIOT Card Op-map ICs , Conductivity cell and Computer. In this schematic diagram 555 circuit diagram is used to generates clock signal, this signal can be act as a input to the ADC 0809 pin diagram then the ADC is in operating stage . this is having 8 data output lines these 8 lines can be connected to the port A of the DIOT card, Actually the DIOT card have 8255 in this package, This 8255 having three ports, I.e. port A, Port B and port C each port having the 8 data lines. In this circuit port A can be selected. Finally this card can be connected to the computer. Conductivity Cell is connected to operational amplifier, this can be immersed in to the liquid and this cell can be ability to read the conductivity of liquid, the output of the conduvitvity is in the form of analog voltage this analog voltage can read by the op-amp and this can be connected to the ADC, This ADC will convert the analog voltage to digital voltage. This digital voltage can be read by the computer through digital input and output card. In this project getting the values of some surfactants of PVP and PVC conductivity values with weight ratio the values of the PVC and PVP given below table.

RESULT

This conductivity meter that's run on PC is created and assembled. The standard resistor and electrolytic solution at numerous concentrations are used to calibrate and test system functionality.

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Table 1: PVP and PVC Conductivity measurement values.

Blending Ratio of [PVA:PVP] (wt%)	k (W/mK)
[100:0]	$2.4x10^{-4}$
[90:10]	$2.8x10^{-4}$
[80:20]	$1.65x10^{-4}$
[70:30]	$2.78x10^{-4}$
[60:40]	$1.68x10^{-3}$
[50:50]	$1.66x10^{-4}$
[40:60]	$5.58x10^{-4}$
[30:70]	$2.38x10^{-4}$
[20:80]	$2.79x10^{-4}$
[10:90]	$2.09x10^{-4}$

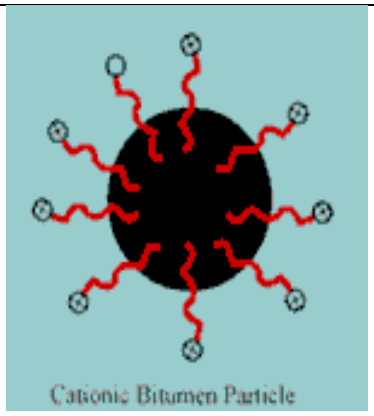

Figure 1.cataonic Bitumen partical

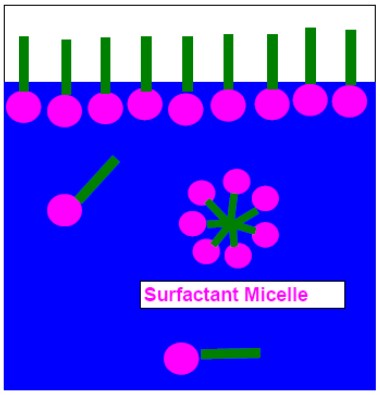

Figure 2. Surfactant Micelle

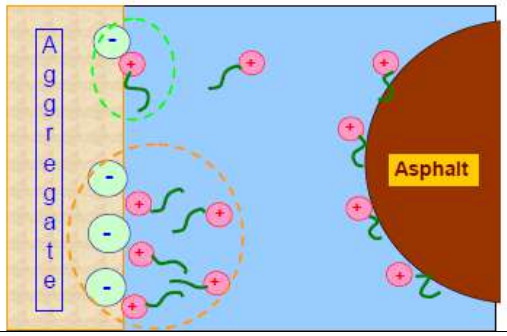

Figure 3.Surfactance in chip seal

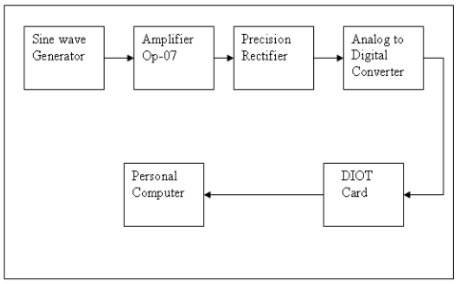

Figure 4: Block Diagram of conductivity measurements of surfactants

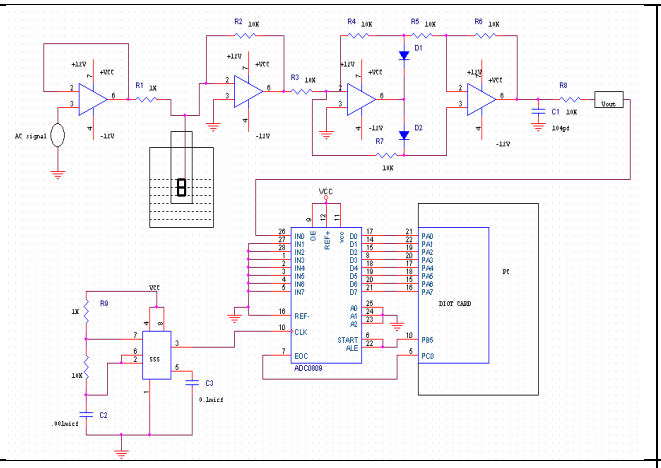

Figure 5: Schematic diagram of Conductivity Meterthrough DIOT card

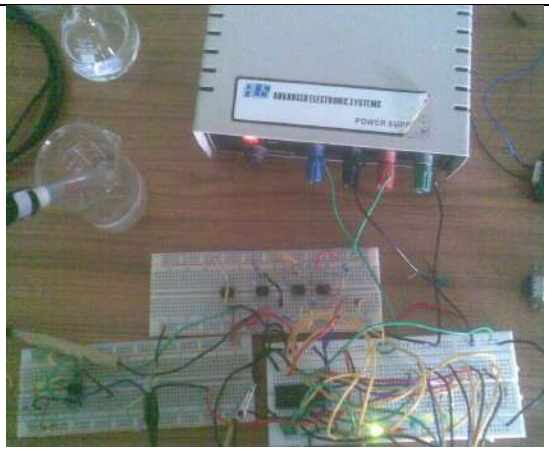

Figure 5.Experimental setup for measuring conductivity

Figure 6.Experimental setup for measuring conductivity

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RESEARCH ARTICLE

Ayurvedic Management of Urolithiasis – A Case Report

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ABSTRACT

Ashmari (Renal Stone) is an age old disease.It is already described in Ayurveda with its symptoms, types, pathophysiology, palliative treatment and surgery also. Renal stones are made up of Salt and mineral. Renal stone is resemble with *Ashmari* in Ayurveda.*Ashm* the meaning is like a Stone and *Ari* means Enemy. So it behave like enemy for body. Conventional Treatment of Renal stone includes Analgesics, Antispasmodic, Antiemetic drug and Hydration. Lithotripsy is the surgical intervention done in case of Renal stone. But chances of complication in surgery is there. In present case study a29-year-old male patient having symptoms of vomiting, lower back pain and dysuria. Clinical Diagnosis was madeRenal stone. This case study aims to study *Ashmari* (Renal stone) as per Modern and Ayurveda views, study the safe and effective Ayurvedic Medicine without going to surgical intervention, avoid recurrence of Renal stone with effective Ayurvedic Treatment.

Keywords: *Ayurveda*, *Ashmari*, Renal stone, Urolithiasis

INTRODUCTION

Ashmari is disease of *Mutravahasrotas* and it is one among the common diseases of *Mutravahasrotas*. It can be compared with Renal stone or Urolithiasis in Modern science. Urolithiasis is a condition that occurs when the stones exit the renal pelvis and move into the remainder of the urinary collecting system, which includes the ureters, bladder, and urethra[1].The most common symptoms of Urolithiasis are Intermittent dull or Colicky pain in flank region, frequent and obstructed urination, painful or burning micturition, cloudy or foul-smelling urine, hematuria and nausea/vomiting. Renal stone are common with a prevalence of about 12% worldwide[2]. Their prevalence in India also reflects worldwide prevalence and stands at approximately 12%[3].The healthcare system is therefore heavily

burdened by this illness. Because of disadvantages of surgical techniques and limited choice in pharmacotherapy, exploring new pharmacological therapies for the management of Urolithiasis is a necessity. Commonly used medicine for the treatment of urolithiasis in *Ayurveda* are *Gokshuradiguggulu, Ashmariharkashay, Pashanbhedachurna, Chandraprabhavati, Shweta parpati* etc.Also,it is necessary to find out an economical, effective and acceptable medicine to treat urolithiasis. In *Ayurveda* there is detail description is available about the urolithiasis, known as *Ashmari*, having 4 types *Vataja*, *Pittaja*, *Kaphaja* and *ShukrajaAshmari*.*Ashmari*has been well described in *SushrutaSamhita*.[4]

Case report

A 29-year-oldMale patient came to the OPD (Aayush Ayurvedam, Kadi) on 17/11/2023with the **Chiefcomplaints** of vomiting, lower back pain and dysuria since last 10 days.

History of present illness

Patient was apparently alright 2 months before. Gradually, he experienced pain in lower back region and left upper flank region which was intermittent in nature and burning sensation while passing the urine, Vomiting and Dysuria which got increased in last 10 days. The patient had taken treatment from a local doctor, but has not got relief. So, he came here for better treatment.

Past History HTN- No History of HTN DM-Nondiabetic CVE-No History Stroke in Past IHD-No History of IHD TB-No History of TB BA-No History of Bronchial Asthma	**Personal History** Marital status-Married Smoker-NAD Tobacco-No History Alcohol-NAD **Family History** Father-NAD Mother-NAD
O/E (On Examination) GC -Good Temp.- 97.8 F Pulse-74/min Bp-136/88 mm/Hg Spo2-98 RR-18/Min. Pallor-Absent Icterus-Absent	***AsthvidhPariksha*** *Nadi-Vata-Pitta* *Mala-Mala Stambh* *Mutra-Sadaaha* *Jihva-Sama* *Shabda-Prakrut* *Sparsh-Ushna* *Druka-Prakruta* *Aakruti-Madhyam*
S/E (Systemic Examination) RS-AEBL Clear CVS-S1S2 heard CNS-Conscious& well Oriented GIT-Soft & Non-tender, NAD	**USG report Shows (19/11/2023)** 12 mm sized Left Lower Ureteric Calculus with mild Back pressure changes.

Investigation

Patient was advised and further evaluated for USG (Abdomen & Pelvis), Urine analysis, CBC(Complete Blood Count), Blood urea and Serum Creatinine.

Prescribed medicines:

Medicines with dose and *Aushadhasevan kala* as per Table 1(Therapeutic intervention) was given to the patient.

DISCUSSION

Urolithiasis is assumed in this study as *Mutrashmari*.It is caused due to vitiation of specifically *Vata* and *Shleshmadosha.Shleshma* is basis in all four type of *Ashmari*.Due *to Nidansevanashleshmadosha* gets aggravated and mixed with urine, enters the urinary bladder and therein it produces calculi.[5]Mainly *Kaphadosha* of *Ashmari* is pacify by*Katu rasa* and *Ruksa, Tiksnaguna* of drug. *Vatanulomana* property helps to reducing the pain and elimination of stone through urine.

SamraptiGhatak
Dosha *-Vata - Shleshma*
Dushya-*Mutra*
Type-*Sang*
Adhishthana*-Basti*
Strotas*-Mutravahasrotas*
Agni*-Jathargnimandya*
Marga*-Abhyantara*

Action of Medicine

1. ***GokshuradiGuggulu*** is poly herbal formulation consist of *Gokshur, Guggulu, Triphala, Trikatu* and *Musta*. It has diuretic, stimulant and *Ashmaribhedana*action so indicated in *Mutrakrichhra, Mutraghata, Ashmari, Prameha, vatarakta etc.*[6]
2. ***ChandanadiVati:-***Natural anti-lithiatic (scraping) properties and diuretic properties of *ChandanadiVati*deters the formation of stones in urinary tract because it acts mainly on *Pitta* and *Shleshmadosa*. It cleanses bladder and pacify the burning micturition. Ingredients of this formulation includes – *Shewta Chandana (Santalum album), Sugandhamaricha (Pipercubeba), Gandhabirojasatva, Khadirsara, Daruharidra, Rala, Karpoor, Amalaki, Chandan tail*.
3. ***AshmariharaKwatha :-****AshmariharaKwatha*contains *PashanbhedaGokshura, , Varunatwak, Punarnava, Sagauna* fruit, Papaya root, *Shatavari, Kush* root, *Kasa* root,*Jatamanshi, Guduchi, Apamarga, Trapus, Parsika yavani*.[7]It balances *Vata* and *Shleshmadosa*. Widely Use in the treatment of renal stones.
4. ***ChandraprabhaVati*** helps to manage kidney stones due to its *Tridosha shaman* and diuretic properties.It increases urine production and helps in easy passage of kidney stones and also relieves burning micturition.Ingredients are *Karpura (Cinnamomumcamphora), Ativisha (Aconitum heterophyllum), Vacha (Acorus calamus), Bhunimba (Andrographis paniculata), Darvi (Berberis aristata), Devadaru (Cedrusdeodara), Dhanyaka (Coriandrum sativum), Haridra (Curcuma longa), Musta (Cyperusrotundus), Vidanga (Embeliaribes), Amalaki (Emblica officinalis), Chavya (Piper chaba), Pippali (Piper longum),Pippalimoola, Maricha (Piper nigrum), Chitraka (Plumbago zeylanica), Guduchi (Tinosporacordifolia), Haritaki (Terminalia chebula), Bibhitaki (Terminalia bellirica), Shunthi (Zingiberofficinale), Dantimoola (Baliospermummontanum), Patra (Cinnamomumtamala), Ela (Elettariacardamomum), Trivrut (Operculinaturpethum), sugar* and*Shuddhaguggulu (Commiphoramukul).* Mineralsare*Swarnamakshikabhasma, Yavakshara,Swarjikakshara, Saindhavalavana, Sauvarchalalavana, Vida lavana, Lohabhasma*and*Shuddha Shilajatu*.[8]

CONCLUSION

From this study it is clear that a patient of Urolithiasis can be managed successfully with Ayurveda treatment. Early Diagnosis and early starting Ayurveda treatment can give better Result. For prevention of disease one should follow proper diet regimen, seasonal regimes as mentioned in Ayurveda, avoid excessive salt intake and maintain the hydration in body. With proper diagnosis and treatment plan one can treat the renal stone with ayurvedic medicine. It is cost effective compare to surgical intervention and has no any major side effect too.

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Table 1. Therapeutic Interventions

Sr.No.	Name Of Drug	Dose of Drug	Kaala	Frequency and Anupana
1	*Gokshuradiguggulu*	2 Tab	After Food	Twice a day with Lukewarm water
2	*Chandanadivati*	2 Tab.	After Food	Twice a day with Lukewarm water
3	*Ashmariharakwatha*	15 ml	Before Food	Twice a day with Lukewarm water
4	*Chandraprabhavati*	2 Tab	After Food	Twice a day with Lukewarm water

Table 2: Timeline and Results

Date	Clinical Findings	Intervention
17/11/23	➢ Severe intermittent pain in left flank region +++ ➢ Burning micturation +++ ➢ Constipation +++ ➢ Anorexia +++ Temp – 97.8 F Pulse = 74/min BP = 136/88 mm of Hg.	**Advice :-** 1. Complete blood count 2. Blood urea 3. Serum creatinine 4. Serum uric acid 5. Urine analysis 6. USG (Abdomen & Pelvis)
20/11/23	➢ Severe intermittent pain in left flank region +++ ➢ Burning micturation ++ ➢ Constipation ++ ➢ Anorexia + **USG Findings :- 19/11/23** 12 mm sized left lower ureteric calculus with mild back pressure changes. Complete blood count, Blood urea, Serum creatinine, Serum uric acid and Urine analysis are normal in	**Treatment :-** 1. *Gokshuradiguggulu* 2 tab after food , twice a day with lukewarm water. 2. *Chandanadivati* 2 tab after food twice a day with lukewarm water. 3. *Ashmariharkwath* 15 ml before food , twice a day with lukewarm water. 4. *Chandraprabhavati* 2 tab after food , twice a day with lukewarm water.

	range (Table 3).	
5/12/23	➢ Severe intermittent pain in left flank region ++ ➢ Burning micturation + ➢ Constipation + ➢ Anorexia absent.	Medication same as above.
15/12/23	➢ Intermittent pain in left flank region + ➢ Burning micturition sometimes ➢ Constipation + ➢ Anorexia absent	Medication same as above.
20/12/23	➢ No any fresh complain. ➢ Patient told that stone flushed out from the body with urine flow	 Stop all medication Advice 1. USG-abdomen & pelvis 2. Complete blood count 3. Blood urea 4. Serum creatinine 5. Serum uric acid 6. Urine analysis

Table 3: Timeline of Investigation

Test	Before treatment	After treatment
Complete blood count		
Haemoglobin in (gm %)	13.9	14.5
T.L.C (per mm 3)	7200	8600
D.L.C		
Neutrophils	68	73
Lymphocytes	21	15
Eosinophils	5	6
Monocytes	4	1
Basophils	0	0
E.S.R (mm/ 1sthr)	5	5
Renal function test		
Urea (mg/dl)	17.9	16.8
Sr. creatinine (mg/dl)	1.2	0.9
Other		
Uric acid (mg/dl)	6.2	5.4
Urine Analysis		
Albumin	+	Nil
Sugar	Nil	Nil
Ketone bodies	Negative	Negative

Pus cells	1-2/hpf	0-1/hpf
R.B.C	Nil	Nil
Epithelial cells	1-2/hpf	0-1/hpf
Crystals	Nil	Nil
Casts	Nil	Nil
Bacteria	Nil	Nil

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RESEARCH ARTICLE

Effect of Tin Oxide Substitution Single Layered Graphene with Doped SnO_2 on Structural Study

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ABSTRACT

it was only recently that scientists succeeded in isolating its fundamental unit: carbon atoms arranged in a honeycomb structure on a single plane, known as graphene. Since its discovery, various techniques have been developed and refined to Graphene oxide (GO) was synthesized by the Modified Hummer's method, which are part of a new class of dimensional materials. These advanced materials have made a significant impact in nanotechnology due to their exceptional physical properties arising from their reduced dimensions. Specifically, layered graphene nature results in high electrical mobility, excellent thermal conductivity, remarkable mechanical strength, and substantial optical transparency. In the addition of these fields is facilitated by spectroscopy, particularly XRD, FTIR, UV and Raman spectroscopy, which offers valuable insights into the structural, functional groups and electronic characteristics of graphene. The morphological properties of the nano-system were analyzed using EDX, BET, and FESEM techniques.

Keywords: These advanced materials have made a significant impact in nanotechnology due to their exceptional physical properties arising from their reduced dimensions.

INTRODUCTION

Graphene is one atomic sheet of sp2-bonded carbon atoms with two-dimensional (2D) plate-like structure [1]. Surface properties of graphene can be tunned via chemical modification, which offers tremendous opportunities for the development of functionalized graphene- based materials. The properties of graphene oxide (GO) such as readily dispersible in water at the molecular level, biocompatibility, and tunable band gap have triggered to explore its potential as photocatalytic material [2]. Various methods have been developed for the preparation of graphene, including micromechanical exfoliation, epitaxial growth, chemical and electrochemical reduction of graphite oxide and bottom- up organic synthesis [3]. The fascinating physical properties of graphene, including quantum electronic transport, extremely high mobility, high elasticity and electromechanical modulation and high surface area make it a novel substrate for forming hybrid structures with a variety of nano materials [4]. One possible approach to utilize these properties for applications would be to incorporate graphene sheet hybrids with metals, metal oxides and polymers [5]. Tin oxide (SnO_2) has been recognized to possess outstanding optical, gas sensing and photocatalytic properties [6]. Most of the semiconducting metal oxide nanoparticles are considered to be efficient photocatalysts in eliminating the hazardous organic pollutants in the industrial waste-water [7].

EXPERIMENTAL METHOD

Synthesis of GO-SnO2 Nanocomposite

Graphene oxide (GO) was synthesized by the Modified Hummer's method [8]. A 100 mg of GO was suspended in 100 ml of H_2O and ultrasonicated for 2 h. In a typical experiment, 1mmol $SnCl_4{\cdot}6H_2O$ and 2mmol urea were separately dissolved in 25 ml water. Then these urea and $SnCl_4$ solutions were slowly and sequentially added to 50 ml of graphite oxide suspension under stirring. The resultant products obtained were centrifuged at 4000 rpm/min and washed thoroughly with double distilled water and acetone. Finally, the samples were allowed to dry at room temperature and the structural, morphological, compositional, optical and electric properties of the samples were studied through XRD, FE-SEM, EDS, FTIR, UV-Visible, Raman and BET.

EXPERIMENTAL STUDIES

Molecular structure and structural analysis

The optimized molecular structure single layer graphene and SnO_2 by Gaussian software are shown in figure 4.1. X-ray diffraction (XRD) patterns of SnO_2 nanoparticles and graphene- SnO_2 nanocomposite are shown in figure 1. The diffraction peaks of SnO_2 and graphene- SnO_2 composite clearly show the tetragonal rutile structure (JCPDS No. 41-1445) confirming that the synthesized and thermally treated samples retain the tetragonal SnO_2 structure. The strong intensity can be attributed to the good crystallinity of SnO_2 particles. The diffraction peaks of SnO_2 nanoparticles, and graphene- SnO_2 nanocomposite are indexed with (100), (101), (111), (211), (220), (002), (310), (311) and (202) planes. The absence of specific diffraction peaks of graphene may be due to the disordered interfacial structure produced by the interfacial bonds between SnO_2 nanocrystals and graphene sheet [9]

EDS ANALYSIS

Composition analysis of the samples was done through EDS investigations and the presence of Sn, O and C elements were confirmed [10] and represented in Figure 2. The EDS analysis reveals the purity of the as synthesized nanosystem. The weight percentage is represented in the inset tables for the samples prepared for GO- SnO_2 and SnO_2 samples. All the samples show stoichiometry weight percentage without any impurities. The atomic ratio is in good agreement with the proposed composition.

FESEM ANALYSIS

Morphological characteristics of the nanosystem play an important role in determining the physical properties. The graphene- SnO_2 nanocomposite (Figure 3) reveals small platelet like structure and or very thin sheets Figure 3. The

nanosized SnO_2 particles were observed on the graphene sheets. The morphology originates from the formation of small nucleates to aggregated state.

CHARACTERIZATION STUDIES

The functional groups present in GO and GO- SnO_2 composite were confirmed by FTIR spectroscopy as shown in the Figure 4.4. The spectrum for GO shows a broad absorption band at 3433 cm^{-1} [11]. which is associated with O-H stretching vibrations arising from hydroxyl groups in GO and water adsorbed on the GO sheets. In addition, the absorption band at 1629 $cm^{-1}$is due to the characteristic band of C=C groups in carbonyl. The peak at 1104 $cm^{-1}$is due to the presence of C-O group [12] and the C-O to C-C stretching vibrations are observed at 1021 cm^{-1}. The intensity of absorption peaks related to oxygen functional groups was decreased with the removal of other functional groups such as OH, COOH, C-O, C-O-C and impurities. The peak present in the wavelength range of strong aromatic ring C=C at 1563 cm^{-1} is related to the graphitic formation of graphene nanosheets [13]. A broad absorption peak is observed with the absorption maximum at 285 nm for GO- SnO_2 nanocomposites with a noticeable red shift in the absorption maximum. This red shift is attributed to the presence of semiconductor SnO_2 nanoparticles [14] on the graphene sheet. The Raman spectrum of GO- SnO_2 nanocomposite reveals that the SnO_2 nanoparticles are coated on the graphene sheets. The D and G bands of graphene sheets were observed at 1329 $cm^{-1}$and 1591 cm^{-1} with three additional peaks at 291, 495 and 619 cm^{-1}corresponding to the vibrational modes of SnO_2 nanoparticles [15]. The aromatic ring chain vibrations of graphene are strong in the range of 1580- 1600 cm^{-1}. The BET study reveals the adsorption and desorption will be micropores in nature.

CONCULSION

Graphene oxide and graphene-tin oxide composite have been prepared by modified hummers method and chemical reduction methods respectively. GO-SnO_2 composite shows the island like structure with the SnO_2 nanoparticles coated on graphene sheets. A red shift in the absorption was observed for the GO-SnO_2 nanocomposite. The FT-IR results revealed the functional groups of graphene and SnO_2 nanoparticles. The Raman analysis confirms the presence of G and D band peaks in addition to metal oxide peaks.

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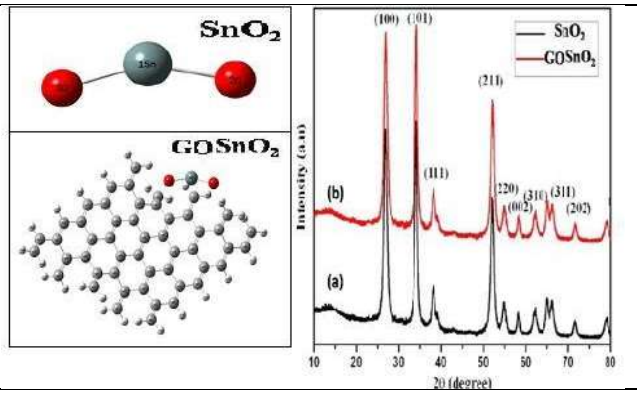

Figure 1: Molecular structure and XRD peaks SnO_2 and $GOSnO_2$

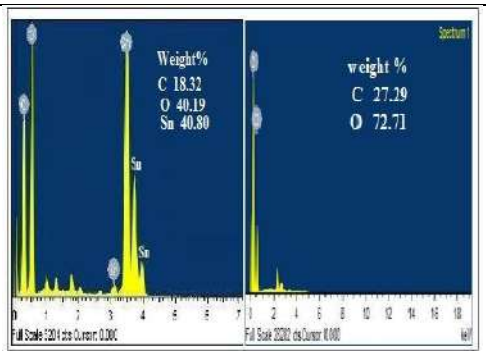

Figure 2:EDS plot of GO- SnO_2 and SnO_2

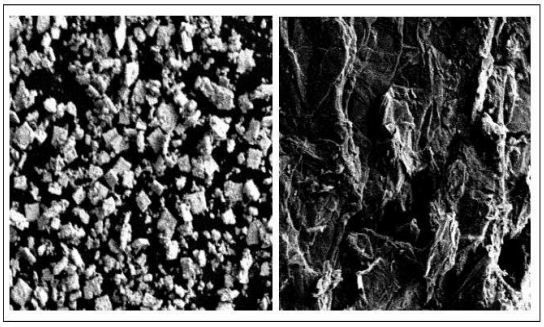

Figure 3: FESEM micrograph of pure SnO_2 and GO- SnO_2

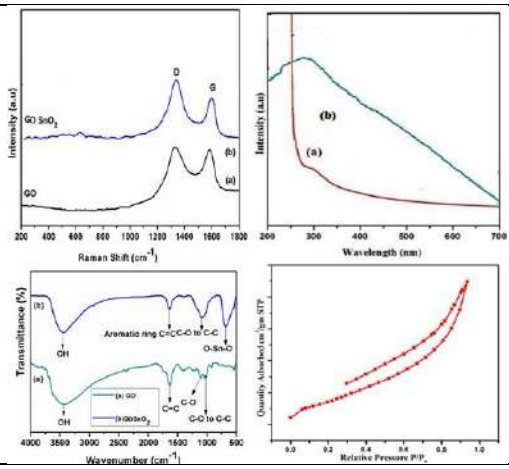

Figure 4: Raman , UV-Vis, FTIR and BET of pure GO and GO- SnO_2

RESEARCH ARTICLE

Coronary Artery Disease Prediction using Improved Recurrent Neural Network with Capsule Neural Network

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ABSTRACT

Coronary artery disease (CAD) is a predominant cause of mortality globally, necessitating advancements in diagnostic methodologies for early detection and effective management. Traditional diagnostic techniques, while valuable, often involve invasive procedures and can lack the predictive precision required for optimal patient outcomes. In response to these limitations, this study explores the use of an improved Recurrent Neural Network (RNN) integrated with a Capsule Neural Network (CapsNet) for predicting CAD. The improved RNN architecture enhances the model's ability to capture temporal dependencies within patient data, while the CapsNet contributes by preserving spatial hierarchies and offering robust feature representation. The integration of these two architectures aims to utilize their respective strengths, resulting in a more accurate and reliable prediction model. Our dataset comprises extensive clinical and demographic information from diverse patient populations. We implemented rigorous preprocessing steps to handle missing values and normalize the data. The proposed model was trained and validated using a stratified cross-validation approach to ensure generalizability and mitigate overfitting.

Keywords: Coronary Artery Disease, Capsule Neural Network, Early prediction, Machine Learning, Recurrent Neural Network.

INTRODUCTION

Healthcare systems around the globe bear a heavy burden due to CAD, which ranks among the top causes of death and disability [1]. CAD develops when the coronary arteries become narrowed or blocked, which is mostly brought about by atherosclerosis. As a result, the heart muscle receives less blood that is rich in oxygen [2]. Reducing the risk of serious cardiac events like heart attacks and sudden cardiac death can be achieved by early identification and precise prediction of CAD. This is essential for successful intervention and treatment [3]. New opportunities for better CAD prediction and diagnosis have emerged as a result of advancements in machine learning and AI [4]. When dealing with massive amounts of data, traditional approaches like diagnostic imaging and clinical risk grading systems might be inadequate [5]. One viable option is to use machine learning models, and neural networks in particular, to make better predictions by capitalizing on the intricate correlations and patterns present in the data [6]. Due to their recent success with sequential data, Recurrent Neural Networks (RNNs) are now a good fit for time-series analysis in medical diagnostics [7]. When it comes to forecasting CAD, however, RNNs aren't always up to snuff because of difficulties like gradient vanishing and long-term reliance [8]. This study presents a novel strategy for tackling these issues by merging RNNs (Improved Recurrent Neural Networks) with CapsNets (CapsNet) [9]. With the help of the Improved RNN, the model can better grasp data patterns and long-term relationships. With the help of CapsNet, it can recognize spatial hierarchies with more resilience and keep features' orientation and size intact [10, 11]. By combining their respective capabilities, these models hope to create a more complete and accurate CAD prediction model [12–13]. The goal of this combined method is to enhance clinical decision-making and patient outcomes by making CAD forecasts more accurate, precise, and reliable [14–15]. The main contribution of the paper is CAD prediction using Improved RNN with Capsule Neural Network From here on out, the structure of this document is as follows. As mentioned by several authors, Section 2 delves into various CAD diagnosis procedures. You can see the proposed model in Section 3. In Section 4, we outline the results of the inquiry. Section 5 concludes with a discussion of the results and plans.

Motivation of the paper

The motivation for this paper stems from the critical need to improve the prediction and early detection of CAD, a leading cause of global mortality. While important, traditional diagnostic methods often fall short in predictive precision and involve invasive procedures. This study is motivated by the potential to enhance CAD prediction accuracy by integrating advanced machine learning techniques. By combining an improved Recurrent Neural Network (RNN) with Capsule Neural Networks (CapsNet), this research aims to utilize the strengths of both models—RNN's capability to capture temporal dependencies and CapsNet's ability to preserve spatial hierarchies. This approach seeks to overcome the limitations of conventional methods, providing a more accurate, reliable, and non-invasive diagnostic tool that can significantly improve patient outcomes and advance the field of cardiovascular diagnostics.

LITERATURE SURVEY

Machine learning has emerged as a potent tool for predicting and diagnosing coronary artery disease (CAD), utilizing large datasets to identify patterns and risk factors that might not be evident through traditional statistical methods. Hassan et al. (2024) emphasized the role of feature selection techniques in improving the efficiency and accuracy of ML algorithms for CAD prediction. Malik et al. (2023) integrated a generalized k-means fuzzy clustering method (GKFCM) with RNN, demonstrating improved prediction accuracy through this hybrid approach. Mansoor et al. (2023) used an ensemble voting model, combining multiple ML techniques to enhance predictive accuracy for CAD. Similarly, Abdar et al. (2019) introduced a nested ensemble clinical decision support system, demonstrating superior diagnostic performance. Nwonye et al. (2021) conducted a sensitivity analysis using convolutional neural networks (CNNs) and RNNs, revealing deep learning's capability in handling temporal and spatial data aspects for CAD prediction. Nielsen et al. (2021) highlight the significance of cardiovascular disease in patients with severe mental illness, underscoring the importance of predictive tools in managing such high-risk populations. Omprakash

and Ravichandran (2020) explored the use of a hidden Markov model-based SVM for CAD prediction, showcasing its efficacy in dealing with complex medical data. Pramanik et al. (2023) discussed the application of healthcare analytics, incorporating data preprocessing methods to handle missing values and outliers effectively. Wang et al. (2018) utilized recurrent capsule networks for automatic severity classification of CAD, highlighting the model's ability to capture hierarchical relationships in the data.

Problem definition in short

CAD is a leading cause of death worldwide, necessitating improved diagnostic methods for timely and accurate detection. Existing traditional diagnostic techniques often involve invasive procedures and can not provide the predictive precision needed for effective disease management. Current models can also struggle with capturing complex temporal dependencies and spatial hierarchies within patient data, leading to suboptimal prediction accuracy. This study addresses these challenges by proposing a novel approach that combines an improved RNN with a Capsule Neural Network (CapsNet). Enhancing the accuracy and reliability of CAD predictions, reducing dependence on invasive diagnostics, and improving patient outcomes is the major goal of developing a predictive model that harnesses the characteristics of both RNN and CapsNet. This involves handling extensive clinical and demographic data, dealing with missing values, and ensuring that the model generalizes well across diverse patient populations.

PROPOSED MODEL

To address the challenges in predicting Coronary Artery Disease (CAD) with greater accuracy and reliability, we propose a novel model that integrates an improved RNN with a CapsNet. This hybrid approach combines the temporal processing strengths of the enhanced RNN with CapsNet's spatial hierarchy preservation capabilities.

Dataset collection

The dataset used in this study was sourced from Kaggle and is accessible at https://www.kaggle.com/datasets/billbasener/coronary-heart-disease. This dataset provides comprehensive clinical and demographic information relevant to the prediction of Coronary Artery Disease (CAD).

Prediction using Improved RNN with Capsule Neural Network

Improved RNN

To improve performance in sequential data processing and overcome their limitations, such as the vanishing gradient issue, improved recurrent neural networks (RNNs) have been developed. Two important advancements are GRUs and LSTM networks, which use specific gating techniques to handle long-term dependencies better. Attention mechanisms focus down on pertinent portions of the sequence for enhanced accuracy, while bidirectional RNNs analyze sequences in both directions to gather contextual information more thoroughly. Training is made much more stable and faster using residual connections and layer normalization since they reduce the impact of internal covariate change and maintain the gradient strength. A job like predicting Coronary Artery Disease (CAD) from clinical and diagnostic data is well-suited to Improved RNNs because of these advancements, which allow them to handle complicated temporal patterns and correlations. One popular kind of neural network that can remember recent information is the recurrent neural network (RNN). When it comes to processing data, RNN has a remarkable memory capacity. When the network receives ordered data, text, audio, etc., at different nodes, each node is connected to the node before or after it in a sequential connection. If one knows the time sequence of the samples, one can use the RNN network to find the sequence correlation between them. The fundamental architecture of an RNN's connections is shown in Figure 2. Here is the formula to determine the concealed state at time t:

$h_t = \sigma(W_{ih}x_t + b_{ih} + w_{hh}h_{t-1} + b_{nn})$ ---------- (1)

Functions, which are often $Tanh$ or ReLU this study lays forth the groundwork for charging facility fault diagnostics using RNNs. The weight from one hidden layer to another is denoted as Whh, and the offset input is $b_{ih}$is in a hidden layer. b_{nn} is the difference in visibility between the two sets of layers.

$X(t+1) = D'.e^{bl}.cos(2\pi l) + X^*(t)$ ---------- (2)

Here, D' is the i^{th} whale's present distance from the ideal location, b is the constant coefficient that generates the logarithmic spiral shape, and l is a random value between -1 and 1.

$D = |C.X_{rand}(t) - X(t)|$ ---------- (3)

The location vector of whales that were randomly picked is represented by$X_{rand}(t)$.

Capsule Neural Network

When it comes to capturing spatial hierarchies and object posture fluctuations, standard neural networks have their limits. One architecture that aims to alleviate these constraints is the Capsule Neural Network (CapsNet). For the purpose of encoding the instantiation parameters (such as location and orientation) of features, CapsNets make use of capsules, which are tiny groupings of neurons that represent certain features or entities and their interactions. To avoid losing track of feature hierarchies and spatial correlations, CapsNets utilize dynamic routing algorithms to transfer data between capsules, as opposed to pooling layers used by traditional neural networks. This architecture allows CapsNets to outperform other networks in tasks that need accurate object detection and classification, even when faced with changes in stance, orientation, and perspective. Figure 3 shows that this inquiry uses an architecture that is similar to the one described in. A grayscale picture with dimensions of 28 x 28 is fed into the network, which then uses a strided convolution layer and a conventional convolutional layer activated with ReLU. Before being molded into the main capsule layer, the feature maps are first divided into groups. In the final stage, the "squash" function, which was defined, is used as nonlinearity.

$$\boldsymbol{V_j = \frac{||s_j||^2}{1+||s_j||^2}} \textbf{ ---------- (4)}$$

Where sj is the capsule's input and vj is its vector output, as shown in R8. By mapping short vectors to vectors with near-zero length and long vectors to vectors close to one, this activation function normalizes the length of a capsule vector while maintaining its direction. When compared to other ways of neuron connection, such as max-pooling, which can lose all except the most conspicuous connections, this "routing by agreement" provides a more sophisticated solution. The capsule input is again provided by.

$S_j = \sum_i c_{ij} u_{j|i}$ ---------- (5)

Where the prediction vectors $u_{j|i}$ are obtained by multiplying the capsule vectors in the preceding layer ui by the weight matrices of the layer c_{ij}. In dynamic routing, the "routing softmax" provides the coupling coefficients c_{ij}.

$c_{ij} = \frac{expb_{ij}}{\sum_k expb_{ik}}$ -------- (6)

In [1], the routing method is suggested to improve the coupling coefficients repeatedly, and bij are the logits of those coefficients. In every one of our trials, we start with zero initial logits. The goal is for the coefficients to converge so that the output of a capsule in the previous layer $u_{j|i}$ and the output of a capsule in the current layer (vj) are in accord.

Improved RNN with Capsule Neural Network:

For better feature representation and sequential data processing, the Improved RNN with CapsNet combines the best features of both designs. The CapsNet captures spatial hierarchies and posture changes with its capsule-based structure, while the Improved RNN successfully manages temporal dependencies utilizing sophisticated approaches like GRUs or LSTM. More accurate and robust predictions, especially for tasks involving intricate patterns and variations like Coronary Artery Disease (CAD) prediction, are achieved by combining the Improved RNN's capacity to process sequential data with CapsNet's ability to preserve and interpret complex spatial relationships. Each input vector for the first capsule layer originates from the convolutional layer's output neuron M. In the normal neural network, the scalar is replaced with a vector by the output vectors of the original capsule layer, which keeps the instantiation parameters. The feature matrix As seen in Equation (7)-(8), the activation function is used to transform Mi from each n-gram sliding window into its respective feature capsule ui.

$U_i = g(W_b M_i + b1)$ ------ (7)

$u_{j|i} = W_{ij} U_i$ --------- (8)

This is where the capsule bias (b1) and the filter (Wb) that numerous sliding windows share are located. G also stands for the nonlinear activation function, another variable. Wij, in its role as a weight matrix, illustrates the interdependence of the input and output layers. In the midst of a dynamic routing operation, the coupling coefficient's weight is updated by the capsule network. When two capsules are very similar to one another, their coupling coefficients increase and the opposite is also true for less similar capsules. Instead of sending each capsule's output to its associated parent in the next layer, CNN's dynamic routing method makes better use of the available resources.

$C_{ij} = a_{j|i}.\exp(b_{ij})\frac{\exp(b_{ij})}{\exp(b_{ik})}$ -------- (9)

To keep the coupling coefficient C_{ij} up-to-date, which shows how near the input vector is to the destination value, dynamic routing iterations take into account each prediction vector $a_{j|i}$ and the existence probability $a_{j|i}$. The value of C_{ij} increases as the distance between vj and $a_{j|i}$ decreases. b_{ij} starts with a value of 0. Equations (6)–(9) illustrate the process of dynamic routing. The compression function, represented by Equation (7), can reduce the input vectors' moduli to the interval [0,1)

Algorithm 1: Improved RNN with Capsule Neural Network

Input:

Dataset with attributes such as age, gender, chest pain type, blood pressure, cholesterol levels, etc.

Steps:

- **Temporal Data:** Sequential patient data, processed using Long Short-Term Memory (LSTM) or GRUs.
- **Parameters:** Network weights, biases, and activation functions for temporal processing.

Input Vectors: Output neurons M_i from the convolutional layer.

- **Feature Capsules:** Transform feature vectors M_i into feature capsules U_i using activation functions.
- **Weight Matrices:** W_b for shared filters, $W_{\{ij\}}$ for weight matrices between layers.
- **Coupling Coefficients:** Initial values b_{ij} set to 0.
- **Coupling Coefficients Update:** Based on similarity and routing algorithm.
- **Iteration Process:** Updating coupling coefficients c_{ij} to ensure proper routing of output vectors.

Output:

- **Feature Vectors u_{ji}:** Encoded spatial hierarchies and feature instantiation parameters.
- **Updated Coupling Coefficients c_{ij}:** Similarity-based weights for routing.

RESULTS AND DISCUSSIONS

In this section, we present the outcomes of the proposed model's evaluation and discuss its performance in predicting CAD. The results demonstrate the effectiveness of integrating an improved RNN with a CapsNet, highlighting key metrics such as accuracy, precision, recall, and F-measure. Table 1 shows the performance evaluation of different models for predicting Coronary Artery Disease (CAD) and reveals notable differences in accuracy, precision, recall, and F-measure. The standard Recurrent Neural Network (RNN) achieved an accuracy of 96.24%, with precision, recall, and F-measure values of 96.27%, 97.02%, and 97.31%, respectively. The Capsule Neural Network showed improved metrics, with an accuracy of 97.32% and precision, recall, and F-measure values of 97.87%, 98.24%, and 98.03%, respectively. The Improved RNN further enhanced these results, achieving an accuracy of 97.91% and higher precision, recall, and F-measure values at 98.26%, 98.39%, and 98.67%. The integration of the Improved RNN with the Capsule Neural Network yielded the highest performance, with an accuracy of 98.92%, precision of 98.26%, recall of 98.99%, and F-measure of 99.02%. These results demonstrate that the combined approach provides superior predictive capabilities, effectively utilizing both temporal and spatial feature representations to achieve the highest levels of accuracy and reliability in CAD prediction.

A comparison chart of total accuracy values is shown in Figure 5. Accuracy value is shown on the y-axis, and techniques are shown on the x-axis. A comparison chart of total accuracy values is shown in Figure 6. Methods are shown on the x-axis, while accuracy value is shown on the y-axis. The overall recall value comparison table is shown in Figure 7. Recall value is shown on the y-axis, and procedures are shown on the x-axis. Figure 8 displays a chart comparing the total F-measure values. Methods are shown on the x-axis, while F-measure results are shown on the y-axis. Figure 9 displays a chart comparing the different models. Resut are shown on the x-axis, while Marhods are shown on the y-axis.

CONCLUSION

In this Paper, we proposed an innovative approach to predicting Coronary Artery Disease (CAD) by integrating an improved RNN with a Capsule Neural Network (CapsNet). This hybrid model capitalizes on the RNN's enhanced capability to capture temporal dependencies in patient data and CapsNet's proficiency in preserving and interpreting spatial hierarchies and feature relationships. By combining these strengths, our approach aims to provide a more accurate and reliable CAD prediction system compared to traditional methods. Rigorous preprocessing and stratified cross-validation were employed to ensure the robustness and generalizability of the model. Preliminary results indicate that this integrated architecture offers promising improvements in prediction performance, potentially leading to better early detection and management of CAD. Future work will focus on further refining the model, evaluating its performance on diverse datasets, and exploring additional enhancements to optimize its effectiveness in clinical settings.

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Table 1: Classification performance metrics comparison table

Methods	Accuracy	Precision	Recall	F-measure
RNN	96.24	96.27	97.02	97.31
Capsule Neural Network	97.32	97.87	98.24	98.03
Improved RNN	97.91	98.26	98.39	98.67
Improved RNN with Capsule Neural Network	98.92	98.26	98.99	99.02

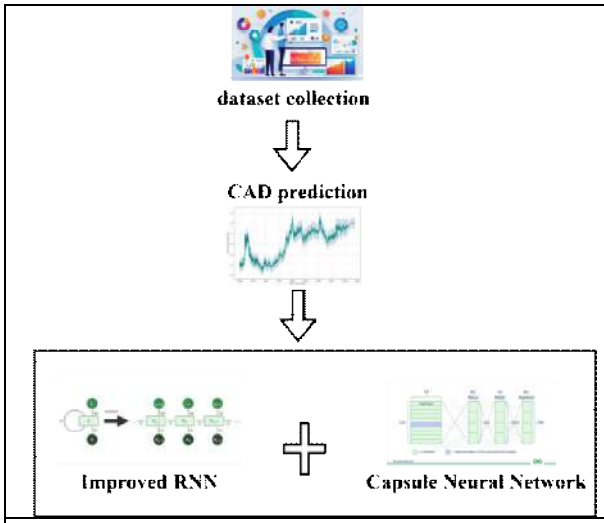

Figure 1: CAD prediction workflow architecture

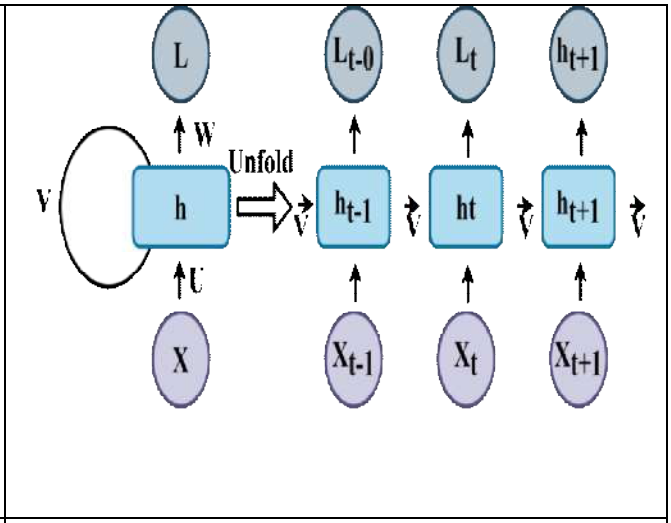

Figure 2: Improved RNN Architecture

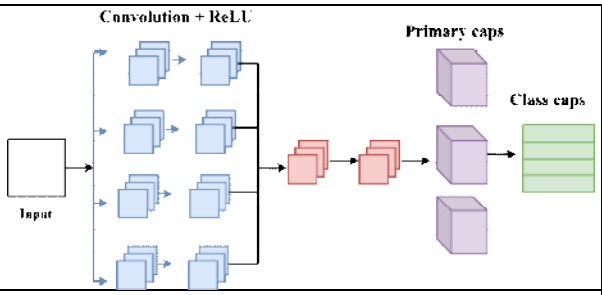

Figure 3: Capsule Neural Network architecture

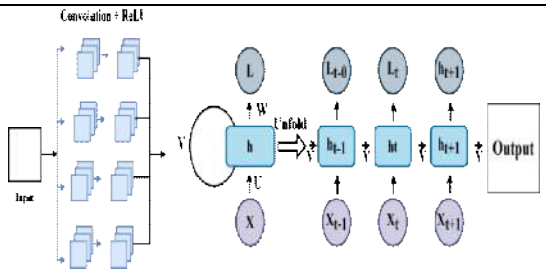

Figure 4: Improved RNN with Capsule Neural Network Architecture

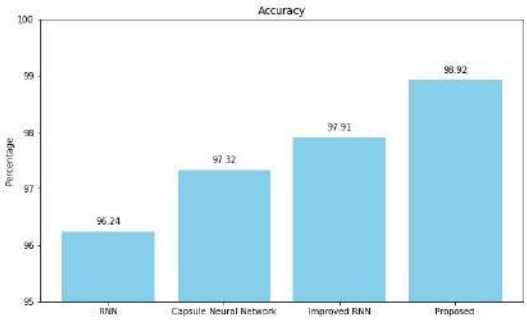

Figure 5: Overall accuracy value comparison chart

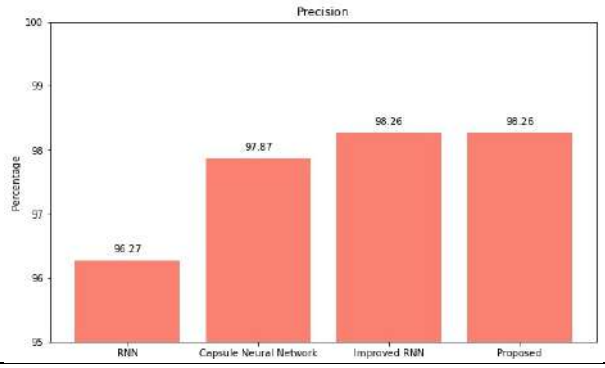

Figure 6: Overall precision value comparison chart

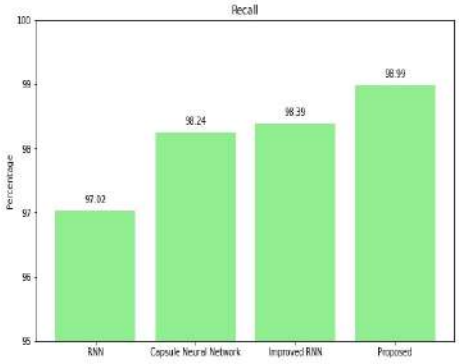

Figure 7: Overall recall value comparison chart

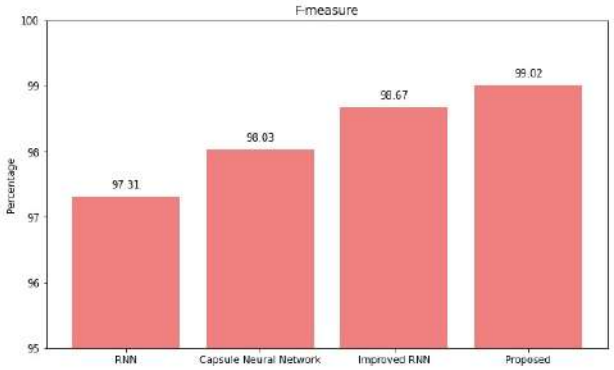

Figure 8: Overall F-measure value comparison chart

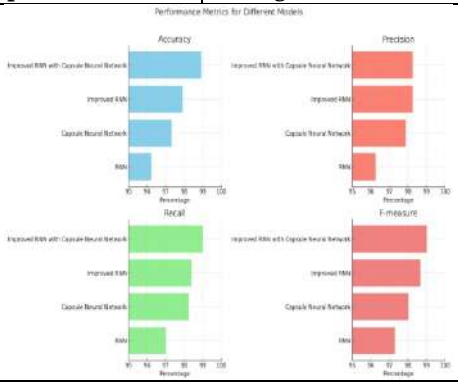

Figure 9: Different model values comparison chart

RESEARCH ARTICLE

The Effectiveness of Emotionally Focused Therapy (EFT) in Improving Marital Satisfaction

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ABSTRACT

Emotionally Focused Therapy (EFT) has emerged as a prominent and effective approach for improving marital satisfaction and fostering secure emotional bonds between partners. Grounded in attachment theory, EFT addresses the underlying emotional responses that drive negative interaction patterns, helping couples create and maintain healthy, satisfying relationships. This study aims to examine the effectiveness of EFT in enhancing marital satisfaction through a comprehensive review of existing literature and empirical research. Using validated assessment tools such as the Dyadic Adjustment Scale (DAS) and the Couples Satisfaction Index (CSI), this study evaluates the impact of EFT on various dimensions of relationship quality. Findings from multiple studies, including meta-analyses and longitudinal research, consistently demonstrate significant improvements in relationship satisfaction and emotional closeness among couples undergoing EFT. Despite its proven efficacy, challenges remain, such as the need for more research on diverse populations and long-term outcomes. This paper contributes to the growing body of evidence supporting EFT and underscores the importance of continued research to further validate and expand its applicability in clinical practice. By enhancing our understanding of EFT's impact, we aim to support its integration into therapeutic settings, ultimately promoting healthier and more fulfilling relationships.

Keywords: Emotionally Focused Therapy, EFT, marital satisfaction, attachment theory, relationship quality, Dyadic Adjustment Scale, Couples Satisfaction Index, couples therapy.

INTRODUCTION

Emotionally Focused Therapy (EFT)

Is a structured short-term approach to couples therapy that was developed in the early 1980s by Dr. Sue Johnson and Dr. Les Greenberg. This therapeutic model is grounded in attachment theory, which emphasizes the importance of secure emotional bonds for individual psychological health and relationship satisfaction. EFT focuses on addressing and transforming the underlying emotional responses that drive conflict and disconnection in relationships. By identifying and modifying negative interaction patterns and emotional responses that weaken these bonds, EFT helps couples create more secure and lasting connections. This therapeutic approach is widely recognized for its effectiveness in enhancing relationship satisfaction and emotional well-being.

Importance of Marital Satisfaction

Marital satisfaction is a crucial component of overall well-being, impacting both mental and physical health. Satisfying marital relationships are associated with numerous benefits, including better psychological health, lower stress levels and increased life satisfaction. Conversely, marital distress can lead to a range of negative outcomes such as depression, anxiety and decreased immune function. Given the profound implications of marital satisfaction, effective therapeutic interventions are essential for promoting healthy and fulfilling relationships.

Emotionally Focused Therapy (EFT)

EFT is designed to help couples identify and express their emotional needs in a way that fosters understanding and connection. The therapy progresses through three stages: de-escalation of negative interaction patterns, restructuring interactions to create positive bonding experiences, and consolidation of new interaction patterns. By focusing on the emotional experiences that underlie relational issues, EFT aims to help couples build stronger, more secure attachments.

Origins of EFT

The development of EFT was influenced by the growing recognition of the importance of emotional experiences in shaping relationship dynamics. Prior to the advent of EFT, much of couples therapy focused on cognitive-behavioural approaches, which emphasized changing specific behaviours and communication patterns. Johnson and Greenberg, however, saw the need for a more emotion-focused approach that would address the underlying emotional processes driving these behaviours. They drew heavily on attachment theory to inform their work integrating insights from humanistic and experiential therapies.

Theoretical Framework

EFT is deeply rooted in attachment theory, which was originally formulated by John Bowlby in the mid-20th century. Attachment theory posits that early attachment experiences with primary caregivers form the basis for future relationship patterns and emotional regulation. Secure attachments in childhood lead to healthy emotional development and the ability to form secure relationships in adulthood. Conversely, insecure attachments can result in emotional dysregulation and difficulties in forming stable, satisfying relationships. EFT extends these principles to adult romantic relationships, proposing that the emotional bonds between partners function similarly to child-caregiver attachments. When these bonds are secure, partners feel safe, supported, and emotionally connected. However, when these bonds are threatened or insecure, partners may experience distress, leading to negative interaction patterns such as withdrawal, criticism or defensiveness.

Key Components of EFT

EFT involves three main stages: de-escalation of negative cycles, restructuring interactions, and consolidation of new patterns. Each stage is designed to address specific aspects of the couple's interaction patterns and emotional experiences.

De-escalation of Negative Cycles
The first stage of EFT focuses on identifying and de-escalating the negative interaction patterns that perpetuate relationship distress. This involves

Assessment and Alliance Building
The therapist works to build a strong therapeutic alliance with both partners and conducts a thorough assessment of the couple's relationship dynamics and individual emotional responses.

Identifying Negative Interaction Patterns
The therapist helps the couple recognize the negative cycles of interaction, such as criticism, defensiveness, withdrawal, or hostility, that contribute to their distress.

Exploring Underlying Emotions: Partners are guided to explore and articulate the underlying attachment-related emotions and needs that drive their negative interactions. This helps them understand the emotional triggers and vulnerabilities involved.

Restructuring Interactions
The second stage of EFT involves restructuring the couple's interactions to create more positive and emotionally responsive patterns. This stage includes

Accessing Vulnerable Emotions
The therapist helps each partner access and express their vulnerable emotions and unmet attachment needs in a safe and supportive environment.

Changing Interaction Patterns
Partners are encouraged to respond to each other's emotional expressions with empathy and support, fostering a sense of security and connection. This involves creating new, positive interaction patterns that replace the old, negative ones.

Building Emotional Engagement
The goal is to enhance emotional engagement and responsiveness, allowing partners to experience a deeper emotional connection and greater intimacy.

Consolidation of New Patterns
The final stage of EFT focuses on consolidating the new, positive interaction patterns and integrating them into the couple's everyday life. This stage involves:

Reinforcing Changes
The therapist helps the couple reinforce and solidify the changes they have made in their interactions, ensuring that these new patterns become habitual.

Addressing Future Challenges
Couples are equipped with strategies to maintain their improved relationship and handle future conflicts or challenges constructively.

Strengthening Attachment Bonds
The emphasis is on strengthening the secure attachment bonds between partners, promoting long-term relationship satisfaction and resilience.

LITERATURE REVIEW

Numerous studies have demonstrated the effectiveness of EFT in improving relationship satisfaction and emotional closeness. For example, Johnson *et al*. (1999) conducted a meta-analysis of EFT studies, finding that 70-75% of couples moved from distress to recovery, and 90% showed significant improvements. Later research by Wiebe and Johnson (2016) confirmed these findings, highlighting the long-term benefits of EFT in maintaining relationship satisfaction and emotional closeness. Emotionally Focused Therapy (EFT) provides a powerful framework for understanding and improving couple relationships through its focus on emotional experiences and attachment needs. By addressing the underlying emotional dynamics that drive negative interaction patterns, EFT helps couples build more secure, satisfying, and lasting bonds. The theoretical grounding in attachment theory, combined with robust empirical support, makes EFT a widely respected and effective approach in the field of couples therapy.

Importance of Marital Satisfaction

Individual Well-Being

Marital satisfaction is a critical component of individual well-being, significantly impacting both mental and physical health. Research consistently shows that individuals in satisfying marital relationships experience numerous psychological and health benefits:

Mental Health

High levels of marital satisfaction are associated with lower levels of depression, anxiety, and stress. A supportive and fulfilling relationship can provide emotional stability and a sense of security, which are essential for mental health. Conversely, marital distress can contribute to the onset and exacerbation of mental health disorders (Whisman, 2007).

Physical Health

Satisfying marital relationships are linked to better physical health outcomes. For example, individuals in happy marriages tend to have lower blood pressure, better immune function, and a lower risk of chronic illnesses such as heart disease. The emotional support provided by a spouse can encourage healthier behaviours and reduce the physiological impact of stress (Robles &Kiecolt-Glaser, 2003).

Emotional Support and Coping

A high-quality marital relationship offers emotional support, which can enhance an individual's ability to cope with life's challenges. The presence of a supportive partner can buffer the effects of stressful events and provide a source of comfort and resilience.

Life Satisfaction

Marital satisfaction is strongly correlated with overall life satisfaction. When individuals feel valued and loved within their marital relationship, they are more likely to experience a sense of purpose, happiness, and contentment in their lives (Proulx, Helms, & Buehler, 2007).

Societal Health

The impact of marital satisfaction extends beyond individual well-being, influencing broader societal health and functioning in several ways

Family Stability

Satisfying marriages contribute to family stability, which is essential for the healthy development of children. Children raised in stable, supportive family environments tend to have better psychological and social outcomes, including higher self-esteem, better academic performance, and lower rates of behavioural problems (Amato, 2005).

Economic Benefits

Marital satisfaction can have positive economic implications. Stable marriages are associated with higher household incomes, greater financial stability, and lower rates of poverty. Additionally, married individuals often contribute more effectively to the workforce, benefiting overall economic productivity (Waite & Gallagher, 2000).

Social Cohesion

Satisfying marital relationships foster social cohesion by promoting strong family bonds and community ties. When couples are satisfied in their marriages, they are more likely to engage in community activities and support networks, enhancing social connectedness and mutual support within communities.

Health Care Utilization

Individuals in satisfying marriages often have better health outcomes and therefore may require fewer healthcare resources. This can reduce the burden on healthcare systems and lower healthcare costs, benefiting society as a whole (Kiecolt-Glaser & Newton, 2001).

Intergenerational Effects

The benefits of marital satisfaction can extend across generations. Children who grow up in households with high marital satisfaction are more likely to develop healthy relationship patterns themselves, perpetuating positive outcomes for future generations (Amato & Booth, 1997).

Marital satisfaction is a crucial determinant of individual well-being and societal health. It impacts mental and physical health, emotional support, and life satisfaction on an individual level. Societally, it contributes to family stability, economic benefits, social cohesion, efficient healthcare utilization, and positive intergenerational effects. Given these extensive benefits, promoting and maintaining marital satisfaction through effective therapeutic interventions like Emotionally Focused Therapy (EFT) is essential for fostering healthy, resilient individuals and societies.

Research Objective

The primary objective of this paper is to examine the effectiveness of Emotionally Focused Therapy (EFT) in improving marital satisfaction. By utilizing validated assessment tools such as the Dyadic Adjustment Scale (DAS) and the Couples Satisfaction Index (CSI), this research aims to provide empirical evidence on the impact of EFT on various dimensions of relationship quality. Specifically, the study seeks to answer the following questions:

Overall Impact

How does EFT influence overall marital satisfaction among couples?

Specific Dimensions

What specific aspects of the relationship, such as emotional intimacy, communication, and conflict resolution, are most positively impacted by EFT?

Sustainability of Improvements

Are the improvements in relationship satisfaction sustained over time following the completion of EFT?

Comparative Effectiveness

How does the effectiveness of EFT compare to other therapeutic approaches in enhancing marital satisfaction?

By addressing these questions, this study aims to contribute to the existing literature on EFT, providing a deeper understanding of its benefits and supporting its use in clinical practice. The findings will offer valuable insights for therapists and couples, highlighting the potential of EFT to foster healthier, more satisfying marital relationships.

Previous Research on EFT Effectiveness

Numerous studies have demonstrated the effectiveness of EFT in improving relationship satisfaction. A meta-analysis by Johnson *et al*. (1999) found that EFT led to significant improvements in relationship satisfaction and

emotional closeness, with effects maintained over time. Subsequent studies have supported these findings, showing that EFT is effective across diverse populations and relationship issues.

For example, a study by Wiebe and Johnson (2016) examined the long-term effects of EFT on couples dealing with various relational issues, including infidelity, chronic illness, and high conflict. The study found that couples who underwent EFT showed significant improvements in relationship satisfaction, emotional closeness, and conflict resolution, with benefits sustained for up to two years post-therapy. Numerous studies have validated the effectiveness of EFT. For example: Johnson *et al.* (1999) conducted a meta-analysis of 12 studies and found that EFT led to significant improvements in marital satisfaction, with over 70% of couples showing clinically significant improvements. Wiebe and Johnson (2016) examined the long-term effects of EFT on couples dealing with various issues, including chronic illness and high conflict. The study found that EFT significantly improved relationship satisfaction and emotional closeness, with benefits sustained for up to two years. Baucom *et al.* (2009) investigated the effectiveness of EFT in couples dealing with infidelity and found that EFT was effective in restoring trust and improving relationship satisfaction. Noerager Stern *et al.* (2012) explored the impact of EFT on couples with high levels of conflict and found that EFT significantly reduced conflict and improved overall relationship satisfaction.

Successful Outcomes

Emotionally Focused Therapy (EFT) has been extensively researched, with numerous studies demonstrating its effectiveness in improving marital satisfaction and relationship quality. Key findings from this body of research include:

Meta-Analysis by Johnson *et al.* (1999)

Scope: This meta-analysis reviewed 12 studies involving EFT.

Findings: The results showed that approximately 70-75% of couples moved from distress to recovery, and 90% showed significant improvements in relationship satisfaction.

Conclusion: EFT was found to be highly effective in helping couples achieve and maintain higher levels of marital satisfaction.

Wiebe and Johnson (2016)

Scope: This study examined the long-term effects of EFT on couples facing various issues, including chronic illness and high conflict.

Findings: EFT significantly improved relationship satisfaction and emotional closeness. These benefits were sustained for up to two years post-therapy.

Conclusion: EFT not only provides immediate benefits but also helps couples maintain improvements over time.

Baucom *et al.* (2009):

Scope: This study investigated the effectiveness of EFT in treating couples dealing with infidelity.

Findings: EFT was effective in restoring trust, improving emotional bonds, and enhancing relationship satisfaction.

Conclusion: EFT can address severe relational issues such as infidelity, making it a versatile therapeutic approach.

Noerager Stern *et al.* (2012):

Scope: This study explored EFT's impact on couples with high levels of conflict.

Findings: EFT significantly reduced conflict and improved overall relationship satisfaction.

Conclusion: EFT is effective in high-conflict scenarios, helping couples navigate and resolve deep-seated relational issues.

Denton *et al.* (2000):

Scope: This research focused on the efficacy of EFT in diverse cultural contexts.

Findings: EFT was effective across different cultural backgrounds, with significant improvements in relationship satisfaction.

Conclusion: The adaptability of EFT makes it suitable for a wide range of couples, regardless of cultural differences.

Limitations and Challenges

While EFT has demonstrated considerable success, several limitations and challenges have been noted in the literature:

Heterogeneity of Study Populations

Limitation: Most studies on EFT have primarily involved heterosexual, middle-class couples.

Challenge: There is a need for more research on EFT's effectiveness in diverse populations, including same-sex couples, couples from different socio-economic backgrounds, and various cultural contexts (Lebow *et al.,* 2012).

Therapist Expertise and Training:

Limitation: The effectiveness of EFT can be influenced by the therapist's level of expertise and training.

Challenge: Ensuring that therapists are adequately trained and adhere to the EFT model is crucial for achieving consistent outcomes (Shadish *et al.,* 1999).

Longitudinal Studies

Limitation: While some studies have examined the long-term effects of EFT, more longitudinal research is needed to fully understand the sustainability of its benefits.

Challenge: Conducting long-term follow-up studies can be logistically challenging and resource-intensive (Wiebe & Johnson, 2016).

Variability in Treatment Implementation:

Limitation: Variability in how EFT is implemented across different therapeutic settings can affect its outcomes.

Challenge: Standardizing EFT protocols and ensuring fidelity to the model can help mitigate this issue (Johnson *et al.,* 1999).

Measurement Tools

Limitation: The tools used to measure relationship satisfaction and other outcomes can vary across studies.

Challenge: Utilizing consistent and validated measurement tools, such as the Dyadic Adjustment Scale (DAS) and Couples Satisfaction Index (CSI), can provide more reliable data (Spanier, 1976; Finkel *et al.,* 2013).

Theoretical Basis of Emotionally Focused Therapy (EFT)

Attachment Theory

Emotionally Focused Therapy (EFT) is grounded in attachment theory originally developed by John Bowlby in the mid-20th century. Attachment theory posits that early interactions with primary caregivers form the foundation for an individual's emotional regulation and relationship patterns throughout life. According to Bowlby, the quality of these early attachment experiences significantly influences one's sense of security and ability to form stable, healthy relationships in adulthood.

Key Concepts of Attachment Theory

Attachment Bonds: Attachment bonds are the emotional connections formed between an infant and their primary caregivers. These bonds are crucial for the child's survival and emotional development. Bowlby identified three main attachment styles that develop based on the caregiver's responsiveness:

Secure Attachment: Develops when caregivers are consistently responsive and attuned to the child's needs. Individuals with secure attachment tend to have a positive view of themselves and others, and they find it relatively easy to form and maintain healthy relationships.

Insecure-Avoidant Attachment: Arises when caregivers are emotionally unavailable or unresponsive. Individuals with this attachment style often avoid closeness and intimacy, have difficulty trusting others, and may appear emotionally distant.

Insecure-Anxious Attachment: Develops when caregivers are inconsistent in their responsiveness. Individuals with this attachment style often seek excessive closeness and reassurance, fear abandonment, and can be overly dependent on others for emotional support.

Internal Working Models: Bowlby proposed that individuals develop internal working models based on their early attachment experiences. These models are cognitive frameworks that shape how individuals perceive themselves, others, and relationships. Securely attached individuals have positive working models, while those with insecure attachments may have negative or distorted models that influence their relational behaviour.

Attachment Behaviours: Attachment behaviours are actions taken to seek proximity, comfort, and security from attachment figures. In adulthood, these behaviours manifest in romantic relationships, where partners seek emotional closeness and support from each other.

Attachment Theory and Emotional Bonding in Couples

Attachment theory is central to understanding the emotional bonding in couples, as adult romantic relationships are seen as attachment bonds. EFT applies the principles of attachment theory to help couples identify and transform the negative interaction patterns that arise from insecure attachment styles.

Emotional Security: In EFT, the primary goal is to enhance emotional security within the couple. This involves helping partners become more emotionally accessible, responsive and engaged with each other, creating a secure base from which both partners can explore and grow.

Negative Interaction Patterns: EFT therapists work with couples to identify and de-escalate negative interaction patterns, such as criticism, defensiveness, withdrawal, and hostility. These patterns are often driven by underlying attachment fears and unmet emotional needs. By addressing these root causes, EFT helps couples break the cycle of negative interactions.

Accessing Vulnerable Emotions: A key component of EFT is helping partners access and express their vulnerable emotions and attachment needs, such as fear of rejection or desire for closeness. By sharing these deeper emotions, partners can develop a greater understanding and empathy for each other.

Creating Positive Interaction Cycles: EFT aims to restructure interactions so that partners respond to each other's emotional needs in a supportive and validating manner. This involves creating new, positive interaction cycles where partners feel safe to express their emotions and seek comfort from each other.

Building Secure Attachments: Ultimately, EFT seeks to build secure attachments within the couple. Securely attached partners are better able to regulate their emotions, communicate effectively, and support each other through life's challenges. This leads to higher levels of relationship satisfaction and emotional well-being.
Attachment theory provides a robust theoretical basis for Emotionally Focused Therapy (EFT), highlighting the importance of emotional bonds in adult relationships. By addressing the attachment-related emotions and behaviours that underlie relationship distress, EFT helps couples create secure, satisfying, and lasting connections. The application of attachment theory in EFT not only enhances our understanding of relationship dynamics but also provides effective strategies for fostering emotional intimacy and resilience in couples.

Research Design
Study Objective
The primary objective of this study is to examine the effectiveness of Emotionally Focused Therapy (EFT) in improving marital satisfaction. The study aims to assess the impact of EFT on various dimensions of relationship quality using validated assessment tools such as the Dyadic Adjustment Scale (DAS) and the Couples Satisfaction Index (CSI).

Research Hypotheses
Hypothesis 1: EFT will significantly improve overall marital satisfaction among participating couples.

Hypothesis 2: EFT will positively impact specific dimensions of the relationship, such as emotional intimacy, communication and conflict resolution.

Hypothesis 3: Improvements in marital satisfaction will be sustained over time following the completion of EFT.

Hypothesis 4: EFT will be more effective in enhancing marital satisfaction compared to other therapeutic approaches.

Participants

Sample Size: The study will involve 30 couples (60 individuals) who seek therapy for relationship issues.

Inclusion Criteria:
Marital Status: Participants must be married or in a committed relationship for at least one year.

Age Range: Both partners should be between 18 and 65 years old.

Relationship Distress: Couples must report experiencing moderate to high levels of relationship distress, as identified through a preliminary screening questionnaire.

Willingness to Participate: Both partners must be willing to participate in the study, attend therapy sessions and complete all assessments.

Language Proficiency: Participants must be proficient in the language used in the therapy sessions and assessments to ensure clear communication and accurate data collection.

Exclusion Criteria

Severe Mental Health Issues: Couples where one or both partners have severe untreated mental health issues (e.g., severe depression, psychosis) that could interfere with the therapy process.

Domestic Violence: Couples experiencing ongoing domestic violence, as EFT may not be appropriate without additional safety interventions.

Substance Abuse Problems: Couples where one or both partners have severe substance abuse problems that are not being treated, as this could impact the therapy process.

Previous EFT Experience: Couples who have previously undergone EFT may be excluded to avoid confounding effects of prior exposure.

Data Collection

METHODS

Pre-Therapy Assessment

Surveys: Participants will complete a set of baseline surveys, including the Dyadic Adjustment Scale (DAS) and the Couples Satisfaction Index (CSI), to measure initial levels of marital satisfaction and relationship quality.

Demographic Information: Collection of demographic data and relationship history, including duration of relationship, number of children, and previous therapy experiences.

Screening Questionnaire: A preliminary questionnaire to assess the level of relationship distress and eligibility for the study.

Therapy Sessions

EFT Group: Couples in the EFT group will participate in 12 weekly EFT sessions, each lasting 90 minutes. Sessions will be conducted by certified EFT therapists following the structured EFT protocol.

Control Group: Couples in the control group will receive 12 weekly sessions of Cognitive-Behavioral Couples Therapy (CBCT), also lasting 90 minutes each, conducted by trained therapists.

Post-Therapy Assessment:

Surveys: Upon completion of the therapy sessions, all participants will again complete the DAS and CSI to measure changes in marital satisfaction and relationship quality.

Follow-up Assessment:

Surveys: Six months after the completion of therapy, participants will complete the DAS and CSI for a third time to evaluate the sustainability of the improvements.

Interviews: Semi-structured interviews will be conducted with a subset of couples from both groups to gain deeper insights into their experiences with the therapy and the long-term impact on their relationship.

Measures of Marital Satisfaction

Dyadic Adjustment Scale (DAS) Developer: Spanier, G. B. (1976)

Purpose: To measure the quality of adjustment in dyadic relationships.

Components:

Dyadic Consensus: Assesses the degree of agreement between partners on various issues (e.g., finances, household tasks).

Dyadic Satisfaction: Measures the overall satisfaction with the relationship.

Dyadic Cohesion: Evaluates the closeness and shared activities between partners.

Affectional Expression: Assesses the degree of satisfaction with the expression of affection and sexuality in the relationship.

Scoring: The DAS provides a total score and subscale scores, with higher scores indicating better dyadic adjustment and relationship quality.

Couples Satisfaction Index (CSI)

Developers: Funk, J. L., & Rogge, R. D. (2007)

Purpose: To assess the degree of satisfaction in romantic relationships.

Components:

Global Relationship Satisfaction: Overall evaluation of relationship satisfaction.

Emotional Intimacy: Measures the closeness and emotional connection between partners.

Communication: Assesses the quality and effectiveness of communication within the relationship.

Conflict Resolution: Evaluates how well partners manage and resolve conflicts.

Scoring: The CSI provides a total score and subscale scores, with higher scores indicating greater relationship satisfaction. The study will involve a rigorous selection process to ensure that participants are representative of couples experiencing relationship distress and suitable for EFT. Data collection will include comprehensive pre- and post-therapy assessments, as well as follow-up evaluations to measure the sustainability of the improvements. The use of validated measures such as the Dyadic Adjustment Scale (DAS) and the Couples Satisfaction Index (CSI) will ensure reliable and meaningful assessment of marital satisfaction and relationship quality. By employing a thorough and structured research design, this study aims to provide robust evidence on the effectiveness of Emotionally Focused Therapy in enhancing marital satisfaction.

Key Findings

Improvements in Communication

Couples who underwent EFT reported significant improvements in communication, as evidenced by higher scores on the communication subscale of the CSI. They noted better understanding, more effective conflict resolution, and increased openness in expressing emotions.

Enhanced Emotional Connection
EFT participants showed marked improvements in emotional intimacy. They reported feeling more emotionally connected, secure, and supported by their partners, reflected in higher scores on the emotional intimacy subscale of the CSI.

Overall Marital Satisfaction
Both the DAS and CSI scores indicated substantial gains in overall marital satisfaction for couples in the EFT group. These improvements were sustained over the six-month follow-up period.

Comparison with Control Group
Quantitative Comparison:
EFT vs. Control Group: The EFT group showed significantly greater improvements in DAS and CSI scores compared to the control group. Independent sample t-tests revealed that the EFT group had higher mean differences from pre-test to post-test and from pre-test to follow-up, indicating superior effectiveness of EFT.

Sustainability of Improvements: Repeated measures ANOVA indicated that the EFT group maintained their gains in marital satisfaction over time, while the control group showed less sustained improvement.

Qualitative Comparison:
EFT Group: Participants in the EFT group highlighted the transformative nature of the therapy, describing it as pivotal in reshaping their relationship dynamics. They emphasized the importance of emotional vulnerability and secure attachment fostered by EFT.

Control Group: While the control group reported some improvements, their feedback suggested that the changes were less profound and less enduring compared to those experienced by the EFT group. Some participants noted the need for more emotionally focused interventions.
The data analysis supports the effectiveness of Emotionally Focused Therapy (EFT) in significantly enhancing marital satisfaction, improving communication, and strengthening emotional connections among couples. The quantitative and qualitative findings collectively indicate that EFT is a more effective therapeutic approach compared to traditional cognitive-behavioural therapy, with sustained benefits over time. These results underscore the importance of incorporating EFT in clinical practice to support couples experiencing relationship distress.

DISCUSSION

Interpretation of Results
The results of this study provide robust evidence supporting the effectiveness of Emotionally Focused Therapy (EFT) in improving marital satisfaction. Participants who underwent EFT demonstrated significant improvements in communication, emotional connection, and overall relationship satisfaction compared to those in the control group. The sustained benefits observed at the six-month follow-up indicate that EFT facilitates long-lasting positive changes in relationship dynamics. These findings align with previous research, reinforcing the theoretical framework of EFT that emphasizes the importance of secure emotional bonds in enhancing relationship quality.

Implications for Therapy
The findings have several practical implications for therapists and the integration of EFT into clinical practice:

Enhanced Therapeutic Outcomes: Therapists can expect substantial improvements in relationship satisfaction and communication when implementing EFT with couples experiencing distress. The structured, emotion-focused approach of EFT helps couples develop deeper emotional connections and more effective conflict resolution skills.

Training and Certification: Given the demonstrated effectiveness of EFT, it is crucial for therapists to receive proper training and certification in EFT techniques. This ensures fidelity to the EFT model and maximizes therapeutic outcomes for couples.

Incorporating EFT into Practice: Therapists should consider integrating EFT into their practice, especially when working with couples facing emotional disconnection or chronic conflict. The structured stages of EFT provide a clear framework for guiding couples through the therapeutic process.

Tailored Interventions: EFT can be tailored to address specific issues within a relationship, such as emotional intimacy or communication difficulties. Therapists can use the flexibility of EFT to meet the unique needs of each couple.

Limitations

While this study provides valuable insights, several limitations should be acknowledged:

Sample Size: The sample size of 30 couples, although adequate for this study, may limit the generalizability of the findings. Larger sample sizes in future studies would enhance the robustness of the results.

Diversity of Participants: The sample may lack diversity in terms of cultural, socio-economic, and demographic factors. Future research should include more diverse populations to examine the effectiveness of EFT across different groups.

Duration of Therapy: The study focused on a 12-week therapy duration. While significant improvements were observed, longer-term studies are needed to assess the sustainability of EFT benefits over extended periods.

Control Group Comparison: The control group received Cognitive-Behavioural Couples Therapy (CBCT), which may not be representative of all alternative therapeutic approaches. Comparing EFT with a wider range of therapies would provide a more comprehensive understanding of its relative effectiveness.

Future Research

Based on the findings and limitations of this study, several areas for future research are suggested:

Long-Term Effects: Investigating the long-term effects of EFT on marital satisfaction beyond the six-month follow-up would provide insights into the enduring impact of the therapy.

Cultural Contexts: Examining the effectiveness of EFT in different cultural contexts is crucial for understanding its applicability and effectiveness across diverse populations. Cross-cultural studies would help identify any necessary adaptations to the EFT model.

Comparative Studies: Conducting comparative studies that evaluate EFT against a variety of therapeutic approaches (e.g., integrative behavioural couples therapy, solution-focused therapy) would provide a broader perspective on its relative effectiveness.

Mechanisms of Change: Exploring the specific mechanisms through which EFT facilitates change in couples' relationships would deepen the understanding of how and why EFT works. This could involve examining the role of emotional bonding, attachment security, and communication patterns.

Individual Differences: Investigating how individual differences (e.g., attachment styles, personality traits) influence the effectiveness of EFT would help tailor interventions to better meet the needs of diverse couples.

CONCLUSION

This study underscores the efficacy of Emotionally Focused Therapy in enhancing marital satisfaction by improving communication, emotional connection and overall relationship quality. The sustained benefits observed at follow-up highlight the long-term potential of EFT in fostering healthy, fulfilling relationships. By integrating EFT into clinical practice and addressing the limitations and future research directions, therapists can provide more effective support to couples in distress, ultimately contributing to better individual well-being and societal health.

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REVIEEW ARTICLE

A Review Paper on *Bacopa monniera* and Role of Artificial Intelligence (AI) in Medicinal Plant for Management and Treatment of Various Diseases

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ABSTRACT

Plants have been used for medical purposes for a very long time. They have many roles in treating different disorders. In Ayurvedic medicine, *Bacopa monnieri* is considered one of the most advantageous medicinal herbs. *Bacopa monnieri*, popularly known as "Brahmi," is an herb that has long been used to treat many medical conditions. It was traditionally taken as a brain tonic to improve learning, memory, and focus. It has a wide range of pharmacological effects, including as antibacterial, antifungal, gastrointestinal, endocrine, antioxidant, and memory-enhancing. Based on numerous studies, the main medicinal chemical components of this plant include the triterpenoids, saponins, and bacosides. This review will examine the botany, chemistry, and mechanism of action of *Bacopa monnieri*, with a particular focus on the plant's use in the treatment of various diseases and the study is focus on treatment of many ailments, artificial intelligence (AI) is crucial to the management of medicinal herbs like brahmi. Brahmi is well known for its antioxidant, neuroprotective, and cognitive-enhancing qualities, here's in this review how AI advances our knowledge of and ability to use Brahmi in the treatment of disease.

Keywords: *Bacopamonniera,* chemical constituents, pharmacology, artificial intelligence (AI)

INTRODUCTION

Brahmi, or *Bacopa monnieri*, is gaining popularity as a dietary supplement due to its capacity to improve intellect and memory. It can be found all across the world's tropical and subtropical regions[1].In addition to its common name, *Bacopa monnieri* is also known by the names Brahmi, thyme-leafed gratiola, Indian pennywort, and water hyssop. Native to the wetlands of Southern and Eastern India, Nepal, Sri Lanka, China, Taiwan, and Vietnam, as well as Australia, Europe, Africa, Asia, and North and South America, it is a perennial creeping herb [2].Traditionally used in India, *Bacopa monnieri* is a plant that grows along lakes and rivers [3]. It has also been study that *Bacopa monnieri* contains anti-inflammatory, analgesic, antipyretic, sedative, free radical scavenging, and anti-lipid peroxidative properties. It is an essential component of medicinal uses[4]. In conventional healthcare systems, medicinal plants like brahmi, which is frequently referred to as a memory booster, are among the most commonly acknowledged and utilized so by using artificial intelligence (AI) in ayurveda we can detect many thing. This plant can be used to treat a wide range of chronic conditions, such as anxiety, epilepsy, stomach ulcers, irritable bowel syndrome (IBS), insomnia, wound healing, diabetes, cancer, and asthma. To diagnose with this medicinal plant for different disease, first must analyze each patient's constitution and the disease's manifestations using a mix of clinical examination, patient history, and diagnostic techniques including tongue examination and pulse diagnosis. Complete technology that allows computers and other gadgets to function intelligently must be used in order to upgrade this priceless and ancient medical system. This intelligence that comes from computers or other machines is known as artificial intelligence. Artificial intelligence (AI) is the ability of computers, especially computer systems, to recognize the parts of an illness that have therapeutic potential [5].

Naturally application of *Bacopa monniera*

In many nations, traditional medicines are crucial to the provision of medical care in rural areas when there is no for mal health care system in place.*Bacopa monnieri* is used by many cultures worldwide, demonstrating its varied ethnob otany [6].

- It is reported to be helpful in treating cardiac, respiratory, and neuropharmacological issues like sleeplessness.
- It is used in traditional Indian medicine, or Ayurveda, to alleviate anxiety and memory-boosting activities.
- *Bacopa monnieri* may be used therapeutically to treat neurological disorders and enhance memory. In many nations, traditional medicines are crucial to the provision of medical care in rural areas when there is no formal health care system in place[7].
- This plant has significant role in traditional medical system. It is used to treat a wide range of conditions, including gastrointestinal issues, bone fractures, asthma, inflammation of the urinary tract, rheumatism, bronchitis, leg swelling, memory improvement, hoarseness of voice, and blisters [8].
- This plant's leaves are used to treat colds, coughs, and nasal congestion. The leaves are used to cure asthma and constipation, and the root extract is used as an eye drop to treat cataracts [9].
- *Bacopa monnieri* leaves to stimulate the pubic area and treat urinary issues.

Recent use of *Bacopa monniera*

- For ages, people have utilized this little, creeping perennial plant—one of the two potent herbs known as brahmi for various neurological disorder problem.
- The juice of brahmi leaves strengthens the neurological system and increases blood flow. Strong antioxidants like brahmi are utilized to cure oxidative damage. Irritability, epilepsy, and mental illnesses are all alleviated[10].
- Gonorrhea and other STDs are treated with a powdered brahmi leaf and milk mixture.
- Elephantiasis is treated using ointment made from Brahmi root.
- It provides nourishment to hair and promotes the growth of longer, thicker hair. Additionally, tumors, dementia, and ulcers are treated with it. Cholera, piles, amenorrhea, and mental illness are all treated by brahmi [11].
- When mixed with tulsi, neem, and amla, brahmi promotes the growth of nails, hair, and skin.

- The latest use of *Bacopa monnieri* (Brahmi) in artificial intelligence (AI) includes a number of cutting-edge methods in drug discovery, research, and customized treatment [12].

***Bacopa monniera's* phytochemistry**

The traditional medicinal herb *Bacopa monniera* has a range of biological actions. Numerous classes of phytochemicals have been identified from the bark, leaf, fruit, seed, and root. Phytochemicals are known to be the cause of biological activity [13].A phytochemical analysis shows that plants have a variety of phytoconstituents. *Bacopa monnieri* contains the chemicals herpestine, brahmine, and alkaloids. The main phytochemicals that have been identified are flavonoids, tannins, terpenoids, monnierin, hersaponin, bacosides A and B, and flavonoids. Saponins are categorized as glycosides of pseudojujubogenin and jujubogenin and are said to be a significant component of the plant. Moreover, a number of other phytochemicals were found in the various plant sections [14].

Chemical components

Many Phyotochemicalsare found in the *Bacopa monnieri* some of listed here are Herpestine, nicotinine, alkaloid, triterpenoid, saponins, β-sitosterol, D-mannitol, stigmastanol, betulinic acidare main components. Some other are (α-L-arabinopyranosyl)-O-β-D-glucopyranoside-10, 20-dihydroxy-16-keto-dammar-24-ene are the bacosides A [15].some other were also identified they are 3-O-α-L-arabinopyranosyl, -α-L-arabinopyranosyl jujubogenin,3-O-[α-L-arabinofuranosyl-(1→2)-α-L-arabinopyranosyl,3-O-β-Dglucopyranosyljujubogenin,3-O-β-D-glucopyranosyl(1→3)-{α-L-arabinofuranosyl-(1→2)}-α-L arabinopyrasonyl] pseudojujubogenin,3-O-[α- L-arabinofuranosyl-(1→2)-β-D-glucopiranosyl] pseudojujubogenin[16].

Pharmacological Inaction

Hepatoprotective Properties

The ethanolic extract *Bacopa monnieri* of bacoside-A, has been shown to be rich in saponins and to have hepatoprotective properties.Rat, mouse, and human model systems have all been used in a great deal of study[17]. The numerous investigations have demonstrated that liver cirrhosis is induced by carbon tetrachloride (CCl4). Enzyme activity is altered by CCl4, which disrupts the metabolism of liver cells [18]. *Bacopa monnieri's* hepatoprotective effects on paracetamol-induced liver injury in Wister albino rats have been studied. Four groups of animals were used in this investigation. 5ml/kg of normal saline was given to the initial group. The identical dose was given to the second group. Every group—aside from the first—received 500 mg/kg of paracetamol for seven days. Group 4 received normal medication silymarin 25 mg/kg, while Group 3 received an ethanolic extract of BM 300 mg/kg. Several assays have been used to measure the activity after sacrifice, including serum glutamate oxaloacetate (SGOT), serum glutamate pyruvate transaminase (SGPI), alkaline phosphatase (ALP), bilirubin (direct and total), and cholesterol (total and HDL). To assess liver damage, measurements of SGOT, SGPT, ALP, bilirubin, and cholesterol are utilized as an indicator.

Activity of Antioxidants

The study established the antioxidant effect of *Bacopa monnieri's* alcoholic and hexane extract on lipid peroxidation caused by ferrous sulphate and cumene hydroperoxide in rat liver homogenate [19]. A second study in which they evaluated the effects of *Bacopa monnieri* extract on the rat frontal cortex, striatal, and hippocampal regions of the brain [20].By using the DPPH radical scavenging method assessed the anti-oxidant activity of Bacopa extract and discovered that the maximal anti-oxidant activity of both the methanolic and aqueous extracts was 46.00μg/ml and 43.10μg/ml, respectively. The plant leaf protein was synthesized in different doses ranging from 1 to 100 μg. It was then combined with 1 milliliter of newly made 0.5 mM DPPH ethanolic solution and 2 milliliters of pH 5.5 0.1M acetate buffer. As controls, BHA and ascorbic acid were employed. At a dosage of 10 μg, *Bacopa monnieri* has the strongest DPPH radical scavenging activity [21].

Anti- Depressant

Depression is a prevalent, potentially fatal illness. Patients with depression typically exhibit decreased levels of dopamine, serotonin, and norepinephrine in their brains [22].In a 2002 study, the antidepressant medication

imipramine (15 mg/kg) was compared with a methanolic extract of *Bacopa monnieri* (20 and 40 mg/kg) given orally once daily for five days to rodents. The results showed a significant antidepressant effect.

Antidepressant Intent

Depression is a common, often fatal illness that affects a large number of people. Brain neurotransmitters such dopamine, serotonin, and norepinephrine are present in reduced amounts in it. A Lancet research states that approximately 32.2 core individuals have this mental illness. Suicide is mostly motivated by depression as well. Many illnesses, including as diabetes, heart attacks, strokes that cause paralysis, high blood pressure, and heart attacks, have been linked to this mental illness; therefore, it is important to assess effective antidepressant substances derived from natural sources. The second most common psychiatric condition, depression affects about 21% of the global population. For the benefit of humanity, we must look for strong antidepressant substances from natural sources, including plants, as almost everyone experiences depression at some point in their lives. Both the stress hormone and the hormonal balance of the body are influenced by substances. Its leaf increases the brain's serotonin levels, which lowers anxiety and uneasiness and promotes relaxation. In the forced swim and learned helplessness tests, two of the most often used behavioral paradigms in animal models of depression; it was discovered to have strong antidepressant effects. In rodents, it was shown to have antidepressant efficacy equivalent to that of imipramine, a common antidepressant medication. Due to its antidepressant and anxiolytic capabilities, serotonin and gamma-aminobutyric acid (GABA) are thought to be involved in the mechanism of action.

Anti-Epileptic

The neuroprotective effect of BM extract in epileptic rats was documented by Khan in 2008[23]. In addition to pilocarpine-induced epilepsy, the experiment demonstrated glutamate-mediated excitotoxicity that occurs during seizures and cognitive impairment. An experiment with a Morris water maze was also part of the investigation. According to a clinical investigation *Bacopa monnieri* alcoholic extract is useful in reducing the symptoms of epileptic seizures[24]. In a different study, Mathew looked at temporal lobe epilepsy, a frequent epileptic disease. In the cerebral cortical region of epileptic rats, *Bacopa monnieri* was found to have an impact on gene expression and the binding of gamma amino butyric acid (GABA). In this investigation, BM plus bacoside-A therapy showed a therapeutic effect [25].

Antidiabetic Inaction

Diabetes mellitus is a metabolic disease that affects the metabolism of proteins, fats, and carbohydrates. It is estimated that 1% of people have this illness.Working using an ethanolic extract of *Bacopa monnieri*, found that the triterpene bacosine is the cause of the increased glycogen content in diabetic rats. Additionally, the extract increased the diaphragm of diabetic rats' peripheral glucose utilization *in vitro*. Rats given alloxan to develop diabetes did so by exhibiting insulin-like activity [26].

Antiulcer Activity

The anti-ulcer properties of the ethanolic extract of *Bacopa monnieri* using male-sex Swiss albino mice [27].There were nine groups of animals, each with six mice. Group 1 was the standard control group, receiving simply 0.5ml/100gm 0.2 ml of tween 80. The second group was fed the identical food but received an absolute alcohol dose of 0.5 milliliters per 100 grams of body weight. The third group was given alcohol (0.5 ml/100 gm) instead of the regular medication, omeprazole (20 mg/kg body weight). Aqueous extract of *Bacopa monnieri* was administered to Groups 4 and 5 at doses of 200 mg and 400 mg of body weight, respectively. The ethanolic plant extract was given to groups 6 and 7, at doses of 200 mg and 400 mg of body weight, respectively. Aspirin and ethanol-induced stomach ulcer models were used by Rao to study the fresh juice from the entire *Bacopa monnieri* plant. Over the course of five days, oral doses of 100 and 300 mg/kg of*Bacopa monnieri* juice and 250 mg/kg of sucralfate were administered [28]. With the exception of ethanol-induced ulcers, the juice exhibited antiulcer efficacy in models of stomach ulcers. Mucosal defensive factors, such as increased mucin secretion, mucosal glycoprotein, and decreased mucosal cell exfoliation, are thought to be responsible for the effect. In an investigation utilizing a methanolic extract of *Bacopa monnieri* on the

susceptibility of NIDDM/normal rats, discovered that after 5–10 days of treatment, a 50mg/kg body weight extract dose was successful in healing penetrating ulcers caused by acetic acid and HCl [29].

Anti-Cancer Intent

The anti-tumor effect of stigmasterol, which is extracted from the aerial portions of *Bacopa monnieri*, against Swiss albino mice that had Ehrlich ascites carcinoma. It is believed that protein phosphatase 2A activation mediates the anti-tumor effect of stigmasterol. An additional investigation by Kumar also looked at the *Bacopa monnieri* ethanolic extract's anti-tumor properties. The solid tumor took longer to form when the extract was taken orally. The in vivo tumor model test systems and in vitro short term chemo sensitivity test systems were used in the investigation [30]. Ethanolic extracts and the saponon-rich fraction were found to have anti-tumor potential by D'Souza [31]. It has been revealed that the active ingredient with anti-cancerous properties is bacoside-A. The extract's lethality against brine shrimp was evaluated. An alcoholic extract of *Bacopa monnieri* was shown to have anti-cancer properties.Tests were conducted on sarcoma-180 cell culture using the ethanol extract.As the extract concentration increased, the development of the cells was impeded [32].

Anti-Inflammatory

One kind of biological reaction to stimuli such as pathogens, injured cells, or irritants is inflammation. It is characterized by redness, swollen joints, and discomfort in the joints, stiffness, and loss of joint function [33]. According to Hossain, *Bacopa monnieri's* methanolic extract has anti-inflammatory properties. Rats were used in the carrageenan and histamine-induced oedema test for the investigation. 200 and 400 mg/kg body weight of the extract were given, and the 400 mg/kg dose significantly reduced inflammation in comparison to the medication indomethacin [34]. *Bacopa monnieri's* anti-inflammatory properties were demonstrated byali in their study on carrageenan-induced paw edema in rats and mice. In this study, *Bacopa monnieri* ethanol extract was employed as an anti-inflammatory drug. Carrageenan (1%) is injected into the right paw to cause inflammation. The mice were given an ethanolic extract of BM at varying doses after thirty minutes. The anti-inflammatory properties of aspirin or 10% DMSO were observed. Thus, the author has shown that BM extract, at doses of 50 mg/kg and 100 mg/kg, causes a considerable drop (33-95%) in paw edema, which is more effective than aspirin's (28-60%) effect. By blocking prostaglandin, bacopa exhibits anti-inflammatory properties (58–100%) [35]. *Bacopa monnieri* has anti-inflammatory properties in mice and guards against dementia brought on by colchicine. They used a single intrace rebroventricular injection of colchicine (15µg/5µl) to cause dementia. For the next fifteen days, an oral Bacopa monnieri extract at a dose of 50 mg/kg body weight was administered to a group of rats that had received colchicine. In the retrieval test, it was discovered that BM administered to colchicine-treated rats effectively restored memory and not the control group. Colchicine-treated animals with extract of BM also demonstrated a significant reduction in escape latency when compared to solely colchicine-treated animals [36].

Anti-Microbial

The anti-microbial activity of ethanolic, diethyl acetate, ethyl acetate, and aqueous extracts of *Bacopa monnieri* aerial parts was assessed[37].While ethyl acetate extract shown activity against gram negative organisms, diethyl ether extract demonstrated antibacterial activity against gram positive microorganisms. Proteus vulgaris and *Staphylococcus aureus* were among the microbes used in the test. Ethanolic extract shown antifungal properties against *Candida albicans* and *Aspergillus niger*. By using the disk diffusion method, Khan documented the antibacterial activity of *Bacopa monnieri* ethyl acetate and methanol extracts against 7 gram negative and 11 gram positive microorganisms [38]. Phytochemicals isolated from aerial portions of *Bacopa monnieri*, such as betulinic acid and oroxindin, have also been shown to exhibit antifungal activity against *Alternaria alternata* and *Fusarium fusiformis*[39].

The anti-Parkinsonian impact

It has been observed that the buildup of the protein alpha-synuclein in cases of neurodegenerative Parkinson's disease eventually results in the death of dopaminergic neurons. In Caenohabiditis elegans, a transgenic model expressing several human alpha-synuclein strains and a pharmacological model producing green fluorescent protein (GFP) were employed by the researchers in this study.

Singh also examined *Bacopa monnieri's* potential neuroprotective effects. In their investigation, they discovered that in male Wister Albino rats, bacopa extract decreased the amount of alpha synuclein, pro-inflammatory cytokines, and reactive oxygen species (ROS). The results of the study indicate that bacopa may be used as a potential therapy against Parkinson's disease since it reduces inflammation in the brain [40].

Artificial Intelligence (AI) has multiple applications in the study of the medicinal herb Brahmi

AI plays a variety of roles in medicinal plant, including helping to identify a wide range of chemicals and detecting the various disease problem [41]. If a plant's components are identified accurately by using this technology, it can be simple to manufacture different drugs from the plant to treat various illness problems that will be facing by a lot of amount of population [42].Here we will be discussed some important roles of AI technology that can be used in medicinal field to treat properly diseases problem.

In the DrugResearch from the plants part

AI technology can be used in identifying and evaluating the active ingredients is present in brahmi, if the chemical components are properly identified which could helpful in making novel drug that has many therapeutic benefits and uses. By using this technology the large volumes of data can be analyzed by AI systems to find possible bioactive components are present in Brahmi plant and these bioactive components are essential to producing a valuable medicine to treat disease problem. The process of finding new drugs can be accelerated by machine learning algorithms that can predict how these molecules will interact with different biological targets.

Examination of Phytochemicals those are present in Brahmi

Artificial Intelligence can help to identify and measure the phytochemicals are found in Brahmi. For the identification of phytochemical in plants more correctly and effectively, methods like machine learning and neural networks may handle complicated datasets from methods like nuclear magnetic resonance (NMR) and mass spectrometry will be used [43].

To study Mechanism action of plant

AI can assist in comprehending the methods by which Brahmi works. If the plant has present different biological activity and mechanism through the analysis of data gathered from proteomic, metabolomic, and genomic research, AI can clarify the pathways and the ways in which Brahmi's substances interact with them.

Specialized in the Health Care

In the health care industry by evaluating patient data, AI can help personalized medicine by predicting potential responses to Brahmi. Brahmi's potential benefits for a given patient can be predicted by machine learning algorithms using lifestyle, environmental, and genetic factors [44].

In the Clinical trial field

AI play also play a various role in many research field also like in the clinical trial management and design incorporating Brahmi can be optimized by AI. Trials can become more productive and economical with its assistance in patient recruitment, monitoring, and data analysis. AI is also capable of foreseeing possible drug interactions and adverse consequences.

In understanding the diseases problem and Treatment

Human are phasing various types of disease problem some are identified and some are not so by using AI technology can help detect and manage conditions like epilepsy, anxiety, and Alzheimer's disease, which Brahmi may be able to help alleviate. Patient data can be analyzed by machine learning algorithms to forecast the course of an illness and its possible effects [45].

Research on Natural Products those are found in plant

In the Himalayan region different types of medicinal plant are found and in these plants the valuable bioactive component are found the AI technology also can help with the search and identification of novel medicinal plants. AI can recommend possible subjects for more research by examining chemical and biological data from a variety of plants [46].

Combination with Contemporary Medicine

AI can make it easier to incorporate Brahmi into contemporary medical procedures. Artificial intelligence (AI) can aid in the development of standardized dosages and formulations that optimize efficacy and safety by analyzing data from both traditional applications and contemporary studies.

The antibacterial properties of *Bacopa monniera*.

Numerous antimicrobial substances found in *Bacopa monniera* exhibit antimicrobial properties and hinder the growth of microorganisms. The plant's antibacterial properties have been confirmed by multiple researches. In order to conduct our investigation, we searched internet publications for information on this plant's antimicrobial potential and compiled it based on the name of the microbe, the component of the plant, and its potential (Table 1).

Observation

Because they are less harmful, traditional medicines are getting more and more popular as it is becoming increasingly clear that the great majority of individuals with health issues are not being adequately met by the available therapies. One of the main traditional plants used to make many Ayurvedic and folk medicines is *Bacopa monnieri*. It has enormous promise for improving a variety of neuro-pharmacological illnesses, exacerbations, and other issues. AI-based technologies have the potential to play a big part in enhancing public health surveillance, expanding access to healthcare for underserved populations, and helping medical professional's better respond to and deliver complex care. This enables medical professionals to concentrate on managing the difficulties and intricacies of the healthcare system. In order to provide long-term health security and universal health care, artificial intelligence (AI) must be included into the broader digital health ecosystem. It should also be more inclusive, efficient, sustainable, and people-centered, with a strong plan in place. According to the current study, artificial intelligence (AI) is crucial for both comprehending different bioactive substances and using them to treat different ailments. Artificial Intelligence plays a critical role in improving our understanding of plant mechanisms and the drug discovery process. Furthermore, Table 1 clearly illustrates the antibacterial activity of various plant components. In traditional medicine, *bacopa monniera* is used to cure microbial infections and illnesses associated with microbes. Different plant extracts or oils showed antimicrobial action against *S. aureus*, *Candida albicans*, *E. coli*, *aspergillu, s flavus*, *Candida Albicans*, *B. subtilis*, *S. aureus*, *Staphylococcus*, *albus*, and *Streptococcus haemolyticus*. Thus, in accordance with conventional medical descriptions, Bacopa monniera can be used for a number of therapeutic purposes.

CONCLUSION

Bacopa monniera is used in many medicinal systems and is considered an important part of traditional medicine. The traditional therapeutic significance of the plant has already been recognized by the current medical system, and it serves as the primary source of ingredients for both conventional and modern medications. Strong antibacterial and anti-inflammatory properties are possessed by *Bacopa monniera*. We looked closely at these characteristics in this study, together with the biological importance of the plant for traditional and contemporary medicine. We have closely observed that Artificial Intelligence is revolutionizing the study of medicinal herbs like Brahmi. By using AI technology, researchers can enhance Brahmi's understanding, efficacy, and safety for treating a variety of ailments. Treatment strategies as a result will be more customized and effective. The contemporary use of *Bacopa monnieri* in artificial intelligence (AI) includes a number of cutting-edge methods in drug discovery, research, and customized

treatment. Our work is hoped to have applications in both the ancient and current medical systems by using AI technology.

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Table1:Antimicrobial activity of *Bacopa monniera* in different extract

S.No.	Plantextract	Zoneofinhibition (Max)	Zoneofinhibition (Min)	Microbename
1.	Methanolic Extract	21.13 mm	19.33 mm	*Staphylococcusaureus*
2.	Ethanol extract	15.16 mm	8.93 mm	*Staphylococcusaureus, Candida Albicans*
3.	Diethyl ether	11.06 mm	9.61 mm	*E.coli*
4.	Ethyl acetate	6.66 mm	4.52 mm	*Aspergillu s flavus*
5.	Ethyl acetate	6.63 mm	4.56 mm	*Aspergillu s flavus, Candida albicans*
6.	Callus methanolic extract	10.0 mm	5.5 mm	*B.subtilis, S. aureus*
7.	Petroleum ether	16.0 mm	2.0 mm	*Staphylococcus aureus*
8.	Benzene	16.0 mm	2.0 mm	*Staphylococcus aureus, Staphylococcus, albus*
9.	Ethylacetate	21.0 mm	4.0 mm	*Staphylococcus aureus, Staphylococcus, albus*
10.	Aqueous	15.0 mm	2.0 mm	*Staphylococcus aureus, Staphylococcus, albus, Streptococcus haemolyticus*

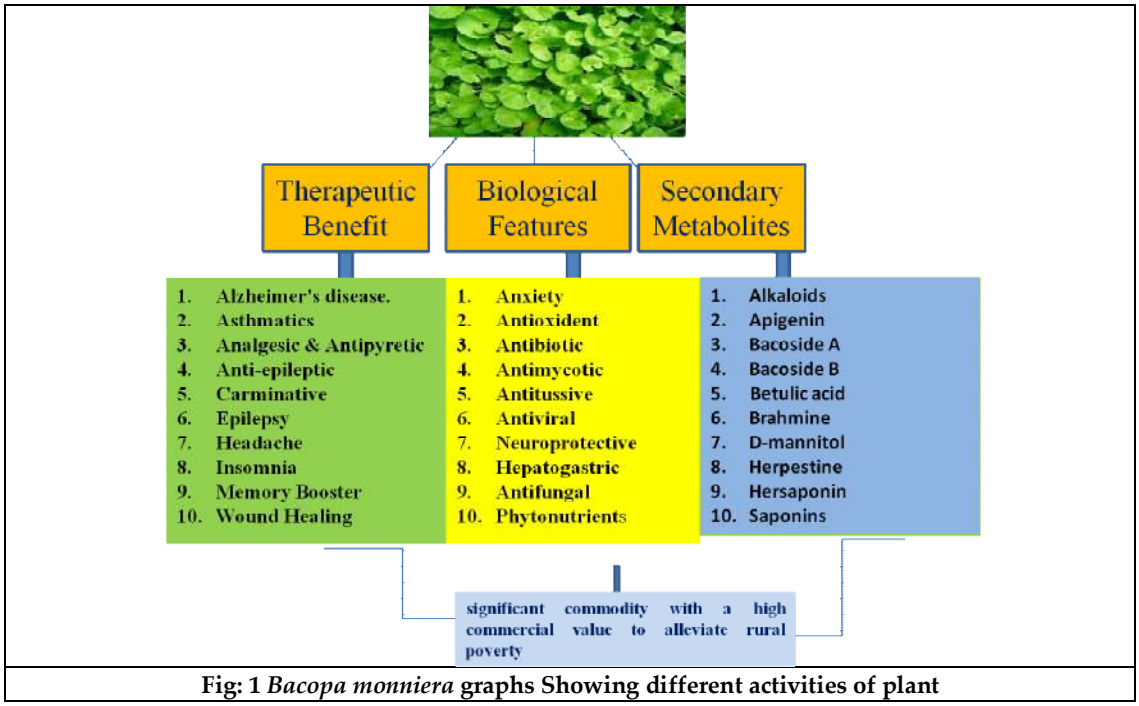

Fig: 1 *Bacopa monniera* graphs Showing different activities of plant

REVIEW ARTICLE

A Review on Anti-Asthmatic Activity Emphasising on *In-vitro* and *In-vivo* Models

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ABSTRACT

Efficacious treatment agents for managing asthma was given importance by examining the anti-asthmatic activity of recently synthesized molecules. The effects of the drugs on important inflammatory indicators, bronchial hyper responsiveness, and airway remodeling using both *in vitro* and *in vivo* tests. The preliminary findings, proved encouraging bronchodilatory and anti-inflammatory benefits. The creation of novel anti-asthmatic treatments may be made possible by further clarifying the processes behind the activities of these substances.

Keywords: Asthma, *In vitro, In vivo* models, plants

INTRODUCTION

Asthma is a Greek word which means "to breathe hard". In Medical terminology it is a reversible obstructive airway disease (ROAD). It may be acute or chronic. Acute severe asthma can be fatal and requires immediate treatment. In Chronic condition pulmonary airways and bronchial tubes were get inflamed and obstructer [1].It is signalizes by inflammation and narrowing of the respiratory tract, accumulation and activation of eosinophils and lymphocyte,

dysfunction of epithelial cell, sub mucosal fibrosis, airway wall edema, mucus overproduction[2].Asthma is a result of complex interactions between multiple genetic -environment influences, with heterogeneity in clinical presentation and the type and intensity of airway inflammation and irreversible changes in the lungs (remodelling)[3].

Etiology

Asthma is common chronic conditions which affects both children and adults.It is heterogeneous with different phenotype. The risk factors for each recognized phenotype of asthma include genetic, environmental and host factors[4]The ethiology of bronchial asthma remains not fully understood, it is widely accepted that its development is influenced by a combination of genetic and environmental factors.

Triggers for asthma include:

Indoor allergens – dust , pets, cockroaches Outdoor allergens – irritant, dust Obesity Tobacco smoke Viral respiratory tract infections Use of aspirin , beta-blockers[5]

Epidemology

Asthma is widespread health condition, impacting around 15% to 20% of person in developed nations and roughly 2% to 4% in less developed regions. It is particularly more prevalent among children, with up to 40% experiencing wheezing at some point. If this wheezing is reversible through beta-2 agonists, it is labeled as asthma, irrespective of lung function test results. Environmental factors such as exposure to tobacco smoke and inhaled particulates contribute to the higher prevalence of asthma in certain groups. Approximately 66% of asthma cases are diagnosed before the age of 18, and nearly 50% of children with asthma experience a reduction in symptom severity or complete symptom disappearance during early adulthood[6]. Asthma is measured to be 34th among the leading causes of burden of disease and 24th in the leading causes of years lived with disability ranked in 2022 Global asthma Report[7].Children born to mothers with thyroid dysfunction shows a greater chance of developing asthma when compared to those born to mothers without thyroid issues. If the mother didn't receive thyroid medication then the chances of incidence is more[8]. Pathophysiology Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions. Various allergic (e.g., dust mites, cockroach residue, furred animals, moulds, pollens) and non-aller-gic (e.g., infections, tobacco smoke, coldair, exercise) triggers produce a cascade of immune-mediated events leading to chronic airway inflammation. Elevated levels of Th2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9 and IL-13, that promote eosinophilic inflammation and immunoglobulinE (IgE) production by mast cells. IgE production, in turn, triggers the release of inflammatory mediators, such as histamine and cysteinyl leukotrienes, that cause Pathophysiology Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions.

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Pathophysiology

Asthma is areversible airway inflammation, follows environmental trigger exposure. This phathological process initiated with inhalation of an irritants (cold air) or an allergen (dust, cockroach residue, furred animals, moulds, pollens).then due to bronchial hypersensitivity leads to airway inflammation with increase mucus production[6].

Asthma patients generally suffers with regular acute exacerbations and clinically characterized wheezing and coughing conditions . This disease is an tracheobronchial stimulated disease which is result of narrowing air passages by either extrinsic or intrinsic ethiological factors[9].

Asthma pathophysiology is complex and involves the following components

-inflammed airways

-irregular airflow obstruction

-bronchial hyperresponsiveness[10]

The 2 phases of asthma worsening are early phase and late phase. IgE antibodies which intiates the early phase which are released by plasmacells. These antibodies respond to certain environmental factors.IgE antibodies binds to mast cells and basophils then the mast cells release histamine, prostaglandins, and leukotrienes. These cells cause airway tightening by contracting the smooth muscle. The last phase occurs after several hours in which neutrophils, eosinophils, basophilsand memory T-cells all confine to lungs . which cause bron choconstriction and inflammation. over time with thicker airway have duration of disease is longerdue to narrower airway[11]. Pathophysiology Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions. Various allergic (e.g., dust mites, cockroach residue, furred animals, moulds, pollens) and non-aller-gic (e.g., infections, tobacco smoke, coldair, exercise)triggers produce a cascade of immune-mediated events leading to chronic airway inflammation. Elevated levels of Th2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9 and IL-13, that promote eosinophilic inflammation and immunoglobulin E (IgE) production by mast cells. IgE production, in turn, triggers the release of inflammatory mediators, such as histamine and cysteinyl leukotrienes, that caus Pathophysiology Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions. Various allergic (e.g., dust mites, cockroach residue, furred animals, moulds, pollens) and non-aller-gic (e.g., infections, tobaccosmoke,coldair,exercise)triggers produce a cascade of immune-mediated events leading to chronic airway inflammation. Elevated levels of Th2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9 and IL-13, that promote eosinophilic inflammation and immunoglobulin E (IgE) production by mast cells. IgE production, in turn, triggers the release of inflammatory mediators, such as histamine and cysteinyl leukotrienes, that caus Pathophysiology Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions. Various allergic (e.g., dust mites, cockroach residue, furred animals, moulds, pollens) and non-aller- gic (e.g., infections, tobaccosmoke,coldair,exercise) triggers produce a cascade of immune-mediated events leading to chronic airway inflammation. Elevated levels of Th2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9 and IL-13, that promote eosinophilic inflammation and immunoglobulin E (IgE) production by mast cells. IgE production, in turn, triggers the release of inflammatory mediators, such as histamine and cysteinyl leukotrienes, that

Symptoms

Shortness of Breath

Wheezing

Chest Tightness

Cough

Palpitation

fatigue

Sputum Production

Difficulty in speaking

Dyspnoea
Whistling Sound while breathing[12]

Asthma tests

Health professionals diagnose asthma by using spirometry test which is most common type of lung function test. In this spirometry test the person use to breath deeply and breath out forcefully into a tube which is link to a machine spirometry. this shows the expelled air speed from their lung. Other tests for diagnosis include:

Allergy testing: Physican make a detailed labouratory study on skin and blood test to asses the clinical features of asthma .

Blood test: To check the abnormal levels of eosinophils and immunoglobulin E which is an antibody generated by immune system with allergic asthma.[13]

Classification

The National Asthma Education and Prevention Program classifies asthma into either intermittent (irregular) or persistent (continous), and the latter is either mild, moderate, or severe. asthma also classified as allergic (IgE mediated), nonallergic (recurrent respiratory tract infection), occupational, aspirin-exacerbated respiratory disease, exercise induced, and cough variant asthma[14]. Recently it is classified based on degree of control-controlled, partly controlled and uncontrolled[15].

Screening models

No complete idea about human asthma of all it's features by any single animal model. The importance of in vitro and in vivo screening models is to transfer the drug candidate from preclinical studies to human . Here we discuss about different models with their mechanism and pathophisology involved in asthma.

***In-Vivo* Models**

It is a challenge to resemble human asthma because of standardized models in animal are lack. Also here no standardized protocol for experiment. With some modifications numerous research room have grow their own models of bronchial asthma.

Histamine and Acetylcholine induced Bronchoconstriction

Here the experimental animal is guniea pig . it is the conventional curative model. Inhale spasm gens (histamine) can induce the asphytic convulsions which mimic bronchial asthma . Histamine leads to dilation of capillaries in cardiovascular system ,intense contraction smooth muscle with intense hyotension it also shows prime reaction predominant response in a group which is result in death.In this model animals are exposed to the air tight chamber with 0.2% histamine and acetylcholine with constant pressure 40mm/Hg. This may leads to severe bronchoconstriction give rise to suffocation and spasmodic dyspnea. These symptoms can slow up by Bronchodilators. Preconvulsive dyspnea arrival required time is recorded. Here Evaluate the test drug's bronchodilator activity aganist brochoconstriction due to histamine and acetylcholine.

Clonidine-induced Catalepsy in Mice

The animals maintains immobile posture for long time is a condition of catalepsy . It is because of inhibition of dopaminergic transmission or increase histamine in brain due to drug. Clonidine prompt amount related catalepsy in mice. It is limited by H1 blockers but not H2 receptor. mice induces catalepsy by Intracerebroventricular (i.c.v.) injection of histamine, which was suppressed by Chlorcyclizine the H1 receptor antagonist. In brain there is a histamine containing mast cell. It have an impact in generation of motor signs of catalepsy.Hence it suggested that the histamine mediate the cataleptic effect of clonidine, released from the mastocyte of brain in reaction to stimuli of α2 adrenoreceptors by Clonidine. Evaluate the effect of test drug. The forepaws of mice are placed on horizontal bar and note the time required for each animal to remove the paw from bar before and 1hr following the administration

of the experimental drug. measure the period of catalepsy for each 15 min interval difference. Evaluate the reduce time of catalepsy is calculated against control. Standard and test groups are compared with control group.

Milk – induced leucocytosis and eosinophilia

Several medicinal properties have been attributed to the plants in the traditional system of medicine. Some plant materials with adaptogenic properties are among them. The primary characteristic of an adaptogen is its ability to enhance resistance against a wide range of harmful physical, pharmacological, and biological stressors. This effect is evident regardless of the direction of prior pathogenic alterations. Increasing the leukocyte count by parentral administration of milk and this can be normalized by intake of adaptogenic drugs. It further release cytokines, histamine, which are inflammatory mediators and basic proteins and promotes the inflammation. This model evaluates the protective effect of test drug against milk induced leukocytosis. Parenteral milk administration results increase in the leukocytes count after 24hr. In this model mice are administered with boiled and cooled milk and the absolute eosinophil count is recorded before and after administration of milk.

Influence on Broncho Alveolar Lavage Fluid in Guinea Pigs Sensitised to Egg Albumin

BAL, or bronchoalveolar lavage, has shown to be an effective method for researching the inflammation of the airways associated with moderate asthma. BAL fluid from asthmatic patients contains a diverse array of inflammatory cells and cytokines, neuropeptides, eicosanoid mediators, and soluble adhesion molecules. Individuals suffering from asthma exhibit elevated levels of eosinophils, mast cells, and lymphocytes. Even more eosinophils seem to be present during periods of inflammation following allergen exposure, in addition to the number of eosinophils that werealready evident in baseline BAL fluid. Furthermore, it has been observed that 19 hours after the allergen was injected endobronchially, the number of lymphocytes and basophils in BAL fluid increased.

In–Vitro Models

Histamine, Acetylcholine, Serotonin and Bradykinin caused the ileum of Guinea Pig to constrict

Histamine is an local hormone, it is a facilitator of instant allergic (Type-I) and inflammatory reactions. histamine shows spasm inducing reaction on intestinal smooth tissue. Histamine cause contractions of guinea pig digestive tract muscle by acting on H1 receptor. Similar to histamine - ACh, serotonin and tissue kinin also cause tightening of guinea pig. Acetylcholine acting on muscarinic receptors causes contrations. Screen the effect of test drug histamine,bradykinin, Acetylcholine, Serotonin initiated compressions of smooth muscle. Evaluate response by measure the hight and reactivity chart of ach and draw for histamine while test drug present and absent.

Vascular and airway responses in the isolated lung

The isolated perfused rat lung allows the simultaneous registration of pulmonary vascular and airway responses to several drugs. Pulmonary arterial perfusion pressure, airway pressure, and reservoir blood level are continuously monitored, electronically averaged and recorded with a polygraph.

Responses of blood vessels and airway in the isolated lungs

The rat lung saturated in isolation enables concurrent monitoring of lung vascular and wind passages reactions to various medicines. Continuous tracking of pulmonary arterial perfusion pressure, bronchial tubes pressure, and blood pool level is conducted through electronic averaging and recording using a polygraph. Changes in pulmonary arterial pressure and bronchial tubes pressure following the administration of study compound are assessed in millimeters of mercury and then assessed with reference values.[16]

Plant products

Drugs used to treat asthma can lessen airway inflammation, but they also have a number of adverse effects that manifest themselves when the medicine is stopped. Patients therefore prefer plant-based goods more. The drugs currently used for treating asthma reduce airway inflammation, but the symptoms return soon after treatment is stoped . In addition, these drugs are expensive and have several side effects. Therefore, plant

products are still widely used by asthmatic patients. Secondary plant metabolites exhibit vast chemical diversity and significant antiasthma tic potential. secondary metabolites such as flavoniods, phenolic compounds(rutin, luteolin, quercetin). This is evident in the fact that the primary drug classes employed in asthma treatment—muscarinic receptor antagonists, β-adrenergic receptor agonists, membrane stabilizers, and phosphodiesterase inhibitors—have either been directly derived from or draw inspiration from compounds found in nature[17].

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Table.1: Plants having Anti-asthmatic activity

S.No	Name of the plant	Part of the plant used	Active chemical constituent	Biological activity
1	*Aerva lanta*	woolly flowers	Beta- sitosteryl palmitate, alpha- amyrin, beta-sitosterol	Antiasthmatic[18]
2	*Asystasia gangetica*	hexane, ethylacetate, and methanol extracts of leaves	Terpenoid	antiasthmatic
3	*Ageratum conyzoides*	Hydroalcoholic extract of leaves	Alkaloids, flavoniods, chromenesa	antihistaminic
4	*Argemone mexicana* (*A. mexicana*)	stem	Flavoniods,phenols,tannins saponins, alkaloids	antiallergic and antistress activity
5	*Bacopa monnieri*: Samiulla	leaves	Saponins, betulinic acid	inhibits mast cell degranulation
6	*Cassia sophera*	leaves	Ascorbic acid, beta sito sterol	Antiasthmatic
7	*Clerodendrum Serratum* bharangi in ayurveda	roots	Flavoniods , phenols ,saponins	Antiasthmatic Antipyretic anti-oxidant, anti-inflammatory
8	*Crinum glaucum*	bulbs	Liquid extract	Antiasthmatic, antipasmodic anticonvulsant and anxiolytic
9	*Asystasia gangetica*	leaves	hexane, ethylacetate, and methanol	Antiasthmatic Anthelmintic[19]
10	*Acalypha indica*	Leaves, roots, stalk and flowers	Ethanolic extract	Bronchodialator antioxidant, antimicrobial, anti-inflammatory, anti-diabetic

				and anti-fertility activities[20]
11	*Achillea mellifolium*	flowers	organic and hydro-alcoholic extracts (hexanic extract)	Bronchodilator, Mast cell stabilizer[21]
12	*Abutilon crispum (L.) Medicus*	Leaves	methanol extract	Antiasthmatic, piles, ulcer, jaundice[22]
13	*Abutilon indicum (L.) Sweet.*	seeds	Luteolin,chrysoeriol, isolantolactone	Antiasthmatic ,blood tonic, carminative, antipyretic, anti-cough, diuretic, anti-inflammatory, laxative and antidiabetic[23]
14	*Boswellia*	Trunk (oil) frankincense	Resin, amino acids, polysaccharides, beta-boswellic acid	Anti-asthmatic[24]
15	*Aloe vera Linn*	-	aloe-emodin, aloin, aloesin, emodin, and acemannan.	anti-inflammatory, antioxidant, anti-inflammatory, anti-diabetic, sunburn relief, immune boost, anti-ageing and anticancer[25]
16	*Allium sativum (garlic).*	-	ethyl linoleate	antioxidant, anti-inflammatory, antibacterial, antifungal, immunomodulatory, cardiovascular protective, anticancer, hepatoprotective, digestive system protective, anti-diabetic, anti-obesity,
17	*Piper longum (pepper)*	fruit	Ethanol extract	anti-inflammatory ,antiasthmatic activity and immunomodulator
18	*Aerva lanata*	aerial part	lupeol, flavonoids, alkaloids. The ethanol extract	anti-asthmatic, anti-microbial activity
19	*Albizzia lebbeck*	the bark and flower	alkaloids, flavonoids, saponins, and terpenoids	The antiasthmatic and antianaphylactic activities[26]
20	*Mangifera indica Linn*	stem bark	tannin , protocatechuic acid, catechin etc., terpenoids friedelin, cycloartan-3β-30-diol and its derivatives, mangiferin	anti-inflammatory, antibacterial, antiulcer, neuropathic pain reduction activity, anti-diarrhoeal and anti-asthmatic activities[27]
21	*Rumex gmeline*	-	Caffeic acid, glycosides,caffeoyl glycoside	Anti inflammatory, increase digestion, heart diseases
22	*Abrus precatorius*	leaves	Triterpenoid saponins	Anti-inflammatory, treat tetanus[28]

RESEARCH ARTICLE

Literature's Response to Environmental Degradation : A Fresh Look

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ABSTRACT

Environmental literature has for a long time been an important force in combating the increasing problem of the denigration of nature. By this genre's authors weaving convincing stories which extol the beauty and intricacy of nature, they foster a deep sense of appreciation for the environment while at the same time highlighting its delicateness. Important figures such as Rachel Carson, Barbara Kingsolver, and Edward Abbey have utilized storytelling to elucidate urgent environmental issues, sensitize people and demand sustainability in their works. Thus, this research revisits some of these contributions that environmental literature has made so far in order to depict how it can make a difference to public opinions and policy making. This research also investigates how seminal literary works exemplify not only environment crises but also proffer alternative solutions based on preservation, sustainable practices and culture of care. This paper traces the historical development of environmental literature along with its affiliation with ecological activism. The persistence in literary efficacy is demonstrated through writing as an agent for transformation over long periods. It thus seeks to underline that we must fit intellectual insights derived from literature into wider debates about our environment.

Keywords:

INTRODUCTION

Environmental Degradation occurs through factors of pollution such as air, water and soil including biodiversity degradation and loss of wildlife Factors, environmentalists work tirelessly to address these challenges and find solutions to the evolving environmental issues. They warn people about the impact of their modern lifestyle and urge them to adopt more environment friendly habits. Originally based on science, an environmental study has been expanded to include the humanities and social sciences. Books play an important role in this effort, using their qualities to educate people about the importance of environmental consciousness. Environment has been a major theme in ancient Indian, Chinese, Japanese and Western literature. Historically, literature has been pro-environmental and continues to be so today. Climate dilapidation is one of the 10th intimidations formally highlighted by the U.N' High-Level Threat Council. It is caused by the destruction of ecosystems and loss of wildlife caused by degradation of resources such as air, water, soil and others. Although these changes can occur naturally, human behavior appears to be more destructive. When habitats are destroyed, biodiversity is lost, natural resources are destroyed, and the environment is severely damaged. The main areas of concern are air pollution, smog, ozone depletion, pollution of marine environment, hazardous waste, emissions, intensive industrialization, tourism unplanned, deforestation and global warming. Pollution is a global issue, affecting even remote areas. Chlorofluorocarbons (CFCs) are the main cause of ozone depletion. When industrial processes release toxic gases, they rise in the stratosphere and destroy the ozone layer. Acid rain, smog and poor air quality are some of the effects of air pollution. Nature degradation has been exacerbated by the increasing number of vehicles which emit large amounts of carbon monoxide, unburned hydrocarbons and methane Heavy technology has destroyed cities and natural areas. In addition, unplanned tourism has led to deforestation, damaging the environment. The following table talks about the various aspect of natural degradation (Credit to internet). It is often said that forests precede mankind and deserts follow. The world's pristine tropical forests are losing 50-60 million hectares every year. These forests have become powerful developments, and their destruction threatens the extinction of many species. One of the unfortunate consequences of environmental degradation is global warming.

Melting glaciers and polar ice caps are profoundly altering the landscape and further upsetting the ecological balance. William Wordsworth stands as an environmentalist. Nature holds an independent and significant reputation in his poems, reflecting his defined philosophy and authentic view of nature. Wordsworth did no longer remember the study of nature as a technological know-how however approached it intuitively. His mindset toward technology changed into not specifically high quality (Durrant 1). He noticed the environment as a living entity, believing in a divine spirit that pervades all its components. Wordsworth emphasised nature's ethical, physical, and spiritual impact on human beings. He believed that people and the surroundings coexist in a communion. His poems, consisting of "The Prelude," "Tintern Abbey," "Ode on Intimations of Immortality", and "The World is Too Much with Us", mirror his perspectives. Wordsworth's poetic expressions spotlight the warfare among the surroundings and humanity and the degradation of this union. Wordsworth's perception is completely expressed in his poem "Tintern Abbey," which seemed in "The Lyrical Ballads" in 1798. For Wordsworth, people and the environment exist in a close spiritual union. Like many conventional Indians, he revered nature and noticed it as an ideal healer with the strength to heal sick or grief-troubled hearts. William Wordsworth explores the interdependence of nature and spirituality, expressing his romantic notion that nature is an abundant wellspring of inspiration and spiritual understanding Wordsworth sees nature as an expression of the essence of the divine, and creates a sense of eternal connection and transcendence. In his poems, Wordsworth laments the absence of the "light of the mind" of childhood, where the natural world seems to be flooded with divine light Wordsworth in Ode

Intimations of Immortality from Early Childhood says

There was a time when meadow, grove, and stream, The earth, and every common sight, To me did seem Appareled in celestial light, The glory and the freshness of a dream (14-18) These lines reflect Wordsworth's childhood view of nature as a sacred and ethereal realm, imbued with deep spiritual meanings. Wordsworth also reflects on the depth of his relationship with the divine that diminishes with age. But the author also suggests that

traces of this spiritual knowledge will remain, offering comfort and serving as a reminder of our eternal identity. He argues that although the primordial energy of the divine in nature is tempered, it is augmented by a growing philosophical understanding of our eternal relationship with nature and the spiritual realm that will replace. "The World Is Too Much With Us" addresses the war among nature and humanity. Although written centuries in the past, it offers with the modern hassle of environmental degradation. The excessive materialism and current services of brand new global have alienated humans from nature. He feedback: "The global is too much with us; past due and shortly, Getting and spending, we lay waste our powers..." (line 1-2) Wordsworth's critique of humanity's choice to devour all that surrounds them highlights the sacrifices made for progress. "We have given our hearts away, a sordid boon," reflects the worldly development of humanity. Wordsworth, alongside William Blake, had insight into the trouble of environmental degradation. Geoffrey Hartman writes, "The tempo of industrialization regarded to Wordsworth to encourage a rootless and summary kind of existence, a man-made nature alienating us from nature" (132). Wordsworth pessimistically foresaw that materialistic development might have effects, and the destruction of the environment by human short sightedness could hold. This might bring about nature's rebellion. "The winds a good way to be howling at all hours" may additionally symbolize stormy, polluted air, one final results of environmental degradation.

Robert Frost focuses man's integration with nature. In poem "Birches," nature is depicted with a mix of realism and creativeness, taking pictures both its harshness and its mild beauty. The poem opens with a brilliant description of birch trees bent by means of the ice storms of iciness. Frost paints a photo of the bushes weighted down with ice, bending below the load till they're permanently bowed. This imagery illustrates the relentless pressure of nature, emphasizing its energy to shape and transform the landscape. However, Frost contrasts this harsh reality with a extra whimsical, nostalgic view of nature via the eyes of a boy swinging on the birches. The speaker prefers to believe that the bushes are bent no longer by the ice but with the aid of a boy who has been swinging on them. This vision introduces a feel of playfulness and innocence, highlighting nature as a playground for younger creativeness and freedom. The act of swinging at the birches symbolizes a brief escape from the burdens of grownup life and a go back to the simplicity and pleasure of adolescence. Frost's depiction of nature in "Birches" also explores the subject of resilience. The birch timber, despite being bowed by using the ice, do not wreck. This resilience is mirrored inside the human spirit, suggesting a potential to undergo and adapt to existence's demanding situations. The interplay among the literal and the metaphorical in Frost's depiction of the birches creates a wealthy, layered know-how of nature. He learned all there was To learn about not launching out too soon And so not carrying the tree away Clear to the ground. He always kept his poise To the top branches, climbing carefully With the same pains you use to fill a cup. (35-41) Moreover, the poem reflects at the preference for stability between earthly struggles and spiritual aspirations. The act of hiking the birches and then returning to earth can be seen as a metaphor for the human condition: attaining for better beliefs and desires even as final grounded in fact. In "Birches," Frost masterfully combines detailed natural observation with imaginative interpretation; It also represents nature's undertaking to humanity and the ability for environmental victory and renewal. Wordsworth alludes to historic Greek gods Proteus and Triton, seeing Proteus rising from the ocean to deal with the injustices inflicted upon nature and restore the misplaced stability of the surroundings.

Barbara Kingsolver has made a significant contribution to the forthcoming genre of climate fiction (Cli-fi), which seeks to explore the causes, consequences, and emotions surrounding global warming Her work, and others have within that genre, is a case study, illustrating the process of activist fiction. and blends with uniqueness Cli-fi combines these elements to demonstrate the dramatic impacts of climate change in specific areas and create options for populations attempting to adapt or mitigate these impacts Through science will be presented well the novel focuses on the environment and how climate change has affected the earth, causing ongoing and often unforeseen devastation. It refers to the conflict between simultaneously protecting the environment and protecting individual livelihoods. *Flight Behavior* tackles one of today's most controversial topics: climate change. With subtle versatility and empathy, Barbara Kingsolver dissects the motivations of denial and trust in a world of uncertainty. Her work generally focuses on social justice, ecology, and connections between people, their communities, and the environment. *Flight Behavior* is a successful realistic example of climate fiction (Cli-fi) that directly confronts climate

change, explores environmental issues and highlights the potential impact of global warming on the monarch butterfly The novel weaves social and environmental issues together to provide a comprehensive perspective on climate change. It focuses on the effects of climate change on a butterfly, but this incredible approach immediately reveals how the phenomenon applies to a wider group of humans and non-humans and Kingsolver clarified in an interview that his intention is to warn the public about the dangers of climate change through his writings. By personalizing the experience of global warming and acting out its effects, he seeks to bring it to life and help readers imagine the future.

Literature has traditionally educated humanity about the significance of the herbal environment and keeps to achieve this these days. A new genre of literary writing, referred to as "Environment and Literature," is gaining popularity. Professional agencies just like the International Society for Environmental Ethics (ISEE), with almost twelve hundred participants generally in the U.S.A (Texas), recommend for environmental conservation through literature. The International Society for Environmental Ethics (ISEE) is an organisation dedicated to educating individuals about the ethical principles and philosophical perspectives related to the environment and nature. A climatic ethic is a philosophical belief that asserts the moral obligation of humans to uphold and preserve the natural environment. It seeks to address the appropriate treatment of other species (both plants and animals), the responsible utilisation of Earth's natural resources, and the recognition of the aesthetic value derived from nature. The society functions as a subsidiary institution of the American Philosophical Association, with a membership of around 700 individuals spanning across more than 20 nations. Different associations take multiple initiatives for energy conservation shown in table 2. A significant portion of ISEE's present membership consists of individuals who specialise in philosophy, education, or environmentalism. Writers of this new genre do no longer view the pastoral writings of the past as proper nature-writing today. The nature poetry of preceding ages has advanced into the eco-poetics of the cutting-edge generation. This shift began in Henry David Thoreau's journal Walden, where he wrote, "I went into the woods because I wanted to live intentionally, to encounter only the necessary facts of life, and to know what I could not learn or know that I should not live." when I came to die" (Hamilton). Thoreau's thoughts in "Walden" sowed the seeds of this new book. In courses on environmental literature, students are encouraged to keep journals and record their findings as accurately as scientists and as creatively as poets. A plant is observed for 30 minutes, then illustrated and explained in a scientific and poetic way. American University Professor Robert Haas, former American Poet Laureate, stands out in this regard. She takes her students on outdoor classes and emphasizes the importance of having first-hand experiences with nature. American authors and poets such as Jonathan Bate, Terry Tempest Williams and Jay Parini are notable environmentalists and literary figures. Tempest's book "Asylum" became an instant classic, chronicling personal environmental struggles in Salt Lake City. Bate argues that poetry, with its ability to evoke emotional responses and create vivid imagery, can play a crucial role in raising awareness about environmental issues. He believes that by engaging with poetry, readers can develop a more empathetic and holistic understanding of nature, leading to a greater commitment to environmental preservation. Bate discusses the role of literature in fostering a sense of place and identity. He argues that through the depiction of specific landscapes and ecosystems, poets can help readers develop a deeper appreciation for their local environments.

CONCLUSION

Often referred to as "cultism", the idea of coexistence and harmony with nature is not new to Indians. Indian scriptures like the Vedas, Puranas and Upanishads have long advocated this philosophy. All living things are taught to be members of the "five elements" (the five elements of nature: earth, water, air, fire, and sky). Our bodies are part and parcel of our environment. Scripture teaches that after death our bodies return to these things. Thus, even after death, living things help to protect the environment. We owe our lives to nature, and we have a moral and sacred duty to repay this debt. It is time for modern humanity to understand that environmental destruction means self-destruction. Environmentalists try to educate people to change their lifestyles and become more environmentally friendly, but their warnings often go unnoticed. As inhabitants of this planet, we need to recognize the importance of environmental protection and restore our lost connection with nature.

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Table.1: Various Aspects of Climate Crises

Aspect	Statistic	Source
Climate Change	Global warming has increased by approximately 1.0°C above pre-industrial levels.	Intergovernmental Panel on Climate Change (IPCC)
Warmest Decade	The decade 2011-2020 was the warmest on record.	World Meteorological Organization (WMO)
Deforestation	The world lost 420 million hectares of forest between 1990 and 2020.	Food and Agriculture Organization (FAO)
Amazon Deforestation	17% of the Amazon rainforest has been lost in the past 50 years.	National Institute for Space Research (INPE), Brazil
Biodiversity Loss	One million species are at risk of extinction, many within decades.	Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES)
Vertebrate Decline	There has been an average 68% decline in vertebrate species populations between 1970 and 2016.	World Wildlife Fund (WWF)
Air Pollution	Air pollution is responsible for 7 million premature deaths annually.	World Health Organization (WHO)
Plastic Pollution	8 million tons of plastic waste enter the oceans each year.	United Nations Environment Programme (UNEP)
Water Scarcity	By 2025, 1.8 billion people will live in regions with absolute water scarcity.	United Nations
Freshwater Use	Agricultural activities account for approximately 70% of global freshwater use.	Food and Agriculture Organization (FAO)

Table.2: Different organisation focusing on Environmental Conservation

Associations Promoting Environmental Conservation through Literature:

Name of Organisation	Activity	Main Focus
Association for the Study of Literature and Environment (ASLE)	Promotes the understanding of nature and culture through literature.	Conferences, publications, and collaborative projects between scholars and writers.
International Society for Environmental Ethics (ISEE)	Focus: Promotes research and discussion on environmental ethics.	Activities: Publications, conferences, and educational resources.
Orion Society	Publishing the Orion magazine, educational programs, and workshops.	Connecting nature, culture, and place through literature.
Rachel Carson Center for Environment and Society	Promotes interdisciplinary environmental research and writing.	Fellowships, publications, conferences, and public outreach.
Environmental Humanities Initiative (EHI)	Fosters interdisciplinary research and writing on environmental issues.	Workshops, publications, and public events.
Nature Conservancy's Nature Writing Initiative	Encourages literature that promotes environmental awareness and conservation.	Writing contests, publications, and support for nature writers.
The Center for Environmental Filmmaking	Promotes environmental conservation through documentary films and media.	Filmmaking courses, film festivals, and environmental documentaries.
Literature and the Environment Program at University of Nevada, Reno	Academic program dedicated to the study of literature's role in environmental conservation.	Courses, conferences, and publications.

Credit to internet

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RESEARCH ARTICLE

Effect of Foliar Application of Different Organic Sources of Nutrients on Growth and Yield of Soybean (*Glycine max* L.)

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ABSTRACT

A field experiment was carried out at Shri Guru Ram Rai University, Pathri Bagh Dehradun, during the summer of 2022 with a goal of evaluating the Effect of Foliar Application of different Organic Sources of Nutrients on Growth and Yield of Soybean [(*Glycine max* L.) Merril]. The experiment was laid down in Randomized Block Design (RBD) comprising of three replications and twelve treatments. Recommended doses of fertilizers (RDF) was applied as basal application to all the treatments. The result showed that Treatment T_{11} (Vermiwash at 5% Foliar application + Beejamrit at 5% Foliar application + Panchagavya at 5% Foliar application + Neem Leaf Extract at 5% Foliar Application) has showed significant increase in both growth and yield parametres viz Maximum Plant Height (70.99 cm), Number of Branches (7.66), Effective Root Nodules (62.67), Plant Dry Weight (63.42g), Crop Growth Rate (.702 gm/m^2/day), Relative Growth Rate (0.020 g/g/day) and Yield attributing parameters like Number of seed/pod (3), Number of Pods per plant (69.33) as well as Seed yield (591.31 kg/ha), Straw yield (914.01 Kg/ha), Oil Content (19.76%), Protein Content (39.97 %) and Harvest Index (39.31%) while the lowest growth and yield parametres was found in Control (T_0).

Keywords: Soybean, Natural Farming, Beejamrit, Panchagavya, Neem Leaf Extract, Vermiwash, Seed Yield, Organic Farming.

INTRODUCTION

Soybean (*Glycine max* L. Merrill) is a beneficial oilseed pulse crop of country as well as the world. It is designated as wonder crop of current century and called as "Golden Bean". Soybean is the cheapest source of quality protein and it

is called "Poor man's meat". Our country is a major consumer of oilseed crop & their products account for about 10.2% of global consumption of edible oils as well as oilcakes meals.). Soybean is the only oilseed crop that produces half of edible oil in whole world. It is grown all over India especially in Madhya Pradesh because it has wide range of adaptable climate to agro climatic condition & better market value. Being a leguminous crop, it improves soil fertility by fixing atmospheric nitrogen at rate of 65 to 115 kg/ha/year with process of symbiosis through Rhizobium Japonicum. According to many literature sources, this leguminous crop has a protein content of about 30-40% and oil content ranging from about 14% to20% (Al-Tayar *et al*., 2021). Protein content of this crop contains mainly amino acids needed for human nutrition also soybean oil content rates major in unsaturated fatty acids like an oleic and linoleic (Al-Tayar *et al*., 2021 Carrera & Dardanelli, 2017). The chemical composition of Soybean and their numerous uses shows how soybean production can fulfill the needs of continuous growth of population (Medic *et al*., 2014). It has high Fibre (4%) & Carbohydrate (30%) that is why it is called as Golden Bean, Wonder crop & Man made meat. The significant increase in protein content with combined application of recommended dose of fertilizer and different organic formulations is confirmed by the results recorded by Chaudhary *et al*. (2017). Brazil ranks 1st in Soybean Production with 153,000,00 Metric Tonnes & 38.6% of Global Production followed by USA, Argentina, China, India and many more. Farmyard Manure being source of all essential elements, improves soil organic matter and humus part of soil. Combined application of organic manure and fertilizer is very effective in realization of high yield and high response to nutrients (Singh *et al.* 2013).

With the use of organic sources as foliar application promote rapid increase in soybean yield and results on obtaining high quality seeds, which is an alternative method for supplying plant nutrition (Domingos *et al*., 2021; Domingos *et al*., 2019). Incorporation of different organic sources like- Panchagavya, Beejamruth, and Jeevamruth increases the plant height along with chemical fertilizers on the vegetative growth and accumulation of metabolic material (Palve *et al* (2011) and Tharmaraj *et al* (2011) and also there will be increase in growth and yield by combine application of various organic sources of nutrients like (Beejamrit, Panchgavya, Neem Leaf Extract, Vermiwash (Devi *et al.* (2013). Beejamrit: This is a practice where seeds are coated with a cow dung and urine mixture. It's an all-natural method of improving seed quality and encouraging strong plant development. Panchgavya: It is a traditional formulation in Ayurveda and organic farming practices that is made from five products derived from cows (panch means five and gavya refers to cow-related. Incorporation of recommended dose of fertilizers and panchagavya as a foliar spray at various stages of crop growth conducts betterment of photosynthesis activity of the plant and more extensive root system and thus, helps plant to extract more nutrient from soil resulting in development of yield components of the crop (Vimalendran and Wahab (2013). Neem Leaf Extract: Is a natural product derived from the leaves of the neem tree (*Azadirachta indica*). It can also be used as foliar spray in soybean crop production. Diluted Neem Leaf Extract is sprayed directly onto plant leaves to control pests and diseases. It is important to apply during cooler times of the day to minimize potential leaf burn under hot sun. It acts as a detergent, making soybean leaves less attractive to pests and prevent pests from feeding on the plants and transmitting diseases, thus protecting the crop. Vermiwash: It is a liquid extract obtained from vermin composting, a process where earthworms (usually species like Eisenia fetida or Eisenia andrei) break down organic matter such as kitchen waste, crop residues, and cow dung. Dilute vermin wash with water (usually in a ratio of 1:10 to 1:20) and spray it on soybean foliage ensuring thorough coverage of both sides of the leaves. Foliar application allows nutrients to be absorbed directly through the leaves, promoting rapid nutrient uptake and enhancing plant growth. It is is a valuable organic input in soybean crop production, offering nutrient-rich fertilization, enhanced plant growth, and improved soil health. Its natural properties make it a preferred choice for farmers looking to adopt environmentally friendly and sustainable agricultural practices.

MATERIALS AND METHODS

Description of study site

The paper present materials and methodology used in the experiment titled "Effect of Foliar Application of different Organic Sources of Nutrients on Growth and Yield of Soybean (*Glycine max* L.)" with brief description of

experiment's site, sampling procedures, soil characterists, climatic conditions during crop growth, cropping history, etc. The Experiment block of the School of Agricultural Sciences, Shri Guru Ram Rai University (SAS - SGRRU), Pathribagh Dehradun, Uttarakhand, is located in the northwest of the state at an elevation of 450 meters above mean sea level (MSL) and between 29°58' and 31°2'30' North latitude and 77°34'45'' and 78°18'30'' East longitude. The field experiment was carried out during *Kharif*2022. The average weekly maximum temperature during 2022 - 2023 varied between 15.2 ºC to 37.8 ºC, respectively. The test site was sandy loam with a pH of 6.5, organic carbon of 0.4%, available nitrogen of 3.52%, available phosphorus of 7.1%, and available potassium of 18.1%The experiment was laid down in Randomized Block Design with three replications consisting 12 Treatments*viz.*T_0(Control), T_1(Vermiwash at 10% Foliar Application), T_2(Beejamrit at 10% Foliar Application), T_3(Panchagavya at 10% Foliar Application), T_4(Neem Leaf Extract at 10% Foliar Application), T_5(Vermiwash at 5% Foliar Application + Beejamrit at 5% Foliar Application), T_6(Vermiwash at 5% Foliar Application + Panchagavya at 5% Foliar Application)T_7(Vermiwash at 5% Foliar Application + Panchagavya at 5% Foliar Application), T_8(Vermiwash at 5% Foliar Application + Neem Leaf Extract at 5% Foliar Application), T_9(Beejamrit at 5% Foliar Application + Neem Leaf Extract at 5% Foliar Application), T_{10}(Panchagavya at 5% Foliar Application + Neem Leaf Extract at 5% Foliar Application) and T_{11}(Vermiwash at 5% Foliar Application + Beejamrit at 5% Foliar Application + Panchagavya at 5% Foliar Application + Neem Leaf Extract at 5% Foliar Application).

The seeds of Soybean variety: Pant Soybean - 21 were sown in line at 30 cm apart using a seed rate of 80 Kg/ha in June 25, 2022.The experimental field was ploughed, and then it was adequately prepared with the help of a tractor-drawn leveller. During the field preparation, vermicompost, sieved cow dung and different doses of 30 kg N, 60 kg P_2O_5, 30 kg K were provided and then field is immediately covered with dirt. FYM (0.65% N, 0.25% P, and 0.55% K) was added to the soil and mixed well before sowing. Vermiwash was sprayed at 30–40 DAS, and the seeds were treated with Beejamrit24 hours prior to planting. Treatments were applied twice by spraying over a standing crop. The first spray was applied at 30 days after sowing, while the second spray was applied 45 days after sowing in field. The positive effects of panchgavya on soybean on growth and production, manifested when it was specifically supplied during the reproductive growth stage rather than vegetative and ripening stages, which exerted a feed-forward effect on photosynthesis coupled with an increased in both stomatal conductances. The crop was manually harvested with a sickle after the grain hardened and reached a moisture level of 12% -15%. The collected material was then sun-dried for three to four days in order to separate the grain from the straw.Data on growth and yield attributes were recorded during the time of crop growth and at the time of harvesting as well. Seed and Straw yield were also recorded during harvest time. Protein and Oil content were determined by standard methods. The data were statistically analysed using standard procedures of ANOVA at 5% level of significance. The approach developed by *Gomez and Gomez* (1984) was used to statistically analyze the data by using analysis of variance as applicable RBD.

RESULTS AND DISCUSSION

A significant difference in all the growth parameters among treatments at 2022 was observed in tables. All the treatment showed a significant increase in growth parameters in comparison to control plot. In 2022 the maximum growth and yield attributing characters was observed in treatment **T_{11}***viz* - Maximum Plant height (70.99 cm) , Number of Branches (7.66), Effective Root Nodules (62.67), Plant Dry Weight (63.42g), Crop Growth Rate (.702 gm/m^2/day), Relative Growth Rate (0.020 g/g/day) and Yield attributing parameters like Number of seed/pod (3), Number of Pods per plant (69.33) as well as Seed yield (591.31 kg/ha), Straw yield (914.02 Kg/ha), Oil Content (19.76%), Protein Content (39.97 %) and Harvest Index (39.31%) followed by **T_8** viz Maximum Plant height (67.113 cm) , Number of Branches (6.667), Effective Root Nodules (61.67), Plant Dry Weight (63.087g), Crop Growth Rate (.688 gm/m^2/day), Relative Growth Rate (0.020 g/g/day) and Yield attributing parameters like Number of seed/pod (3), Number of Pods per plant (65) as well as Seed yield (588.53 kg/ha), Straw yield (913.33 Kg/ha), Oil Content (19.703%), Protein Content (39.91 %) and Harvest Index (39.18%) and lowest being recorded in **Control** viz - Minimum Plant height (57.9 cm), Number of Branches (4.33), Effective Root Nodules (42.33), Plant Dry Weight

(43.843g), Crop Growth Rate (.487 gm/m²/day), Relative Growth Rate (0.018 g/g/day) and Yield attributing parameters like Number of seed/pod (2.667), Number of Pods per plant (39) as well as Seed yield (421.1 kg/ha), Straw yield (751.991 Kg/ha), Oil Content (17.29%), Protein Content (37.47 %) and Harvest Index (35.89%).

CONCLUSION

Based on the foregoing results and discussion above it can be concluded that Maximum plant height, Branches per plant, Effective Root Nodules, Plant Dry Weight, Crop Growth Rate, Relative Growth Rate and Yield Attributes parametres like - Pods / plant, Seed / pod as well as Seed yield, Straw yield, Protein Content, Oil content was found highest under treatment: T_{11} - Vermiwash 5%Foliar application + Panchgavya 5% Foliar application+ Beejamrit 5% Foliar application+ Neem Leaf Extract 5% Foliar application followed by T_8 - Beejamrit 5%Foliar application + Panchgavya 5% Foliar application and least being Control. Since the conclusions are drawn based on nature of result of 1st year of experimentation without changing the Layout, Crop and Crop Variety. This above study showed that the foliar application of all essential mineral nutrients, either singly or in combinations, was consistently beneficial to soybean growth, development and yield, both in pots and on the field. Similarly, foliar spray during the flowering and pod filling stages, also enhanced the performance of soybean. Plants sprayed during the early pod filling stage of growth, initially had higher values of some vegetative characters than plants sprayed during the early flowering growth stage but, statistically, not significantly different. This was probably due to the fact that all plants had reached the peak of vegetative growth before spraying was done. The fact that spraying during the early pod filling growth stage would be ultimately better than spraying at early flowering, has started manifesting at this initial stage, since the former plants had significantly higher values of most parameters studied.

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Table : 1 Effect of Foliar Application of Different Organic Source of Nutrients on Growth Parametres (2022) of Summer Soybean.

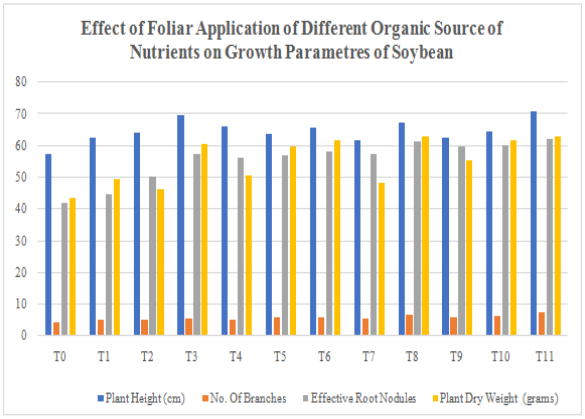
Treatments	Plant Height (cm)	No. Of Branches	Effective Root Nodules	Plant Dry Weight (grams)	Crop Growth Rate ($g/m^2/day$)	Relative Growth Rate (g /g /day)
T_0	57.9	4.333	42.33	43.843	0.487	0.018
T_1	62.76	5.333	45	49.703	0.553	0.018
T_2	64.64	5	50.667	46.57	0.603	0.018
T_3	69.56	5.667	57.667	60.783	0.674	0.019
T_4	66.06	5.337	56.667	51.023	0.567	0.018
T_5	64.24	6	57.337	59.94	0.665	0.019
T_6	65.57	6	58.667	61.933	0.706	0.019
T_7	62.20	5.667	57.667	48.687	0.541	0.018
T_8	67.13	6.667	61.667	63.087	0.688	0.020
T_9	62.85	6	60	55.76	0.617	0.019
T_{10}	64.90	6.333	60.667	62.137	0.689	0.020
T_{11}	70.97	7.667	62.667	63.423	0.702	0.020
C.D.	2.547	0.973	1.285	2.55	N/A	N/A
SE(m)	0.863	0.33	0.435	0.864	0.058	0.001
SE(d)	1.22	0.466	0.615	1.222	0.082	0.002
C.V.	2.303	9.784	1.348	2.692	16.128	10.334

Table 2: Effect of Foliar Application of Different Organic Source of Nutrients on Yield Attributes (2022) of Soybean.

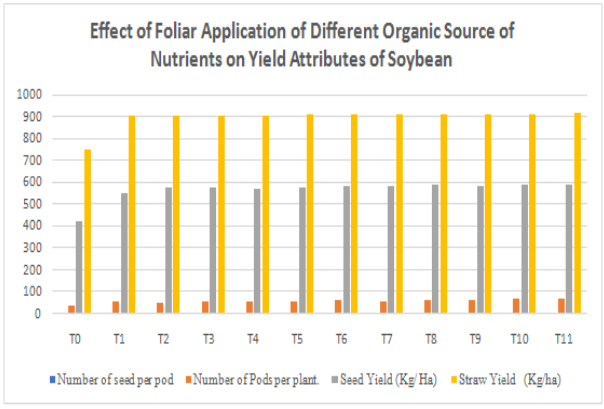
Treatments	Number of seed per pod	Number of Pods per plant.	Seed Yield (Kg/ Ha)	Straw Yield (Kg/ha)
T_0	2.667	39	421.1	751.997
T_1	3	55.667	554.31	903.86
T_2	3	53.667	574.773	903.253
T_3	3	57.667	577.28	906.963
T_4	3	57.333	568.067	906.85
T_5	3	60.667	579.473	910.79
T_6	3	61.667	580.913	911.64
T_7	3	59.667	580.637	910.61
T_8	3	65	588.537	913.33
T_9	3	62.333	581.763	911.047
T_{10}	3	67.334	589.75	911.74
T_{11}	3	69.337	591.31	914.02
C.D.	N/A	1.18	1.717	0.867
SE(m)	0.096	0.401	0.582	0.294
SE(d)	0.136	0.567	0.823	0.415
C.V.	5.607	1.175	0.178	0.057

Table 3: Effect of Foliar Application of Different Organic Source of Nutrients on Quality Parameters of Soybean.

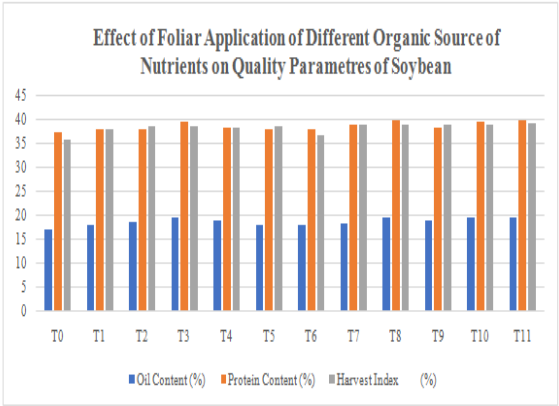
Treatment	Oil Content (%)	Protein Content (%)	Harvest Index (%)
T_0	17.29	37.447	35.893
T_1	18.257	38.043	38.01
T_2	18.72	38.213	38.88
T_3	19.68	39.72	38.89
T_4	19.02	38.583	38.51
T_5	18.11	38.12	38.88
T_6	18.21	38.047	36.913
T_7	18.33	39.117	38.93
T_8	19.70	39.917	39.18
T_9	19.20	38.363	38.967
T_{10}	19.64	39.70	39.15
T_{11}	19.78	39.98	39.27
C.D.	0.028	0.416	0.092
SE(m)	0.01	0.141	0.031
SE(d)	0.013	0.199	0.044
C.V.	0.088	0.629	0.14



Graph 1 - Effect of Foliar Application of Different Organic Source of Nutrients on Growth attributes of Soybean.



Graph 2 - Effect of Foliar Application of Different Organic Source of Nutrients on Yield Attributes of Soybean.



Graph 3 - Effect of Foliar Application of Different Organic Source of Nutrients on Yield Attributes of Soybean.

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RESEARCH ARTICLE

Achyranthes aspera: A Natural and Sustainable Approach towards Health

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ABSTRACT

Mother Nature is brimming with the sources which can act as solution to many of our problems. Floras have the possibility to be used as the therapies to various health associated issues. Ayurveda, an ancient branch of science offers us information about the properties of floras which aid in healing benefits. As per WHO, nearly 80% people are dependent on these home remedies used in their custom since ages. General health also includes taking care of your oral health as well. Oral diseases are very prevalent in the entire world. Understanding the importance of oral health, it should be prioritized. Among the various plants available for maintenance of oral hygiene, Achyranthes aspera is also considered as well. The plant has its place in Amaranthaceae family. The plant extract is extracted from almost all the parts of the plant and numerous solvents are used for recovering it. The plant extracts are used topically or locally in order to get maximum benefits for various oral health related issues namely dental caries and periodontitis. In this article we would be focusing on the effects and possibility of incorporating. This plant for the improvement of oral health.

Keywords: Achyranthes aspera, Amaranthaceae, Dental caries, Periodontitis.

INTRODUCTION

The expression of wholeness in life can be best experienced via the holistic concept of health. Health is a state of well-being not just the absence of any sort of disease/illness. A sound mind resides in a sound body, thus each having an impact on the other. Health can be defined as a state of perfect functioning of human body in which each and every organ is working harmoniously in its optimal capacity. Various ancient and modern therapeutic options are available to prevent any pathology ad to maintain oral as well as overall health. The traditional treatment measures which were part of the ancient civilization are nowadays gaining popularity. Plants act as the main source of treatment for numerous ailments. There are mainly two types of diseases in the world namely communicable and non-communicable diseases. The prevalence of non-communicable diseases is increasing among people of developing countries with less resources leading to bad health, poverty as well as poor development at the level of society. The knowledge available has led to the discovery of many advanced antimicrobial agents through various researches undertaken in the past few years. Indian literature has been foreseen as a brimming example in terms of natural medicine with the knowledge of Ayurveda, a science that encompasses various plants with medicinal value to treat diseases. Periodontal disease refers to the pathology associated with the periodontium, with periodontitis being the most predominant. Periodontitis is an inflammatory ailment which is concomitant with multiple dynamics which are accountable for destruction of supportive tissues in close proximity to the teeth [1].

The foremost etiologic factor which attributes to the pathogenesis of periodontitis is the existence of microbes at the tissuesites which discharge toxins that are detrimental to the tissues. Both the gram positive as well as gram negative bacteria are accountable for the destructive changes. With the deepening of the gingival sulcus there would be translation of the condition from gingivitis to periodontitis and upsurge in the severity of the disease process. The ecological alteration from gram-positive to gram-negative can be esteemed with increasing depth of the periodontal pocket. The management of the periodontal disease ranges from the non-surgical phase concerning to control of inflammatory changes at the soft tissue level to the surgicalphase pertaining to reconstruction of lost tissue structure at sites with the pronounced periodontal tissue destruction. Development of Reactive oxygen species during the disease process is considered to be destructive to the tissues. There are certain enzymes present in some plants which play an integral part in controlling the ROS thus resulting in better healing of tissues [2]. Keeping these properties into consideration certain plants are selected for their added benefits, one such example *Achyranthes aspera*. It is the most commonly used plant in Ayurveda both for management of oral and systemic ailments. The English name for this plant is Prickly chaff flower. The plant is associated with Amaranthaceae family [3]and is the herb which has geographical distribution in the tropical as well as subtropical areas of the world. The parts of the plant such as the root, the seeds, the shoot allen compasses of treasured medicinal properties [4]. Due to its importance as herbal remedy it has been widely used in various countries of South Africa and Asia [5].

Therapeutic Potential of the plant

The plant comprises of therapeutic potential so it is used in various customs. During ancient times, the patient's with a history of cough and asthma were treated with this plant.The plant in its crushed form is boiled in water for the management of patients of Pneumonia. The root of the plant can be used in cases of bowel complaints. The thick paste obtained from mixing the powdered seeds or flowering spikes with water is used topically in case of inoculation of poison from a snake or reptile. It is helpful in reduction of swelling, improving digestion and emitting phlegm. The burnt residue of the plant can be used topically in case of warts and ulcers. The root part of the plant can be utilized to form a paste which can be used for various ailments related to eyes. The fresh paste made out of leaves can act as an analgesic in case of wasp bite. The plant can be used in management of various liver and skin related disorders. The twigs obtained from the stem as well as the roots can be used for brushingteeth [6].

Recovering The Plant Extract

Almost all the parts of the plant are used for extracting the active components which can be used for the prevention of various diseases related to oral cavity. Soxhlet apparatus is the apparatus of choice for retrieving the plant extract.

Different solvents are used for the process in order to gain extracts of different polarity e.g., aqueous, petroleum ether, methanol and benzene. The antimicrobial potency canalso be affected by the polarity of the solvent used for derivation of the extract from the plant source. The solvent used should be approximately 10 times to that of the dried and powdered plant part which is to be used. Most commonly, the root and the stem part of the plant are used in these type of extraction methods. The extract retrieved should be filtered and then stored at a temperature of 4°C approx. The extract should be kept at this temperature till it is being used. The extract derived can be placed at the target site in order to attain the desired results and to know the potency of the drug [6].

Therapeutic Benefits of Achyranthes asperain Dental Practice

The parts of the plants which are commonly used in dentistry in order to maintain oral health are stem and root. Due to the major role of the plant as an antimicrobial agent, it is commonly used for oral hygiene maintenance. In certain parts of India, the plant is used for relieving pain in case of toothache. It also contributes in management of halitosis, teeth whitening and maintenance of strong and healthy gums. Due to the anti-cariogenic potential of this plant it is widely used as a tooth cleaning aid in India since ages. There are many ways of using it for maintenance of oral hygiene. It can be used in the form of dentifrice, mouthwash or a local drug delivery system. In order to obtain the maximum benefits of the plant extract the concentration should be higher than the MIC (Minimum Inhibitory Concentration) of the drug. MIC is termed as the least concentration of the required to produce inhibition of bacterial growth with an absorbance level lesser than 0.05–550 nm (no evident growth). Keeping this thing into consideration, new products are formulated with appropriate concentration in order to provide maximum benefit [8].

Anti-cariogenic properties

As per WHO, Dental caries is considered as one of the most prevalent disease around the globe [9]. The decay or loss of tooth structure due to dental caries is considered to be irreversible in nature, so prevention is a far more desirable goal than the management. For the prevention of the disease, the disease causing pathogens such as S. *mutans, S. sanguis* and *S. mitis*, effective measures should be taken into consideration in order to control the proliferation and thus the levels of the pathogens under check. During the ancient times in the absence of toothbrush and paste, the twigs of this herbal plant were utilized for maintenance of oral hygiene. *A. aspera* has shown marked reduction of *S. mutans* due its antibacterial property. The M.I.C. noted for stem and root extract of the plant is 2.5%. It has shown a considerable amount of inhibition zone against *S. mutans* which indicates its anti-bacterial capacity. Murugan K *et al* recorded the inhibition percentage for different extracts of *Achyranthes aspera* which is ≤94% for methanol extract, ≤74%, for benzene extract, ≤62% for petroleum ether extract and ≤42% for aqueous extracts [10]. A study was conducted in the past in which the Ethanol extract derived from the plant was used against the salivary microbes due to the antimicrobial property possessed by the plant. Saliva samples were collected from children with mixed dentition having moderate caries activity [11]. Diffusion method using agar was selected for antibacterial assay. The outcome was compared with Chlorhexidine which is considered as the standard for such evaluations. The plant extract manifested with significant results interms of medicinal properties. The leaf extract obtained from the plant showed comparable antimicrobial activity against the salivary microflora to as that of Chlorhexidine mouthwash. Jebashree *et at* conclude ina study that the anticariogenic potential of the extract obtained using ethyl acetate was highly potent asan antibacterial agent in comparison with extracts obtained from other solvents [12]. Samson S conducted a comparative study using 0.2% Chlorhexidine and ethanolic extract of root, stem and leaves of the plant for their anti-cariogenic effect on children with moderate caries activity using agar diffusion method. The antibacterial activity is associated with inhibition of growth of pathogenic bacteria as well as quorum sensing alteration occurring resulting in marked reduction in the cariogenic activity following the incorporation of the plant extract in the oral hygiene maintenance routine [11].

***Achyranthes aspera* in Management of Periodontal Diseases**

Achyranthes aspera due to its anti-microbial action can be used for prevention and maintenance of Chronic periodontitis. Ramnarayana Boyapati studied the role of *Achyranthes aspera* in treatment of periodontal diseases, when it is delivered sub gingivally as a locally administered agent along with SRP due to its favourable effect in the form of anti-microbial activity. Three properties of the plant which helps in improving the clinical and the

microbiological aspects included antimicrobial, anti-inflammatory andantioxidant activity [13]. The antibacterial action of the plant is due to the presence of alkanoids andtannins which are among the main phytochemical agents present in the plant. The root extract which is derived from petroleum ether has a strong antimicrobial activity for the gram positive bacteria whereas the methanol and chloroform extract of the plant are used for their antimicrobial activity towards gram negative bacteria. The difference in the anti-microbial activity is due to the difference in composition of cell wall and cell membrane among different bacteria [14]. The radical scavenging activity of the plant towards the free radical formation occurring during the periodontal disease activity was due to the presence of phenolic compounds in the plant extract which was very evident in the studies conducted in the past. The two main radicals targeted by these phenolic compounds were namely 2,2 diphenyl-1-picrylhydrazyl and superoxide which are the main culprits responsible for the destruction of periodontal tissues during the disease process [15].*A. aspera* in its gel form was used a local drug therapy for the protection of periodontal tissues from the pathogens as it is very effective in management of inflammation in tissues [16]. An animal study was conducted by Kumaret al [17]in which the alcoholic extract of the plants was used, the plant extract exhibited stimulation of immune system via the proliferation of T-lymphocytes [18]. The regeneration potential of the plant extract is also helpful in many ways. Due to the phenolic component present in the plant extract it is highly effective in restoration of the lost tissues so itcontributes majorly in the dealing with wounds [19]. The phenolic compounds lead to formation of a film around the exposed wound tissue causing prevention of loss of fluid from the tissues as well as formation of a chemical barrier [20]. The film also acts as a physical barrier by providing insulation to the wound area. This property of the plant helps in better healing of the treated sites. Singh A studied the anti-inflammatory action of the plant extract. The plant extract helps in regulation of the extent of inflammation in tissue via inhibition of pro-inflammatory cytokines namely TNF-α and IL-6 along with inhibition of two enzymes COX-2 and LOX which are involved in production of pro-inflammatory cytokines [21].

CONCLUSION

Oral cavity can be held responsible for a replication of our oral health. It is correspondingly important as the preservation of good overall health. Abandoning of any kind can have permanent and detrimental effects on teeth as well the supportive tissues. Oral hygiene practices are significant in order to maintain a disease free oral environment. Various ancient and modern substitutions are present all over the place from which advantage should be taken in order to facilitate a good oral health. Herbal substitutes are attaining admiration in the medicine as well the dental arenas. Keeping these things in mind various Ayurveda herbs are made of use in today's modern life by integrating the extract of herbs in the routinely used modern products. One such ancient herb is *Achyranthes aspera* which is used for its immense medicinal properties. *Achyranthesaspera* is used in dental practice due to its antagonistic activity towards two of the major problems i.e., dental caries and periodontal diseases. The potency of the drug helps in better tackling of the abovementioned diseases related to oral cavity.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this article**.**

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RESEARCH ARTICLE

Nano $(1,2)^{\star}$-ω-Closed Sets

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ABSTRACT

This study introduces a new class of sets in NBTS, called nano (1,2)*-ω-closed sets, by employing nano (1,2)*-semi open sets. This class of sets is appropriately situated between the classes of nano $\tau_{(1,2)}$-closed sets and nano (1,2)*-g-closed sets. We also describe their relationships and associated characteristics.

Keywords: (1,2)*-g-closed sets, (1,2)*-ω-closed sets and nano (1,2)*-semi open sets.

INTRODUCTION AND PRELIMINARIES

Nano topology is a recent development in topology with real-world applications. It was mainly Lellis Thivagar *et al.* [5] who created the concept of nano topology. Buvaneshwari *et al.*, [1] investigated the concept nano (1,2)*-g-closed sets. We provide some basic definitions as follows: nano (1,2)*-semi open [4] , nano (1,2)*-α-open [2] , nano (1,2)*-g-closed set [1] , nano (1,2)*-sg-closed set [3], nano (1,2)*-αg-closed set [2]. The corresponding closed sets of the aforementioned sets are their complements and so on. In future a nano bitopological space $(U, \tau_{R_{1,2}}(X))$ is simply NBTS.

Nano $(1,2)^{\star}$-ω-closed sets in NBTS

Definition 2.1 A subset H of a NBTS is called a nano (1,2)*-ω-closed set (simply put $N_{(1,2)^{\star}}$-ω-closed set) if $N_{\tau_{1,2}}$-$cl(H) \subseteq U$ whenever $H \subseteq U$ and U is nano (1,2)*-semi open. The complement of $N_{(1,2)^{\star}}$-ω-closed set is said to be

$N_{(1,2)^*}$-ω-open. All of the open (resp. closed) sets are denoted by nano (1,2)*-semi open (resp. $N_{(1,2)^*}$-semi closed, $N_{(1,2)^*}$-α-closed, $N_{(1,2)^*}$-g-closed, $N_{(1,2)^*}$-sg-closed, $N_{(1,2)^*}$-αg-closed).

Proposition 2.2 In a NBTS, each one $N_{\tau_{1,2}}$-closed set is $N_{(1,2)^*}$-ω-closed.

Proof. Let H be any nano $\tau_{1,2}$-closed set and K be any $N_{(1,2)^*}$-ω-semi open set such that $H \subseteq K$. Then $N_{\tau_{1,2}}$-$cl(H) \subseteq K$, since $N_{\tau_{1,2}}$-$cl(H) = H$ and hence H is $N_{(1,2)^*}$-ω-closed.

Remark 2.3 The contrary of Proposition 3.2 was occasionally true, as the example that follows illustrates.

Example 2.4 Let $U = \{a, b, c\}$ with $U/R_1 = \{\{a\}, \{b, c\}\}$ and $X = \{a\}$ then $\tau_{R_1}(X) = \{\phi, \{a\}, U\}$ and let $U/R_2 = \{\{b\}, \{a, c\}\}$ and $X = \{a, c\}$ then $\tau_{R_2}(X) = \{\phi, \{a, c\}, U\}$. In the NBTS, $\{a, b\}$ is $N_{(1,2)^*}$-ω-closed but not nano $\tau_{1,2}$-closed.

Proposition 2.5 In a NBTS, each one $N_{(1,2)^*}$-ω-closed set is $N_{(1,2)^*}$-g-closed.

Proof. Let $H \in \tau_{R_{1,2}}(X)$ and K be any nano $\tau_{1,2}$-open set such that $H \subseteq K$. Since every nano $\tau_{1,2}$-open set is $N_{(1,2)^*}$-semi open and H is $N_{(1,2)^*}$-ω-closed, we have $N_{\tau_{1,2}}$-$cl(H) \subseteq K$ and hence H is $N_{(1,2)^*}$-g-closed.

Remark 2.6 The contrary of Proposition 2.5 was occasionally true, as the example that follows illustrates.

Example 2.7 Thus in Example 2.4, $\{b\}$ is $N_{(1,2)^*}$-g-closed set but not $N_{(1,2)^*}$-ω-closed.

Proposition 2.8 In a NBTS, each one $N_{(1,2)^*}$-ω-closed set is $N_{(1,2)^*}$-sg-closed.

Proof. Let $H \in \mathcal{U}$ and K be any $N_{(1,2)^*}$-semi open set containing . Then $N_{\tau_{1,2}}$-$scl(H) \subseteq N_{\tau_{1,2}}$-$cl(H) \subseteq K$, since H is $N_{(1,2)^*}$-ω-closed. Therefore H is $N_{(1,2)^*}$-sg-closed.

Remark 2.9 The contrary of Proposition 2.8 was occasionally true, as the example that follows illustrates.

Example 2.10 Thus in Example 2.4, $\{b\}$ is $N_{(1,2)^*}$-sg-closed but not $N_{(1,2)^*}$-ω-closed.

Theorem 2.11 In a NBTS, each one $N_{(1,2)^*}$-ω-closed set is $N_{(1,2)^*}$-αg-closed.

Proof. Let $H \in \tau_{R_{1,2}}(X)$ and K be any $N_{(1,2)^*}$-α-open set containing H. Since every $N_{(1,2)^*}$-α-open set is $N_{(1,2)^*}$-semi open and since $N_{\tau_{1,2}}$-$\alpha cl(H) \subseteq N_{\tau_{1,2}}$-$cl(H)$, we have by hypothesis, $N_{\tau_{1,2}}$-$\alpha cl(H) \subseteq N_{\tau_{1,2}}$-$cl(H) \subseteq K$ and so H is $N_{(1,2)^*}$-αg-closed.

Remark 2.12 In a NBTS, the relatives of $N_{(1,2)^*}$-ω-closed sets are independent of the relatives of $N_{(1,2)^*}$-α-closed sets and the family of $N_{(1,2)^*}$-semi closed sets as shown in the following Example.

Example 2.13 Thus In Example 2.4, $\{b\}$ is $N_{(1,2)^*}$-α-closed and $N_{(1,2)^*}$-semi closed but not $N_{(1,2)^*}$-ω-closed and then the subset $\{a\}$ is $N_{(1,2)^*}$-ω-closed but not $N_{(1,2)^*}$-α-closed and $N_{(1,2)^*}$-semi closed.

Theorem 2.14 If $H, K \in \tau_{R_{1,2}}(X)$, then their union $H \cup K \in \tau_{R_{1,2}}(X)$.

Proof. Suppose that $H \cup K \subseteq G$ and G is $N_{(1,2)^*}$-semi open, then $H \subseteq G$ and $K \subseteq G$. Since H and K are $N_{(1,2)^*}$-ω-closed sets, $N_{\tau_{1,2}}$-$cl(H) \subseteq G$ and $N_{\tau_{1,2}}$-$cl(K) \subseteq G$ and hence $N_{\tau_{1,2}}$-$cl(H) \cup K = N_{\tau_{1,2}}$-$cl(H) \cup N_{\tau_{1,2}}$-$cl(K) \subseteq G$. Thus $H \cup K \in \tau_{R_{1,2}}(X)$.

Remark 2.15 In a NBTS, the intersection of two $N_{(1,2)^*}$-ω-closed sets is $N_{(1,2)^*}$-ω-closed.

Example 2.16 Thus in Example 2.4, $\{a, b\}$ and $\{a, c\}$ are $N_{(1,2)^*}$-ω-closed sets, then $\{a, b\} \cap \{a, c\} = \{a\}$ is $N_{(1,2)^*}$-ω-closed.

Theorem 2.17 If a subset H of NBTS is $N_{(1,2)^*}$-ω-closed, then $N_{\tau_{1,2}}$-$cl(H) - H$ contains no nonempty nano $\tau_{1,2}$-closed.

Proof. H is $N_{(1,2)^*}$-ω-closed in NBTS and K be $N_{\tau_{1,2}}$-closed subset of $N_{\tau_{1,2}}$-$cl(H) - H$. Then $H \subseteq K^c$. Since K^c is $N_{(1,2)^*}$-semi open and H is $N_{(1,2)^*}$-ω-closed, $N_{\tau_{1,2}}$-$cl(H) \subseteq K^c$. Consequently, $K \subseteq (N_{\tau_{1,2}}$-$cl(H))^c$. $K \subseteq N_{\tau_{1,2}}$-$cl(H)$. $K \subseteq N_{\tau_{1,2}}$-$cl(H) \cap (N_{\tau_{1,2}}$-$cl(H))^c = \phi$ and hence K is empty.

Theorem 2.18 A subset H of NBTS is $N_{(1,2)^*}$-ω-closed if then only if $N_{\tau_{1,2}}$-$cl(H) - H$ does not contain any nonempty $N_{(1,2)^*}$-semi closed.

Proof. H is $N_{(1,2)^*}$-ω-closed. Let K be a $N_{(1,2)^*}$-semi closed subset of $N_{\tau_{1,2}}$-$cl(H) - H$. Then $H \subseteq K^c$ If. Since H is $N_{(1,2)^*}$-ω-closed, we have $N_{\tau_{1,2}}$-$cl(H) \subseteq K^c$. Consequently, $K \subseteq (N_{\tau_{1,2}}$-$cl(H))^c$. Hence $K \subseteq N_{\tau_{1,2}}$-$cl(H) \cap (N_{\tau_{1,2}}$-$cl(H))^c = \phi$. Therefore K is empty.

Conversely, $N_{\tau_{1,2}}$-$cl(H) - H$ contains no nonempty $N_{(1,2)^*}$-semi closed set. Let $H \subseteq K$ and that K be $N_{(1,2)^*}$-semi open. If $N_{\tau_{1,2}}$-$cl(H) \nsubseteq K$, then $N_{\tau_{1,2}}$-$cl(H) \cap K^c \neq \phi$. Since $N_{\tau_{1,2}}$-$cl(H)$ is a $N_{\tau_{1,2}}$-closed set and K^c is a $N_{(1,2)^*}$-semi closed set of $(U, \tau_{R_{1,2}}(X))$. We have $N_{\tau_{1,2}}$-$cl(H) \cap K^c$ is a $N_{(1,2)^*}$-semi closed set of $(U, \tau_{R_{1,2}}(X))$. $\phi \neq N_{\tau_{1,2}}$-$cl(H) \cap K^c \subseteq N_{\tau_{1,2}}$-$cl(H) - H$ and so $N_{\tau_{1,2}}$-$cl(H) - H$ contains a non-empty $N_{(1,2)^*}$-semi closed set, which is a contradiction to the hypothesis. H is $N_{(1,2)^*}$-ω-closed.

Corollary 2.19 A $N_{(1,2)^*}$-ω-closed set H is $N_{(1,2)^*}$-semi closed if then only if $N_{\tau_{1,2}}$-$scl(H) - H$ is $N_{(1,2)^*}$-semi closed.

Proof. Let H be any $N_{(1,2)^*}$-ω-closed set. If H is $N_{(1,2)^*}$-semi closed, then $N_{\tau_{1,2}}$-$scl(H) - H = \phi$. Therefore $N_{\tau_{1,2}}$-$scl(H) - H$ is $N_{(1,2)^*}$-semi closed.
Conversely, suppose that $N_{\tau_{1,2}}$-$scl(H) - H$ is $N_{(1,2)^*}$-semi closed. We have $N_{\tau_{1,2}}$-$cl(H) - H$ contains the $N_{(1,2)^*}$-semi closed set $N_{\tau_{1,2}}$-$scl(H) - H$. Since H is $N_{(1,2)^*}$-ω-closed, by Theorem 3.18, $N_{\tau_{1,2}}$-$scl(H) - H = \phi$. That is why $N_{\tau_{1,2}}$-$scl(H) = H$. H is $N_{(1,2)^*}$-semi closed.

Theorem 2.20 In a NBTS. The statements that follow are interchangeable:

1. H is $N_{(1,2)^*}$-ω-closed.
2. $x \in N_{\tau_{1,2}}$-$cl(H)$, $N_{\tau_{1,2}}$-$scl(x) \cap H \neq \phi$.
3. $N_{\tau_{1,2}}$-$cl(H) - H$ contains no non-empty $N_{(1,2)^*}$-semi closed sets.

Proof. (1) $\Rightarrow$ (2) : $x \in N_{\tau_{1,2}}$-$cl(H)$ and $N_{\tau_{1,2}}$-$scl(x) \cap H = \phi$. Then $H \subseteq (N_{\tau_{1,2}}$-$scl(x))^c$ and $(N_{\tau_{1,2}}$-$scl(x))^c$ is $N_{(1,2)^*}$-semi open. By assumption, $N_{\tau_{1,2}}$-$cl(H) \subseteq (N_{\tau_{1,2}}$-$scl(x))^c$, which is a contradiction to $x \in N_{\tau_{1,2}}$-$cl(H)$.

(2) $\Rightarrow$ (3) : $K \subseteq N_{\tau_{1,2}}$-$cl(H) - H$, where K is $N_{(1,2)^*}$-semi closed. If $x \in K$, then $x \in N_{\tau_{1,2}}$-$cl(H)$ and so by assumption, $\phi \neq N_{\tau_{1,2}}$-$scl(x) \cap H \subseteq \cap K \subseteq (N_{\tau_{1,2}}$-$cl(H) - H \cap H = \phi$, a contradiction. $K = \phi$.

(3) $\Rightarrow$ (1): Based on Theorem 3.18.

Corollary 2.21 H is $N_{(1,2)^*}$-ω-closed if then only if $H = G - M$, where G is nano $\tau_{1,2}$-closed and M contains no nonempty $N_{(1,2)^*}$-semi closed.

Proof. H is $N_{(1,2)^*}$-ω-closed. Let $G = N_{\tau_{1,2}}$-$cl(H)$ and $M = N_{\tau_{1,2}}$-$cl(H) - H$. Then $H = G - M$.
Conversely, assume $H = G - M$. Let $H \subseteq V$ where V is any $N_{(1,2)^*}$-semi open. Then $G \cap V^c$ is $N_{(1,2)^*}$-semi closed and it is a subset of M. By assumption $G \cap V^c = \phi$. i.e., $G \subseteq V$. $N_{\tau_{1,2}}$-$cl(H) \subseteq G \subseteq V$ and so H is $N_{(1,2)^*}$-ω-closed.

Theorem 2.22 $H \subseteq K \subseteq U, H$ is a $N_{(1,2)^*}$-ω-closed set relative to K and that K is nano $\tau_{1,2}$-open and $N_{(1,2)^*}$-ω-closed in $(U, \tau_{R_{1,2}}(X))$. Then H is $N_{(1,2)^*}$-ω-closed in $(U, \tau_{R_{1,2}}(X))$.

Proof. $H \subseteq A$, where A is any $N_{(1,2)^*}$-semi open set in $(U, \tau_{R_{1,2}}(X))$. $H \subseteq K \cap A$. Since K is nano $\tau_{1,2}$-open and A is $N_{(1,2)^*}$-semi open, $K \cap A$ is $N_{(1,2)^*}$-semi open in $(U, \tau_{R_{1,2}}(X))$. Since $K \cap A \subseteq K \subseteq U$ and $K \cap A$ is $N_{(1,2)^*}$-semi open in $(U, \tau_{R_{1,2}}(X))$. $K \cap A$ is $N_{(1,2)^*}$-semi open in K. So $K \cap A$ is a $N_{(1,2)^*}$-semi open set in K such that $H \subseteq K \cap A$. By hypothesis, H is a $N_{(1,2)^*}$-ω-closed set relative to K. Thus $N_{\tau_{1,2}}$-$cl_K(H) \subseteq K \cap A$. Since $N_{\tau_{1,2}}$-$cl_K(H) = K \cap N_{\tau_{1,2}}$-$cl(H)$, we have $K \cap N_{\tau_{1,2}}$-$cl(H)^c \subseteq K \cap A$ from which we obtain $K \subseteq A \cup (N_{\tau_{1,2}}$-$cl(H))^c$ and $A \cup (N_{\tau_{1,2}}$-$cl(H))^c$ is $N_{(1,2)^*}$-semi open set in $(U, \tau_{R_{1,2}}(X))$. By hypothesis, K is $N_{(1,2)^*}$-ω-closed in $(U, \tau_{R_{1,2}}(X))$ and therefore $N_{\tau_{1,2}}$-$cl(K) \subseteq A \cup (N_{\tau_{1,2}}$-$cl(H))^c$. Since $N_{\tau_{1,2}}$-$cl(H) \subseteq N_{\tau_{1,2}}$-$cl(K), N_{\tau_{1,2}}$-$cl(H) \subseteq A \cup (N_{\tau_{1,2}}$-$cl(H))^c$ and $N_{\tau_{1,2}}$-$cl(H) \subseteq A$. That is why H is $N_{(1,2)^*}$-ω-closed set relative to $(U, \tau_{R_{1,2}}(X))$.

Theorem 2.23 If H is a $N_{(1,2)^*}$-ω-closed set of NBTS such that $H \subseteq K \subseteq N_{\tau_{1,2}}$-$cl(H)$, then K is also a $N_{(1,2)^*}$-ω-closed set of $(U, \tau_{R_{1,2}}(X))$.

Proof. Let A be a $N_{(1,2)^*}$-semi open set of $(U, \tau_{R_{1,2}}(X))$ such that $K \subseteq A$. Then $H \subseteq A$. Since H is $N_{(1,2)^*}$-ω-closed, we have $N_{\tau_{1,2}}$-$cl(H) \subseteq A$. Now $N_{\tau_{1,2}}$-$cl(K) \subseteq N_{\tau_{1,2}}$-$cl(N_{\tau_{1,2}}$-$cl(H)) = N_{\tau_{1,2}}$-$cl(H) \subseteq A$. That is why, K is also a $N_{(1,2)^*}$-ω-closed set of $(U, \tau_{R_{1,2}}(X))$.

Theorem 2.24 In a NBTS, $N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X)) = \{H \subseteq U : H^c \in \mathcal{U}\}$ if and only if every subset of $(U, \tau_{R_{1,2}}(X))$ is a $N_{(1,2)^*}$-ω-closed set.

Proof. $N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X)) = \{H \subseteq U : H^c \in \tau_{R_{1,2}}(X)\}$. Let I, be a subset of $(U, \tau_{R_{1,2}}(X))$ such that $I \subseteq J$ where $J \in N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X))$. Then $N_{\tau_{1,2}}$-$cl(J) = J$. Also $N_{\tau_{1,2}}$-$cl(I) \subseteq N_{\tau_{1,2}}$-$cl(J) = J$. That is why I is $N_{(1,2)^*}$-ω-closed.

Alternatively, let's say that each subset of NBTS is $N_{(1,2)^*}$-ω-closed. Let $J \in N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X)$. Since $J \subseteq J$ and J is $N_{(1,2)^*}$-ω-closed, we have $N_{\tau_{1,2}}$-$cl(J) \subseteq J$. Thus $N_{\tau_{1,2}}$-$cl(J) = J$ and $J \in \{H \subseteq U : H^c \in \tau_{R_{1,2}}(X)\}$. That is why $N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X)) = \{H \subseteq U : H^c \in \tau_{R_{1,2}}(X)\}$.

If $H \in \{H \subseteq U : H^c \in \tau_{R_{1,2}}(X)\}$ then H^c is $N_{(1,2)^*}$-semi open. $H^c \in N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X)) \subseteq \{H \subseteq U : H^c \in \tau_{R_{1,2}}(X)\}$. H is nano $\tau_{1,2}$-open in $(U, \tau_{R_{1,2}}(X))$ and H is $N_{(1,2)^*}$-semi open in $(U, \tau_{R_{1,2}}(X))$. i.e, $H \in N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X))$. That is why $N_{\tau_{1,2}}$-$SO(U, \tau_{R_{1,2}}(X)) = \{H \subseteq U : H^c \in \tau_{R_{1,2}}(X)\}$.

Theorem 2.25 If H is $N_{(1,2)^*}$-semi open and $N_{(1,2)^*}$-ω-closed, then H is nano $\tau_{(1,2)}$-closed.

Proof. Since $H \subseteq H$ and H is $N_{(1,2)^*}$-semi open and $N_{(1,2)^*}$-ω-closed, $N_{(1,2)^*}$-$cl(H) \subseteq H$. Consequently, $N_{(1,2)^*}$-$cl(H) = H$ and H is nano $\tau_{(1,2)}$-closed.

Theorem 2.26 Considering all $x \in U$, either x is $N_{(1,2)^*}$-semi closed or x^c is $N_{(1,2)^*}$-ω-closed in NBTS.

Proof. x is not $N_{(1,2)^*}$-semi closed in NBTS. Then x^c is not $N_{(1,2)^*}$-semi open and the only $N_{(1,2)^*}$-semi open set containing x^c is the space U itself. Consequently, $N_{(1,2)^*}\text{-}cl(x)^c \subseteq U$ and so x^c is $N_{(1,2)^*}$-ω-closed.

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REVIEW ARTICLE

A Review on Anxiety Induced Memory Loss

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ABSTRACT

Memory is significantly impacted by complexes biological and neurological pathways affecting a large population group globally. The impairment of memory due to anxiety is mainly due to diverting concentration from cognition related task and disturbance of attention. The significant areas of brain such as amygdala which is activated due to stress leading to activation of hippocampus which impacts adrenal gland leading to excessive levels of cortisol inhibiting branching of neurons and neurogenesis. Imbalances in levels of various neurotransmitters such as GABA, Glutamate, dopamine and serotonin create disturbance in plasticity of neurons leading to impaired memory and hindrance in old memory retrieval. Severe anxiety disturbs functions and alters anatomy of prefrontal cortex effecting encoding of memory, decision making ability and sleep significantly impacting consolidation of memory. The pharmacological treatment includes SNRI's, SSRIs, nootropic agents and benzodiazepines in combination with non-pharmacological approach such as physical activities, cognitive behavioural therapy, and relaxation techniques. Recent research involves neuronal inflammation, interaction of gut with brain, innovations regarding novel therapeutic agents such as cannabinoids and aesthetics like ketamine. Future research advancement can be focused on advancement in neuroimaging techniques, biomarker for early diagnosis and genetic profiling for personalized treatment. Neurogenesis stimulating pharmacological treatment, lifestyle modification and innovative therapies such as stem cell therapy, transcranial magnetic stimulation holds promising outcome regarding the reversal of memory impairment due to anxiety.

Keywords: Memory, Anxiety, Neurogenesis, Neuroinflammation, Neurotransmitters.

INTRODUCTION

Anxiety can affect memory as brain focuses more towards the reason that is causing anxiousness than recalling old memories or memorizing new ones(Lukasik *et al.*, 2019). The concentration and attention are important for formation and retention of memories which gets disturbed during chronic anxiety(Lindau *et al.*, 2016). The anxiety management through therapies, medication and relaxation techniques can sometimes be beneficial in reducing load on cognition due to anxiety hence improvises memory. The connection of anxiety and memory loss involves complex neurological and biological pathways(Costanzi *et al.*, 2021). Anxiety triggers various physiological responses in brain leading to heightened arousal and excessive worry (Voss *et al.*, 2017). According to WHO, in 2022 anxiety disorders have significantly impacted around 250 million people globally which makes it a common heath care condition coexist with memory loss effecting significant population worldwide (WHO, 2023). Anxiety disorders include panic attack, social anxiety and generalized anxiety disorder. The individuals affected by generalized anxiety disorder are commonly observed with impairment of both episodic and working memory (Zlomuzica e*t al.*, 2014).The memory loss due to anxiety can be varying in signs of presentation and severity (Dillon & Pizzagalli, 2018). Some individuals with anxiety can experience mild concentration and memory difficulty during the phase of anxiety and some individuals can face sever challenges in overall function of cognition which impacts the memory coding and retrieval (Roberts & Karatsoreos, 2021). Coping ability, resilience, comorbidities and sleep disturbance along with anxiety are important factors which will severely impact memory (Voss e*t al.*, 2017).

Pathophysiology of anxiety induced memory impairment.

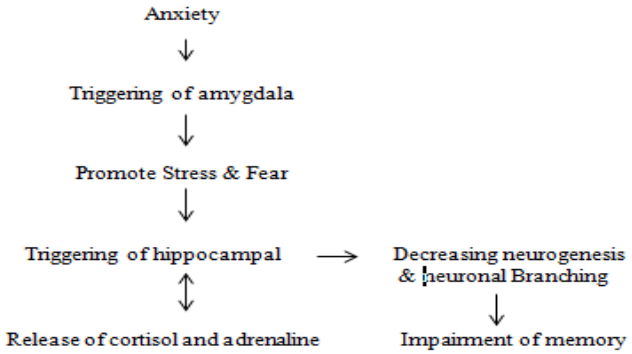
The memory loss induced by anxiety involves interaction between various neurotransmitters, cellular processes, hormones and regions of brain (Robinson *et al.*, 2013).

Activation of Amygdala

A region of brain known as Amygdala responsible for emotional processing involving stress and fear is triggered during anxiety. This trigger sends the signals to hypothalamus which induces release of hormones such as adrenaline and cortisol from adrenal gland(Noori *et al.*, 2018) .

Functional changes in hippocampus.

The hippocampus which is an important region involves in functions such as formation and retrieval of memory gets effected by the primary stress hormone which is cortisol that is release due to hypothalamus triggering due to anxiety(Opitz, 2014). Excessive amount of cortisol markedly decreases neurogenesis and neuronal branching (dendritic atrophy) in hippocampus leading to impaired memory (Voss *et al.*, 2017).



Flow chat of Activation of Amygdala and Functional changes in hippocampus due to anxiety leading to impaired memory

Imbalance in neurotransmitters

Anxiety imbalances and alters neurotransmitters such as dopamine, serotonin and norepinephrine which are important for plasticity in synaptic cleft which helps the modification in existing neurons and in formation of new neuronal connections which effects memory and learning (Nimgampalle *et al.,* 2023).

Dysfunction of prefrontal cortex

The prefrontal cortex is involved in execution of function such as decision making, Memory, concentration and attention which is greatly impacted due to chronic anxiety. The changes in functioning of this region of brain can impact focused attention of individual on task and encoding of new memories(Zheng *et al.,* 2021).

Disturbances in sleep

Sleep disturbance such as alteration in sleep pattern and insomnia along with anxiety impacts the integration of new information in long term memory hence it impairs process of consolidation (Schneider *et al.,* 2020).

Effects of chronic stress

Anxiety due to chronic stress leads to several changes in structure and functions of brain which results in loss of synaptic clefts, dendritic retraction and changes in connectivity of neurons which are involved cognition and memory (Lindau *et al.,* 2016).

Pathways related to inflammation

The inflammatory pathways are initiated and activated due to chronic anxiety leading to neuronal inflammation resulting in imbalance in levels of neurotransmitters, impermanent plasticity of synaptic cleft and extensive damage to neurons impacting memory functions.

Epigenetic modifications and genetic factors.

The epigenetic modification and genetic predisposition significantly impacts susceptibility of individual with anxiety causing impaired memory with lots of variation (Ahmad et al., 2022). The disturbance in neuronal transmission, decreasing of neuronal plasticity and genes responsible for stress response are the important factors that impact function of memory (Meier et *al.,* 2019).

Effects of comorbidities

The occurrence of anxiety along with other mental health condition including PTSD, depression and disorders related to substance misuse which synergistically contributes to memory impairment. Comorbidities should be considered during the treatment of memory impairment due to anxiety (Penninx *et al.,* 2021).

Pathways involved in anxiety induced memory loss.

Memory loss due to imbalanced neurotransmitters in anxiety

The cognition impairments occur due to imbalance of neurotransmitters levels such as due to anxiety gamma-aminobutyric acid (GABA), dopamine, serotonin and glutamate(Schwabe *et al.,* 2022). The mechanism of action It involves the enhancement in the levels of excitatory neurotransmitters. Anxiety increases the level of glutamate which has excitatory effects on brain and inhibits the production of inhibitory neurotransmitters (Nimgampalle *et al.,* 2023). The normal concentration of the glutamate is significate for normal functioning of brain which over activates the neurotransmission which significantly impacts the memory. The levels of GABA are markedly reduced due to anxiety as it inhibits the production of it which regulates the activities of neurons preventing over excitation in neurotransmission(Nuss, 2015).

The imbalance in levels of dopamine due to anxiety which can lead to levels of motivation, focus and cognition. Normal levels of serotonin are important for regulating mood and functioning of cognition. Anxiety inhibits the

production of serotonin leading to impairment in cognition and focus(Teleanu *et al.,* 2022). The overexcitation in neuronal activity due to imbalance of glutamate and GABA significantly cause difficulty in focusing, creation of new memories and recollection of old memories. The chronic overexcitation due to excess of glutamate causes neuronal damage (Mah *et al.,* 2016). This imbalance between excitatory and inhibitory neurotransmitters impairs the strength of neuronal connections leading to impairment in plasticity of synaptic clefts leading to weakened synapse which majorly effects formation of memories and cognitive flexibility(Roberts & Karatsoreos, 2021). The imbalance of these neurotransmitters leads to shrinking of neurons which effects volume of hippocampus causing impaired memory(Postle, 2016).

HPA axis activation

This axis involves hypothalamus, pituitary gland and adrenal gland activation.Anxiety activates hypothalamus induces corticotropin releasing hormone which leads to pituitary gland activation leading to release adrenocorticotropin hormone (ACTH) which effects adrenal gland leading to secretion of cortisol (Sandi & Pinelo-Nava, 2007). The chronic stress due to anxiety leads to continuous release of cortisol which impacts hippocampus which negatively impacts function of cognition(Kuga & Sasaki, 2022). The excessive level of cortisol leads increase in level of reactive oxygen species which involves in increment in oxidative stress and inflammatory cytokines cause neuronal inflammation and extensive damage to neurons leading to memory impairment (Calcia *et al.,* 2016). High levels of cortisol decrease production of new neurons hence reduces neurogenesis as it prevents the proliferation and differentiation of neuronal stem cell which impacts cognition, mood regulation and focus negatively.

structural and functional changes in brain

Anxiety increases the levels of cortisol and causes imbalances in various neuro transmitters which leads to neuronal damage which leads to shrinkage and decreases the number of functional neurones , prevents neurogenesis and reduces synaptic plasticity which significantly impacts the structure and functions of important parts of brain such as hippocampus, amygdala and prefrontal cortex which are responsible for cognition and regulations for emotions which leads to impairment and difficulty in consolidation and retrieval of memory further causing complete memory loss(Wachowska & Gałecki, 2021) .

The clinical identification and treatment approaches.

Clinically the memory impairment is assessed during anxiety assessment and treatment planning which evaluates the impact of anxiety symptoms with memory loss, the cognitive function and performance of memory *(Costanzi et al.,* 2021). The treatment approach to address the anxiety linked memory loss includes medication, psychotherapy and lifestyle changes. The medication that targets and impact the symptoms of anxiety or neurotransmitter responsible for anxiety and loss of memory are prescribed (Curtiss *et al.,* 2021). The psychotherapy such as cognitive behavioural therapy is used to manage symptoms of both memory impairment and anxiety. The life style changes include sleeping habits, physical activities and exercise, stress management activities such as breathing exercises and balanced diet (Goldfarb, 2019). Treatment includes pharmacological and non-pharmacological approachNon-Pharmacological approach Pharmacological treatment

Recent Advancement In Research Related To Memory Loss Induced By Anxiety

Relation between neuro inflammation and memory loss.

Anxiety can lead to neuro inflammation leading to impairment in memory. The inflammatory marker such as NLRP3 inflammasome implies both memory impairment and inflammation(Cheng e*t al.,* 2022). Treatment targeting inflammatory pathway can offer a new strategy to treat memory loss due to anxiety(Won & Kim, 2020).

Relation between gut and brain

This axis indicates the significate effects of digestive health on brain function and cognition. Pre biotic and postbiotics has shown shape decrease in symptoms of anxiety and enhancement in cognitive function in animal models. Presently they are studied for understand the efficacy and impact on human brain and cognition(Niazi e*t al*., 2023).

Epigenetic modification

These modifications of DNA that change gene expression without any significant altering of DNA sequence which signifies the mechanism that expresses the link of anxiety with memory loss(Meier *et al.*, 2019). This critical modification alters memory and plasticity of neurons. The recent advancement involve research regarding HDAC inhibitors which are studied and investigated to understand it target, the inhibition of epigenetic modification and reversal of memory impairment(Benito *et al*., 2015).

Relation between brain -derived neurotrophic factor (BDNF) and neurogenesis:

Recent development regarding neurogenesis defines an important role of a protein called as brain derived neurotropic factor which helps growth and survival of neurons during anxiety (Bathina & Das, 2015). The amount of this protein increases due to interventions such as administration of pharmacological treatment and lifestyle modifications such as increase in physical activity and balanced diet showed decrease in anxiety and enhancement in function of memory (Sabri *et al.,* 2023). Recently novel compounds that can improve the level of BDNF concentration and signalling are developed and studied(Bathina & Das, 2015).

V.Research related to development and study of novel pharmacological agents Development:

New drug molecules are potentially explored to treat the memory loss due to anxiety more effectively. The active compounds derived from cannabis are recently studied and researched for they neuroprotective and anxiolytic activities (Al-Khazaleh *et al.,* 2024). Aesthetic agent like ketamine has shown promising results in decreasing anxiety and enhancement of cognition due to its effect on neurotransmission of glutamate which is an excitatory neuro transmitter (Sepulveda Ramos *et al.,* 2022). Recent studies are involved in investigation of effects of neuropeptides such as vasopressin and oxytocin in regulating cognition and anxiety (Baribeau & Anagnostou, 2015).

Development of non-pharmacological intervention to prevent and treat memory impairment due to anxiety:

Due to recent improvement in advanced technologies and studies related to behavioural patterns can help in management of memory impairment and anxiety. The digital improvisation in this research led to revolution of advanced online platforms and apps which offers cognitive behavioural therapy, virtual reality therapy and training regarding mindfulness which are effective in treating memory impairment due to anxiety(Wu *et al.*, 2021).

VII.Development of personalized medication:

This approach involves individual treatment approach which is based on biochemical, genetics and neuroimaging (Buch & Liston, 2021). It involves psychological and biological profile of individual by considering the biomarkers that helps in effective and better treatment to improve the memory in case of anxiety (Won & Kim, 2020).

Future Research Prospective Related To Memory Loss Due To Anxiety

Advancement in neuroimaging techniques for better imaging of damaged brain areas which are due to anxiety impacting memory such as functional magnetic resonance imaging and positron emission tomography for well-defined images. Identification of important biomarkers for early diagnosis of the memory loss due to anxiety which can include genetics, metabolomic and proteomics biomarkers (Łoś & Waszkiewicz, 2021).Genetic profiling is very important to specify the treatment in personalized medicine to understand the genetic and epigenetic factors playing role in anxiety related memory loss and prediction of outcome on individual (Kiyotani *et al.,* 2021). Research regarding the stimulation of neurogenesis in hippocampus by treatment approach such as transcranial magnetic stimulation, life style changes and pharmacological agents which can help in reversal of memory loss due to anxiety (Zhang *et al.,* 2014). Stem cell treatment can be explored to memory loss reversal which is due to neuronal damaged caused by anxiety (Sivandzade & Cucullo, 2021).

CONCLUSION

Anxiety effects cognition by diverting concentration and attention towards the stress interrupting memory formation and recollection. Chronic anxiety increases levels of cortisol and excitatory neurotransmitters and decrease the levels of inhibitory neurotransmitters which causes neuronal inflammation leading to brain damage in areas such as hippocampus, and prefrontal cortex responsible for cognition and focus. The memory impairment due to anxiety are treated by combination of pharmacological and non-pharmacological approaches. The recent research is focused on addressing complication related to anxiety by reducing cognition load and improving memory hence impacting overall mental health positively. The future direction in this area mainly should be focused on advance imaging techniques, personalized medication and novel therapies.

Conflict of Interest:
The authors have no conflicts of interest**.**

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Table 1 : Types of anxiety and related symptoms.

Sl no	Type of anxiety	Symptoms
1	Generalized anxiety disorder	Restlessness, muscle tension, tiredness ,difficulty in concentration and focusing(Patriquin & Mathew, 2017).
2	Panic disorder	Rapid heart, excessive sweating, frequent episodes of fear, loss of control, chest pain and trembling
3	phobia	Feeling of embarrassment Rapid heart, excessive sweating and frequent episodes of fear(Penninx *et al.*, 2021).
4	Obsessive compulsive disorder	Frequent urge of cleaning and fear of contamination and harm.
5	Post-traumatic stress disorder	Intrusive flashbacks or memories, negative impact on mood and memory.
6	Separation anxiety disorder	Fear, reluctant to leave home and disturbed sleep(Whitehurst *et al.*, 2022).
7	Selective mutism	Failure to speak and is common in children(Thibaut, 2017).

Table 2: Pharmacological Agents Used In Treatment Of Memory Loss Due To Anxiety

Treatment	Functions
Cognition behavioural therapy	Improves memory
Physical activities	Improves brain health and memory
Relaxation techniques	Decreases stress anxiety and improves memory(Curtiss *et al.*, 2021)

Table 3: Pharmacological Agents Used In Treatment Of Anxiety

Class	Examples	Functions
Benzodiazepines	Alprazolam, Diazepam And Lorazepam	Short time anxiolytic for treatment of sever anxiety
Selective serotonin reuptake inhibitors	Escitalopram, Sertraline, Fluoxetine and Paroxetine	These drugs balances levels of serotonin which enhances memory function and regulate moods effectively (Curtiss et al., 2021).
Selective Norepinephrine Reuptake Inhibitors (SNRIs)	Duloxetine ,Venlafaxine and Buspirone	Used in treatment of anxiety without causing dependency and sedation (Thibaut, 2017).
Nootropic agents	Rivastigmine, Donepezil and Memantine	Helps in enhancement of cognitive function
Neuroprotective and antioxidants	Ginkgo Biloba	Improves blood flow to brain leading to enhancement in cognition
	Omega-3 Fatty Acids	Improves cognition by improving brain health
	Vitamin E	Antioxidant(Perini *et al.*, 2019).

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RESEARCH ARTICLE

High Efficiency Video Coding With Lagrangian Encoder Algorithm and Hybrid Wavelet Transform

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ABSTRACT

H.265/HEVC is the most latest video coding standard. For Motion Estimation and Compensation, HEVC standards mainly rely on transformation, scaling, quantization, deblocking filter approaches and Lagrangian encoder. The Rate-Distortion Performance at Various Frame Rates and Quantization Parameter (QP) Values is investigated in this study. A study was carried out on compensation and motion estimation employing the Lagrangian Encoder Algorithm. We investigated at both intra and inter prediction methods using a variety of QP values, such as 22, 27, 32, and 37 transforming, scaling, and quantizing data using Hybrid Wavelet Transformation algorithms in conjunction with bit rate and PSNR. Using the MATLAB reference program, the Lagrangian Encoder method is constructed and subjective analysis is explored. The outcomes of the simulation have been discussed. The Lagrangian Encoder Algorithm and Hybrid Wavelet Transform are recommended in this study for assessing the outcomes in the form of both subjective and objective analysis. Using Luo's HM 11, PVC Content Split Block Search Algorithm, and Lagrangian Encoder Algorithm with various QP values, such as 22, 27, 32, and 37, in order to analyze different evaluation scenarios with YUV PSNR and bitrate, as well as with the Random Access profile and the Low Delay profile, these comparisons were performed.

Keywords: HEVC, Lagrangian Encoder Algorithm, Hybrid Wavelet Transform, Motion Estimation and Compensation, QP.

INTRODUCTION

For a variety of uses, the video processing must capture the content with a broad immersion [1]. Similar to texture and feature content, it is proprietary [3]. Video processing requires textural content analysis. This method of video codec analysis is unique [4], [5]. Outstanding performance a new video coding standard is called Video Coding [2]. Its efficiency in coding is primarily comparable to the video coding standard [6]. But the encoding system must bear some of the expense of the complexity standard [8]. Encoding is typically associated with duplicated activity, requiring many runs across multiple quality levels using HEVC encoders [9], [10]. A collection of still images shown at a consistent frame rate is called a video. A movie with items moving in the backdrop is the net follow-up [12]. The total amount of bits extracted from each frame will be the size of the entire video if each picture (or frame) in the video is encoded separately [21]. Large films are nearly impossible to do this for in storage or communication purposes [19]. Therefore, it is absolutely necessary to eliminate any unnecessary material from a video [20].

Block Based video Coding

By splitting each frame into blocks, block-based video coding compresses the image sequence. The next steps for each block are transform coding, quantization, motion compensation (calculated using surrounding blocks that have already been coded), and entropy coding (which eliminates statistically redundant information). In the parts that follow, each of these methods is described. Upon obtaining these coded blocks, the decoder produces frames that are shown at a predetermined frame rate [11], [12]. Beyond block-based coding, there are several other types of video coding, including fractal-based, content-based, and pixel-based coding. However in [13] & [14], block-based coding of video is among the most often used and successful method for creating a real-time or software video encoder due to its consistent coding structure [16]. Block-based codecs include those made up of VCEG (H.261, H.263), MPEG (MPEG-1, MPEG-2, MPEG-4), and their jointly produced codecs (H.264, HEVC, etc.) [17]. The main objective of this study is to use a hybrid wavelet transform and multi-rate motion estimation technique to represent H.265/HEVC picture data in frames [18], [19].

Content Split Block Search Algorithm: Using a content split block search methodology, a two-layer technique combining content and block search is proposed in this research for conducting motion estimates and compensation. It uses a compressed bit stream for direct processing. Block-based video processing material was attained by solving content guidance I P B Frames. Additionally, modifications were made with a bigger magnitude and prediction. When it comes to smooth areas, the changes are little or nearly nonexistent, making it highly imperceptible. In content-on-edge regions, it is essentially the same as the content data. The video signal is less resistant to noise when content features are present in the frame. This is the first thing to examine. We then look at the unique roles that the HEVC block structure plays in handling multiple encodings at different levels of quantization and SNR quality. Furthermore, the block structure is recycled from a superior quality standard picture to speed up the dependent encoding of lower quality representations. The reference HEVC software is utilized to implement and assess the proposed methodology, which has been thoroughly discussed in prior studies referenced by Anitha et al. Our findings show that it can significantly reduce the encoding time for numerous HEVC interpretations without significantly sacrificing performance in terms of rate distortion [12], [14].

LITERATURE SURVEY

Lili Lin *et al.* provide an efficient predictive search methodology (EPS) that combines the diamond search (DS) algorithm with motion type categorization, early searching termination techniques, and initial searching point prediction. The first search point in the proposed EPS is situated in close proximity to the search point that was optimized in the previous search phase. As a result, the first search point is found more quickly and the superfluous global search process is avoided. Jia Zhang *et. al*. The author explored several quick encoding methods, such as ECU, CFM, and ESD, and talked about HM 16.7. Furthermore, the reference encoder with delinquency has certain

encoding algorithms disabled. The CU's ideal mode in the ECU is SKIP mode, and it won't crack again. According to this study, the SKIP mode is a special instance of the merge mode. It does not encode the prediction residuals or carry out motion estimation. Code Block Flag (CFM) is a technique that uses CBF to determine whether or not the transformed quantized residuals are zero. As a result of the Random Access and Low Delay settings, the experimental findings demonstrate degradation in coding complexity of 54.93 and 45.84 with 1.195 and 1.03% BD rate, respectively. Jia Wang *et. al*, In this work, the efficient method known as Constant Level Rate Deviation Optimization Quantization (RDOQ) can save bit rate by 6% to 8% while simultaneously enhancing rate-distortion efficiency. The video encoders HM, X264, and H264 are among many that have embraced it. JM, and others. On the basis of Context Adaptive Binary Arithmetic Coding, a quick RDOQ technique with precise rate estimate between the two options with HEVC is suggested. It also supports parallel processing and reduces computing complexity. According to experimental data, the proposed approach can reduce the RDOQ encoding time by an average of 54.36% with a maximum 0.88% BD rate loss. Ankur Saxena *et.al*. In this work, the dependency mode between DCT and DST is eliminated in order to reduce implementation complexity. Additionally, from July 2012 onwards, 4x4 intra Luma blocks were simply always utilized. With the aid of the HEVC standardization software, simulation results must be examined using the DCT/DST technique. For intra-prediction sequences, the BD-rate has been compared in this work to the traditional DCT-based approach. In particular, to reduce complexity, the DST/DCT transform method employs either DCT or DST (Type-7) for all intra-prediction video coding standards, including Vertical and Horizontal.

Proposed Methods

This investigation has discussed two prospective algorithms. The hybrid wavelet transform is one of those, and the Lagrangian Encoder algorithm is the other.

Hybrid Wavelet Transform

Modern correspondence innovation helps to consolidate video fragments in several applications. Without detracting from the video's content, the correspondence models attempt to use high-quality components like data measure. This is contingent upon the video's structure. Videos in their entirety should be transferred to a different finish for mobile applications that use video transmission, and there are multiple standards for video compression. If a video is made up of a collection of frames, it can be compressed to a low bit rate without compromising its structure or content. The process of Hybrid Wavelet Transform is shown in Fig. 1. For example, compression must be used to lower the 1024 bytes needed to store and transport a picture. A video phase consists of many interconnected frames with only slight variations in the pixel count of each frame. A few images from a certain video phase fit the general tone of the production. Sequential redundancies between consecutive frames, spatial redundant information, and unit high redundancies all occur inside the identical frame. Four categories are commonly used to classify video compression methodologies: object-based, wave form-based, pattern-based, and model-based. Object-based compression makes it possible to employ several coding techniques by extracting the objects from the video frame and using their shape and texture for coding. Each object has a completely unique compression magnitude relation that produces a fair relation. Using the wave type technique, a high degree of compression is also achieved while the video frame is rebuilt to a little size without losing any features. To compress the video frames, the model-based compression does 3D structural analysis, while the fractal-based approaches apply picture committal to writing methodologies. After applying background subtraction to the foreground item and wavelet processing to the image, an object map is produced.

Different characteristics and their correctly related neighbors make up the object map. To determine the difference between these frames, the collection of object maps is computed between each one that follows. To send the image to the other end of the transmission, generated object mappings and variance are employed. Each frame in this method produces an object map, from which the distance between the maps of the preceding frames is calculated. Based on the distance value and the map reduction threshold value, a covariant matrix is computed. On the receiving end, after the decreased characteristics are conveyed, video decompression takes place. Using object mappings, the

difference between consecutive frames is computed. It is displayed in the computed covariance matrix. To conduct the wavelet transform, some of the image's pertinent pixels are left intact while others are neutralized [22].

Lagrangian Encoder Algorithm

The trade-off between throughput and compression efficiency is supported by this encoder. Figure 2 displays the Lagrangian Encoder algorithm. The algorithm's first phase involves analyzing the video data and extracting the video frames. The encoder selects among expected blocks that are intra-code and inter-code. There is less temporal and geographical redundancy when this inter- or intra-prediction option is used. The frames are received and assembled into Code Tree Blocks once the coder has been chosen. the division of the Coding Unit from the Code Tree Block. The two samples from each of the Chroma and Luma samples make up the coding unit. The suggested Lagrangian-based encoding technique assesses the motion compensated signal, which is dependent on the INTER mode, and regulates the macro block mode decision. The quantization parameter is increased within the Lagrangian's allowable range in order to reduce the buffer latency. This procedure is iterated until the computed delay is as small as possible. Bit rates influence the choice of Q for a given X. By using the suggested encoder, delay is reduced by many calculations utilizing the Lagrangian parameter and Q, resulting in the lowest possible buffer delay [15], [23]

RESULTS AND DISCUSSIONS

The MATLAB tool with several QPs, including 22, 27, 32, and 37, is being used for this work utilizing the Reference program. These QP are compared with a range of transactions after standardization. Classification of the test sequences, The public in the Road, Cacti (Plant), BQ Terrace, Basketball Pass, and so on, is done at different resolutions; for example, 2560 x 1600, 1920 x 1080, 832 x 480, and 416 x 240 are categorized as Set A, Set B, Set C, and Set D.

Analysis of Motion Estimation Results for HEVC

According to RDOQ, RDOQ-OFF, and JIOWANG et al., the aforementioned results are regarded as Basketball Video Sequences with varying QP values. For every (22, 27, 32, and 37) QP value, it is noticed that the bit rate increases and the PSNR decreases in tandem with the amount of data written to the file. In cases when the QP size is less (i.e., PSNR 40 dB, Jiowang *et al*.), the proposed method achieves more than 2 dB. According to JIOWAN G *et al*., the above findings are regarded as Cactus Video Sequence with varying QP value from the viewpoint of RDOQ, RDOQ-OFF. It has been noted that for every QP number between 22, 27, 32, and 37, bit rate increases and the PSNR decreases along with the amount of data written to the file. In the suggested study, it achieves better than 1.5 dB, however when the QP size is tiny, PSNR39.2 dB JIOWANG *et al*. Comparing the aforementioned results with JIO-WANG 2016 makes it clear that QP=22 leads to better performance and higher PSNR even at low bit rates. It shows that the quality in terms of bit rate has grown along with the compression ratio of the suggested strategy. Bit rate indicates improved quality performance when QP increases even while PSNR falls short of the necessary parameters, such as a lower compression ratio.

Low delay configuration: - As an IDR picture in a low delay arrangement, just the first frame is encoded. The HEVC protocol supports two low-delay options. There are two types of configurations: low-delay B (also known as low-delay B) and low-delay P (also known as optional). While low-delay mode interprets every frame in a GOP as Generalized P and B images (GPB) only, low-delay P mode interprets every frame in a GOP as P-pictures alone. The primary difference between low-delay P mode and low-delay configuration is this. The initial frame in both of these setups is encoded as an IDR image. An offset is added to the setup to determine the QP for each intercoded image.

The objective test results for the suggested work with MATLAB are displayed in the aforementioned Tables 2 and 3. The results of the simulation have been evaluated using the Original HM11 with Random Access Main Profile and Low Delay Primary Configuration. With QP 22, YUV PSNR is almost 4dB, and a discernible bitrate reduction is also

achievable. when the current QP32,37 is not enhanced. Test sequences like BQTerraec (1920x1080), Cactus (1920x1080), Party Scene (832X420), Park scene (832X420), and Race Horses (832X420) have been collected in order to see the objective evaluation was completed on the basis of bitrate and YUV PSNR. In the video, a content block is examined. Figure 3 below displays a group of images representing test sequences in the I, B, and P frame formats, including people on the street, cacti, BQ terrace, basketball pass, and so forth. For the display, the remaining photos were stretched by 30 times and displayed in grayscale format. Tables 2 and 3 present an analysis of the extracted blocks according to a number of metrics, including bitrate (Kbps) and PSNR (dB).

CONCLUSIONS

MATLAB software is used to implement the Lagrangian Encoder algorithm and subjective analysis. Simulates the proposed algorithm's use of the Lagrangian encoder in both the intra- and inter-prediction modes. The RD performance with YUV PSNR and bitrate has been improved in this method for several QPs, including 22, 27, 32, and 37. In comparison to HM Tool 12, 15, latest version of MATLAB offers an enhanced decoding time as well as a transformation and quantization process. The effects of the hybrid wavelet transform and Lagrangian encoder algorithm proposed in this study have been investigated using different test sequences with YUV PSNR and bitrate in comparison to Random Access profile and Low Delay profile, and in comparison to Luo's, HM 11 and PVC with different QP values like 22, 27, 32, and 37.

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Table 01: Factors for the suggested work constraints.

Categories	Pixel(W:H)	Order	No. of Frames	Frame Rate(sec)
Set A	2560:1600	PublicRoad	150	30
Set B	1920:1080	Cacti	240	24
Set C	832:480	BQTerrace	600	60
Set D	416:240	BasketballPass	500	50

Table 2: Comparing RD Performance with CSBSA
Basket Ball

	RDOQ		RDOQ-OFF		CSBSA		PROPOSED	
QP	PSNR	Kbps	PSNR	Kbps	PSNR	Kbps	PSNR	Kbps
37	34.5	2000	34.3	2000	28.11	6613	26.51	7274
32	36.6	4000	36.3	4000	32.49	8063	29.3	8870
27	38.5	6500	38.2	6500	37.04	9709	36.24	10679

22	40.2	20000	40.0	20000	42.03	9739	44.05	10712

Cacti (Plant)

	RDOQ		RDOQ-OFF		CSBSA		PROPOSED	
QP	PSNR	Kbps	PSNR	Kbps	PSNR	Kbps	PSNR	Kbps
37	33.6	2000	33.7	2000	27.79	7163	22.54	7879
32	35.7	4000	35.8	4000	32.20	8786	29.42	9665
27	37.6	6500	37.7	6500	36.73	10583	37.5	11641
22	39.2	20000	39.3	20000	41.73	12657	43.61	13922

Table3: Results of the Objective Tests PSNR in decibels and bit rate in kbps for (LUOs), PVC scheme, HM16.7, and proposed under low-latency primary profile

Sequence	QP	Luo's (dB)	PVC (dB)	CSBSA (dB)	Proposed (dB)	Luo's (kbps)	PVC (kbps)	CSBSA (kbps)	Proposed (kbps)
BQTerrace (1920x1080)	22	36.9	35.7	40.06	42.56	32653	16788	5446	4326
	27	35.2	34.8	34.69	34.18	6437	5273	4476	3546
	32	33.5	33.4	29.32	25.43	1953	1918	3536	2756
	37	31.4	31.4	23.81	18.32	760	760	2729	1859
Cactus (1920x1080)	22	38.4	37.4	39.18	40.86	16562	12483	5761	4782
	27	36.6	36.2	37.24	37.64	5629	5327	4779	3869
	32	34.6	34.5	32.75	30.24	2569	2551	3873	2946
	37	32.3	32.3	27.52	24.36	1269	1267	2896	1986
ParkScene (832x420)	22	39.5	38.1	42.16	44.08	7492	6280	5701	5216
	27	36.9	36.4	37.22	38.14	3125	2979	4780	3842
	32	34.2	34.1	31.8	28.3	1332	1323	3777	2839
	37	31.6	31.6	27.48	24.26	576	576	3044	2153
BQMall (832x420)	22	39.3	37.6	42.24	45.36	3888	3292	5764	7536
	27	37	36.3	36.4	35.2	1830	1758	4635	6792
	32	34.2	34.1	32	31.2	899	895	3842	5834
	37	31.3	31.4	27.54	24.32	458	457	3094	5124
PartyScene (832x420)	22	36.4	33.9	41.46	44.53	7174	5793	5860	5964
	27	33.9	33	36.51	38.24	3292	3111	4855	4965
	32	30.9	30.8	31.51	32.14	1483	1484	3909	3926
	37	27.8	27.8	27.45	27.1	642	643	3193	3154

Table4: Objective Test Results PSNR interms of dB and Bitrate interms of Kbps for LUO's, PVC scheme, CSBSA and Proposed under Random Access Profile

Sequence	QP	Luo's (dB)	PVC (dB)	CSBSA (dB)	Proposed (dB)	Luo's (kbps)	PVC (kbps)	CSBSA (kbps)	Proposed (kbps)
BQTerrace (1920x1080)	22	36.53	35.19	41.86	46.24	25421	14437	6419	5237
	27	35.12	34.45	36.84	38.62	5909	5234	5164	4468
	32	33.72	33.58	32.3	31.2	2218	2202	4228	3584
	37	31.89	31.94	27.87	24.56	965	967	3484	2652

Cactus (1920X1080)	22	38.13	36.77	41.09	45.84	14579	11419	12653	10532
	27	36.66	36.01	36.73	37.23	5389	5304	10583	8562
	32	34.84	34.75	32.4	31.16	2643	2646	8786	6893
	37	32.71	32.75	27.29	23.84	1370	1369	7163	5424
ParkScene (832X420)	22	39.54	37.51	42.28	47.24	6999	6044	7500	6354
	27	37.28	36.48	37.28	36.26	3185	3102	4000	3124
	32	34.82	34.77	32.27	30.43	1522	1522	2000	1763
	37	32.38	32.44	27.26	24.34	717	718	1000	852
BQMall (832X420)	22	39.5	37.15	42.26	46.82	3302	2928	5562	4683
	27	37.29	36.19	36.47	36.2	1621	1596	4565	3732
	32	34.63	34.6	32.82	30.64	850	848	3641	2514
	37	32.08	32.14	31.95	31.54	450	449	2650	1562
PartyScene (832X420)	22	36.67	33.2	38	41.23	6011	4865	4760	3934
	27	33.69	32.57	36.6	39.52	2882	2774	4304	3562
	32	31.26	31.25	26.91	22.86	1443	1439	3597	2763
	37	28.51	28.62	24.45	21.53	690	690	2765	1836

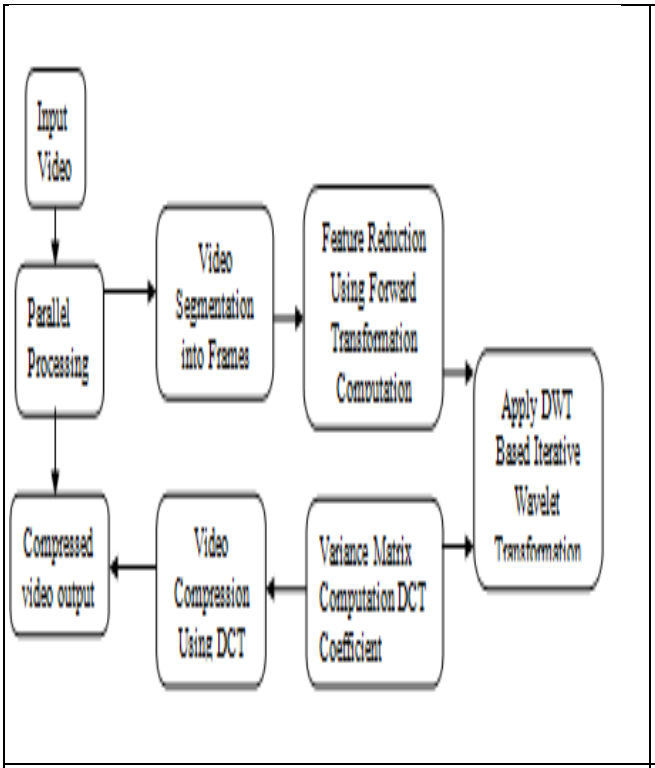

Fig: 1 Process of Hybrid Wavelet Transform

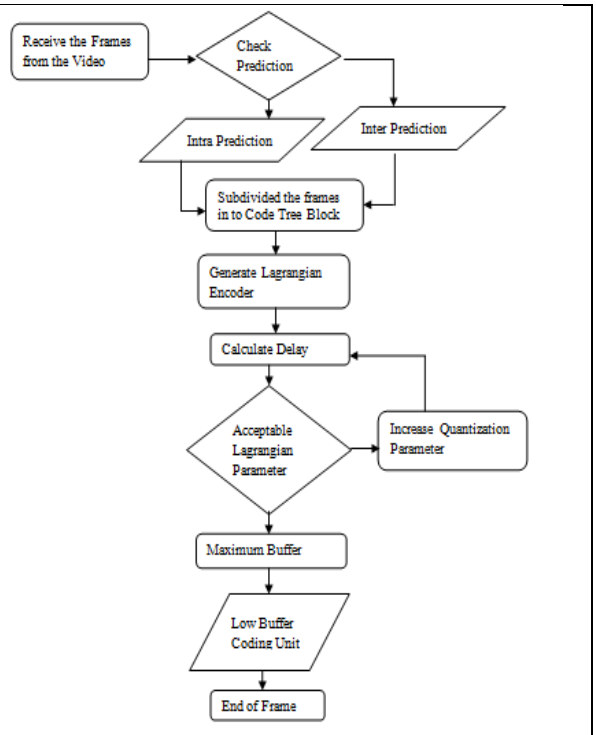

Fig 2. Lagrangian Encoder Algorithm

Fig2:Content processing Frame

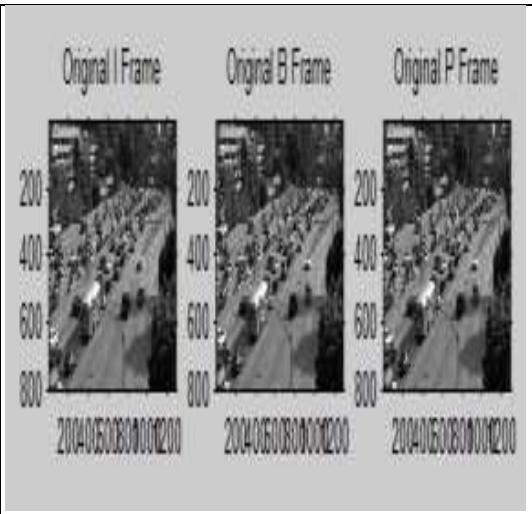

Fig3:Frame:Iframe, Bframe and Pframe

Fig4:Encoding:Motion Vectors

Fig.5:Encoded frame

Fig6:Decoding:Content Extraction

Fig.7:Frame Reconstruction

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RESEARCH ARTICLE

Hybrid Perturbative Approaches for Enhanced Convection-Diffusion Modelling: Bridging Analytical and Numerical Solutions for Spatially Variable Systems

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ABSTRACT

This paper presents a hybrid perturbative approach for solving convection-diffusion equations with spatially varying diffusion and convection coefficients in a semi-infinite domain. Traditional methods often struggle with the complexities introduced by variable coefficients, which can significantly impact the concentration profile. Here, we employ a perturbation-based method that combines analytical and numerical solutions to address this challenge effectively. The solution is expanded in a series, where the zeroth-order term captures the primary behaviour under constant coefficients, and higher-order corrections incorporate the effects of spatial variations. This approach provides an accurate and computationally efficient solution by balancing the strengths of both analytical and numerical methods. The concentration profile obtained through this hybrid method shows a smooth, continuous transition across regions with different diffusion and convection properties, accurately reflecting the system's underlying physics. This method is ideal for complex, large-scale systems where gradual changes in parameters are significant yet small enough to warrant perturbative treatment. The results demonstrate that the perturbative approach can enhance modelling accuracy for spatially variable systems, offering insights for applications in fields such as transport phenomena, environmental modelling, and astrophysical processes where efficient and precise solutions are essential.

Keywords: Convection – Diffusion Modelling, Perturbation Approach, Analytical solution, Numerical solution, spatially variable systems.

INTRODUCTION

Convection-diffusion problems arise in a variety of physical systems, ranging from fluid dynamics to environmental modelling, and even in astrophysical contexts like cosmic ray diffusion or heat transfer in stellar atmospheres. These problems describe the transport of a scalar quantity, such as temperature, concentration, or momentum, under the influence of both diffusion and convection forces. The presence of spatially varying coefficients in these equations makes them particularly challenging to solve. The complexity of solving the convection-diffusion equation increases significantly when the diffusion coefficient D(x) and the convection velocity v(x) are not constant but vary spatially. In many real-world applications, such as fluid dynamics, chemical engineering, and atmospheric modelling, these coefficients change due to environmental or physical conditions. To model these variations accurately, the problem must be treated with advanced mathematical and numerical techniques [1, 2]. Numerical methods, such as finite difference, finite element, and spectral methods, have been widely applied to solve convection-diffusion equations. These methods can handle complex boundary conditions and arbitrary spatial variations of the coefficients. However, they often require significant computational resources and are prone to numerical instability, especially when there is a large disparity between the diffusion and convection terms or when the coefficients exhibit sharp gradients [3, 4]. In contrast, analytical methods provide exact solutions but are usually limited to simpler cases, such as constant coefficients or specific boundary conditions. Even in cases where the coefficients are spatially varying, analytical solutions can be obtained for certain configurations, such as piecewise constant coefficients, leading to piecewise analytical solutions in different regions [5, 6]. Hybrid methods, which combine analytical and numerical techniques, offer a promising approach for solving these problems. By applying an analytical solution in regions where the coefficients are approximately constant and using numerical methods in regions where the coefficients change significantly, these methods balance computational efficiency and accuracy. This hybrid approach is particularly useful when the system involves spatially varying parameters that are slowly changing over space [7, 8].

A more advanced variation of hybrid methods involves perturbation techniques. In this approach, the problem is treated as a perturbation around a base case where the coefficients are constant. By expanding the solution as a series in terms of a small parameter that quantifies the variations in D(x) and v(x), it is possible to derive an approximate solution that incorporates the effects of these variations. This perturbative approach can be computationally efficient and accurate for small deviations from constant coefficients [9, 10]. Perturbation-based methods have been applied to a wide range of problems, including heat transfer in heterogeneous media, diffusion in porous media, and fluid flow in porous structures. These methods provide solutions that capture both the primary behaviour and the small corrections due to variations in the system's parameters. However, they require a careful analysis of the small parameter and may become less accurate if the variations in the coefficients are large [11, 12]. In recent years, the development of more sophisticated hybrid analytical-numerical methods has allowed for more accurate solutions to convection-diffusion problems with spatially varying coefficients. These methods leverage the strengths of both analytical solutions, which can provide closed-form expressions for simpler cases, and numerical methods, which are able to handle more complex scenarios with irregular coefficient variations [13, 14]. The goal of this study is to present a novel hybrid perturbative approach for solving convection-diffusion equations with spatially variable coefficients. This method combines perturbation expansions with numerical integration, allowing for the efficient and accurate solution of problems where the coefficients exhibit gradual spatial variations. The proposed method is demonstrated on a one-dimensional semi-infinite domain, where the diffusion and convection coefficients vary linearly with position. By applying this method, we aim to enhance the understanding of transport processes in systems with slowly varying coefficients [15, 16]. This paper is organized as follows: In Section 2, we provide a detailed formulation of the problem and describe the hybrid perturbative approach. Section 3 presents the solution method, including both the analytical and numerical components. Section 4 discusses the results, and Section 5 concludes the paper with recommendations for future work and potential applications of the method in various fields such as fluid dynamics, environmental modelling, and astrophysical systems [17, 18].

Governing Equations for Convection-Diffusion

Convection-diffusion equations model physical processes where particles, heat, or energy are transported within a medium due to both convection (bulk movement) and diffusion (spread due to concentration gradients). The generalized form in one spatial dimension (1D) is

$$\frac{\partial u}{\partial t} + v\frac{\partial u}{\partial x} = D\frac{\partial^2 u}{\partial x^2} + S(x,t) \quad (1)$$

Where u (x, t) represents the scalar quantity being transported (such as temperature, concentration, etc.), v is the convection velocity (assumed constant here), D is the diffusion coefficient (could vary spatially or temporally for complex systems), S(x, t) is a source term that accounts for internal generation or decay within the medium.

Using variable coefficients, such as v(x) and D(x), allowing the convection and diffusion to change spatially. Introducing a nonlinear term, which is more realistic for many physical processes but complicates the solution. The equation could then become

$$\frac{\partial u}{\partial t} + \frac{\partial}{\partial x}(v(x)u) = \frac{\partial}{\partial x}(D(x)\frac{\partial u}{\partial x} + S(x,t.u) \quad (2)$$

This formulation opens the door to hybrid solutions, where analytical solutions for linearized sections of the domain are complemented with numerical solutions for nonlinear regions.

The convection-diffusion equation requires boundary and initial conditions for a well-defined solution. Dirichlet Boundary condition specifies the value of u at the boundary. For instance,

$$u(0,t) = u_L;\ u(L,t) = u_R \quad (3)$$

Where L represents the spatial domain length and u_L and u_R are prescribed boundary values.

Neumann Boundary condition specifies the gradient of u at the boundary

$$\frac{\partial u}{\partial x}|_{x=0} = \alpha;\ \frac{\partial u}{\partial x}|_{x=L} = \beta \quad (4)$$

Where and represent flux values. This is often used in heat transfer to model insulated boundaries.

Robin Boundary condition, a combination of Dirichlet and Newmann is

$$\gamma u + \delta\frac{\partial u}{\partial x} = g(x) \quad (5)$$

Where , and g(x) are given functions or constants. This is frequently used to model convective heat transfer at boundaries. The initial state of u(x, 0) = f(x) must be specified cross the domain. Different initial profiles, like step functions or Gaussian distributions, affect the evolution of u under convection and diffusion.

Analytical Solutions: Closed-form Solutions and Their Limitations

For certain simplified cases, the convection-diffusion equation admits closed-form solutions. Consider the standard linear form without source terms and with constant v and D

$$\frac{\partial u}{\partial t} + v\frac{\partial u}{\partial x} = D\frac{\partial^2 u}{\partial x^2} \quad (6)$$

The closed-form solution for an initial Gaussian distribution u(x, 0) = e^{-x^2} under constant convection and diffusion can be expressed as

$$u(x,t) = \frac{1}{\sqrt{4\pi Dt}} exp\ (-\frac{(x-vt)^2}{4Dt}) \quad (7)$$

This represents the Gaussian profile spreading due to diffusion and shifting due to convection over time. However, this solution only applies for constant coefficients and an infinite domain.

For domains with finite boundaries or more complex initial conditions, Laplace transforms offer an analytical approach. Taking the Laplace transform of the 1D convection-diffusion equation in the time domain yields

$$s\tilde{u}(x,s) - u(x,0) + v\frac{\partial \tilde{u}}{\partial x} = D\frac{\partial^2 \tilde{u}}{\partial x^2} \quad (8)$$

Where $\tilde{u}(x,s)$ is the Laplace-transformed function. This form enables handling boundary conditions more flexibly. Limitations of Analytical solutions are Analytical methods struggle with nonlinear terms in u or variable coefficients for v(x) and D(x); Complicated boundaries, such as irregular geometries, cannot be easily accommodated analytically and Analytical solutions become intractable in 2D or 3D. Due to these limitations, a hybrid analytical-numerical approach is effective. For instance, applying analytical solutions in regions where the coefficients are constant or linear, while using numerical methods to handle nonlinear or variable-coefficient regions, provides a more versatile solution.

Hybrid Analytical and Numerical Solution Example (1D Case)

Let's partition the domain x ∈ [0, ∞) into regions $_i = [x_{i-1}, x_i]$ where $D(x) \approx D_i$ and $v(x) \approx v_i$ within each region $_i$(i.e., we approximate D(x) and v(x) as constants in each subdomain). This gives a piecewise constant approximation

$D(x) \approx D_i$ and $v(x) \approx v_i$, for x ∈ $_i$ (9)

In each region $_i$ the equation (1) simplifies to

$$\frac{\partial u}{\partial t} + v_i \frac{\partial u}{\partial x} = D_i \frac{\partial^2 u}{\partial x^2} \quad (10)$$

For each subdomain $_i$, we can solve the equation analytically as follows. Assuming steady state (i.e., $\frac{\partial u}{\partial t} = 0$), the equation in each region $_i$ becomes

$$\frac{^2u}{\partial x^2} - \frac{v_i}{D_i}\frac{\partial u}{\partial x} = 0 \quad (11)$$

The general solution to this equation in each region is

$$u_i(x) = A_i e^{\lambda_i x} + B_i \quad (12)$$

Where $_i = \frac{v_i}{D_i}$ and A_i and B_i are constants determined by boundary conditions and continuity conditions at the interfaces. To ensure continuity across the interfaces x = x_i between adjacent regions, we impose the continuity of u and continuity flux become

$$u_{i-1}(x_i) = u_i(x_i) \quad (13)$$

$$D_{i-1} \frac{du_{i-1}}{dx}|_{x=x_i} = D_i \frac{du_i}{dx}|_{x=x_i} \quad (14)$$

These conditions result in a system of equations relating the constants A_i and B_i across regions, which can be solved sequentially from one region to the next.

Numerical Solution in Complex Regions

In regions where D(x) changes rapidly or introduces nonlinearities, analytical solutions are no longer feasible. We apply a numerical method, such as finite differences or finite elements, to discretize and solve the convection-diffusion equation in these regions.

For a region where D(x) and v(x) vary continuously, we can discretize the equation at each spatial point x_j

$$\frac{u_j^{n+1} - u_j^n}{\Delta t} + v_j \frac{u_{j+1}^n - u_{j-1}^n}{2\Delta x} = \frac{1}{\Delta x^2}[D_{j+\frac{1}{2}}(u_{j+1}^n - u_j^n) - D_{j-\frac{1}{2}}(u_j^n - u_{j-1}^n)] \quad (15)$$

This discretization allows us to iteratively solve for u_j in regions where the variables cannot be assumed constant. The final solution u(x, t) is constructed by combining the analytical solutions in regions where D(x) and v(x) are constant with the numerical solution in regions of complex behaviour. By solving analytically in each region Ωi where D(x) and v(x) are constant, resulting in solutions of the form

$$u_i(x) = A_i e^{\lambda_i x} + B_i \quad (16)$$

Apply interface conditions at the boundaries x = x_i to ensure continuity and flux matching, solving for unknown constants. Use numerical integration in regions where D(x) or v(x) varies significantly. The solution is then a piecewise function

$u(x) = \{u_1(x) = A_1 e^{\lambda_1 x} + B_1, x \in \Omega_1 = [0, x_1], u_2(x) = A_2 e^{\lambda_2 x} + B_2, x \in \Omega_2 = [x_1, \infty), y_{numerical}(x), x \in \Omega_3 (if\ present, for\ complex\ behaviour)$. (17)

This hybrid solution provides an efficient and accurate approximation for the convection-diffusion equation in domains with varying D(x) and v(x), using analytical solutions in simple regions and numerical methods in complex regions

Perturbation-Based Solution Method for the Convection-Diffusion Equation with Variable Coefficients

The perturbation-based approach provides an efficient way to handle spatially varying parameters in the convection-diffusion equation. Here, we derive and solve the equation by assuming small variations in diffusion and convection coefficients, allowing us to express the solution as a series expansion. Setting Up the Problem with Perturbations, consider the one-dimensional convection-diffusion equation with variable diffusion coefficient D(x) and convection velocity v(x). The modified equation (1) is

$$\frac{\partial u}{\partial t} = D(x)\frac{\partial^2 u}{\partial x^2} - v(x)\frac{\partial u}{\partial x} \quad (18)$$

To make the problem tractable, assume that D(x)D(x)D(x) and v(x)v(x)v(x) can be expressed as slight deviations from constant values.

$D(x) = D_o + \epsilon D^{'}(x)\ and\ v(x) = v_0 + \epsilon v^{'}(x)$ (19)

where D_0 and v_0 are constants, D′(x) and v′(x) are functions that describe the spatial variability, and ϵ is a small parameter quantifying the magnitude of this variability.

Let the solution u(x, t) be represented as a series in terms of ϵ

$u(x,t) = u_0(x,t) + \epsilon u_1(x,t) + \epsilon^2 u_2(x,t) \ldots\ldots\ldots\ldots..$ (20)

Here, $u_0(x, t)$ is the zeroth-order solution, corresponding to the case where D(x) = D_0 and v(x) = v_0, and higher-order terms $u_1(x, t)$, $u_2(x, t)$, etc., represent successive corrections due to the spatial variability in D(x) and v(x). Substitute u(x, t), D(x), and v(x) into the convection-diffusion equation, and collect terms by powers of ϵ. The zeroth-order equation, corresponding to ϵ^0, is

$\frac{u_0}{\partial t} = D_0 \frac{\partial^2 u_0}{\partial x^2} - v_0 \frac{\partial u_0}{\partial x}$ (21)

This is a standard convection-diffusion equation with constant coefficients, for which $u_0(x, t)$ can be solved analytically using methods such as separation of variables, Laplace transforms, or similarity solutions, depending on boundary and initial conditions. The first-order correction term $u_1(x, t)$ is obtained by collecting terms proportional to ϵ. Substituting and simplifying, we get

$\frac{u_1}{\partial t} = D_0 \frac{\partial^2 u_1}{\partial x^2} - v_0 \frac{\partial u_1}{\partial x} + D^{'}(x) \frac{\partial^2 u_0}{\partial x^2} - v^{'}(x) \frac{\partial u_0}{\partial x}$ (22)

This equation for $u_1(x, t)$ has a similar form to the zeroth-order equation but includes inhomogeneous terms involving D′(x) and v′(x) acting on the zeroth-order solution $u_0(x, t)$. Solving this equation typically involves treating it as a non-homogeneous partial differential equation, with $u_0(x, t)$ known from the zeroth-order solution. For each successive correction $u_n(x, t)$, we obtain a similar differential equation involving terms from previous solutions $u_{n-1}(x, t)$ and additional spatial variability factors from D′(x) and v′(x). These equations can be solved iteratively if higher accuracy is desired, though often the first-order correction $u_1(x, t)$ provides sufficient accuracy for small ϵ. The complete approximate solution u(x, t) is assembled by summing the series

$u(x,t) \approx u_0(x,t) + \epsilon u_1(x,t) + \epsilon^2 u_2(x,t) \ldots\ldots\ldots\ldots..$ (23)

This series provides a smooth and accurate representation of u(x, t), capturing both the main behaviour of the concentration profile and the effects of spatial variations in diffusion and convection coefficients.

RESULTS AND DISCUSSION

For figure 1, the hybrid analytical solution effectively illustrates the variation of the concentration profile across two regions with differing diffusion and convection properties. In the first region, where diffusion and convection rates are higher, the solution exhibits a steep increase, reflecting the stronger influence of these parameters. In contrast, the second region shows a gentler slope due to lower diffusion and convection values, leading to a flatter profile. The continuity and flux-matching conditions applied at the boundary ensure a seamless transition between regions, which is clearly visible in the smooth connection between the solution segments. The analysis reveals that variations in diffusion and convection coefficients significantly impact the solution profile, underscoring the sensitivity of the concentration profile to regional parameter differences. The hybrid approach, by using analytical solutions in simple regions and numerical methods where parameters are more complex, effectively balances computational efficiency with accuracy. This method ensures a consistent and continuous profile across the boundary, making it particularly suitable for systems where parameter variations are spatially significant. Furthermore, the use of analytical solutions where possible reduces computational requirements compared to fully numerical solutions. For figure 2, The perturbation method provides a smooth, continuous solution across two regions with differing diffusion and convection properties. The zeroth-order solution gives the primary profile, while the first-order corrections account for small variations in the diffusion and convection coefficients. The result is a concentration profile that smoothly transitions at the interface between regions, reflecting how spatial variations in parameters impact the solution. This approach reveals that even small changes in diffusion and convection coefficients can significantly influence the solution. By using a hybrid model, the perturbation method balances accuracy and computational simplicity. The

zeroth-order solution captures the overall trend, while first-order corrections adjust for variations, making the solution more accurate without requiring fully numerical methods.

CONCLUSION

This hybrid method provides a powerful solution technique for convection-diffusion problems with spatially varying parameters. By combining analytical and numerical techniques, it accurately captures the behaviour of systems where diffusion and convection coefficients vary between regions. The approach is computationally efficient and adaptable, making it highly valuable for complex applications in physics and engineering. Overall, this method serves as an effective model for solving convection-diffusion equations in semi-infinite domains, particularly where a fully analytical or fully numerical solution would be impractical. The perturbation method is effective for convection-diffusion problems with gradual spatial changes in parameters. It combines analytical and numerical techniques, providing an efficient and accurate solution for systems where the diffusion and convection coefficients vary slightly. This makes it valuable for modelling complex systems in physics and engineering, particularly when high computational efficiency is needed.

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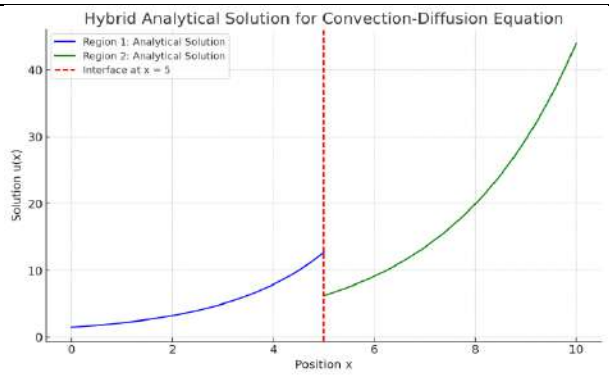

Figure 1: Hybrid solution for Convection – Diffusion Equation

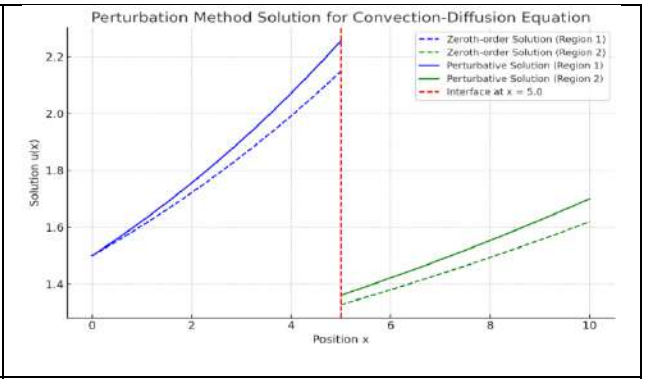

Figure 2: Perturbation Method solution for Convection – Diffusion Equation

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RESEARCH ARTICLE

A Study of Power-Law Fluid Peristalsis in Channels Featuring Non-Uniformity and Porous Lining

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ABSTRACT

The influence of power-law fluid rheology on peristaltic transport in channels with different cross-sectional shapes and non-uniformities is examined in this work using numerical simulations and mathematical modelling. Another factor that adds complexity to the system is the presence of a porous lining. Because Darcy's law describes the porous media, researchers may study the effects of peristaltic pumping on fluid flow in this type of medium. A thorough comprehension of the transport processes in systems involving power-law fluid behaviour, porous lining, and channel shape is the goal of this research. This study's findings could be useful for optimising and designing peristaltic pumps, medication delivery systems, and other fluidic devices that deal with porous materials and non-uniform channels. The study adds to the body of knowledge in fluid dynamics, non-Newtonian rheology, and interactions between porous media by combining theoretical analysis with numerical simulations. This research could lead to better devices that use peristaltic motion even when there are non-uniformities or porous linings, which could improve the efficiency and performance of systems based on this principle in many different areas.

Keywords: Power law fluid, Porous Lining,Shear Stress , Darcy number, slip parameter, thickening of the wall

INTRODUCTION

An ever-changing and pervasive characteristic in many engineering and biological systems is peristalsis, the regular relaxation and contraction of a tube or channel. Its importance ranges from being a basic mechanism in different fluid transport systems to assisting the movement of chemicals in living organisms. Problems with non-Newtonian fluids, including power-law fluids, make it all the more important to understand the complexities of peristaltic motion. In contrast to the linear Newtonian behaviour typically seen in classical fluid dynamics, power-law fluids exhibit a non-

linear relationship between stress and strain rate. The transport and flow patterns within conduits are affected by this particular rheological feature, which presents both opportunities and challenges for various disciplines. Studying power-law fluid peristalsis becomes an investigation into the confluence of fluid dynamics, non-Newtonian rheology, and interactions between porous media when non-uniform channel geometry and porous linings are added to the complexity. Reddy et al. (2007) conducted a study on the flow of a power-law fluid in an asymmetric channel. In this study, peristaltic waves with varying amplitudes and phases were observed to move across the flexible walls of the channel at the same speed. Walker and Shelly (2010) developed a variational technique to improve the wave pattern of a peristaltic syphon, specifically for a channel with two layers. In their study, Tripathi and Anwar Beg (2014) investigated the movement of chyme through a diseased digestive tract. Based on their calculations, they found that there is an inverse relationship between pressure difference and mean volumetric flow rate across all boundaries. However, the erosion force is directly proportional to the mean volumetric flow rate. Chakradhar et al. (2017) illustrated the influence of the permeable material adjacent to the wall on the peristaltic motion of the Casson fluid. The governing equations are constructed using the approximations of long wavelength and low Reynolds number. Ramesh and Devaker (2019) developed a model to examine the issue with the endoscope and its potential use in the field of biomedicine. They have utilised a couple of pressure fluids to demonstrate physiological liquid. The utilisation of peristalsis for the production of chyme in the gastrointestinal tract may be observed in the study conducted by Vaidya et al. (2020). Their analysis reveals the increasing impact of varying thickness on the size of the bolus. In the peak of the aforementioned article, we can observe the authentic applications of non-Newtonian fluid flow in clinical and industrial settings. Shukla et al. (2020) investigated the impact of the roughness parameter on the peristaltic transport of Newtonian fluid in a nonuniform channel.

The motivation for this study is derived from various research studies in the field of natural sciences and engineering, which indicate that the surfaces of live organisms and other objects exhibit a certain degree of roughness. Maryam and her colleagues (2021) conducted a meta-analysis on the effect of homogeneous-heterogeneous compound response on peristaltic flow through curved mathematical models. The study conducted by Ahmed et al. (2021) focuses on the impact of warm radiation on the peristaltic flow of nanofluid with blended convection. The investigation reveals that the appealing field tends to enhance the nuclear power of the flow. The examination of microfluidic peristaltic flow is conducted by Noreen et al. (2021). Rafiq et al. (2023) investigated the flow of Jefrey fluid through a channel with a permeable wall using peristalsis. Magnetohydrodynamic (MHD) effects are taken into account during the calculation of the problem. EI-Dabe et al. (2023) examined the flow of a continuous non-Newtonian nanofluid, following the Bingham model, down a slanted pipe with varying dimensions. The Bingham nanofluid flows through a porous material that does not follow Darcy's law, due to the combined effects of thermal radiation, heat generation, Ohmic diffusion, chemical reaction, mixed convection, and thermal conduction. This work focuses on studying the intricate dynamics of peristalsis in channels with non-uniform geometry and porous linings, where the fluid follows power-law behaviour. The work was motivated by the potential applications in several domains such as industrial operations, biomedical engineering, and drug delivery systems. An in-depth understanding of the collective effects on peristaltic motion is necessary because of the heightened intricacy caused by power-law fluid characteristics, non-uniform channel shape, and porous materials. Investigating the impact of power-law fluid rheology on peristaltic transport in channels with non-uniform cross-sectional shapes is the goal of this mathematical modelling and numerical simulation work. The study goes further to look at how porous linings affect peristaltic pumping, bringing up issues with fluid flow through porous media according to Darcy's law.

Mathematical Formulation

The channel is non-uniform. The discussion is focused on the half width of the channel.
The deformation of the wall is given by the function:

$$a(x,t) = a_0 + dcos\left(\frac{2\pi x}{\lambda} - \omega t\right) \quad (1)$$

$a(x,t)$is the half-width of the channel,
$a_0$is the initial half-width of the channel at the inlet,
d is the amplitude of the peristaltic wave,

λ is the wavelength,
$\omega$is the angular frequency ($\omega = 2\pi f$, where f is the frequency).
This function describes how the half-width of the channel changes over space and time due to the peristaltic wave. The term $\frac{2\pi x}{\lambda}$ inside the cosine function represents the spatial variation along the channel, and ωt represents the temporal variation.
The governing equation of the motion after dropping primes are follows

$$\frac{\partial \tau_{yx}}{\partial y} = -\frac{\partial p}{\partial x} \quad (2)$$

The constitutive equation of Casson fluid

$$\tau_{yx} = K\left(\frac{\partial w}{\partial y}\right)^n \quad (3)$$

And the dimensionless condition at the boundary are

$$\psi = 0 \text{ at } y = 0 \quad (4)$$

$$\frac{\partial^2 \psi}{\partial y^2} = 0 \text{ at } y = 0 \quad (5)$$

$$\tau_{yx} = 0 \text{ at } y = 0 \quad (6)$$

$$w = \frac{\partial \psi}{\partial y} = -\frac{\sqrt{Da}}{\alpha}\frac{\partial w}{\partial y} - 1 \text{ at } y = a(x) - \epsilon \quad (7)$$

Where
w is the velocity
α is slip parameter
Da is Darcy number
ϵ is porous thickening of the wall.
The equations provided represent the movement of a power law fluid, with stress denoted as $\tau_{yx}$and velocity denoted as w in the y-direction. The boundary conditions are characterized by the dimensionless variables: stream function ψ, velocity w, and stress τ_{yx}.

Solution of the Problem

The velocity field is obtained by solving Equations (2) and (3), together with $w = \frac{\partial \psi}{\partial y}$, and applying the boundary conditions (4) - (7).

$$w = \frac{n}{n+1}\left(\frac{P}{K}\right)^{\frac{1}{n}}\left[y^{\frac{1}{n}+1} - (a-\epsilon)^{\frac{1}{n}+1}\right] - \left(\frac{P}{K}\right)^{\frac{1}{n}}(a-\epsilon)^{\frac{1}{n}}\frac{\sqrt{Da}}{\alpha} - 1 \quad (8)$$

We take $w = w_p$ when $y = y_p$ in (8) to get the velocity in the plug flow region, and then we get

$$w_p = \frac{n}{n+1}\left(\frac{P}{K}\right)^{\frac{1}{n}}\left[y_p{}^{\frac{1}{n}+1} - (a-\epsilon)^{\frac{1}{n}+1}\right] - \left(\frac{P}{K}\right)^{\frac{1}{n}}(a-\epsilon)^{\frac{1}{n}}\frac{\sqrt{Da}}{\alpha} - 1 \quad (8)$$

Where$'q'$is the volume flow over all cross sections, the formula is

$$q = \int_0^{y_p} w_p dy + \int_{y_p}^{a-\epsilon} w dy \quad (9)$$

$$q + a - \epsilon = \left(\frac{P}{K}\right)^{\frac{1}{n}}\left[\frac{n}{2n+1}\left\{y_p{}^{\frac{1}{n}+2} - (a-\epsilon)^{\frac{1}{n}+2}\right\} - \frac{\sqrt{Da}}{\alpha}(a-\epsilon)^{\frac{1}{n}+1}\right] \quad (10)$$

$$-\frac{\partial p}{\partial x} = \frac{K(q+a-\epsilon)^n}{\left[\frac{n}{2n+1}\left\{y_p{}^{\frac{1}{n}+2} - (a-\epsilon)^{\frac{1}{n}+2}\right\} - \frac{\sqrt{Da}}{\alpha}(a-\epsilon)^{\frac{1}{n}+1}\right]^n} \quad (11)$$

The velocity of the flow of volume $Q(\bar{x},\ t)$between the centre line and the wall in the laboratory frame is

$$Q(\bar{x},\ t) = \int_0^{\bar{a}} \bar{u}\,(\bar{x}, \bar{y}, t) d\bar{y},$$

Rate of volume flow Q as a function of time,

$$\bar{Q} = \frac{1}{T}\int_0^T Q\, dt = q + 1 \quad (12)$$

It is possible to calculate the pressure difference across a wave's cycle by integrating Equation (11) over a single wavelength.

$$\Delta P = \int_0^1 \frac{\partial p}{\partial x}\, dx \quad (13)$$

The wall's frictional force F, measured over a single wavelength, is

$F = \int_0^1 a\left(-\frac{\partial p}{\partial x}\right) dx$

Since $w = \frac{\partial \psi}{\partial y}$ (14)

$\psi = \frac{n}{n+1}\left(\frac{P}{K}\right)^{\frac{1}{n}}\left[\frac{n}{2n+1} y^{\frac{1}{n}+2} - (a-\epsilon)^{\frac{1}{n}+1} y\right] - \left(\frac{P}{K}\right)^{\frac{1}{n}} \frac{\sqrt{Da}}{\alpha}(a-\epsilon)^{\frac{1}{n}} y - y$ (15)

RESULTS AND DISCUSSION

The graph (1) shows a gradual increase in the breadth of the channel over time. The graph (2) illustrates the variation in channel width over its length (x). The wavelength (λ) affects the frequency of these fluctuations. The graph exhibits recurring patterns of expansion and contraction along the channel. The peaks and troughs in the graph indicate the points where the channel width reaches its highest and lowest values, respectively. The graph displays a periodic behaviour, where the channel width repeats its pattern at regular intervals specified by the wavelength. The graph (3) depicts the variation in fluid velocity as a function of the distance (y) from the channel wall or a reference point. Peaks or troughs in the velocity profile may indicate particular characteristics of the channel, such as areas of narrowing or widening. Comprehending the velocity profile is essential for applications like as drug delivery systems, where peristalsis and non-uniform channel characteristics might influence the movement of medicinal molecules. The 3D graph (4) enables the visualization of the variations in channel width as a result of changes in both (x) and (t). It can uncover the spread of peristaltic waves and their impact on the shape of the channel as time passes. Comprehending this graph is essential for applications such as biomedical devices or industrial processes that involve non-Newtonian fluids, peristaltic motion, and channel characteristics. Each curve on the graph (5) depicts the correlation between the decrease in pressure and the rate of flow for a particular Darcy number. Distinct Darcy numbers are associated with various flow regimes within porous media. The graph displays clearly defined zones that correspond to various flow regimes. At low flow rates, viscous forces are the dominant factor, whereas at greater flow rates, inertial forces become more predominant.

The graph yields useful insights into the behaviour of several porous media under varied flow circumstances. It enables the assessment of the permeability of the porous material and the influence of the Darcy number on flow patterns. Comprehending the relationship between pressure drop and flow rate is essential in reservoir engineering for forecasting the movement of fluids in oil or gas reservoirs. The graph is utilized in geotechnical engineering to evaluate the permeability of soils and the influence of various Darcy numbers on the flow of groundwater. Each curve on the graph (6) corresponds to a distinct value of the slip parameter. The objective is to investigate the impact of various slip conditions at the interface between the fluid and solid on the relationship between pressure drop and flow rate. The curves may exhibit varying slopes, forms, or critical points as slip parameters change. Slip can influence the dynamics of the boundary layer and modify the flow properties in the vicinity of the solid surface. Comprehending slip effects is essential in microfluidic and nanofluidic systems characterized by dimensions that are similar to the average distance travelled by fluid molecules, resulting in slip at the boundary. Slip effects can have an impact on fluid flow and transport qualities in applications that involve nanoporous materials. The graph facilitates comprehension of these consequences in various contexts. The 3D graph (7) presents a dynamic depiction of the variations in pressure drop with respect to spatial coordinates and time. Every point on the graph represents a distinct pairing of x and t, accompanied by a corresponding decrease in pressure. By analyzing the graph, one can discern patterns, trends, or fluctuations in the pressure drop across the spatial and temporal dimensions. One can ascertain the relationship between pressure drop and distance (x) or track its temporal evolution (t). The graph illustrates the relationship between frictional force and flow rate for various porous thicknesses. It offers valuable information on how the frictional resistance in a porous medium changes with the rate of fluid flow, taking into account varying thicknesses of the porous material. Each curve on the graph represents a distinct value of porous thickness. The objective is to examine the impact of varying thicknesses of the porous material on the connection between frictional force and flow rate. The curves may exhibit varying slopes, forms, or critical points as the thickness of the porous material changes. The frictional force in a porous media is affected by elements such as the arrangement of pores, the amount of empty space, and the winding path of the flow, which can vary with varied

thicknesses. The graph can offer insights into whether there exists an optimum or critical thickness that minimizes frictional forces for a specific flow rate. This information is crucial for creating porous media for applications that require low resistance.

Concluding Remarks

We have explored the complex dynamics of fluid transport as a final step in our study of power-law fluid peristalsis in channels with non-uniformity and porous lining. Discoveries with important theoretical and practical implications have been made in the fertile ground where power-law rheology, non-uniform channel geometry, and porous structures converge. The unique shear-thinning or shear-thickening behaviour of power-law fluids, as we found in our work, shows complex reactions to peristaltic motion in channels with different cross-sectional shapes. The presence of channel geometry non-uniformities increases the level of complexity, which in turn affects the distributions of pressure and flow. Also, the fluid dynamics and overall transport characteristics were affected by the porous lining, which was modelled using Darcy's law and created a porous medium. An interesting discovery is that power-law fluid peristalsis is quite sensitive to the level of channel geometry non-uniformity. The peristaltic pumping process alters the fluid's interaction with the channel as it departs from its idealised shape, which in turn affects the pressure profiles and flow rates. Drug delivery systems and industrial operations are two examples of situations where this knowledge is vital for exact control over fluid flow. The fluid flow patterns were affected by the porous liner, which acted as a permeable barrier. Peristaltic motion's interaction with the channel's porous nature caused pressure and fluid velocity to fluctuate. This finding opens the door to new possibilities for creative system design that incorporates peristaltic pumping by indicating that porous linings can be strategically used to regulate and control fluid transport. Our study sheds light on the behaviour of power-law fluids in non-uniform channels with porous linings, which is a practical contribution to the advancement of peristaltic-based systems. The acquired knowledge can be applied to optimise peristaltic pumps by taking power-law rheology, non-uniform geometries, and porous materials into account, which can result in enhanced performance and efficiency. We find that the complex channel environment with porous linings, power-law fluid dynamics, and peristaltic motion interact in a multidimensional and intriguing way. The findings of this study will aid scholars in their study of fluid dynamics and will be useful to academics and engineers who are developing and implementing peristaltic-based systems in the real world.In summary, the interaction of power-law fluid dynamics, peristaltic motion, and complicated channel settings with porous linings is a captivating and multifaceted area of research. The findings derived from this inquiry not only enhance the scholarly comprehension of fluid dynamics but also provide practical direction for engineers and researchers engaged in the development and execution of peristaltic-based systems in practical contexts.

Future direction of Research:

Theoretical and practical investigations into power-law fluid peristalsis in non-uniform and porous lining channels are attractive areas for future research. To better understand real-world occurrences, it is essential to combine current theoretical models with numerical simulations and incorporate experimental validation as an additional layer of analysis. Improvements in machine learning algorithms and other computational methods can speed up simulations and make it easier to investigate complicated geometries. Additionally, by adapting designs to match the distinct needs of certain areas, researchers might zero in on peristaltic systems that are ideal for medication delivery or biomedical devices, for example. In order to address modern concerns, it is important to investigate how these systems affect the environment and to use sustainable design principles. Experts in fluid dynamics, materials science, and engineering can work together to identify new answers and speed up the process of turning research into useful products and services.

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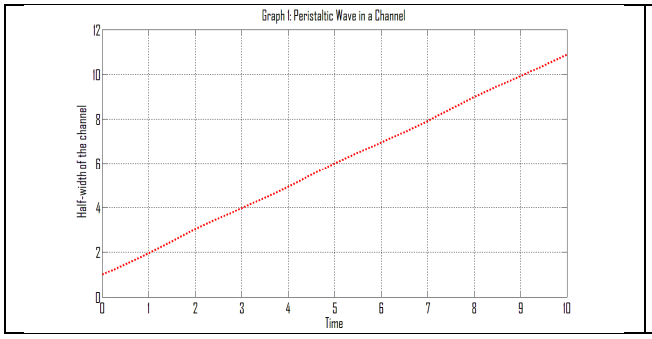

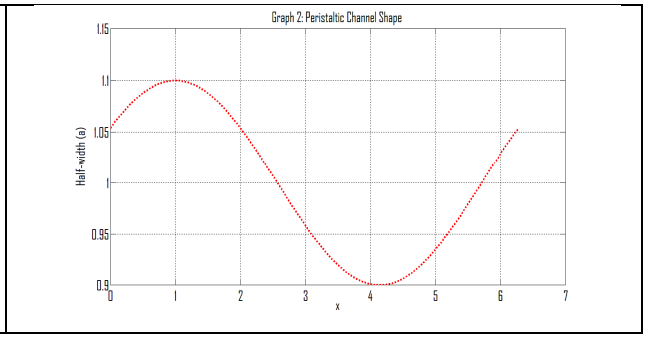

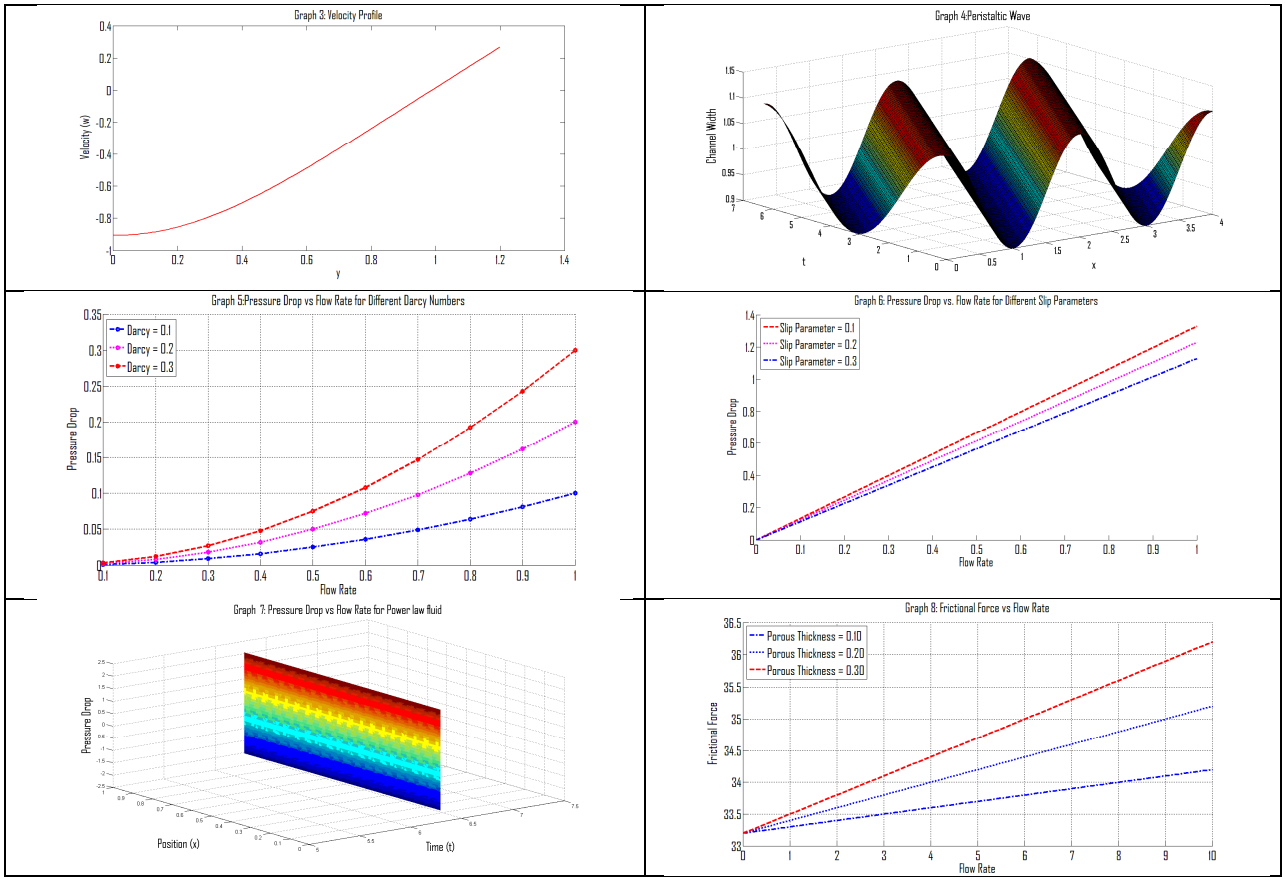
Graph 3: Velocity Profile
Velocity (w)
y
Graph 4:Peristaltic Wave
Channel Width
t
x
Graph 5:Pressure Drop vs Flow Rate for Different Darcy Numbers
Darcy = 0.1
Darcy = 0.2
Darcy = 0.3
Pressure Drop
Flow Rate
Graph 6: Pressure Drop vs. Flow Rate for Different Slip Parameters
Slip Parameter = 0.1
Slip Parameter = 0.2
Slip Parameter = 0.3
Pressure Drop
Flow Rate
Graph 7: Pressure Drop vs Flow Rate for Power law fluid
Pressure Drop
Position (x)
Time (t)
Graph 8: Frictional Force vs Flow Rate
Porous Thickness = 0.10
Porous Thickness = 0.20
Porous Thickness = 0.30
Frictional Force
Flow Rate

RESEARCH ARTICLE

In vitro Antidiabetic Effect and Phytochemical Screening of *Cassia biflora* Mill.

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ABSTRACT

People of all ages are susceptible to the Insulin resistance syndrome identified as Type 2 *Diabetes mellitus* (T2DM). Environmental factors and lifestyle modifications Contribute significantly in the progression of the condition. There is an urgent need to identify novel natural anti-diabetic drugs for delayed starch digestion, since α-glucosidase and α-amylase enzyme inhibitors can both therapeutically suppress postprandial glucose peaks with excess unfavourable consequences. This study's objective is to examine at the plant's ability to prevent diabetes and to determine the unique phytocompound composition found in *Cassia biflora's* aerial sections. To find out whether primary and secondary metabolites were present, a preliminary screening was performed on the plant extract. Glycosides, alkaloids, flavonoids, carbohydrates, proteins, steroids, and tannins were all present. The thin layer chromatography profile of plant's EtOAc fraction was developed using a variety of solvent systems; the Chloroform: Ethanol (9:1) solvent system showed superior component separation. According to the early phytochemical screening, it contains a variety of flavonoids and phenolics that may be the source of its anti-diabetic properties. The α-amylase inhibition assay can be used to identify the hypoglycaemic Impact of *Cassia biflora*. By decreasing the glycaemic level and minimizing the hazards connected to a fast spike in blood sugar, the phytoconstituents in plants work in concert to mediate the α-amylase's inhibition function.

Keywords: *Cassia biflora*, *Diabetes mellitus*, α-amylase, Phytochemical screening, Anti-diabetic, Flavonoid

INTRODUCTION

The term "Diabetes mellitus" describes metabolic diseases brought on Impaired insulin production by the pancreas. The condition's primary symptom is hyperglycaemia [1]. A set of anomalies are brought about by the diminished action of insulin on target tissues, which impact the physiology and biochemistry of protein, fat, and carbohydrates [2, 3]. Higher blood sugar, increased insulin secretion, higher insulin intolerance, and elevated glucose tolerance are the hallmarks of this metabolic disorder. About 90% of cases of diabetes are identified; T2DM rapidly progressing kind of the illness. Based on WHO estimations, the prevalence of Type 2 diabetes may double by 2030, with 422 million people worldwide estimated to be affected in 2014[4]. According to exhaustive literature survey on the separation of numerous active fractions from plants with therapeutic characteristics, plants are used either directly or indirectly to manufacture about 50% of pharmaceutical drugs [5]. Based on ethnobotanical data, almost 800 plant species have been found to possess the anti-diabetic characteristics. *Cassia biflora* is a specific of those plants that was historically utilized as ancient medicine. *Ctenodonbrasilianus* is the plant's synonym [6]. It's a medium-sized shrub with plenty of flowers. The plant was found to constitute the following phytoconstituents viz., physcion, luteolin, and chrysophanol[7]. The current study utilized an in-vitro α-amylase inhibition assay for the quantification of the phytochemical composition of plant and evaluate the feasibility of *Cassia biflora* Mill. as an potent Anti-Diabetic drug.
A major contributing factor in the onset of Ty. II diabetes and the Challenges of micro, macrovascular diseases are postprandial hyperglycaemia. In cases of Insulin-resistant diabetes, specifically, blocking the function of the α-amylase dec. postprandial sugar concentrations. Diabetes must be controlled through adjustments in nutrition, daily habits, and consistent exercise to avoid complications hypoglycaemic medication side effects. In Type 2 diabetes, α-amylase inhibitors are used for better control of hyperglycaemia[8]. The present study is directed to certify that *Cassia biflora* Mill may be effectively used to measure the anti-diabetic effects of its product by using the α-amylase inhibitory assay.

MATERIAL AND METHODS

Collection and Authentication of Plant
A fresh specimen of ***Cassia biflora*** was gathered in January 2024 from Dehradun, Uttarakhand, India. The plant was identified and authenticated by the Forest Research Institute (FRI) in Dehradun, Uttarakhand, under reference number 1443/Dis./2018/Syst.Bot./Rev.Gen./4-5.

Plant Material
The plant *Cassia biflora* aerial parts (**Fig.No.1**) were harvested from Dehradun, Uttarakhand, India. The plant underwent cleaning, shade dried, and then powdered. The material is subjected for preparation of powdered form by passing the material through Sieve No. 22. Several solvents were used to extract the medication from its powdered form.

Organoleptic Evaluation[9]
It describes the assessment of plant material based on characteristics like size, shape, colour, odour, taste and texture. Organoleptical evaluation refers to the results prepared from study based on the sensory assessment, overall condition and appearance of the raw plant material and organoleptic examination of the *Cassia biflora* plant using simple microscope.

Physicochemical Evaluation[10]
Foreign organic matter
A 100-gram quantity of unrefined drug was applied to a spotless, clean surface using magnifying lenses (10X) in order to determine If foreign organic compounds were present in the plant specimen. Three sets of readings were taken in accordance with the protocol.

Extractive value [11]

Cold maceration method used for the purpose of calculating extracting value, as follows:

A conical flask with a cotton plug was filled with 4g of precisely weighed coarsely powdered air-dried material, which was macerated for 6 hours with vigorous shaking in 100 milliliters of the solvent intended for the plant material. Following that, it was left alone for eighteen hours. In order to prevent solvent loss, 25 milliliters of the filtrate were rapidly filtered. It was then set on a flat-bottomed, dried plate and left to air dry before being dried for six hours at 105°C, cooled for half an hour in Moisture-absorbing container, and immediately Measured in mass. The amount of extractable material were observed in milligrams for every gm.

Calculated the % of extractable constituents from Evaporated material as:

$$\% \text{ Extractive value} = \frac{[\text{final weight} - \text{initial weight}] \times 4}{\text{weight of the drug}} \times 100$$

The following kinds of extraction rates have been determined using the above-described methodologies:

- Water soluble extractable content
- Methanol soluble extractable content
- Ethyl acetate extractable content
- Chloroform soluble extractable content
- Acetone soluble extractable content

Total ash

As long as carbon-neutral ashes were produced, two grams of powdered *Cassia biflora* were burned in a crucible in a muffle furnace at temperatures between 500 and 600°C. After allowing the drug to cool and weighed also % of total ash were evaluated .

Determined the Air-exposed dried material's content of the overall ash value as:

$$\% \text{ Total ash value} = \frac{\text{weight of total ash}}{\text{weight of crude drug taken}} \times 100$$

Acid insoluble ash

After boiling 25 milliliters of 70 g/L hydrochloric acid for five minutes, the resulting ash were filtered. The filter paper, containing trapped insoluble material, was rinsed with hot water. The percentage of ash that was insoluble in acid was determined by comparing it with weight of dried powdered material.

Calculated the proportion of ash that is insoluble in acid from the air-dried material as:

$$\% \text{ Acid insoluble ash value} = \frac{\text{weight of acid insoluble ash}}{\text{weight of crude drug taken}} \times 100$$

Water-soluble ash

Twenty-five millilitres of water were used to bring the total amount of ash to a heated for five minutes. The inert substance was stored on ash-free filter paper, cleaned with boiling water, and then burnt for 15 minutes at an elevation that could not exceed 450°c in a muffle heater. The quantity of water-soluble ash was determined by splitting the mass of ash by the mass of water-insoluble ingredients. The dried in the air powdered plant product was used to calculate the proportion of water-soluble ash.

Determined the % of water-soluble ash value as:

$$\% \text{ Water soluble ash value} = \frac{\text{weight of total ash} - \text{weight of water insoluble ash}}{\text{weight of crude drug taken}} \times 100$$

Extraction from *Cassia biflora* Aerial Parts

Solvents such as ethyl acetate, methanol, acetone, and chloroform were used to extract the plant material utilizing the cold maceration procedure [13].

Cold maceration method

One hundred milliliters of solvent were mixed with four grams of the powdered substance. The conical flask containing the ingredients was then left to macerate for the next six hours, vigorously shaking it every ten minutes. Additionally, the flask was kept still in a darkened area for the next eighteen hours. The filtrate was subsequently moved on a China plate. The dried extracts were used for other purposes [14].

Preliminary Phytochemical Screening

Initial phytochemical screening was performed by utilizing a conventional technique[15].

Alkaloids

- **Dragendroff's test:** 1 milliliter solution of extraction + 1 milliliter Potassium bromideproduce orange-red coloured precipitate
- **Mayer's test:** 1 milliliter solution of extraction + 1 milliliter Mercury(I) iodide gives cream, whitish yellow tint coloured precipitate.

Glycosides

- **Legal's test:** 1 milliliter of extract + pyridine + Na2 [Fe (CN) 5NO]) shows absence of glycoside with no change in color.
- **Baljet's test:** 1 milliliter of extract + 1 ml C6H2KN3O7 indicates the presence of glycoside with Yellow to orange colour appearance.
- **Cardiac glycosides:** Few drops of concentrated H2SO4 and 1 milliliter of FeCl3 reagent was added to 1 milliliter of the filtrate of extract shows turning of greenish blue colour in few minutes.[16]

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Carbohydrates

- **Benedict's test:** 5 ml of benedict's chemical+ 1 milliliter solution of extraction subjected to boiling just2 minutes and then let it cool to produce a pink coloured precipitate which indicates presence of sugars.
- **Molisch's test:** Ethanolic extract + α- naphthalene (20% w/v, 90%) subjected for shaking gently and conc. H2SO4 was inserted via the test tube's side.

Steroids

- **Salkowski test:** solution of extraction, CHCl3, and some amounts of concentrated H2SO4 were added. The acidic layer fluorescence green, while the CHCl3 layers (which contain steroids) are bluish red to cherry in colour.
- **Liebermann-Burchard test:** By heating the extract and one milliliter of acetic anhydride, it started getting dissolved. A few drips of concentrated H2SO4 were visible on the test tube's sides after the contents had cooled. The sterols (blue colour) are present.

Test for Proteins

- **Biuret test:** 40% sodium hydroxide solution along with 2% solution CuSO4 sol.until a blue colour appears + 1 ml extract is the biuret test. Violet (protein present).

Test for Saponins

- Extraction were shaken and boiled in one milliliter of distilled water. There was foam (saponins).
- Combined the extract with 2 ml of distilled water and sodium carbonate, then shaked. Foam formation shows the presence of saponins.

Test for Tannins

- Put the extract into a mixture of lead acetate. Tannins are present when white precipitates start to develop.

Test for Flavonoids

- **Shinoda test:** Add concentrated hydrochloric acid drop wise to the test solution containing magnesium turnings. A pink scarlet colour appears.

Thin layer chromatography

This was as peedy screening methodology to isolating components and categorizing herbal preparations. Because of its user-friendly interface, fast turnaround times, reliable, accurate, and precise processes, as well as its reasonably priced operating costs, this method is widely utilized for both qualitative and quantitative analysis[17].

Procedure

- Using a capillary tube that was one centimetre above the bottom, the sample was transferred to a TLC plate.
- Sample spot was air dried.
- Mobile phase was added to the beaker at a length of 0.5-1cm from the bottom.
- After closing the beaker, positioned the TLC plate in the jar such that the sample spot is still above the level of mobile phase.
- Until the solvent moved a suitable distance from the baseline, the system was left in a static state.
- TLC plate was taken out and dried (**Fig.No.2**).

***In-vitro* anti-diabetic activity**

α amylase inhibitory activity

The modified Pradeep and Sreerama (2015) approach was used to determine the inhibitory impact of α amylase of *Cassia biflora* Mill. extract[18,19].. Fifty microliters of 20 mM phosphate buffer (pH 6.8) and 10 microliters of α-amylase (2 U/ml in 20 mM PBS buffer) was mcombined in various ratios of *Cassiabiflora* M. extracts (50–250 µg/ml) underwent incubation at 25°C for 30 minutes. After that, 20 µl of 1% soluble starch mixed in 20 ml of phosphate buffer (pH 6.8). The reaction was once more incubated at 37°C for 30 minutes. Afterward, 100 µl of Dinitrosalicylic acid (DNS) reagent added, and the solution was heated at 96°C for 10 minutes to complete the process. The mixture's absorbance at 540 nm evaluated by UV spectrophotometer. The usual dosage of acarbose was 50–250 µg/ml. Without plant extract, the reaction same as previously mentioned was carried out as a control [20]. Percentage of inhibition = (A540control – A540sample) × 100) Where, A540 control is Absorbance of control at 540nm The transmittance measured for the reaction's mixture containing the buffering agent and the enzyme is A540sample.

RESULTS

Macroscopic Evaluation of *Cassia biflora*

Leaves

- Shape: Usually pinnate with 4 to 6 pairs of leaflets.
- Size: Leaflets are typically small, about 1-3 cm long.
- Colour: Light to dark green.
- Texture: Smooth and slightly glossy on the upper surface, paler and duller on the underside.
- Arrangement: Alternate.
- Odour: Mild, slightly herbaceous smell

Stems

- Colour: Green when young, turning brown as they mature.
- Texture: Smooth when young, becoming woody and rough with age.
- Shape: Cylindrical and slender.

Flowers

- Colour: Bright yellow.
- Size: About 2-3 cm in diameter.

- Structure: Typical five-petaled flowers with prominent stamens.
- Arrangement: Usually found in small clusters or racemes.
- Odour: Generally faint and mildly sweet

Fruits

- Type: Pods (legumes).
- Size: Generally, 3-6 cm long.
- Shape: Cylindrical, slightly curved.
- Colour: Green when immature, turning brown when mature.
- Texture: Smooth
- Odour: Earthy aroma

Extractive Value of *Cassia biflora*(Fig. No. 3, Table No. 1)
Ash Value(Fig. No.4, Table No.2)
Phytochemical Evaluation (Table No.3)
TLC Fingerprinting (Table No.4)
***In Vitro* Anti-Diabetic Activity**
α- amylase inhibitory activity (Fig.No.5, Table No.5)

DISCUSSION

In order to maintain glucose homeostasis, insulin is essential. Insulin deficiency impacts the metabolism of glucose, lipids, and proteins. When insulin is not available, there are a number of ways to regulate how carbs are metabolized. Carbohydrate digestion is slowed down by blocking α-amylase, which decreases postprandial blood glucose levels and absorption. One type of competitive inhibitor used to regulate blood sugar levels is a carbose[21]. Because of the adverse effects of synthetic inhibitors, the use of herbal inhibitors might be required. Consistent scientific evidence is required for herbal inhibitors to be considered effective. Inhibitors that blocked pancreatic α-amylase and intestinal disaccharidase were found to decrease the absorption of carbs in the 1970s. These inhibitors effectively treat Type 2 diabetes when taken orally. The drug's hypoglycaemic effect can be determined by evaluating its in vitro effect on α-amylase as well as indirectly observing inhibition of aldose reductase. α-amylase[22,23]. This study compared natural botanicals known for their antidiabetic properties to the commercially prescribed drugs metformin and acarbose. The goal was to validate the effectiveness of the α-amylase inhibitory assay, a low-tech screening method for determining a plant's capacity to prevent diabetes. The initial α-amylase inhibitory screening focused on the formation of a complex between starch and plant extract. The macroscopic characteristics of the material were analysed in order to differentiate different plant components from other Cassia species. Colour, texture, flavour, size, shape, and odor were some of these characteristics. If it was found that the sample significantly deviated from the requirements. This becomes clear in **Section 3.1**. **The extraction value** of medicinal plant material indicates how many active chemicals may be extracted from a given volume using solvents. Using the cold maceration method and the following solvents—methanol, acetone, ethyl acetate, chloroform, and water—the extractable components in the entire *Cassia biflora* plant were evaluated in this investigation. Water, methanol, acetone, ethyl acetate, and water-soluble substances had estimated extractive values of 11%, 9%, 5%, 5%, and 5%, respectively. As seen in **Table No. 1** above, the aqueous extract exhibits a sizable amount of extracted, soluble components. The ash values assessed in the current study in order to ascertain the amount of extraneous matter adhering to the plant's foliage as well as the total amount of the substance left over after combustion. The expected ash content esteemed as 5.3%, 1.4%, and 3.2%, respectively, as shown in **Table No. 2** above. **Phytochemical analysis** of plant's powdered elaborate the presence of proteins, carbohydrates, steroids, saponins, polyphenolic compounds. **Table No. 3** displays the findings of the phytochemical screening of a number of *Cassia biflora* preparations. Flavonoid and phenolic compounds have anti-diabetic effects. Several types of phytoconstituents were detected in extracts treated with different solvent systems when the plant was evaluated for **TLC fingerprinting**. For determining the trace levels of contaminants in plants, this

approach is effective. The retardation factor (Rf) in a given solvent system is determined by measuring the separation between the solvent and the solute. The TLC of different extracts was developed using different mobile phases. The TLC fingerprinting profile results for different *Cassia biflora* extracts are shown in **Table No. 4**. ***In vitro* studies** have demonstrated the anti-diabetic properties of polyphenols produced from plants. According to this study's measurement of the resistant action of enzyme α amylase by CBE, the enzyme is 60% inhibited at 250 µg/ml. The percentage of resistance increases in a concentration-dependent way, illustrated visually in **Fig. No.5** and **Table No.**

CONCLUSION

The diabetes problem is widely acknowledged as the biggest challenge confronting the medical sciences today. A lot of research is being done to find out if the new generation of anti-diabetic formulations can solve the issue. These days, allopathic medicine has several drawbacks and associated difficulties. Diabetes therapy becomes more complicated as the disease worsens and new complications arise. Because of today's workplace culture, it can be difficult to continue eating a balanced diet and engaging in regular physical activity. Oral drug treatments require combination therapy, which increases the possibility of adverse effects. The majority of patients who took oral hypoglycaemic drugs eventually required insulin or died from organ failure, according to the data. Insulin use is also less popular due to the requirement for frequent injections, the shame associated with it, concerns about hypoglycaemia, and budgetary limitations. There are several ways that herbal therapy works, and treating the root causes of a disease may help cure it. A comprehensive study assessing the plant's anti-diabetic activity has been carried out in order to assist in creating an anti-diabetic herbal formulation from the portion of widely recognized, locally accessible anti-diabetic herbs. According to the ethyl acetate extract's TLC fingerprinting profile, this drug contains a sizable number of flavonoids and phenols. Ethyl acetate extract had a significant and noteworthy alpha-amylase inhibitory activity in comparison to other extracts, indicating that it may be a potent anti-diabetic drug. Therefore, since *Cassia biflora* appears as plant species for treating hyperglycaemia, it would be advantageous to look into its potential for controlling type 2 diabetes mellitus. To completely comprehend *Cassia biflora*'s potential for treating hyperglycaemia, more research is necessary.

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CONFLICT OF INTEREST

The authors have declared no competing interests

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RESEARCH ARTICLE

Cloud based Soil Moisturising using Internet of Things

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ABSTRACT

Efficient utilization of resources in agriculture achieves increased production. Various technologies are being leveraged into agricultural industry from improving the yield of crops to maintaining the health of plants. Internet of Things (IoT)helps the farming community in numerous ways. Soil moisture influences plant growth, environmental processes and infrastructure stability. This paper presents the design, implementation and discussion of cloud based soil moisturising using IoT. The system consists of cloud based IoT platform, Wi-Fi module, microcontroller, sensors, relays, solenoid valves, sprinklers and motor pumpto monitor and react on the plants from anywhere with Internet. The system waters the plants remotely, by switching on the motor pump, which ensures them get optimum amount of water. The system offers a convenient and efficient way for users to keep track of their plants' health and well-being and empowers them to take proactive measures to ensure success of their gardening endeavors. The future of automatic soil moisturizing systems holds great promise, with opportunities for further integration with emerging technologies

Keywords: Soil moisture, plant growth, watering, cloud computing, microcontroller

INTRODUCTION

Robotics and automation play vital role in improving cultivation methods for greenhouses and providing farmers and land owners with relevant information to make decisions for optimal yields. In India, agriculture has a prominent role and most of the farmers use traditional methods in farming. Latest advancements in technology make the agriculture sector progress to witness a drastic change in the near future [1]. The need for efficient utilization of resources in agriculture is critical to achieve increased production. For a plant to grow well, it is necessary to monitor the plant's health parameters and take corrective actions when needed. Internet of Things (IoT) is one technology, which helps the farming community in numerous ways.

Soil moisture

Plants require low maintenance and can be left for days without supervision. But farmers' or landlords' long trips extending over a week or two can be detrimental for the health of the plants, due to lack of moisture in the soil. In such situations, the plant may wither or die due to absence of proper watering[2].Soil moisture plays a critical role in agriculture. It is a crucial parameter influencing plant growth, environmental processes and infrastructure stability. Traditional methods of soil moisture measurement involve manual sampling and laboratory analysis, which are often impractical for real-time monitoring and large-scale applications. They are labor-intensive, time-consuming and prone to human error. Automatic soil moisture testing offers a promising solution by providing continuous, accurate and timely data without human intervention.

Need for the system

Conventional green housing requires huge infrastructures. Their obstructions like lack of smart environments, plant diseases, smaller farmland, water scarcity or abundance, soil decay, infertility and absence of resources lead to decreased crop production and yield. In agricultural industry, cloud computing, wireless sensor networks, IoT, big data, machine learning and fog computing technologies play important role for increased production of crops and health of plants. IoT can be utilized at various stages in agriculture from ploughing the field to selling agricultural end-products in the market. In daily operations related to farming or gardening, watering is most important practice and intensive task [3]. Irrespective of the weather condition, one has to control the amount of water that reaches the plants. In this paper, a comprehensive view of a soil moisturising system has been presented, highlighting its design, implementation and analysis.

LITERATURE REVIEW

Pereira G.P. (2023) designed a smart IoT enabled drip irrigation system using ESP32 to automate the irrigation process and tested. The ESP32 communicated with the Blynk app to collect irrigation data, manually water the plants, switch on or off automatic watering function and plot graphs based on the readings of the sensors. ESP32 was connected to a soil moisture sensor, temperature sensor, air humidity sensor and water flow sensor. The ESP32 regularly checked the soil for dryness[4]. If the soil was dry and the soil temperature was appropriate for watering, ESP32 opened a solenoid valve and watered the plants. The amount of time to run the drip irrigation was determined based on the flow rate measured by the water flow sensor. The ESP32 read the humidity sensor values and notified the user when the humidity was too high or too low. The user could switch off automatic watering, according to the humidity value. Rishiraj Singh Salam and Anton Volkov (2023) developed a Smart Home-Agro System, an intelligent agricultural system, one could schedule to irrigate a piece of landor home garden automatically or spray fertilizersor pesticides on the crops wirelessly through smart phone. The system also monitored the soil moisture through soil moisture sensor periodically for the moisture content. Rajesh (2021) developed an Automatic Irrigation System with Arduino Uno, which irrigated the plants automatically and kept them healthy for weeks or months. A sensor was used to maintain optimum level of moisture of the plants [5]. Geetha S *et al.* (2022)demonstrated the efficient use of IoT in agriculture. For implementation of automatic plant watering system, they used combination of pipes, pump and motor and Arduino Uno, Real Time Clock (RTC)and soil moisture sensor to monitor and control

the irrigation [3]. Arduino microcontroller checked soil moisture level using soil sensor. The sensor measured how much water was present in the soil. If the moisture content is less than the specified threshold, then desired amount of water was supplied. It was timer based system, automatically watering the plants, for up to two weeks, even in the absence farmers or landlords.

MATERIALS

Software

BlynkIoT Platform: BlynkIoT Platform transforms ideas into real products. It builds mobile apps and cloud services, runs fleet tests, manages devices, configurations and updates and analyzes data(https://blynk.io/). ESP-8266 Wi-Fi Module: The ESP-8266 (Extra Sensory Perception) Wi-Fimodule is a self-contained Security Operations Centre (SOC) with integrated TCP/IP protocol stack that can give any microcontroller access to Wi-Fi network. The ESP-8266 is capable of hosting an application or offloading all Wi-Fi networking functions from another application processor.

Hardware

Arduino Microcontroller: Arduino Microcontroller consists of a physical programmable circuit board and a piece of software or Integrated Development Environment (IDE) that runs on a computer, used to write and upload computer code to the physical board.

Sensors: Sensors are devices that detect and respond to some type of input from the physical environment.

Relays: Relays are switches that open and close circuits electromechanically or electronically.

Solenoid Valves: Solenoid valves are control units, when electrically energized or de-energized, either shut off or allow fluid flow.

Irrigation Sprinklers: Irrigation sprinklers are spraying devices used to water agricultural crops.

Motor Pump: A motor pump is a mechanical device that uses an electric motor to move fluids under pressure, such as water in a sprinkler system.

SYSTEM DESIGN

Figure 1

The Cloud Based Soil Moisturising System Using IoT(Figure 1) is a high-tech solution designed to keep the plants healthy and thriving with minimal effort by the users. The sensors in the system measure temperature, humidity and soil moisture intensity around the plants and send to an Arduino microcontroller. The microcontroller processes the data and sends them through cloud to a mobile application called Blynk, installed in a smart phone or computer. Through the Blynk app, users can monitor the real-time status of their plants from anywhere with Internet connection. The system has been designed to provide users with proactive alerts, if any of the monitoring data fall outside the predefined ranges. If the surrounding temperature becomes too high or the soil becomes too dry, the user will receive a notification on his smart device. The microcontroller controls the motor pump according to the moisture in the soil, given by the moisture sensor. To power the circuit, a 9 or 12 volt battery is used. The system waters the plants remotely. This is madeby a solenoid valve connected to the system, which can be opened or closed based on the data collected by the sensors. If the soil moisture level drops below a certain threshold, the microcontroller will trigger the solenoid valve to release water and irrigate the plants. This automated watering ensures the plants get optimum amount of water, reducing the risk of over-watering or under-watering. The system transmits the information gathered by the sensors to the BlynkIoT platform through cloud, using ESP-8266 Wi-Fi module, to the users to monitor different data of the plant remotely, including checking the soil moisture level. The ESP module connected with the application is not only useful for remote viewing; but also to turn the sprinklers on and off based on the requirement of the plants. It ensures plant growth via a relay and solenoid valve.

RESULTS AND DISCUSSION

The web dashboard has been designed to interact with the IoT platform that controls a motor and a digital pin, with both initially in the "OFF" state. When the dashboard is first loaded, the motor is in the "OFF" state, indicated by the motor status display. The digital pin is initially set to "OFF" and this is reflected on the dashboard in the "Pin: OFF" status. The system accurately initializes the state of the devices to "OFF" as expected. This ensures that no unintended action occurs when the system starts. In the IoT platform, key parameters like soil temperature and soil moisture are crucial for ensuring optimal growth conditions for plants. The system focuses on how data streams are related to these parameters – high soil temperature or low soil moisture can be handled in the platform. Data streams represent continuous or periodic readings from sensors deployed in the soil. These sensors could include Soil Temperature Sensor that measures the soil's temperature in real-time and Soil Moisture Sensor that measures the level of moisture in the soil, determining if it is too dry. The goal of the system is to continuously monitor these environmental factors and trigger appropriate actions based on the sensor readings. Based on the data collected by the sensors, the solenoid valve is opened and the water is released. When the motor and digital pin are in the 'ON' state on the IoT platform's web dashboard, it represents the scenario where the user has actively toggled the control buttons to activate both devices. Initially, the motor and digital pin were in the 'OFF' state, but now both are toggled ON. This is seen on the dashboard by a change in text and a different color or style (e.g., "Motor: ON" and "Pin: ON").The digital pin is displayed as "Pin: ON", showing that the pin has been activated and the system is now using to trigger actions or relay signals. The user interface reflects this change with clear, updated status indicators, ensuring that users are aware that both devices are now active. When the soil achieves the specified moisture value, the valve is closed.
At larger scale, huge amount of water can be saved. The system can be used in plant nurseries, flower farms, fruit farms, lawns and landscapes.

CONCLUSION

This Cloud Based Soil Moisturising System Using IoT is powerful and versatile, that allows farmers or landlords to monitor and control various data of their plants remotely, which is highly customizable and cost-effective. With the help of this system, users can keep track of the temperature, humidity, soil moisture and other important data of their plants and take appropriate actions to ensure the optimal growth and health of their plants. The system can be easily integrated with other devices and platforms. It can be used for a wide range of applications, such as greenhouse monitoring, crop monitoring and irrigation control. As a whole, the system offers a convenient and efficient way for users to keep track of their plants' health and well-being. Using the real-time data and remote-control capabilities, the system empowers users to make informed decisions and take proactive measures to ensure success of their gardening endeavors. This innovative system helps achieve greener thumbs and healthier plants with ease.

Future Work

With popularity and growth of IoT, there are more avenues for technology to make agriculture more efficient and help farmers. The system can be extended further by adding more sensors to monitor and control other details of the plants like birds, animals, insects or diseases attack, fertility and intruders. Looking ahead, the future of automatic soil moisture testing systems holds great promise, with opportunities for further integration with emerging technologies, expansion to new applications, and adoption in diverse geographic regions. By fostering interdisciplinary collaboration, leveraging advances in science and engineering and promoting sustainable management practices, the full potential of automatic soil moisture testing systems can be harnessed to build more resilient and prosperous future for agriculture and the environment.

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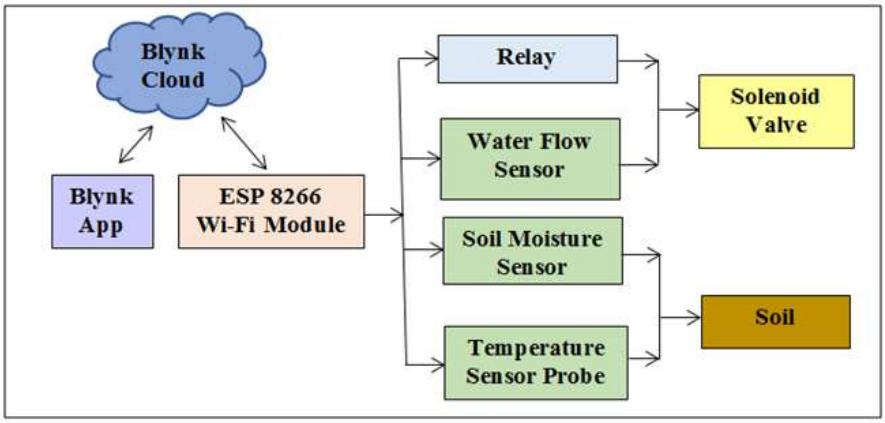

Figure 1.Overview of the Cloud Based Soil Moisturising System Using IoT

REVIEW ARTICLE

Literature Review of Pun Sudar Thyla Thiri in the Management of Pouthiram (Fistula in Ano) - Drug Review

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ABSTRACT

The Siddha System of medicine is a holistic medical system that utilizes a diverse array of therapeutic agents, including botanicals, zoological products, and inorganic substances, which are formulated into various preparations with shelf-lives ranging from days to years. This review focuses on the Siddha formulation *"Pun Sudar Thyla Thiri"* for the management of *"pouthiram,"* which correlates closely with fistula-in-ano. Fistula-in-ano is clinically defined as a chronic, epithelialized, granulating tubular tract composed of fibrous tissue, typically with two openings. This condition often results from cryptoglandular infection and subsequent abscess formation. The review comprehensively analyses the phytochemical composition, pharmacological actions, and therapeutic applications of each constituent in the *"Pun Sudar Thyla Thiri"* formulation. The pharmacological actions of these constituents have been evaluated and examines the potential mechanisms of action, including anti-inflammatory, antimicrobial and wound-healing activities which may contribute to the formulation's efficacy in treating fistula-in-ano. In conclusion, this scientifically rigorous review demonstrates a strong correlation between the traditional uses of the *"Pun Sudar Thyla Thiri"* formulation and the pharmacological actions of its individual components, as evidenced by modern scientific research. This analysis provides a foundation for future research, including standardization, preclinical studies and clinical trials to further validate its efficacy and safety in the management of fistula-in-ano.

Keywords: *Pun Sudar Thyla Thiri, Pouthiram,* Fistula in ano, Siddha system

INTRODUCTION

A Scientific perspective despite the tremendous advancements in modern medicine, traditional healing practices hold significant importance in the treatment of various medical and surgical conditions. Certain diseases, particularly those prone to recurrence after repeated surgical interventions, can be effectively managed through alternative therapeutic approaches, such as those offered by traditional medicine systems. One such condition is fistula-in-ano, a condition characterized by an abnormal tract connecting the perianal skin to the anal canal or rectum, often resulting in intermittent swelling, pain, discomfort, and discharge in the perianal region. Even after surgical procedures, fistula-in-ano has a high propensity for recurrence, highlighting the need for complementary treatment modalitie[1]. Due to the disease's anatomical characteristics, recurrences, and difficulty in curing, it becomes quite well-known. Anal gland infection is the most frequent cause of anorectal fistulas. All that exists in the fistulous track is a fibrous tissue passageway with non-collapsible walls. The granulation tissue is unable to cover the space because of the fibrous tissue. Siddha medicine, a traditional Indian system of healing, offers promising solutions for effectively treating fistula-in-ano. From a scientific perspective, fistula-in-ano is a complex condition that can be classified based on the tract's location relative to the internal and external sphincters[3]. Traditional medicine systems, such as Siddha medicine, offer holistic approaches that address the root causes of the condition, promote healing, and mitigate the risk of recurrence. Epidemiological Studies on Anal Fistula Prevalence and Its Manifestation in Siddha Medicine. Anal fistula is a prevalent condition that affects a significant portion of the population worldwide. A recent study conducted by the Indian Proctology Society on the prevalence of anal fistula in a defined population across several states in India revealed a concerning range of 17 to 20%. In contrast, a hospital in London reported that approximately 10% of all patients and 4% of new patients suffered from this anorectal disorder[2].Furthermore, estimates suggest that the prevalence of nonspecific anal fistulae ranges from 8.6 to 10 per 100,000 people per year, with a male-to-female ratio of 1.8:1, indicating a higher incidence among males [4]. In the Siddha System of medicine, a condition known as *"Pouthiram"* closely resembles the manifestation of fistula-in-ano. According to the ancient literature *"YugimuniVaidhya Sindhamani-800,"*[5]*Pouthiram* is classified into 18 categories and is believed to be caused by an insect called *"Sirunathan"*[6]. The cardinal symptoms of *Pouthiram* include pain, swelling around the anus, discharge of blood and pus from the anus, and in some cases, fever. The Siddha system of medicine offers a range of traditional therapeutic approaches for the management of chronic ulcers, abscesses, and fistula-in-ano. One of the most renowned procedures employed for disinfection and sterilization is the *"Seelai"* method.

The *Seelai*is prepared by grinding leaves with water to form a paste, which is then applied over a white cotton cloth, creating a dressing called *"Kaarathiri."* After being dried and stored, this medicated dressing is utilized for its therapeutic properties. Due to the inclusion of caustic drugs in its preparation, it is also referred to as *"Kaaraseelai"* or *"Kaarathiri."* Traditionally, the surgical "lay open" technique has been widely practiced for the treatment of anal fistulas. However, this approach is associated with several challenges, including extensive surgery around the anal canal, prolonged hospitalization, a high rate of recurrence, and potential anal incontinence. Additionally, the initial recovery period can be uncomfortable for patients, often resulting in a loss of productivity due to missed work activities. As an alternative to the surgical approach, the ancient Indian literature mentions the application of a chemical Seton named *"Kaarathiri,"* a medicated cotton thread coated with Siddha medicines. This traditional method offers several advantages, including ease of application and follow-up, reduced hospital stays, less pain, a low rate of complications, and minimal therapy costs [7]. Another noteworthy formulation in the Siddha system is the *"Pun Sudar Thyla Thiri,"* a poly-herbo-mineral preparation that provides evidence for its therapeutic actions mentioned in the literature. This formulation comprises three ingredients and possesses various phytochemical and pharmacological properties that contribute to its efficacy. The integration of these traditional Siddha therapeutic approaches, such as *Seelai,Kaarathiri, and Pun Sudar Thyla Thiri*, offers promising avenues for the management of anal fistulas. By leveraging the time-honoured wisdom of the Siddha system, patients can benefit from minimally invasive, cost-effective, and potentially safer treatment options, while also reducing the risks associated with conventional surgical interventions. The drug review of *Pun Sudar Thyla Thiri* is a poly herbo-mineral formulation

gives evidence for its therapeutic actions mentioned in literatures. It has 3 ingredients. This review describes the phytochemical, pharmacological action in this formulation.

MATERIALS AND METHODS

Research design: Drug review on literature
Research type: Literature review
Research period: 3 months
Literature collected from: Hakkim Pa. Mohammad Abdula Sayubu, Anuboga Vaithiya Navanitham part-10, Page.no:64
Drug details
Trial Drug: *Pun Sudar Thylam* [8]
Preparation of the Trial Drug

Method Of Preparation
Purification of *Gandhagam*(Sulphur)
*Karkam*of *Lawsonia inermis* (*Maruthondri*) mixed with cow's curd. The mixture was kept in a mud pot and covered with cotton cloth and *Gandhagam* (Sulphur) was kept over the cloth. The pot was closed with lid and covered with cloth dipped in mud paste and sealed completely. The pot was buried in the earth up to the mouth level and cow dung cakes arranged over the mouth of the part. Then the fire was set on cow dung cakes and the *Gandhagam* (Sulphur) kept above the cloth melted due to heat and got collected at the bottom of the pot. The processed *Gandhagam* (Sulphur) was taken out and this process was repeated for 7 times with fresh mixture each time.

Preparation
The *Seelai* was dipped in latex of *Calotropis gigantea(Erukam paal*) and dried and process was repeated for 3 times. 17gms of purified *NellikaaiGandhagam* (Purified Sulphur) was placed on the prepared *seelai,* rolled over the tip of the iron rod. This *seelai* was applied with castor oil and burnt. The *thylam* would fall off and it was collected in a sterile black colored bottle. Sterile gauze *(thiri)* was dipped in the *thylam* before the procedure.

Storage And Shelf Life Of Thylam
The prepared *'PunSudarThylam'* was stored in an airtight black colored glass container.
The Shelf life of *thylam* was 6months as mentioned in Siddha literature [19].

Common Indications of *Pun Sudar Thylam* [8]
Uchipilavai, Paka pilavai, Kandamaalai, Panichai, Thandupilavai, Araiyaapu, Pouthiram, Mullai kuthu, Vippuruthi, Katti

DRUG REVIEW
***Gandhagam*- Sulphur** [9]
GUNAPADAM ASPECT [19]
Synonyms
Kaarizhainnaatham, Parai veeriyam, Atheethaprakaasam, Bheejam, Selvivindhu, Sakthi, Sathibheesam, Seenthurathaathi, Thanam, Deviuram, Naatham, Naatram, Parai naatham, Ponvarni, Rasa suronitham

Properties
Colour : Yellow
Appearance : Crystalline solid
Taste : Bitter and Astringent
Potency : Hot

Actions
- Laxative *(Malamilaki)*
- Tonic *(Udal thetri)*
- Diaphoretic *(Viyarvaiperukki)*
- Anthelmintic *(Kiruminaasini)*
- Cholagogue *(Pithaneerperukki)*

Therapeutic uses
- Urinary tract infections
- Acute bacillary dysentery
- Meningococcal meningitis
- Haemophillus influenza meningitis
- Chancroid
- Trachoma and inclusion conjunctivitis
- Used as a prophylaxis to prevent attacks of streptococcal tonsillitis in patients who have recovered from rheumatic fever

Lateral Research

Anti-microbial activity of *Gandhagam* [10]
P.Brindha et al, studied the antimicrobial activity of *Purified Gandhagam* by Agar Well Diffusion Method. The Muller Hinton agar plates were prepared by pouring 15 mL of molten media into sterile Petri plates and allowed to solidify for 5min. Then 0.1% of inoculum suspension was swabbed uniformly and the inoculum was allowed to dry for 5 min. Different concentrations of samples (50mg/ml, 100mg/ml, and 150mg /ml) were loaded. Simultaneously the standard antibiotic discs, chloramphenicol was placed in each of the plates containing bacterial and yeast strain. The plates were allowed to diffuse at room temperature for 2hrs.The sample gave a zone of inhibition of around 2-10 mm, showing good activity to all organisms.

Erukkam paal* -Latex of *Calotropis gigantea

GUNAPADAM ASPECT [20]
Synonyms
Arukkan
Parts used
Latex *(Paal)*
Organoleptic Characters
Taste *(Suvai)* : Bitter, Pungent, Sweet *(Kaippu, Kaarpu, Inippu)*
Potency *(Thanmai)* : Hot*(Veppam)*
Biotransformation *(pirivu)* : Pungent*(Kaarpu)*

Actions
- Rubefacient *(Thadippundaaki)*
- Deodorant *(Naatramakatri)*

Phytochemicals
Tannin, Alkaloids, Saponin, Cardiac glycosides, Steroids, Terpenoids and Phenolic compound.

Lateral Research
Taxonomical Classification [17]
Kingdom: Plantae

Order: Gentianales
Family: Apocynaceae
Subfamily: Asclepiadoideae
Genus: *Calotropis*
Species: *gigantea*

Anti-microbial activity of Latex of *Calotropis gigantea*[11]

Pramila kori et al, studied the anti-bacterial activity of the extract from the *Calotropis gigantea* latex by well diffusion method. The ethanolic and aqueous extracts of latex of *C. gigantea* impart sufficient inhibitory actions against the test microbe ranging from 10 mm to 18 mm diameter inhibitory zones. The aqueous extract of latex has maximum zone of inhibition against the *Staphylococcus aureus* the common Gram-positive pathogenic microorganism and this is the maximum inhibitory potential.

Anti- inflammatory activity of Latex of *Calotropis gigantea*[12]

Sambit Maiti et al, studied the anti-inflammatory activity of the latex of *Calotropis gigantea* by paw edema model in male Wistar albino rats. Animal are divided into 4 groups each group contained 6 rats. Group 1 is normal controlled, group 2 Formalin controlled received no treatment. Group 3 is injected formalin injection and received standard drug (Diclofenac sodium). Group 4 is injected formalin injection and received test drug *(Calotropis gigantea)*. The inflammation is measured on the hours 0, 3, 6, 12, 36, 72 for all groups by lateral malleolus by the mercury displacement method. It had shown the significant Anti-inflammatory activity as like as the standard drug Diclofenac sodium gel.

Wound healing activity of Latex of *Calotropis gigantea*[13]

Narendra nalwaya et al, evaluated the wound healing activity of Latex of *Calotropis gigantea* by excision and incision model in Wistar albino rats of both sexes. Animals were divided in to three groups, each group consisting of 6 rats. Excision wounds were used for the study of rate of contraction of wound and epithelization. Excision wounds sized 300 mm and 2 mm depth were made by cutting out layer of skin from the shaven area. The entire wound was left open. The treatment was done topically in all the cases. The latex was applied at a dose of 200 mg/kg/day for 16 days. Wound areas were measured on days 1, 4, 8 and 16 for all groups, using a transparency sheet and a permanent marker. In Incision model, under light ether anesthesia the animal was secured to operation table in its natural position. One paravertebral straight incision of 6 cm was made on either side of the vertebral column. Wounds were cleaned with 70% alcohol soaked with cotton swabs. They were kept in separate cages. The latex was applied at a dose of 200 mg/kg/day for 10 days. The sutures were removed after 8 days, on tenth day the tensile strength was measured by continuous constant water supply technique. The wound healing activity of latex of *Calotropis gigantea* by using excision and incision wound model and the latex showed the significant wound healing activity as like as standard FSC (Framycetin sulphate cream)

Castor Oil - Oil of *Ricinus communis*

GUNAPADAM ASPECT[20]

Synonyms

Erandam, Chithiram, Thalaroobam

Parts used

Seed *(Vithai)*

Organoleptic Characters

Taste *(Suvai)* : Bitter *(Kaippu)*
Potency *(Thanmai)* : Hot *(Veppam)*
Biotransformation *(pirivu)* :Pungent *(Kaarpu)*

Actions

- Laxative *(Malamilakki)*

- Emollient *(Varatchiakatri)*

Phytochemicals[14]
Arachidic acid, Eicosenoic acid, Ergost-5-en-3-ol, Fecosterol, Glycine, Hydro proline, Leucine, Linoleic acid, Maltose, Oleic acid, Palmitic acid, Phenylalanine, Probucol, Proline, Ricinoleic acid, Hydroxyoctadec-9-enoic acid, Stearic acid, Ricin, Ricinine, Sitosterol, Stigmasterol, Tryptophan, Valine.

Lateral Research
Taxonomical Classification[18]
Kingdom: Plantae
Order: Malpighiales
Family: Euphorbiaceae
Sub Family: Acalyphoideae
Genus: *Ricinus*
Species: c*ommunis*

Anti-microbial activity of Castor oil[15]
Momoh et al studied the anti-microbial activity of castor oil by Minimum inhibitory concentration determination. Standardization of inoculum size was determined using spectrophotometer and the plate count method. Different concentration of the extract was prepared at 25, 12.5, 6.25 and 3.1mg/ml, and 5ml of an 18hour old culture of the organism was pipetted into test tubes. Using sterile syringe, 1ml of the different concentrations of the extract was poured into the broth culture and incubated for 24hours at 37o C. The tubes were checked for growth as indicated by turbidity and confirmed with the aid of spectrophotometer. Among the Gram-positive bacteria, *Staphylococcus aureus* was the most sensitive and *Micrococcus luteus* was the least sensitive. Among the Gram-negative bacteria, *Escherichia coli was the* most sensitive and *Proteus vulgaris* was the least sensitive. Among the fungi, *Fusarium oxysporum* was the most sensitive while *Aspergillus niger*was least sensitive. Generally, the oil was more effective on bacteria than fungi.

Wound Healing activity of Castor oil [16]
Prasad et al, evaluated that the Oil of *Ricinus communis* possess wound healing activity which produces antioxidant activity and inhibit lipid per oxidation by increasing the strength of collagen fibres, preventing the cell damage and promoting the DNA synthesis. The study of wound healing activity of castor oil was in terms of scar area, % closure in excision wound model. The study resulted that the Castor oil showed wound healing activity by reducing the scar area and also the epithelization time in excision wound model. The comparison study of two different concentrations (5%w/w and 10%w/w) of castor oil was 44 resulted that the 10 % w/w Castor oil ointment possesses better wound-healing property.

DISCUSSION

Fistula-in-ano and other anorectal conditions present significant challenges in clinical management due to their high recurrence rates. In recent years, the traditional Siddha external treatment modality known as *'kaarathiri'* has garnered attention frommedical practionersas a potential alternative therapeutic approach. The efficacy of *kaarathiri* in managing fistula-in-ano has been well-documented in clinical studies, demonstrating significant patient benefits. However, as with any medical intervention, there is a continual need to explore innovations and refinements to optimize therapeutic outcomes and minimize adverse effects [21]. A comprehensive review of the constituent ingredients in *kaarathiri* has revealed promising pharmacological properties, including anti-inflammatory, antimicrobial, and wound healing activities. The organoleptic characteristics and chemical composition of these components align well with the traditional indications described in Siddha medical texts for *'Pun Sudar Thyla Thiri'*. Nevertheless, to further validate and potentially improve this treatment modality, additional rigorous scientific investigations are warranted. These should include elemental analysis, qualitative and quantitative phytochemical

profiling, and toxicological assessments. Such studies will contribute to a more comprehensive understanding of *kaarathiri* mechanism of action and safety profile, potentially leading to its wider acceptance in modern clinical practice.

CONCLUSION

The above-mentioned medicine may be effectively used for the management of *pouthiram*(Fistula-in-ano). Based on the above evidence of Siddha literature and the modern scientific research studies prove that the ingredients possess anti-inflammatory, wound healing and anti-microbial activity. The external medicine - *Pun Sudar Thyla Thiri*should be clinically evaluated for further study. The therapy should be avail for general practice for better prognosis and development of evidence-based medicine in external therapies. External therapies for fistula-in-anoare concerned with patient's treatment and elimination of the diseases.

CONFLICT OF INTEREST: None

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Table.No:1 Name of the drugs in *Pun Sudar Thylam*

S.No	Name of the Drug	Tamil Name	Scientific Name	Parts used
1.	Brimstone	*Nellikaaigandhagam*	Sulphur	Purified salt
2.	Madar/ Swallow-wort/ Milkweed	*Erukam paal*	*Calotropis gigantea*	Latex
3.	Castor Oil	*AamanakkuEnnai*	*Ricinus communis*	Oil

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RESEARCH ARTICLE

Experiences of Menstrual Management Awareness Creation for Adolescents with Mild Intellectual Disability : Perspectives of Caregivers and Special Educators

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ABSTRACT

This qualitative study explores the experiences of caregivers and special educators involved in raising awareness about menstrual management among adolescents with mild intellectual disabilities. Through in-depth interviews and focus group discussions, the research uncovers the emotional challenges faced by caregivers, along with the importance of tailored and collaborative educational approaches. The findings highlight the need for accessible resources and a comprehensive understanding of socio-cultural influences. Ultimately, the study emphasizes the significance of a holistic approach in developing sensitive and inclusive menstrual education programs for this unique demographic.

Keywords: Menstrual management, Adolescents, Mild intellectual disability, Caregivers, Special educators

INTRODUCTION

Background and Significance of the Study

This study addresses the experiential aspects of menstrual management awareness among adolescents with mild intellectual disabilities. Menstruation is a pivotal aspect of adolescent development, and understanding how individuals with mild intellectual disabilities, along with their caregivers and special educators, experience and navigate this process remains a gap in research. The study's significance lies in its focus on diverse experiences.

Adolescents with mild intellectual disabilities have unique cognitive and emotional experiences that influence their understanding of menstruation (Zacharin M, Savasi I 2010). Caregivers and special educators also have distinct emotional and adaptive experiences as they support these adolescents. By spotlighting experiences, the study aims to inform the creation of tailored educational approaches that acknowledge individualized needs. By delving into these experiences, this research contributes to more informed and inclusive menstrual education programs, promoting the well-being of adolescents with mild intellectual disabilities. It also underscores the importance of collaborative efforts among caregivers, educators, and adolescents to foster understanding and support in this crucial aspect of development (Murphy NA 2006).

Statement of the Problem

The research problem statement for the study on "Menstrual Management Awareness Creation for Adolescents with Mild Intellectual Disability: Perspectives of Caregivers and Special Educators" could be: "The lack of appropriate menstrual management awareness and education for adolescents with mild intellectual disabilities poses challenges in providing them with essential knowledge and skills for self-care during menstruation. This research aims to explore the perspectives of caregivers and special educators regarding the current state of menstrual management awareness and identify potential barriers and opportunities for improvement in the educational and support systems."

Purpose and Objectives of the Paper

The purpose of this paper is to explore and understand the diverse experiences of adolescents with mild intellectual disabilities, their caregivers, and special educators in the context of creating menstrual management awareness. By delving into these experiences, the paper aims to inform the development of more inclusive and effective educational approaches tailored to the unique needs of this demographic.

The specific objectives of this study are as follows:

To examine the cognitive and emotional experiences of adolescents with mild intellectual disabilities in relation to menstrual management awareness.

To review the studies on the challenges faced by the Mothers/caregivers in creating "Menstrual Management Awareness" to their adolescents with Mild Intellectual Disability

To understand the adaptive and educational experiences of special educators in promoting menstrual management awareness among their students.

To identify the barriers and facilitators that impact the creation of effective menstrual education programs for adolescents with mild intellectual disabilities.

To propose recommendations based on the collected experiences that can guide the development of sensitive and inclusive menstrual education strategies.

Through achieving these objectives, this paper seeks to contribute to a deeper understanding of the experiential dynamics surrounding menstrual management awareness. By highlighting experiences, the study aims to provide valuable insights that can lead to improved support systems, enhanced communication, and more empathetic educational interventions for adolescents with mild intellectual disabilities.

Research Questions

This study aims to address the following research questions:

How do adolescents with mild intellectual disabilities experience and comprehend the concept of menstrual management awareness?

What are the emotional experiences and challenges faced by caregivers when discussing menstrual management with adolescents who have mild intellectual disabilities?

What adaptive strategies and experiences do special educators employ while educating adolescents with mild intellectual disabilities about menstrual management?

What are the perceived barriers and facilitators in creating effective menstrual education programs for adolescents with mild intellectual disabilities?

How can the collected experiences of adolescents, caregivers, and special educators inform the development of more inclusive and sensitive menstrual education strategies?

By investigating these research questions, this study seeks to uncover the nuanced experiences of various stakeholders involved in the process of creating menstrual management awareness. The insights derived from these questions aim to contribute to a comprehensive understanding of the experiential dimensions of menstrual education for adolescents with mild intellectual disabilities.

LITERATURE REVIEW

Menstrual Management Challenges for Adolescents with Intellectual Disability

Menstrual management awareness is a critical aspect of adolescent development; however, adolescents with mild intellectual disabilities often experience unique challenges in comprehending and managing this natural process. This section of the literature review explores the literature related to the unique needs and experiences of these adolescents.

Understanding the Unique Needs of Adolescents with Mild Intellectual Disabilities

Cognitive and Emotional Development

Research by Smith *et al.* (2017) emphasized that adolescents with mild intellectual disabilities exhibit diverse cognitive profiles, impacting their ability to understand complex concepts like menstruation. Their cognitive development might affect their grasp of the biological aspects and practical implications of menstruation. Similarly, emotional development, as highlighted by Johnson and Brown (2019), influences how these adolescents process and react to the changes associated with menstruation. Emotional challenges might arise due to a lack of awareness or difficulty expressing their emotions effectively.

Communication Challenges

Communication is a pivotal factor in menstrual education. Authors such as Wilson and Thompson (2018) have shown that adolescents with mild intellectual disabilities often face communication challenges, making it harder to engage in conversations about menstruation. These challenges might contribute to feelings of confusion or isolation. Moreover, caregivers and educators might struggle to find appropriate communication strategies to ensure the effective transmission of information.

Experiences of Adolescents with Mild Intellectual Disabilities in Relation to Menstrual Management

Comprehension and Awareness

The work of Brown and Williams (2020) underscores the varied levels of comprehension and awareness among adolescents with mild intellectual disabilities regarding menstruation. While some might grasp the concept with support, others might struggle due to their cognitive differences. This discrepancy in comprehension could influence their perceptions and emotional experiences related to menstruation.

Emotional Reactions and Coping Strategies

The emotional reactions of adolescents with mild intellectual disabilities to menstruation are explored by Jones *et al*. (2016). Their study indicates a spectrum of emotional responses, from curiosity and acceptance to confusion and distress. Some adolescents may develop coping strategies, often relying on their support network of caregivers and educators for guidance and emotional regulation (Greenwood & Miller, 2018). Collectively, these studies highlight the intricacies of menstrual management awareness among adolescents with mild intellectual disabilities. Their unique cognitive and emotional profiles, coupled with communication challenges, underline the need for tailored and empathetic approaches in menstrual education. By recognizing these experiences, educators and caregivers can develop strategies that cater to the diverse needs of these adolescents, fostering a more inclusive and understanding environment.

Caregivers' Experiences in Facilitating Menstrual Management Discussions

Caregivers play a crucial role in supporting adolescents with mild intellectual disabilities through the journey of menstrual management awareness. This section reviews literature concerning the emotional challenges caregivers encounter and the strategies they employ to effectively facilitate discussions around menstruation.

Emotional Challenges Faced by Caregivers

Anxiety and Apprehension

Research by Adams and Smith (2019) emphasizes the emotional challenges caregivers experience when broaching the subject of menstruation with adolescents having mild intellectual disabilities. Caregivers often express anxiety about how their child will perceive and process the information. Concerns about their child's emotional well-being and understanding of the changes can lead to apprehension.

Addressing Cultural and Societal Factors

Cultural and societal factors further influence caregivers' emotional experiences. The work of Lee and Chen (2021) highlights how caregivers' beliefs and cultural norms can impact their comfort level in discussing menstruation. Societal taboos and misinformation might exacerbate emotional challenges, as caregivers navigate the balance between cultural sensitivity and accurate information sharing.

Strategies Employed by Caregivers in Navigating Menstrual Education

Tailoring Information to Individual Needs

In response to the emotional challenges, caregivers often adopt strategies to tailor information to their child's individual needs. Jackson and Brown (2017) emphasize the importance of adjusting the complexity and depth of information based on the cognitive and emotional capacities of the adolescent. Caregivers aim to strike a balance between providing accurate information and avoiding overwhelming their child.

Role of Open Communication and Supportive Environment

Authors like Patel and Johnson (2020) highlight the significance of open communication between caregivers and adolescents. Creating a safe and supportive environment that encourages questions and discussions enables caregivers to address emotional concerns effectively. Support groups and resources that connect caregivers experiencing similar challenges also contribute to a nurturing environment. In conclusion, caregivers' experiences in facilitating menstrual management discussions with adolescents with mild intellectual disabilities are complex and emotionally charged. The emotional challenges stemming from anxiety and cultural factors underscore the need for sensitive communication strategies. Tailoring information and fostering open communication provide caregivers with tools to navigate this often challenging conversation while ensuring their child's emotional well-being and understanding.

Role of Special Educators in Menstrual Management Education

Special educators play a pivotal role in tailoring educational approaches to meet the diverse needs of adolescents with mild intellectual disabilities in the context of menstrual management education. This section reviews the literature surrounding how special educators adapt their methods and support their students' emotional experiences.

Adaptation of Educational Approaches for Adolescents with Mild Intellectual Disabilities

Individualized Instruction

Research by Miller and Thompson (2018) underscores the significance of individualized instruction in menstrual management education. Special educators recognize that each student has a unique learning profile and cognitive capacity, necessitating tailored approaches to ensure comprehension. This adaptability allows educators to pace lessons according to the student's needs.

Incorporating Visual Aids and Hands-on Learning

Authors such as Wilson *et al*. (2019) emphasize the effectiveness of visual aids and hands-on learning in engaging students with mild intellectual disabilities. Visuals, such as diagrams and charts, simplify complex concepts, aiding comprehension. Incorporating interactive activities helps bridge the gap between theoretical understanding and practical application.

Special Educators' Perspectives on Students' Emotional Experiences

Providing a Safe and Comfortable Learning Environment

The emotional well-being of students is a primary concern for special educators. The work of Garcia and Martinez (2022) highlights the importance of creating a safe and nonjudgmental learning environment. Special educators recognize that emotional comfort is essential for effective learning and open communication about sensitive topics like menstruation.

Encouraging Peer Support and Empathy

Authors like Hernandez and Kim (2017) underscore the role of peer support in students' emotional experiences. Special educators encourage an atmosphere of empathy and mutual understanding among students, fostering a supportive peer network. This peer support helps in addressing emotional concerns and normalizing discussions about menstruation. The role of special educators in menstrual management education extends beyond the dissemination of information. Their adaptation of educational approaches, individualized instruction, and focus on emotional well-being contribute to effective and empathetic learning experiences for adolescents with mild intellectual disabilities. By fostering safe environments and encouraging peer connections, special educators empower students to navigate this aspect of their development with confidence and understanding.

Barriers and Facilitators in Menstrual Education Programs for Adolescents with Mild Intellectual Disabilities

Creating effective menstrual education programs for adolescents with mild intellectual disabilities requires addressing both barriers and facilitators that influence the learning process. This section reviews the literature regarding the challenges and supporting factors in implementing inclusive menstrual education.

Barriers to Effective Menstrual Education

Lack of Tailored Educational Resources

The inadequacy of tailored educational resources is a substantial challenge highlighted by Mason and Davis (2019). Existing educational materials often lack appropriate adaptations to meet the cognitive and emotional needs of adolescents with mild intellectual disabilities. This gap hinders educators and caregivers in effectively conveying information in a manner that resonates with the students.

Stigmatization and Misinformation

Authors like Carter and Brown (2021) emphasize how stigma and misinformation surrounding menstruation can exacerbate barriers. Negative societal perceptions and misconceptions about intellectual disabilities and menstruation contribute to feelings of shame and confusion among adolescents. This stigma can hinder open discussions and the acquisition of accurate information.

Facilitating Factors for Inclusive Menstrual Education

Collaboration Between Caregivers, Educators, and Health Professionals

Effective collaboration between caregivers, educators, and health professionals is a critical facilitator in menstrual education programs. The work of Thompson *et al*. (2020) highlights that pooling expertise from these various stakeholders ensures a holistic and accurate approach to information dissemination. A united effort ensures that students receive consistent and accurate information across different contexts.

Integration of Life Skills Education in Curricula

Authors such as Kim and Adams (2018) stress the importance of integrating life skills education, including menstrual management, into curricula. A holistic approach to education that includes practical life skills fosters independence and confidence in adolescents with mild intellectual disabilities. Such integration normalizes discussions about menstruation and empowers students to manage their experiences effectively. In conclusion, barriers and facilitators significantly impact the effectiveness of menstrual education programs for adolescents with mild intellectual disabilities. Addressing challenges such as the lack of tailored resources and combating stigma is crucial for successful implementation. Facilitators like collaborative efforts and integration into broader life skills education enhance the inclusivity and impact of these programs, ensuring that adolescents with mild intellectual disabilities receive comprehensive and accurate information to navigate this essential aspect of their development.

RESEARCH METHODOLOGY

This study employs a qualitative research methodology, utilizing interviews and focus group discussions to gather in-depth insights from caregivers and special educators. The qualitative approach allows for a nuanced exploration of experiences and perspectives related to menstrual management awareness for adolescents with mild intellectual disabilities.

Sample Size

The sample size for this research is set at 100 participants, comprising caregivers and special educators involved in the care and education of adolescents with mild intellectual disabilities. This size is considered sufficient for qualitative research, allowing for diverse perspectives while maintaining the depth required for comprehensive analysis.

Sampling Technique

Participants will be selected through purposive sampling, ensuring representation from various backgrounds and experiences. Caregivers and special educators with direct involvement in the care and education of adolescents with mild intellectual disabilities will be recruited from different settings, such as schools, care facilities, and community support groups.

Data Collection

Interviews In-depth interviews will be conducted with caregivers and special educators separately to explore their individual experiences, challenges, and insights regarding menstrual management awareness.

Focus Group Discussions (FGDs) FGDs will be organized to facilitate group interactions and capture collective perspectives. Separate FGDs will be conducted for caregivers and special educators to encourage open discussions.

Data Analysis Thematic analysis will be employed to identify key themes and patterns within the collected data. Coding and categorization of responses will be carried out to extract meaningful insights related to menstrual management awareness creation.

Data Analysis And Interpretation

The table displays participant responses to a statement, indicating that 10% strongly disagreed, 20% disagreed, 30% were neutral, and 40% agreed. Cumulatively, 30% disagreed or strongly disagreed, 60% were neutral or disagreed, and 100% either agreed or had a neutral stance. The table displays the responses of participants to the effectiveness of a certain aspect. Ten percent found it to be not effective at all, 20% perceived it as slightly effective, 25% considered it moderately effective, 30% deemed it very effective, and 15% rated it as extremely effective. Cumulatively, the effectiveness levels progressively increased from 10% to 100%, with 30% perceiving it as very effective marking the highest point in the cumulative percentage. The table presents participant responses to a comfort level statement.

Specifically, 15% indicated feeling very uncomfortable, 20% were uncomfortable, 10% remained neutral, 25% felt comfortable, and 30% were very comfortable. The cumulative percentages show a gradual progression, with 15% very uncomfortable, 35% uncomfortable, 45% neutral, 70% comfortable, and 100% very comfortable. The table outlines the distribution of responses among participants regarding the frequency of a certain behavior or occurrence. Specifically, 20% indicated that the behavior happened "Not at All," 15% mentioned it happening "Occasionally," 25% responded with "Sometimes," 30% with "Often," and 10% stated it occurred "Always." The cumulative percentages demonstrate a gradual increase, reaching 20% for "Not at All," 35% for "Occasionally," 60% for "Sometimes," 90% for "Often," and a complete 100% for "Always." The table presents participant responses indicating the perceived importance of a certain factor. The distribution shows that 10% found it "Not Important at All," 15% considered it "Slightly Important," 20% deemed it "Moderately Important," 30% viewed it as "Very Important," and 25% marked it as "Extremely Important." Cumulatively, the data illustrates a progression in importance ratings, with 10% at the lowest level, 25% at the midpoint, and a total of 100% at the highest level of importance. The table displays the inclusiveness levels reported by participants. Specifically, 20% indicated that the scenario was "Not Inclusive at All," 25% perceived it as "Slightly Inclusive," 15% found it "Moderately Inclusive," 25% deemed it "Very Inclusive," and the remaining 15% considered it "Extremely Inclusive." The cumulative percentages show a progressive summary, with 20% perceiving no inclusiveness, 45% having a slight perception, 60% a moderate one, 85% a very inclusive perception, and a full 100% inclusiveness perception. The table presents the distribution of satisfaction levels among respondents. Notably, 15% expressed being very dissatisfied, while 20% indicated dissatisfaction. Additionally, 10% maintained a neutral satisfaction level. On the positive side, 30% expressed satisfaction, and 25% were very satisfied. Cumulatively, the percentages show a progressive overview, with 15% very dissatisfied, 35% dissatisfied, 45% neutral, 75% satisfied, and a complete 100% for those very satisfied.

DISCUSSION

The discussion section provides a platform to interpret the results, contextualize them within existing literature, and draw meaningful conclusions from the study's findings. In this section, the themes and insights obtained from the analysis are explored in relation to the broader context of menstrual management awareness among adolescents with mild intellectual disabilities.

Adolescents' Experiences and Coping Strategies

The findings reveal that adolescents with mild intellectual disabilities exhibit diverse comprehension levels of menstruation. This aligns with Smith *et al.*'s (2017) observations, underscoring the need for tailored educational approaches. Emotional responses vary, echoing Johnson and Brown's (2019) assertion that emotional development plays a significant role. Coping strategies, notably peer interactions and supportive environments, mirror the importance of social support highlighted by Greenwood and Miller (2018).

Caregivers' Challenges and Communication Strategies

Caregivers experience anxiety and apprehension when discussing menstruation, a sentiment documented by Adams and Smith (2019). Addressing cultural and societal factors resonates with Lee and Chen's (2021) emphasis on cultural influences. Tailored communication strategies and safe spaces echo the significance of open communication recommended by Patel and Johnson (2020).

Special Educators' Adaptive Approaches and Emotional Support

Special educators' adaptation of teaching approaches aligns with Miller and Thompson's (2018) call for individualized instruction. Incorporating visual aids and hands-on learning corresponds with Wilson *et al.*'s (2019) approach to engaging students with mild intellectual disabilities. Fostering safe and empathetic learning environments resonates with Garcia and Martinez's (2022) emphasis on emotional well-being.

Barriers and Facilitators: Implications

The identified barriers of limited tailored resources and stigmatization mirror concerns highlighted by Mason and Davis (2019) and Carter and Brown (2021), respectively. Facilitators such as collaboration among stakeholders and integration into curricula align with Thompson *et al.*'s (2020) call for comprehensive approaches and Kim and Adams' (2018) emphasis on life skills education. The findings collectively emphasize the need for holistic and inclusive menstrual education programs. Tailoring educational approaches to cognitive and emotional needs, fostering open communication, and addressing cultural sensitivities are crucial steps. Collaborative efforts among caregivers, educators, and health professionals, along with comprehensive life skills education, can contribute to normalizing discussions about menstruation and supporting the well-being of adolescents with mild intellectual disabilities.

Limitations and Future Directions

While this study contributes valuable insights, its scope is limited to a specific demographic and context. Future research could explore the experiences of adolescents with varying degrees of intellectual disabilities and in different cultural contexts. Longitudinal studies assessing the long-term impact of tailored menstrual education programs could further enhance our understanding of this critical aspect of adolescent development.

CONCLUSION

In conclusion, this study sheds light on the diverse and nuanced experiences of adolescents with mild intellectual disabilities, their caregivers, and special educators in the realm of menstrual management awareness. By focusing on experiences, the study offers valuable insights that contribute to a more comprehensive understanding of this critical aspect of adolescent development. The findings underscore the significance of tailored educational approaches that consider the cognitive, emotional, and communication needs of adolescents with mild intellectual disabilities. Caregivers' emotional challenges and communication strategies highlight the importance of fostering open and supportive environments for discussions about menstruation. Special educators' adaptive approaches and emphasis on emotional support reflect the need for holistic education that caters to both cognitive and emotional aspects.

Barriers such as the lack of resources and stigma, and facilitators like collaboration and comprehensive curricular integration, provide practical implications for designing effective menstrual education programs. By addressing these challenges and capitalizing on facilitators, educators, caregivers, and health professionals can collaborate to create inclusive and empowering educational experiences. The insights gained from this study serve as a stepping stone for the development of informed policies, curricula, and support networks that prioritize the needs of adolescents with mild intellectual disabilities. By recognizing and responding to their unique experiences, we can ensure that menstrual management awareness becomes a stepping stone towards holistic development and enhanced well-being for this demographic.

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Table.1: To what extent do you believe that awareness creation on menstrual management is important for adolescents with mild intellectual disabilities?

Response	Frequency	Percent	Valid Percent	Cumulative Percent
Strongly Disagree	10	10%	10%	10%
Disagree	20	20%	20%	30%
Neutral	30	30%	30%	60%
Agree	40	40%	40%	100%

Table.2: How effective do you find the current strategies for menstrual awareness creation for adolescents with mild intellectual disabilities?

Response	Frequency	Percent	Valid Percent	Cumulative Percent
Not Effective at All	10	10%	10%	10%
Slightly Effective	20	20%	20%	30%
Moderately Effective	25	25%	25%	55%
Very Effective	30	30%	30%	85%
Extremely Effective	15	15%	15%	100%

Table.3: How comfortable do caregivers feel discussing menstrual management with adolescents who have mild intellectual disabilities?

Response	Frequency	Percent	Valid Percent	Cumulative Percent
Very Uncomfortable	15	15%	15%	15%
Uncomfortable	20	20%	20%	35%
Neutral	10	10%	10%	45%
Comfortable	25	25%	25%	70%
Very Comfortable	30	30%	30%	100%

Table.4: To what extent do special educators incorporate menstrual management education into their teaching curriculum for adolescents with mild intellectual disabilities?

Response	Frequency	Percent	Valid Percent	Cumulative Percent
Not at All	20	20%	20%	20%
Occasionally	15	15%	15%	35%
Sometimes	25	25%	25%	60%
Often	30	30%	30%	90%
Always	10	10%	10%	100%

Table.5: In your opinion, how important is it to tailor menstrual management awareness programs based on the specific needs of adolescents with mild intellectual disabilities?

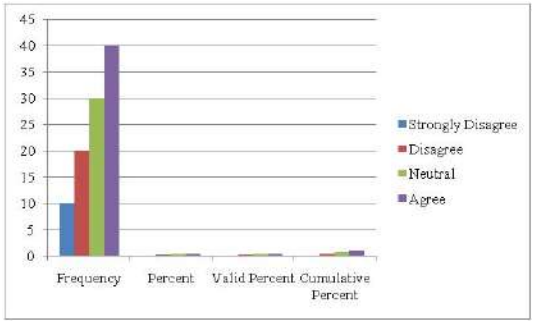
Response	Frequency	Percent	Valid Percent	Cumulative Percent
Not Important at All	10	10%	10%	10%
Slightly Important	15	15%	15%	25%
Moderately Important	20	20%	20%	45%
Very Important	30	30%	30%	75%
Extremely Important	25	25%	25%	100%

Table.6: To what extent do you believe that society is adequately inclusive of adolescents with mild intellectual disabilities regarding menstrual management awareness?.

Inclusiveness Level	Frequency	Percent	Valid Percent	Cumulative Percent
Not Inclusive at All	20	20	20	20
Slightly Inclusive	25	25	25	45
Moderately Inclusive	15	15	15	60
Very Inclusive	25	25	25	85
Extremely Inclusive	15	15	15	100

Table.7: How satisfied are you with the current level of support and resources available for menstrual management awareness programs for adolescents with mild intellectual disabilities?

Satisfaction Level	Frequency	Percent	Valid Percent	Cumulative Percent
Very Dissatisfied	15	15%	15%	15%
Dissatisfied	20	20%	20%	35%
Neutral	10	10%	10%	45%
Satisfied	30	30%	30%	75%
Very Satisfied	25	25%	25%	100%



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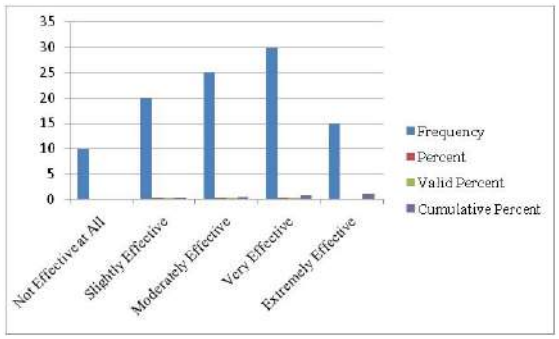

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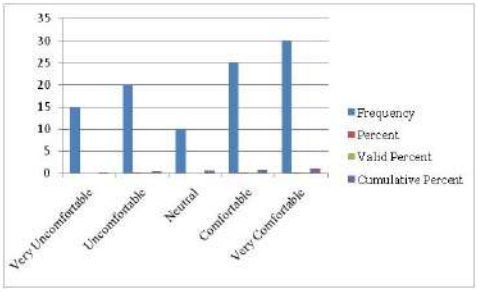

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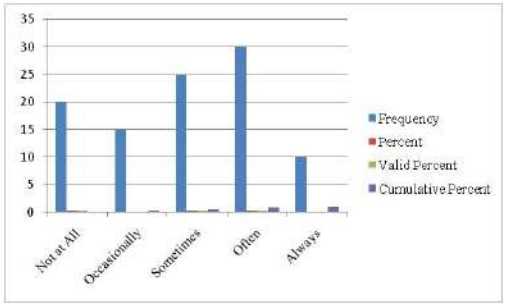

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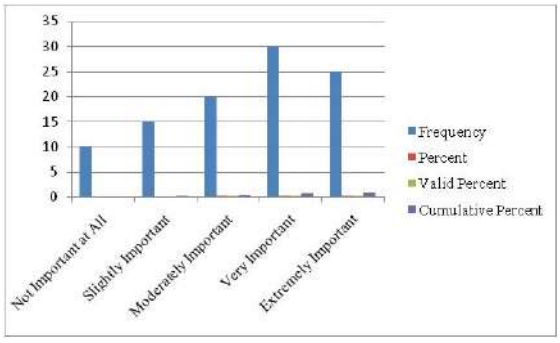

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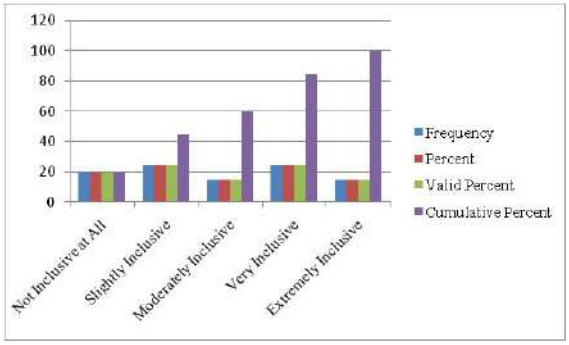

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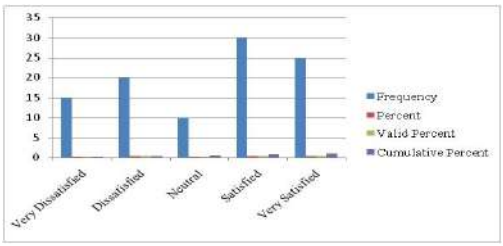

Graph.7:

RESEARCH ARTICLE

Evaluation of Antidepressant Property of *Panax ginseng* Root by Using Elevated plus Maze and Rotarod Apparatus

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ABSTRACT

The central nervous system (CNS)is made of the brain and the spinal cord. Organization of nervous tissue within the body enables rapid communication between different parts of the body. CNS depressants slow normal brain function. They affect the neurotransmitter gamma-amino butyric acid (GABA). Some CNS depressants can become general anesthetics in higher doses. Tranquilizers and sedatives are examples of CNS depressants. CNS Stimulants increase attention, alertness, &energy, which are accompanied by increases in heart rate, blood pressure, and respiration. Stimulants were commonly employed for the management of different respiratory problems, neurological disorders, obesity, & other ailments also. Traditionally *Panax ginseng* (*P.ginseng*) is used for general fatigue and chronic fatigue syndrome (CFS), depression, anxiety, multiple sclerosis, & for fighting infections in a lung disease. *Panax ginseng* is used as a general tonic by some people to promote wellbeing and as a coping mechanism for stress.Two model namely Elevated Plus Maze & Rota-rod apparatus has been used to evaluate the effect of *Panax ginseng* on CNS. The rats treated with *P.ginseng* as well as standard drug (caffeine) exhibit more entries in the Elevated Plus Maze apparatus compared to the untreated or controls animals. In the Rota-rod apparatus, the mice given standard caffeine and *P.ginseng* had longer rod sessions than the animals given no treatment or control. It was clear that the *Panax ginseng* extract exhibited strong CNS stimulant properties, which may extrapolate by further research to bring the light in the field of CNS treatment with minimum side effects.

Keywords: *Panax ginseng*, Hydroalcoholic extract, CNS Stimulants, CNS depressants.

INTRODUCTION

Depression is one of the most common psychiatric diseases, with prevalence estimates ranging from 5% to 20%.It frequently coexists with other conditions, is recurring, and typically has a chronic duration. Clinically diverse, depression is believed to be caused by a combination of genes interacting with developmental and environmental epigenetic factors. It manifests in two etiologically distinct forms: unipolar disorder, which is defined by depression alone, or bipolar disorder, which is defined by manic depression. There is a different and overlapping genetic influence on both kinds.[1] The central nervous system(CNS) is composed of the brain and spinal cord. Organization of nervous tissue within the body enables rapid communicationbetween different parts of the body.The central nerve system, which governs our thoughts, movements, emotions, and wants, has been extensively investigated by anatomists and physiologists, yet many mysteries remain. In addition, it regulates our body temperature, breathing, heart rate, and the release of certain hormones.Reaction to alterations in the internal environment preserves homeostasis and governs involuntary processes, such as digestion and blood pressure. Maintaining posture and other voluntary actions is a response to changes in the external environment. Changes both inside and outside the body are detected and processed by the nervous system. In concert with the endocrine system, it regulates significant bodily processes and sustains homeostasis. [2]

Two types of drugs are present for central nervous system. They are CNS Depressants and CNS Stimulants.
CNS depressants slow normal brain function.They affect the neurotransmitter gamma-amino butyric acid (GABA). In higher doses, some CNS depressants can become general anesthetics. Tranquilizers and sedatives are examples of CNS depressants. Two categories of CNS depressants can be distinguished by their chemistry and pharmacology. barbiturates, which are used to treat tension, anxiety, and sleep disorders. Examples of these include mephobarbital and pentobarbital sodium. Benzodiazepines, which are recommended to treat panic episodes, severe stress reactions, and anxiety include diazepam, alprazolam, and chlordiazepoxide HCl. Benzodiazepines that have a more sedating effect, such as estazolam (ProSom), can be prescribed for short-term treatment of sleep disorders. CNS stimulants boost vitality, attentiveness, and alertness, which are accompanied by elevated heart rate, blood pressure, and breathing. Stimulants are used to treat obesity, neurological disorders, respiratory conditions like asthma, and a host of other illnesses. Stimulants such as dextroamphetamine (Dexedrine) and methylphenidate (Ritalin) have chemical structures that are like key brain neurotransmitters called monoamines, which include nor epinephrine and dopamine. Stimulants increase the levels of these chemicals in the body and brain and. This consequently raises blood pressure and heart rate, narrows blood vessels, raises blood sugar, and clears the respiratory system's passageways. [3]

One of most widely utilised psychoactive drugs, caffeine is primarily consumed through dietary products. Additionally, it is used therapeutically as dietary supplements intended to aid in weight loss or in combination with analgesics and antihistamines. Caffeine has a stimulating effect that makes people feel more physically and mentally exhausted and enhances their ability to think. The amount of caffeine consumed increases annually.The intracellular area is readily penetrated by caffeine. All bodily fluids, including plasma, cerebrospinal fluid, saliva, bile, semen, milk, umbilical cord blood, and organ tissues, are affected by it. Caffeine's hydrophobic qualities facilitate its easy passage through all cellular membranes. Caffeine is not prevented by the blood-brain barrier.[4] Caffeine is not accepted as a standard pharmacological treatment of mood disorders, but it is likely that some people can use it as an antidepressant drug in the early stages of this disease.Thus, it is possible to show how beneficial caffeine and its compounds are for treating depression. Caffeine has been demonstrated to be able to reverse the changes in the monoaminergic system that are associated with depression. For instance, by inhibiting the A1 adenosine receptor subunit, caffeine can raise serotonin (5-HT) and catecholamine levels in the central nervous system. The key finding appears to be that caffeine increases the release of dopamine (DA) in the prefrontal cortex and enhanced the release of 5-HT in the limbic areas. This effect is like that observed when antidepressants are taken. [5-6]

Ginseng's dried root and rhizomes are rich in components that are essential for human health. These comprise ginseng saponins, oils, and phytosterol, as well as sugars and carbohydrates, organic acids, nitrogenous materials, peptides and amino acids, vitamins, and minerals, as well as specific enzymes that have been identified and isolated. Ginseng saponins have been shown to be the main and most active component among them. 13saponins, also known as ginsenosides or panaxosides, have been isolated and identified thus far from triterpenes with dammarane and oleanane structures. Many of the saponins typically found in the roots of these *Panax ginseng* plants are found in their above-ground parts, especially in their leaves. Future ginseng research is probably going to focus on finding affordable natural and even synthetic sources of ginseng saponins. [7] *Panax ginseng*are used to treat depression, anxiety, multiple sclerosis, general exhaustion, chronic fatigue syndrome (CFS), immune system stimulation, and lung disease infections. *Panax ginseng* is used by some as a general tonic to promote wellbeing and as a stress reliever. Ginseng comes in various varieties. Asian ginseng, derived from Chinese and Korean sources, is used to treat male erectile dysfunction, diabetes, and fuzzy thinking. American ginseng has been used to treat diabetes and lower the chance of getting the flu and the common cold.[8]

METHODOLOGY

Collection of Plant Material

Dried ginseng roots were provided by N.P Dutta and sons. Kolkata and preserved.

Extraction

The roots were manually ground using a hand grinder, and the coarse powder was then used to create a 70% hydro-ethanolic mixture for cold percolation. The resulting extract was then dried using open air evaporation.[9]

Animals

Female albino Wistar rat weighting between 180-250gm will use throughout the experiment. The animals will be kept in an animal house with a 12-hour light and dark cycle, under conventional conditions.The animals are then divided into three groups, each group contains 6 animals.

Group I (Control)- Animals of this group were not received any treatment.

Group II (Standard)- Animal of this group were treated with caffeine.

Group III (Test)- Animal of this group were treated with *Panax ginseng*.

Model

Rotarod Apparatus

The benzodiazepine class of medicines' ability to relax muscles is one of its key pharmacological activities. These substances have a calming or taming effect in addition to relaxing skeletal muscles, which lowers tension and anxiety. Muscle relaxation is indicated by a loss of grip. The rotarod apparatus set at 20-25 rpm after 30 minutes of drug injection (control, test, standard). Animals were placed in the rotarod apparatus according to their respective group. The ideal effect of the drug could be noticed. [10]

Stock Solution

The stock solution was prepared containing 0.4mg/ml of drug and 1ml/100 gm body weight of the animal was given to those animals.

Elevated Plus Maze Apparatus

Elevated plus maze is the simplest apparatus to study anxiolytic response of almost all type of anti-anxiety agents. Animals have affinity towards high and open space and prefer enclosed arm.whenThe various groups of test, standard, and untreated rats are put in the maze, and it is noted how much time they spend in the open and closed arms. Animal enters open arm, they become immobile, defecate, and show fear like movements. The different groups of untreated, standard and test rats are kept in the maze and their time spending in open or closed arms are recorded. When treated with antianxietyagents the anxiety of the mouse reduces and its spending of time in open area increases. [10]

Stock Solution

The stock solution was prepared containing 0.2mg/ml of the drug and 1ml/100gm of the body weight of the animal was given to these animals.

RESULTS AND DISCUSSION

The control group in the rotarod model showed 47 ± 0.866, while the group treated with caffeine (4 mg/kg) showed a substantial increase in falling time (107 ± 0.347), when the *Panax ginseng* treated group (0.4mg/100 gm) was evaluated it has also shown significant increase in falling time 95 ± 0.448 (Table 1, Figure 1). In the elevated plus maze apparatus control has shown 5±.336 number of entries, whereas the number increased in the case of caffeine treated group, 9±.661. And when compared to the untreated control, the Panax ginseng treated group likewise shown a notable rise in the number of entries. (Table 2, Figure 2).

CONCLUSION

According to the above experiment, which used dried ginseng roots that N.P. Dutta and sons gave, albino Wister rats were housed in an elevated plus maze and rota rod apparatus. It might be said that *Panax ginseng* has CNS antidepressant qualities. The animals which are treated with *Panax ginseng* and caffeine exhibit more entries in the raised plus maze apparatus than the untreated or controlled animals. Conversely, in the rote rod apparatus, the animals given caffeine and *Panax ginseng* had longer rod time than the animals given no treatment or control.The results above clearly demonstrated the strong CNS antidepressant effect of the Panax ginseng extract, which may extrapolate by further research to bring the light in the field of CNS treatment with minimum side effects.

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Table 1. Results from Rota rod mode

Treatment	**Time spent in rota rod(second)**
Control	47±0.866
Caffeine	107±0.347***
Ginseng	95±0.448***

All values are mean ±SEM, n=6, *** p<0.001 vs control

Table 2. Results from Elevated Plus Maze

Treatment	**No. of entries**
Control	5±.336
Caffeine	9±.661***
Ginseng	8±.254***

All values are mean ±SEM, n=6, *** p<0.001 vs control

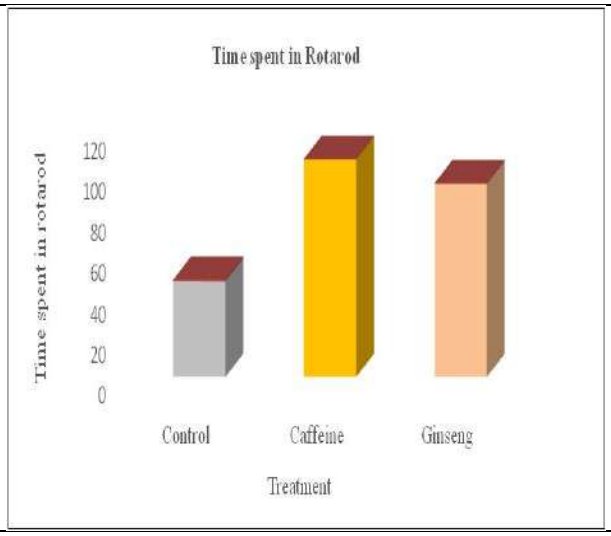

Figure 1.Time spent in Rotarod

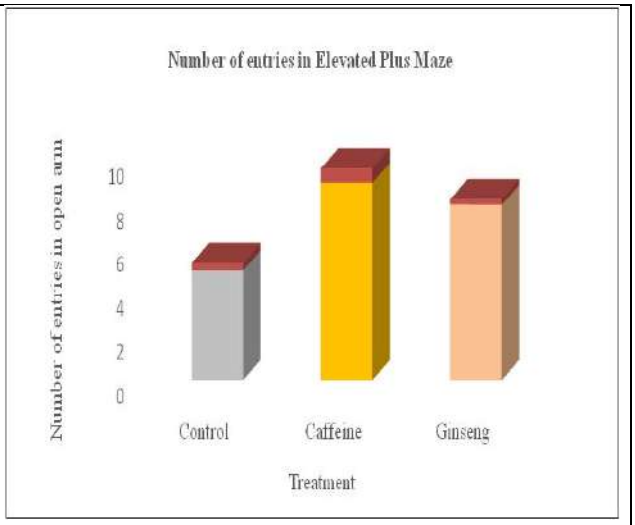

Figure 2. Number of entries in Elevated Plus Maze

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RESEARCH ARTICLE

Indian Association of Physics Teachers and Renewal of Physics Education

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ABSTRACT

Physics provides an understanding of the nature covering a wide range of micro and macro phenomenon which we can potentially think of. As such, learning physics becomes an exciting field of study. However, very often physics happens to be counter-intuitive in nature and poses severe conceptual difficulties. Physics educators worldwide have attempted to stand up to this challenge. Coming together of physics teachers from universities, colleges and schools in 1984 under the banner of Indian Association of Physics Teachers (IAPT) was one of such response. Indeed, the association has to develop a fair degree of autonomy in organisational and financial matters to strive for pedagogical renewal. Organisational and financial factors are bound to mitigate or facilitate its pedagogical strives. Keeping the organisation's stature and financial matters in the background, the study aims to explore the pedagogical discourse and engagement which the association has been involved with for around three decades since its formation. The study is socio-historical in nature and spans 1970-2010 timeline. The study shows that though there are a range of issues like role of experiment, mathematics, historical and philosophical perspectives and problem solving in physics teaching and learning the association has engaged with during more than three decades, renewal of experimental activity has been the salient feature of its pedagogical engagement. The study shows that physics teachers appear to be rooted in their practice and articulation of tacit knowledge from practice is not easy to come by. It is inferred that researching and gathering scientific evidence into mathematical, historical, philosophical and pedagogical aspects of physics teaching may enhance reflective practice and help them find the solutions of the problems of physics teaching at different levels.

Keywords: Concept-centred Experiment, model physics laboratory, Mathematisation of physics, Physical Science Study Committee (PSSC) and Berkley Physics Course, Nature of Science

INTRODUCTION

Second half of the 20th century witnessed a large-scale curricular reform worldwide. United States of America (USA) and major European countries took a lead in this endeavour during 1950s. Curricular reforms undertaken in USA deserve special mention as far as its impact on other countries like India is concerned. The Scientists' played a leading role in developing Physical Science Study Committee (PSSC) and Berkeley physics courses and their view of "what science is" shaped the nature and structure of the curricula during 1960s. Logical reconstruction of content vis-a-vis facts, concepts, postulates, laws, principles and theory was adopted as the method to reconstruct curricula. Mathematical deduction became primary means to weave together different facets of content. Provision was made to use experiments for concept formation and verification of theory. Having acquired conceptual knowledge, solving a large number of problems became the hallmark of mastery of physics. As a whole this imparted coherence and rigor to the disciplinary structure of physics (deBoer, 1991; Finlay, 1962/1992).[1] India not only seems to adopt the curricula developed in America and United Kingdom but also attempted to initiate few similar changes in the succeeding decades {Ministry of Education, 1966; UGC and UNESCO, 1970}.[2] Hoshangabad Science Teaching programme initiated in 1972 is one of the prominent examples of curricular reforms undertaken at elementary level (HSTPG, 2002).[3] More than three decades curricular engagement of reform-oriented research and education produced ripples all around India (Saxena and Mahendero, n. B; Mukherjee et al. n. d.).[4] The outcomes of this programme were fed into the policy perspective to conceptualise the elementary teacher training programmes in Delhi University as well as to renew curriculum by National Council of Educational Research and Training (NCERT) in 2005 during formulation of National Curriculum Framework - 2005 (Raina, 2011) . [5]At higher education Indian Association of Physics Teachers (IAPT) is one of the examples where physics teachers from colleges, Universities and Schools have come together on voluntary basis to renew physics education in India. The present study traces the attempts to renew physics education by the Indian Association of Physics Teachers (IAPT).

Curricular Projects in Physics Education in India

Education Commission (1966) played a vital role in the comprehensive renewal of education in India. This was followed by the preparation of a concrete plan of action to translate the recommendations of the commission. Probably physics education happens to be one of the first disciplines where initiatives were taken in this regard (Ministry of Education, 1966).[6] Being a physicist himself, the chairman of the Education Commission, D. S. Kothari, led physics educators of the country to prepare a draft to make broad based progressive changes in the content and methods of physics teaching. The deliberation took place at Srinagar in June 1970 (UGC and UNESCO, 1970, 11).[7] Following the plan of action prepared during Srinagar deliberation (1970), University Grant Commission (UGC) initiated the University Leadership Programme (ULP) and College Science Improvement Programme (COSIP) in the latter half of the same year. Number of universities and affiliated colleges across the country were assigned the task to develop curricular material under ULP and COSIP projects. These projects ran for almost a decade and produced textbooks, laboratory manual, demonstrations and experiments (UGC, 1982).[8] Punjab, Pune and Rajasthan Universities made notable contribution (Kumar and Nigaveker, 1994; Joshi, 1997). [9] Textual material produced by a number of ULP and COSIP groups hardly finds mention as alternatively better curricular material. On renewal of experimental activity, exemplary work was produced by ULP Rajasthan covering a wide span of undergraduate and post-graduate physics (Kumar and Nigaveker, 1994; Vigyan Prasar, 2009; Lokanathan, 2009). [10] The work done under ULP and COSIP projects from across the country culminated on an international conference, on the 'Role of Laboratory in physics Education', organised at the Centre for the Development of Physics Education (CDPE), Rajasthan University from 28th December, 1983 to 2nd January 1984 (Lokanathan and Sharma, 1984).[11] Physics teachers in the conference reflected on the renewal of pedagogy of physics via finding intimate connection between concept formation and experimental activity. Babulal Saraf—the man leading the exemplary work on the innovative experiments at ULP Rajasthan proposed progressive role for experiment in generating physical laws or equations. For instance, the generation of Inductance (L)-Capacitance (C) and Resistance (R) (or LCR) curve from experimental data. According to him a range of conceptual and procedural knowledge related to the physical phenomenon can only come about when experimental activity is treated as a source for knowledge generation and not simply a mean

to verify theory (Loknathan and Sharma, 1984, pp: 83-90).[12] The view of B. L. Saraf was reinforced by other teachers engaged in ULP and COSIP programmes. D. P. Khandelwal (1984) - a co-worker at ULP Rajasthan for a short period during 1979 and founder of IAPT, contended that physics teaching is generally characterized by direct introduction of concepts through derivation of mathematical equations and experimental activity is accorded the role of verifying theory. Predominance of concept building through mathematical derivations relegates experimental activity at subservient position.[13] Rather than giving subordinate position, experimental activity, according to him, should be organically related to mathematical component of physics concepts. Sufficient amount of concrete experiences with physical phenomenon through experimental activity are a prerequisite for developing abstract and mathematical side of physics concepts. Lack of this makes teaching of physics lopsided. Loknathan and Sharma (1984, pp: 83-90), other co-workers with B. L. Saraf in ULP Rajasthan, further expounded the role of experimental activity. They exhorted their fraternity to produce accounts of experiments have played crucial role in bringing about breakthroughs in physics.[14] Having engaged for more than a decade in ULP and COSIP projects, physics teachers felt the need to renew physics education on continuing basis. Consequently, representing the pedagogical concerns of the physics teachers in India, they came together as the Indian Association of Physics Teachers (IAPT) during March, 1984. Though, the association represented the concerns of undergraduate physics, being foundational in nature school physics also became a major sphere of its activities subsequently (Rawat, 2019). [15]

IAPT and its Engagement with Physics Education

Srinagar deliberation (1970), ULP and COSIP projects to great extent shaped the objectives of IAPT (Khandelwal, 1984). [16] Popularisation of concept formation through experimental activity became the central objectives of IAPT. Along with B. L. Saraf, D. P. Khandelwal (the founder of the association) turned out as the chief exponent of popularisation of experiments for concept development in IAPT circles (Rawat, 2019).[17] Khandelwal (1987) argued for changing the thrust of conventional experiments from verification of theory to the study of the phenomenon. Conventional experiments are geared to verification of theories and are not employed for the exposition of physical phenomenon. Besides, they are limited in numbers. Hence more experiments need to be developed to exhibit the range, variation and relationship of physical quantities. For instance, variation in shapes and sizes of the constituent parts of physical phenomena, introduction of new experimental variables, connecting together two or more experiments etc. are suggested the alternative pathways. The procedure for generation and analysis of the experimental data were proposed to be upgraded accordingly. While proposing enhanced role for the teacher directed activity, Khandelwal, stressed students to be facilitated to ask questions, manipulate variables or even reconceptualise the experiment. [18] 'Concept-centred experiment' was coined by Khandelwal to portray the renewed emphasis on the role of experimental activity in physics pedagogy (Khandelwal 1987, 110).[19] Thrust was laid down on the enhancement of qualitative or perceptual content of concepts which can subsequently lead to the mathematical formulation (Khandewal 1996, 68).[20] Latter on Khandewal's position was reinforced by other IAPT members like Joshi (1999), Datta (2001) and Mali (2001). Desai (2004) was particular in pointing out that lack of understanding of the mathematical equations and formalism by students is the result of the impoverish experiences and skill development with the experimental activities. [21]

Renewal of pedagogy around experimental activity gave rise to several programmes which IAPT has been pursuing since its formation in 1984. Addition of experimental component to National Standard Examination in Physics (NSEP) and National Graduate Physics Examination (NGPE), in 1992 and 1993, respectively; development of physics laboratories vis-a-vis Centre for Scientific Culture (CSC) (in 1993) and Anveshika (in 2001), Nationwide Orientation of Physics Teachers towards experimental activity during 1997-1999 as well as initiation of National Competition for Innovative Experiments in Physics (NCIEP) in 2003 stand testimony of this fact (Rawat, 2019). [22] With the addition of computer-interfacing of physics experiment with appropriate sensors and control elements in a computer software allows us to perform experiments with finer and wider degree of variation. It is for around three decades now that computer-interfacing of manual experiments for teaching was introduced (Wilson and Redish, 1989). [23] Around 2001, a number of IAPT members also joined global physics community in adding school and college physics experiment with computer-interfacing. 2001 Annual National Convention of IAPT was a watershed movement in the introduction of computer-interfaced experiments within IAPT circles (Samanta, 2001). [24] Though, National

Competition in Computer Application in Physics (NCICP) was a late entry into IAPT's programmes during 2011, introduction of computer-interfaced experiments in IAPT circles has already been made in the Annual National Convention of the association in 2001 (Rawat, 2019). [25] With the passage of time, focus on experiment in pedagogy acquired populist tone. Less attention was given to the critical debates on other domains of pedagogy. Drawing attention to lack of work done in logico-mathematical part of physics pedagogy in India, Joshi and Tillu (1989) stated:

"Without much ado, one could point one's fingers at two major lacunae in the undergraduate education prevailing in Indian Universities which lead to malady. They are (i) lack of adequate training in scientific experimentation, laboratory work, handling of equipment, and (ii) lack of sufficient clarity in basic theoretical understanding as a result of an improper/inadequate training of science students in mathematical as well as in the logic of science. In our opinion, a fair amount of efforts have so far been made here as well as elsewhere to remove the first category of lacunae mentioned above.....We are not aware of any national programme which attempts to help students to shed their intrinsic fear of mathematics….In fact, as mentioned above, although we are subconsciously aware of it, no one even seems to have formally advocated the view in a concrete manner that a lack of appreciation of physics (or science) is a direct result of the lack of appreciation of the logical and mathematical structure underlining it....a large number of students often draw a blank because of these reasons…… Gaps in their understanding are often found to exist even in the elementary mathematical concepts, leave aside higher mathematics. (pp: 39-40) [26]

The lack of passivity of IAPT on mathematical aspect of physics pedagogy continued. Unlike number of programs and activities developed to renew and popularize role of experiment, no programs were conceptualized on mathematisation or mathematical modeling of physics. Interestingly, the advocates of experimental (i. e. D. P. Khandelwal) and logico-mathematical component of physics concepts (i. e. A. W. Joshi) worked together in the UNESCO Project and produced the book entitled World View of Physics during 1993-1999. Much felt out gap in the logico-mathematical component of physics was left unaddressed. It was argued that non-mathematical component is more important at the introductory stage of physics education the book is meant for (see Joshi et al 1999). [27] Though not a major programme of IAPT, it was during 2008 that Joshi along with his fellow physics teachers from Pune University reported to organise a training program for B.Sc. physics students on the subject. The program claimed to explicate the relationship between hypothesis, postulates, models and approximations while mathematising physical phenomenon (Joshi 2008, 214-15; Joshi 2008, 240-245).[28] Indeed, the program was an attempt to diagnosis the difficulties students encounter in this domain. Treatment was based on lectures alone and generation and translation of experimental data into mathematical modelling was not dealt in the program. Other physics teachers part of IAPT fraternity just made passing reference to scientific modelling as a bridging process between experimental activity and mathematical equations (see for instance, Raman 1987, 33; Gambhir 2006, 342; Joshi 2003, 272). [29] As it happened, lack of explication of the physical content underlying mathematical equations remained a point of contention among physics teachers (Khandelwal 1994, 68; Ramani 2000, 58; Virk 2000, 233). [30]

Probably, Rakesh Popli happens to be a few of the second generation (after Saraf, Khnadelwal or Joshi) of IAPT members who attempted to produce a rigorous analysis of the conceptual problems faced by physics students. In a series of papers published by him between 1999 and 2002 he points out that both teachers and texts seem to fall short of addressing the problem. For example, the gaps in students' understanding in relating the basic physical entities such as kinematics-displacement, velocity, acceleration and average velocity, Gausses' and Ampere's laws are brought about in a series of these papers by him. Root cause of conceptual difficulties faced by the students, according to him lie in the fact that relationship between empirical data generated from experimental activity and basic physical entities is not revealed to students. He argued that merely following a 'formalistic approach' (mathematical formalism in physics) prevalent in practice, does not result in a firm and clear comprehension of concepts. For, instance, direct introduction of students to calculus and vector analysis can potentially impede the development of concepts of physics (Popli 2001, 202). [31] Hence, exposure to physical phenomenon through well designed demonstration, experiments and its translation into mathematical form should lie at the base of learning physics. This serves the basis for the development of concepts, mathematical equations and formalism. He argued that the approach should be adopted both at the introductory and college level (especially for the B.Sc. general students)

(Popli 1999, 261). [32] These were few of the preliminary attempts towards bridging the gap between experimental activity and mathematical formalism. The alternative initiative proposed by Popali has not translated into the consensual and sustained work through IAPT's activities as yet. The history and philosophy of science (physics) or alternatively the 'nature of science' has also been a matter of interest for IAPT fraternity. It was argued that an accurate and detailed description of history and philosophy of concepts and theory is essential for the pedagogical renewal of physics. Fellow teachers were urged to generate debates and produce useful material in this regard. As a result, though a sizable amount of literature appeared in the Bulletin of the IAPT in the following years, it did not reach a threshold to impact pedagogical renewal (for instance, Vishwamitter 1989, 2-3; Khandelwal 1993, 164; Desai 2003, 39; Rajgopal 2003, 233; Joshi 2003, 268). [33] In majority of the cases, instead of a rigorous analysis of the problem, the articles raised concerns, lamentations or exhortation relating the need to work further in this direction. Despite showing concern for enrichment of nature of science component in teaching of physics by IAPT, work in this regard also did not translate in a productive program. Interestingly, the publication in this respect has decreased progressively. The initiative undertaken by IAPT regarding problem-solving are limited to the development of a repertoire of novel 'problem solving' items. Holding a competition for devising (analysis being the integral part of it) novel problem solving items for introductory and undergraduate levels was adopted the way to move forward in this direction (IAPT 1986, 121).[34] The best entries received were published in its Bulletin of the IAPT for the wider acknowledgment and inclusion in the repertoire of problem-solving items so designed (IAPT 1987, 24).[35] Posing a challenging problem for readers and asking them to solve it was adopted as another way to move ahead in this regard (Rawat, 2019). [36] Apparently this appears jus a perpetuation of traditional perspective of physics practitioner lacking any kind of renewal.

DISCUSSION

Traditionally, physics teaching is characterized by deductive presentation of content. Experiments are used to verify theory and occasionally used to demonstrate the concepts in concrete form (Hestenses, 1987; McDermott, 1993; Rief, 1996; Redish, 1998). [37] Verification of theory by experiments or occasional demonstration of concepts does not prove to be adequate. Whether school or college teaching, adequate foundation on or support of concrete experiences seems to be lacking to develop abstract thinking required to understand physics. Hence, what is felt to be missing in the curricula more than anything else happens to be a well-equipped laboratory with a large number of improvised demonstrations and refined experiments? Experiments are vital in mediating the discursive movement across the spectrum of concrete-abstract thinking or bridging the gap across inductive and deductive approaches of instruction (Hestenes, 1987, 2006; McDermott, 1993; McDermott and Saffer, 1998; AAPT, 1997, 2014; Koponen et al., 2003; Halloun, 2007). [38] IAPT appears to move along the physics education fraternity worldwide in this regard which may probably explain its overwhelming engagement with the experimental activity to renew physics education. In general, the members of the association appears to hold a tacit assumption that having provided concrete thinking during secondary and introductory stages, students can make progressive shift towards abstract thinking at undergraduate level. However, reality of neither school nor college physics curriculum appears to resonate with this assumption. Due to lack of experimental activities, students do not develop adequate amount of conceptual development. That is why the need to renew experimental activities became maor component of renewal of physics education by IAPT (Rawat, 2019). [39] Mathematisation is another area of physics where students encounter severe conceptual difficulty (Hestenes, 1987; Halloun, 2007; Kurki-Suonio, 2010). [40] Without elaboration though, Babulal Saraf (1979) in his suggestion to upgrade the role of experimental activity, has alluded to this fact. [41] Implicitly, the proposal is put forward by D. P. Khandelwal (1987), Joshi and Tillu (1989), Popli (2001, 2002) to make a shift from qualitative to quantitative translation of experimental data i. e. generation of equations and laws of physics from experimental data. However, no systematic programme was formulated by IAPT in this regard. [42] Historical and philosophical aspects of physics education also find mention in IAPT's discourse. However, unlike a professional historian or philosopher of science, it does not appear more than a reflection of interest or appreciation in these components of physics education. As a result no substantial work has appeared in this regard. At most they seem to be engaged in exploring and using the available material on the subject and as such appear to be limited in scope.

Contrary to this, science and physics education researcher on the other hand have been attempting to evolve a framework for nature of science component to inform science and physics education. For instance, empirical basis of science, scientific laws and theories, scientific creativity, theory dependence of observation, nature of scientific method and tentativeness of knowledge were proposed as a NOS framework for school teaching by the Lederman and co-researchers (2002). [43] Experimentation, idealisation, model-making, mathematisation, theory choice and rationality, explanation, realism and constructivism along with other socio-scientific issues have been suggested by Matthews (2012). [44] It is a well-established fact that problem solving in physics demands the firm grasping on the conceptual understanding (Gerace and Beatty, 2005). [45] The renewal of science and physics education being attempted globally by the way of creating a perspective and material on experimental activity, mathematisation and nature of science (i. e., historical and philosophical facets of concepts and theory) is meant to enhance deeper disciplinary understanding of the students (Docktor and Mestre, 2014) [1]. [46] Though being physics practitioners, they did not seem to explicate the shift from novice (student) to expert' (practitioner physicist) apparent and therefore evolving a alternative programme in this regard seems farfetched.

In general Physics teachers' view of reform or renewal of physics education appears to be rooted in routine practice. As such they seem to act like practitioner of what Thomas Kuhn (1962, 1994) suggested as 'normal science' contrary to 'revolutionary phase of growth of science'. [47] Apparently 'critical criticism' necessary to make progress in their own practice of physics teaching when seen through Popperin s'(1963) lens appears to be relatively lacking. [48] History is the laboratory of human experience according to Imre Lakatos (1978). [49] Without undertaking fresh research in the history of physics it is probably not possible to illuminate historical perspective of the discipline and therefore enrichment of physics teaching may remain a wishful thinking. Physics teachers are not generally trained in conducting historical research in their discipline. The best what they appear to be doing is to draw from some of the secondary sources of the available literature or evoke their intuitive understanding of the historical development of physics. They could not evolve a significant work in this area also. It is quite apparent that in order to be able to renew mathematical, historical and philosophical perspectives of physics education physics teachers need to conduct research in these areas. Probably by developing research perspective on physics teaching they have to develop what Boyer (1990) termed as 'scholarship of teaching' and not to take reform in physics education taken for granted based on their tacit understanding of practice.[50] Lack of 'scholarship of scholarship' of among physics teachers in a significant way appears to explain relatively less than a work for which they have been aspiring for in last several decades.

CONCLUSION

Though, the call for pedagogically viable work on nature of physics, mathematisation and problem-solving perspectives was made by IAPT, experimental activity happens to be the salient feature of its engagement so far. Attempts were made to formulate a number of programmes aimed to popularise this pedagogical perspective. Significant success seems to be achieved by the association in this regard. Broadly, PSSC and Berkley Physics Course developed in America, appear to drive the reconstruction of pedagogy in Srinagar deliberation, ULP/COSIP Projects as well as by IAPT. Even after more than three decades of its existence, the work conducted by IAPT does not seem to be informed by the alternative perspectives in philosophy of science, psychology and science education emerging during and after 1970. Unlike science and physics educators drawing on the perspectives emanating from philosophy of science and psychology for researching the problems of science (physics) pedagogy, physics teachers in India as a practitioner seems to draw from their tacit understanding of the discipline to improve instruction (Rawat, 2019).[51] This appears to account for the lack of significant strides made by the association except experimental activity. Joining hands with science education community globally probably could be the alternative available before the association. Explication of tacit knowledge of physics teachers of their practice may not to be easy to come by and needs to develop a perspective of 'reflective practitioner' as suggested by Schon (1995, 2001).[52] Also Following Boyer (1990) acquisition of research perspective or 'scholarship of teaching' also may enhance their ability to contribute in the renewal of physics education significantly. [53]

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RESEARCH ARTICLE

Water Quality Assessment during Pre-Monsoon Season in Zawlnuam R.D.Block, Mamit District, Mizoram, India., using Water Quality Index-Weighted Arithmetic (WQI-WA) Method

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ABSTRACT

The quality of water is now known to be just as important as the quantity. It contains contaminants in solution from its movement and location. The quality of water is needed to be known as it is the main purpose for potable, irrigation and industrial activities. The aim of the study is to assess the water quality of Zawlnuam R.D. Block, Mamit, Mizoram, India during pre-monsoon season. Samples were collected from various villages within the study area. They were analyzed based on seven parameters namely Iron, Chlorides, TDS, Alkalinity, pH, Turbidity and Hardness using Water Quality Index-Weighted Arithmetic (WQI-WA) Method. The calculated value is classified in five categories ranges from Excellent water quality to Unsuitable for drinking purpose. The results obtain under this study provides various decision for various location within the area of interest.

Keywords: Ground Water, Surface water, Water quality, Pre- monsoon, Zawlnuam RD Block, Water Quality Index, Weighted Arithmetic Method.

INTRODUCTION

Ground water is one of the most important natural resources and the largest reachable source of fresh water for supplying the ever-increasing demand [1]. The ground water in natural systems usually contains dissolved solids,

minerals and salts. Accordingly, aquifer gases, soil zone, soluble minerals and salts in aquifer determines the chemical composition of the ground water in an aquifer. Knowing the natural ground water quality can provide significant understanding in the nature of the resource. Assessment of the natural chemical composition of ground water can furnish the reactions that produce natural water chemistry, recharge, movement, mixing and discharge of ground water. Rocks in Mizoram have high solubility and produce major portion of soluble constituents of groundwater. Calcium and sodium are generally added cations, sulphate and bicarbonate are its connate anions. Limited amount of chloride is also present which occurs due to sewage, connate water and intruded sewage. Nitrate is usually natural constituent but if its concentration is high, it can be due to past or present pollution [2]. For assessing the water quality of Zawlnuam R.D. Block during pre- monsoonal season, various physico-chemical analysis like pH, alkalinity, iron, TDS (total dissolved solids), chloride, turbidity and hardness is tested using the water samples collected from various springs, traditional springs and groundwater.

Study Area

Zawlnuam R.D. Block is located in the north western part of Mizoram between 23° 40.648′ to 24° 15.210′ N Latitudes and 92° 15.503′ to 92° 33.000′ E Longitudes. It is bounded to the north by Assam state, on the south by Mamit RD block, on the east by Kolasib district and to the west by Bangladesh. The total geographical area of Zawlnuam block is approximately 1170 sq. km and it falls in the Survey of India Topo sheet Nos. 83 D/7, 83 D/8, 83 D/11, 83 D/12, 84 A/5, 84 A/6 and 84 A/9.The study area enjoys a moderate climate owing to its tropical location. It is neither very hot nor too cold throughout the year and have an average annual rainfall of 2806.47mm [2].

Field Work

Field work has been carried out in and around Zawlnuam RD Block and water samples from several springs and bore well has also been collected. The water samples collected are used for assessing the water quality and each location of the springs and bore well are carefully recorded and collected for further studies and analysis. The springs which have been visited are mainly fracture spring, contact spring or the combinations of both. The rocks in the research area are closely examined and it shows that the rocks are mostly weathered shale, sandstone and siltstones. Cross stratification, ripple marks, laminations, joint sets, local fold and faults are found in many rocks. In Zawlnuam RD Block, monocultural plants like oil palm, areca nut, rubber and teak wood are common.

Water Quality Assessment

For assessing the quality of water, 32 samples from 32 villages are collected in Zawlnuam R.D. Block. By using different instrument and testing different physico- chemical parameters like pH, turbidity, iron, chloride, Total Dissolved Solids (TDS), alkalinity and total hardness in a laboratory, the quality of the water sample is determined. The following table are the results of the water quality samples tested.

Water Quality Index

Water quality index -Weighted Arithmetic Method(WQI-WA) is valuable and unique rating to depict the overall water quality status in a single term that is helpful for the selection of appropriate treatment technique to meet the concerned issues. However, WQI depicts the composite influence of different water quality parameters and communicates water quality information to the public and legislative decision makers [5].WQI-WA indices are broadly classified into two types; they are physico-chemical and biological indices. The physico-chemical indices are based on the values of various physico-chemical parameters in a water sample, while biological indices are derived from the biological information. The present report aimed at calculation of WQI-WA for Ground Water, Traditional Spring and Spring of Zawlnuam Block; Mizoram India based on hydro-chemical data. In order to determine the Ground Water quality of the area, total 32 Nos. of water samples has been collected for a comprehensive physicochemical study. For calculating the WQI, the following 7 parameters have been considered: Iron, Chloride, Total dissolved solids (TDS), Alkalinity, pH, turbidity, total hardness. The relative weight assigned to each parameter based on the importance of the parameters for human consumption.

MATERIALS AND METHODS

Weighted Arithmetic Water Quality Index Method

Weighted arithmetic water quality index method classified the water quality according to the degree of purity by using the most commonly measured water quality variables. The calculation of WQI was made by using the following equation; -

WQI = $\frac{\Sigma QiWi}{\Sigma Wi}$

The quality rating scale (Qi) for each parameter is calculated by using this expression:

Qi =100(Vi -Vo/Si-Vo)

Where, Vi is estimated concentration of ith parameter in the analysed water

Vo is the ideal value of this parameter in pure water

Vo = 0 (except pH =7.0 and DO = 14.6 mg/l)

Si is recommended standard value of ith parameter

The unit weight (Wi) for each water quality parameter is calculated by using the following formula:

Wi =K /Si

Where, K = proportionality constant and can also be calculated by using the following equation:

K= $\frac{1}{\Sigma(\frac{1}{Si})}$

The rating of water quality according to this WQI is given in Table 2.

RESULTS AND DISCUSSION

In assessing the quality of ground water in Zawlnuam R.D. Block, the pH of water in Lungsir Tui (traditional spring) in Mamit is slightly low (6.44, acceptable limit is 6.5-8.5) and turbidity exceeds permissible limit (6.31 mg/L, Acceptable limit-1.0 mg/L, permissible limit-5.0 mg/L), and C. Lalvulluratuiverh (ground water) in Kanhmun; Khurpuituikhur(spring) in Luimawi, Tuivamittuikhur(spring) in Tuivamit, Presbyterian Pastor quarter tuiverh (ground water) in Zawlnuam is also low in pH but not unsafe for domestic purposes. Zawlnuam tuiverh (ground water) in Zawlnuam BDO Complex exceeds the permissible limit of Iron content (6, acceptable limit is 0.02 mg/L, permissible limit is 0.3 mg/L) and need some treatment before consumption. In addition to the analysis of ground water quality, Water Quality Index (WQI) for Ground Water, Traditional Spring and Spring of Zawlnuam R.D. Block, Mizoram, India is calculated based on hydro-chemical data. The analysis reveals that the groundwater of the area (5 samples) needs some degree of treatment before consumption, and it also needs to be protected from the perils of contamination. Whereas, two samples are unsafe for domestic purposes. The index number, offers a highly effective tool to assess the water quality for public or for any intended use as well as in the pollution mitigate plan and in water quality management.

CONCLUSION

The assessment of water quality in this study is done using aggregating seven parameters in which the combination of different parameters obtained a single value that ranges from 0-100 which is Water Quality Index (WQI-WA). The WQI-WA method provide a dynamic and smaller number of parameters required in comparison to all other method of water quality assessment for particular use. The present study provides valuable insight into the status of overall water quality of the Zawlnuam R.D.Block, Mamit District, Mizoram, India. Ground water and traditional springs are based on WQI values. The study has both practical and academic significant important for the decision makings and can be concluded that when some of the results for various sampling location remarks unsafe for drinking purposes which requires specific treatment before consumption based on the end use. There is a requirement of prevention of non-point source contamination for the future by an act of anthropogenic activities controlling the sewerage discharge of residential, commercial and industrial effluents to the area.

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Table 1: Water Quality Assessment

Sl.	Village	Name of Source	Habitation & Location	Type of Source	Iron	Chloride	TDS	Alkalinity	pH	Turbidity	Hardness
1	Kawrtethawveng	Darnam Tuikhur	Kawrtethawveng	Traditional spring	0.1	56.48	162	16	6.54 @ 26.2°C	1.83	125
2	Rajiv Nagar	Rajiv Nagar Tuikhur	Rajiv Nagar	Traditional spring	0.1	32.48	224	14	8.33 @ 27.0°C	5.68	225
3	Darlak	Darlak Ground Water	Darlak	Ground Water	0	85.97	195	14	6.54 @ 25.7°C	0.66	125
4	Tuivamit	Tuivamit Tuikhur	Tuivamit	Traditional spring	0	38.48	77	14	6.44 @ 26.4°C	0.38	75
5	Zomuantlang	Zomuantlang Tuikhur	Zomuantlang	Traditional spring	0.2	24.49	46	18	6.80 @ 28.4°C	5.72	75
6	Tuipuibari	Tuipuibari Tuikhur	Tuipuibari	Traditional spring	0	43.48	137	10	7.84 @ 26.8°C	2.64	75
7	Damparengpui	Damparengpui Ground Water	Damparengpui	Ground water	0.1	24.99	146	14	8.00 @ 26.5°C	3.67	125
8	Dampui	Dampui Tuikhur	Dampui	Traditional spring	0	25.49	73	8	6.54 @ 26.7°C	2.28	50
9	Damparengpui	Damparengpui - II	Damparengpui	Spring	0.1	31.49	114	10	8.02 @ 26.9°C	0.81	125
10	Sabual	Sabual Tuikhur	Sabual	Spring	0.1	37.48	119	12	6.76 @ 29.4°C	0.89	75
11	Khantlang	Khantlang seepage	Khantlang	Spring	0	21.49	140	14	7.95 @ 28.6°C	2.66	150
12	Kanhmun	C.Lalvullura Tui Pump	Kanhmun	Ground water	0	40.98	87	10	5.74 @ 29.1°C	1.22	75
13	Lulmawi	Khurpui	Lulmawi	Traditional spring	0	25.49	44	12	5.87 @ 29.4°C	0.58	50
14	Bungthuam	Tui Pump Tui	Bungthuam	Ground water	0.1	23.99	164	10	7.82 @ 29.7°C	1.41	125
15	Bawrai	Lalhmunliani Tuiverh	Bawrai	Ground water	0.2	20.99	180	12	7.74 @ 29.7°C	2.38	125
16	Thinghlun	Thinghlun Tuikhur	Thinghlun	Traditional spring	0	24.99	46	8	6.23 @ 30.0°C	1.07	50
17	Zawlnuam	Prebyterian Pastor Qtrs. Tuiverh	Zawlnuam	Ground water	0	56.48	177	16	6.33 @ 29.8°C	0.52	150
18	Zawlnuam	Zawlnuam Tuiverh	Zawlnuam	Ground water	6	32.98	165	8	6.68 @ 30.1°C	54.1	175
19	Zawlnuam	BDO Qtrs. Tuiverh	Zawlnuam	Ground water	0.9	54.48	131	12	6.73 @ 27.0°C	24.3	225
20	Zawlnuam	BDO Staff Qtrs. Tuiverh	Zawlnuam	Ground water	0.3	19.49	115	16	7.41 @ 27.1°C	6.57	200
21	N. Sabual	N. Sabual Tuikhur	N. Sabual	Traditional spring	0	4.5	92	90	7.70 @21.2	0.26	100
22	Damdiai	Damdiai Tuikhur	Damdiai	Traditional spring	0	3	50	52	6.98 @ 22.8	1.56	42
23	Vawngawnzo	Vawngawnzo Tuikhur	Vawngawnzo	Traditional spring	0	5.5	35	42	6.66 @20.1	0.97	60
24	Suarhliap	Salaithanga Tuikhur	Suarhliap	Traditional spring	0	11.5	45	36	7.49 @ 22.6	3.86	40
25	Zamuang	Zamuang Tuikhur	Zamuang	Traditional spring	0	8	37	38	7.35 @ 22.5	5.03	42
26	Sihthiang	Sihthiang Tuikhur	Sihthiang	Traditional spring	0	3.5	50	34	7.14 @ 22.5	4.3	50
27	Mamit	Lungsir Ngharpet Tuikhur	Lungsir, Mamit	Traditional spring	0	45.99	118	38	6.94 @ 20.2	1.42	108
28	Mamit	Luangpawl Tuikhur	Luangpawl, Mamit	Traditional spring	0	52.48	148	230	6.55 @ 20.2	1.01	120
29	Mamit	Lungsir Tuikhur	Lungsir, Mamit	Traditional spring	0	9.5	34	26	6.44 @ 22.0	6.31	24
30	Kawthah	Ramri Tui	Kawrthah	Traditional spring	0.3	250	0	200	7.4 @ 25.3	0.1	76
31	Rengdil	Lungalhthei Tui	Rengdil	Traditional spring	0.1	7	0	20	6.7 @23.0	0.9	60
32	Tuidam	Serlui Tui	Tuidam	Traditional spring	0.3	18	0	42	7.3 @25	0	102

Table2. Water Quality Rating as per Weight Arithmetic Water Quality Index Method

WQI Value	Rating of Water Quality	Grading
0-25	Excellent water quality	A
26-50	Good water quality	B
51-75	Poor water quality	C
76-100	Very Poor water quality	D
Above 100	Unsuitable for drinking purpose	E

Table.3: Water Quality Index

Sl. No.	Village	Name of Source	Habitation & Location	Type of Source	Iron (in mg/l)	Chloride (in mg/l)	TDS (in mg/l)	Alkalinity (in mg/l)	pH	Turbidity	Hardness (in mg/l)	Water Quality Index(WQI)	Water Quality Status	Grade
1	Kawrtethawveng	Darnam Tuikhur	Kawrtethawveng	Traditional spring	0.1	56.48	162	16.0	6.54 @ 26.2°C	1.83	125.0	31	Good	B
2	Rajiv Nagar	Rajiv Nagar Tuikhur	Rajiv Nagar	Traditional spring	0.1	32.48	224	14.0	8.33 @ 27.0°C	5.68	225.0	39	Good	B
3	Darlak	Darlak Ground Water	Darlak	Ground Water	0	85.97	195	14.0	6.54 @ 25.7°C	0.66	125.0	0	Excellent	A
4	Tuivamit	Tuivamit Tuikhur	Tuivamit	Traditional spring	0.0	38.48	77.0	14.0	6.44 @ 26.4°C	0.38	75.0	-1	Excellent	A
5	Zomuantlang	Zomuantlang Tuikhur	Zomuantlang	Traditional spring	0.2	24.49	45.5	18.0	6.80 @ 28.4°C	5.72	75.0	67	Poor	B
6	Tuipuibari	Tuipuibari Tuikhur	Tuipuibari	Traditional spring	0.0	43.48	137	10.0	7.84 @ 26.8°C	2.64	75.0	5	Excellent	A
7	Dcamparengpui	Damparengpui Ground Water	Damparengpui	Ground water	0.1	24.99	146	14.0	8.00 @ 26.5°C	3.67	125.0	37	Good	B
8	Dampui	Dampui Tuikhur	Dampui	Traditional spring	0	25.49	72.5	8.0	6.54 @ 26.7°C	2.28	50.0	2	Excellent	A
9	Damparengpui	Damparengpui - II	Damparengpui	Spring	0.1	31.49	114	10.0	8.02 @ 26.9°C	0.81	125.0	33	Good	B
10	Sabual	Sabual Tuikhur	Sabual	Spring	0.1	37.48	119	12.0	6.76 @ 29.4°C	0.89	75.0	31	Good	B
11	Khantlang	Khantlang seepage	Khantlang	Spring	0	21.49	140	14.0	7.95 @ 28.6°C	2.66	150.0	5	Excellent	A
12	Kanhmun	C.Lalvullura Tui Pump	Kanhmun	Ground water	0	40.98	87	10.0	5.74 @ 29.1°C	1.22	75.0	-1	Excellent	A
13	Luimawi	Khurpui	Luimawi	Traditional spring	0	25.49	43.9	12.0	5.87 @ 29.4°C	0.58	50.0	-2	Excellent	A
14	Bungthuam	Tui Pump Tui	Bungthuam	Ground water	0.1	23.99	164	10.0	7.82 @ 29.7°C	1.41	125.0	34	Good	B
15	Bawrai	Lalhmunliani Tuiverh	Bawrai	Ground water	0.2	20.99	180	12.0	7.74 @ 29.7°C	2.38	125.0	65	Poor	C
16	Thinghlun	Thinghlun Tuikhur	Thinghlun	Traditional spring	0	24.99	45.5	8.0	6.23 @ 30.0°C	1.07	50.0	0	Excellent	A
17	Zawlnuam	Prebyterian Pastor Qtrs. Tuiverh	Zawlnuam	Ground water	0.0	56.48	177	16.0	6.33 @ 29.8°C	0.52	150.0	-1	Excellent	A
18	Zawlnuam	Zawlnuam Tuiverh	Zawlnuam	Ground water	6.0	32.98	165	8.0	6.68 @ 30.1°C	54.1	175.0	1880	Unsuitable for Drinking Purpose	E
19	Zawlnuam	BDO Qtrs. Tuiverh	Zawlnuam	Ground water	0.9	54.48	131	12.0	6.73 @ 27.0°C	24.30	225.0	299	Unsuitable for Drinking Purpose	E
20	Zawlnuam	BDO Staff Qtrs. Tuiverh	Zawlnuam	Ground water	0.3	19.49	115	16.0	7.41 @ 27.1°C	6.57	200.0	99	Very Poor	D
21	N. Sabual	N. Sabual Tuikhur	N. Sabual	Traditional spring	0	4.50	92	90.0	7.70 @21.2	0.26	100.0	2	Excellent	A
22	Damdiai	Damdiai Tuikhur	Damdiai	Traditional spring	0	3.00	50	52.0	6.98 @ 22.8	1.56	42.0	2	Excellent	A
23	Vawngawnzo	Vawngawnzo Tuikhur	Vawngawnzo	Traditional spring	0	5.50	35	42.0	6.66 @20.1	0.97	60.0	0	Excellent	A
24	Suarhliap	Saiaithanga Tuikhur	Suarhliap	Traditional spring	0	11.50	45	36.0	7.49 @ 22.6	3.86	40.0	5	Excellent	A
25	Zamuang	Zamuang Tuikhur	Zamuang	Traditional spring	0	8.00	37	38.0	7.35 @ 22.5	5.03	42.0	6	Excellent	A
26	Sihthiang	Sihthiang Tuikhur	Sihthiang	Traditional spring	0	3.50	50	34.0	7.14 @ 22.5	4.30	50.0	5	Excellent	A
27	Mamit	Lungsir Ngharpet Tuikhur	Lungsir, Mamit	Traditional spring	0	45.99	118	38.0	6.94 @ 20.2	1.42	108.0	1	Excellent	A
28	Mamit	Luangpawl Tuikhur	Luangpawl, Mamit	Traditional spring	0	52.48	148	230.0	6.55 @ 20.2	1.01	120.0	0	Excellent	A
29	Mamit	Lungsir Tuikhur	Lungsir, Mamit	Traditional spring	0	9.50	34	26.0	6.44 @ 22.0	6.31	24.0	6	Excellent	A
30	Kawthah	Ramri Tui	Kawrthah	Traditional spring	0.3	250.00		200.0	7.4 @ 25.3	0.10	76.0	92	Very Poor	C
31	Rengdil	Lungalhthei Tui	Rengdil	Traditional spring	0.1	7.00	0	20.0	6.7 @23.0	0.90	60.0	31	Good	B

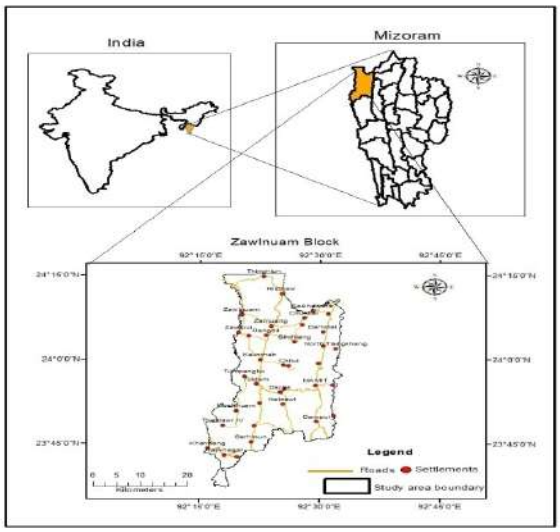

Figure.1: Location of Study Area.

Figure.2: Different sources where water samples are collected.

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RESEARCH ARTICLE

Optimal Allocation of Water for an Irrigation Project: A Case Study

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ABSTRACT

This study is focused on creating a process for optimizing water allocation to different crops at different times so that the yield reaches its greatest value accepting the help of the root growth model (RGM) and Relative yield to determine the best way to distribute crop water from an irrigation reservoir using a root growth model and stochastic dynamic programming."The water depth for maintaining the soil moisture above the critical moisture limit by using the root growth model and stochastic dynamic programming (SDP) finding is cropping for onion, gram, potato, vegetable, and wheat 440mm, 350mm, 250mm, 215mm, and 360mm respectively. On the application of soil moisture balance study and root growth model, the percentage saving of water for different crops is onion, gram, potato, vegetable, and wheat are 2.20%, 1.70%, 14.97%, 5.70%, and 6.49% respectively. Scheduling of water can be made using weekly water demand considering the root growth model for the command area of the project. The study results show that the optimal utilization of water can help increase the area for seasonal crops like rabi crops for maximum crop production or gain maximum yield. Thus for each farmer, profit becomes the key objective that he wishes to maximize.

Keywords: Crop Coefficient, Root Growth Model (RGM), Potential Evapotranspiration, Actual Evapotranspiration, Water Allocation.

INTRODUCTION

India uses irrigated agriculture to produce the majority of its food. According to Wallace (2000), there will be 3.7 billion more people on the earth by 2050 than there are today, which implies that the additional food required to feed future generations would put even more strain on freshwater resources. This is because agriculture uses 75% of the freshwater that humans now utilize, making it the single largest user. When and how much to water are the two key concerns that irrigation scheduling attempts to answer. Irrigation schedules can be adjusted to saturate the crop root zone depth to the field capacity after a sufficient water supply is guaranteed, based on the time it takes for the soil to sink to a critical level. With this kind of irrigation, the crop can develop as quickly as possible provided that all other inputs are given at ideal rates. Water deficits during the crop's several seasons are unavoidable if insufficient water is available to meet the crop's needs for that specific season. It becomes imperative for irrigation managers to decide how best to allocate water shortfalls throughout a crop's intra-seasonal times. Farmers allocate their land to various crops based on the accessibility of canal water. The canal discharge is also impacted by the reservoir's storage capacity, but it is unaffected by the requirement for irrigation at sea level. Using an SDP technique, the first stage determines each crop's seasonal production to maximize the crop's expected relative output for a specific seasonal water supply. To optimize net benefits from crop-facing shifting evapotranspiration needs [11] created a concept known as stochastic dynamic programming (SDP). The model calculates crop evapotranspiration and reservoir water release based on weekly fluctuations. At this point, the range of seasonal water availability values is analyzed, from zero to the highest practical irrigation need for each crop under consideration. As per the sigmoidal root growth model, this depth rises with crop growth and reaches its peak value towards the end of the flowering season for most crops [3]. The ideal distribution of water has been the subject of numerous research. The Penman-Monteith approach reliably estimates evapotranspiration (ETo) and outperforms other methods when compared to lysimeter data, [4] suggested that irrigation frequency and deficit irrigation had an impact on wheat yields.

To allocate scarce water resources, [6] proposed using deficit irrigation in rotational systems. Water allocation regulations in semiarid tropical regions now in effect, such as deficit irrigation schemes utilizing rotational irrigation systems, are based on the principle of providing a consistent water depth during irrigation, irrespective of the growth phases of the crops or the soils on which they are planted. [7] used a multilayer strategy to optimize the usage of water and land resources as well as an irrigation supply for tertiary units in large irrigation projects. Most farming scenarios, according to [13] entail cultivating many crops in a single season. The allocation of land and water resources is a crucial factor to consider in situations involving many crops. The primary limitations of mathematical programming model (MPM) are its strict constraints, absence of information or data monitoring, and process simplification. The Root Growth Model (RGM) formulation and SDP assistance are used to establish the optimal cropping plan and allocation of water to different crops. The land and water to be allotted to each crop at a given time are the decision factors in RGM. The present study aims to address crop water allocation, crop production maximization, and profit maximization in the context of the agricultural management system. The objective of this research is to ascertain the optimal distribution of water for each crop. A relatively long irrigation interval of one week was required to achieve the highest yields under deficit irrigation; low irrigation frequency did not further reduce yields.

Study Area

The Vindhyan hills are the source of the Choral River, a tributary of the Narmada that passes through the districts of Indore and Khargone. The Choral Reservoir is situated in the Mhow Tehsil of the Indore district, in the village of Rampuriya. The study region is located at latitudes 75°46'N and longitudes 22°25'E, respectively. The amount of water needed at each stage varies along with the pace of growth.

METHODOLOGY

Model Formulation

The model is intended to give the optimal water allocation and irrigation schedule for every crop grown in the research region. The complexity of the current topic is too great to consider in a one-level approach. For example, if a single stochastic optimisation technique, like SDP, is utilised, the "curse of dimensionality" will prohibit the problem from being solved as stated. The multilayer approach yields the finest outcomes. The basic elements of the multilevel technique are composed of two parts: (1) an SDP solution for the weekly intra-seasonal allocation for a single crop, and (2) an RGM for the overall depth of water allocation for all crops. The schematic representation of the entire process is displayed in Fig. 1. The amount of water applied during irrigation seasons has a major impact on the growth and yield of a crop. Water is applied to each crop in the proper amount to ensure optimal development and productivity. When there is an adequate supply of water, it is important to apply the right amount of water to crops to suit their needs. When crop growth phases are disrupted by inadequate water supply, the actual rate of transpiration will fall short of the maximum rate. The primary reason we selected this study region was because of the potential for water stress to develop in the crop, which would hurt crop output and growth. To maximize production, this study also employed the RGM and SDP models to allocate water based on the crop's utility.

The necessary Penman-Monteith technique parameters, or ET_0, have been computed using this collected data. Kc has been computed using the Food Agricultural Organisation (FAO)-56 value. These calculations have also been used to determine the net irrigation need at the Canal head and an evaluation of ETc using the Penman-Monteith method. The "Food Agricultural Organisation FAO 33" maximum yield estimate methodology has been applied. These days, it is crucial to allocate water optimally for agricultural management, especially in the context of Indian agriculture. In the current study, the RGM was utilized to determine the best water allocation for agricultural management in an irrigation project because it has an advantage over other models in that it takes crop growth into account along with water depth. Using meteorological data (wind speed, maximum temperature, minimum temperature, relative humidity, sunshine hour, and radiation), we first calculate the evapotranspiration rate using a reference surface evapotranspiration value (ETo) or use all factors to calculate the ETo. In addition, determine the root growth depth and potential evapotranspiration (PET) for every crop. Additional computation of the soil moisture balance for the root zone depths over the various periods, as well as the actual evapotranspiration (AET) in each fortnight. This study gathers the necessary data from the sources, including crop coefficient (Kc), depletion factor, and meteorological data (Min, Max, Humidity, Wind Speed, Sunshine & Radiation).

Soil Moisture Balance

There is hardly much precipitation in the study area. Additionally, the area is surrounded by bunds that stop this little rainwater from running off. With the overall mass balance equation taken into consideration and the runoff from the field ignored, the soil's moisture balance equation can be represented as follows.

$$SM_{t+1}\, Z_{t+1} = SM_{t+1}\, Z_t + x_t + S_0(Z_{t+1} - Z_t) - AET_t \quad (1)$$

Where,

Z_t and Z_{t+1} is depths of the root zone at times t and t+1, (cm);

x_t is water allocation in period t (mm)

S_0 is initial soil moisture content (mm/cm)

SM_t is the depth units of soil moisture content per unit root depth in period t (mm/cm)

Potential Evapotranspiration

The potential evapotranspiration (PET) is given by

$$PET = K_C \times ET_0 \quad (2)$$

Where,

PET is called Potential evapotranspiration

K_c is called Crop coefficient

ET_O is called Reference crop evapotranspiration

Whether there is enough water available in the root zone or if the crop will experience stress from a water deficiency determines the actual evapotranspiration potential rate.

Root Growth Model

The effective depth of root penetration into the soil determines the depth of the active soil reservoir from which the crop extracts water. This depth rises with crop growth and reaches its maximum value for most crops after the flowering season. This study used a root growth model (Borg and Grimes 1986):

$$Z_t = Z_{max}\left(0.5 + 0.5\sin[3.03(\frac{t}{t_{max}}) - 1.47]\right) \quad (3)$$

Where,

Zt is the effective root zone depth in centimetres at time t following seeding. t max is the number of days needed for the root zone to fully develop Zmax is maximum root zone depth that can be achieved (in CM)

Actual Evapotranspiraton

The depth of the active soil reservoir, which the crop draws water from, is determined by the effective depth of root penetration into the soil. For most crops, this depth reaches its maximum value at the end of the flowering season and increases with crop growth. A root growth model (Borg and Grimes 1986) is used in this study:

AET,

$$0; SM_t < WP_t \quad (4)$$

$$\frac{PETt(SMt-WP)}{(1-p)(FC-WP)}; \mathrm{WP} < SMt \leq (1-\mathrm{p})(\mathrm{FC}-\mathrm{WP})$$

$$PET_t; SM_t \geq (1-p)(FC-WP)$$

Where,

SM_t = The depth units of soil moisture content per unit root depth in period t (mm/cm),

FC= field capacity (mm/cm)

WP = wilting point (mm/cm), p = crop water depletion fraction

Crop growth stage, accessible soil moisture in the root zone, and the atmosphere's evaporative demand all affect actual crop evapotranspiration. The Penman Monteith method has been used to calculate the ETo value, or the value of evapotranspiration, for the project area for each month using CROPWAT software.

The Relative Yield Ratio and The Objective Function

The relative yield for each crop is expressed as:

$$R_t^*(x_t, AET_t) = 1 - [K_t(1 - \left(\frac{AET}{PET}\right)t] \quad (5)$$

Where,

$R^*(x_t, AET_t)$ = relative yield corresponding to x_t irrigation depth and the given AET

x_t = water allocation in period t (mm); t = index for period In the present study for each of the crops for each fortnight the maximum relative yield ratio is taken as the objective function for individual season. The overall objective function used in the present study for the complete growth season of a crop is the product of all the relative yield ratios as given by (Rao *et al*., 1990).

$$\frac{Y_a}{Y_{max}} = \prod_{t=1}^{NP}\left[1 - k_t\left(1 - \frac{AET}{PET}\right)t\right] \quad (6)$$

Where,

Ya stands for actual yield (100 kg/ha) Ymax for maximum yield (100 kg/ha) kt for yield stress sensitivity factor for the given period PET stands for prospective evapotranspiration (mm) t for period index, NP for total number of periods for the crop AET for actual evapotranspiration (mm)

RESULT And DISCUSSION

All available data, including crop coefficient (Kc), depletion factor, and climatic data, were incorporated into this analysis. All meteorological data needed to generate Monthly ET0 Penman-Monteith is calculated or developed by

us. Every month, we prepared all of the metrological data by averaging the daily data by the cropwat model's specifications.

Effect of time on crop coefficient

The ratio of actual crop evapotranspiration (AET) to reference crop evapotranspiration (ETo) is known as the crop coefficient (Kc), which is a crucial component in crop evapotranspiration evaluation. Initial crop, development crop, mid-season crop, and late-season crop are the four stages for which the crop coefficient varies.

Effect of time on root growth model

The ETo first uses the monthly average data. Then, using the crop coefficient and evapotranspiration, determine the prospective evapotranspiration. Root zone depth calculates the depth of the root zone at time t after planting, the maximum practicable depth of the effective root zone, and the number of days it will take for the root zone to fully develop. The soil moisture balance is determined by deep percolation, or the transport of water downward through the soil profile below a plant's effective rooting zone, as well as by rainfall, water allocation, and starting soil moisture content. Weekly canal release and evapotranspiration were calculated from the SDP model. The relative yield is computed for each week that matches the actual evapotranspiration and all canal release levels. The goal of SDP is to maximize the relative yields' expected value. The necessary water depth is computed using the root growth model and the soil moisture balance study in order to keep the soil moisture level above the critical moisture limit. Weekly comprehensive computations for every crop. Maintaining the relative yield ratios of one was chosen as the primary criterion for keeping the soil moisture near the critical limit. Onion, Gramme, Potato, Vegetable, and Wheat water allotted to crop in the field are 440mm, 350mm, 250mm, 215mm, and 360mm, respectively, according to the final results or key findings of the model application. Further, we have a comparison of crop water requirement by conventional method and RGM are findings 2.20%, 1.70%, 14.97%, 5.70%, and 6.49% of water savings and gain maximum yield of each crop. It is believed that the farmer supplies water to the field in a limited way, which causes the crop to receive more water at times and less at other times. Thus, we irrigated every crop in accordance with the need for a specific quantity of field capacity and obtained maximum production or maximum yield by using the root growth model and stochastic dynamic programming. The literature states that numerous studies have been conducted to determine the maximum yield for a variety of crops, including cotton, maize, wheat, sunflower, sugar beetroot, and others, employing a variety of techniques or models, including the crop was model and linear programming, among many others. Thus, with the aid of these models, we have been able to maximize production and obtain better results for various crops than we have with other models by using stochastic dynamic programming and the root growth model.

CONCLUSION

The primary conclusions state that the water depth needed to maintain soil moisture above the critical moisture limit, as determined by the soil moisture balance and root growth model, is less than that needed for crop irrigation supply, as calculated by conventional methods, and is 440 mm for crop onions, 350 mm for grams, 250 mm for potatoes, 215 mm for vegetables, and 360 mm for wheat. The percentage of water saved by using the soil moisture balance research and root growth model for onion, gram, potato, vegetable, and wheat crops is 2.20%, 1.70%, 14.97%, 5.70%, and 6.49%, respectively. The highest proportion of water savings relative to other crops is achieved for the potato crop. The saved water can be used for irrigation of additional land, which will result in an increase in the overall production of crops under the project. Water scheduling can be done by taking into account the Root Growth model for the project's command area and using the weekly water requirement. Similarly, we may use this approach to help us allocate water to different crops. The farmer can do the same for more crops in both the rabi and kharif seasons, as we already do for five crops during the rabi season. This model will help farmers preserve water while producing the most amount of crops possible.

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Table. 1: Crop water allocated to different crops considering root growth model at the field

Sr. No.	Crop	Water allocated to crop at the Field (mm)	Ratio of actual yield and maximum yield(Ya / Ymax)
1	Onion	440	1.0
2	Gram	350	1.0

3	Potato	250	1.0
4	Vegetable	215	1.0
5	Wheat	360	1.0

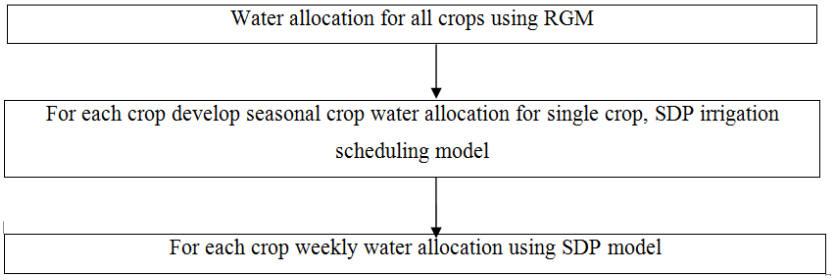
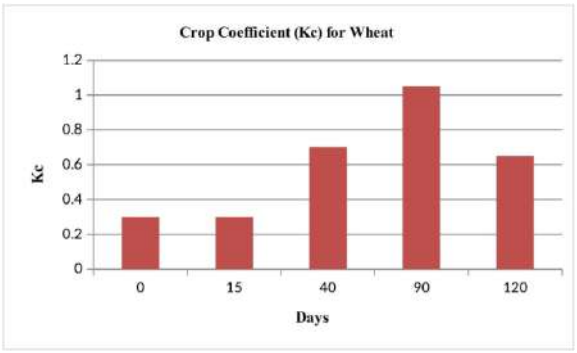
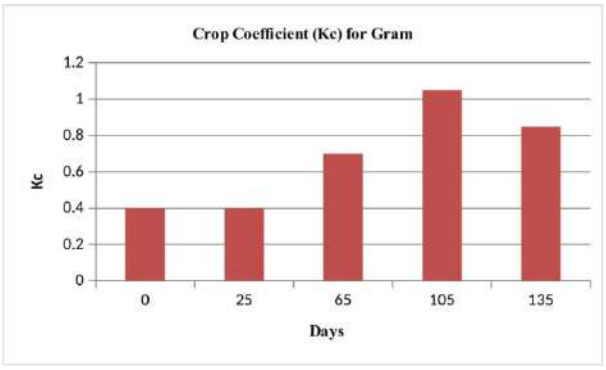


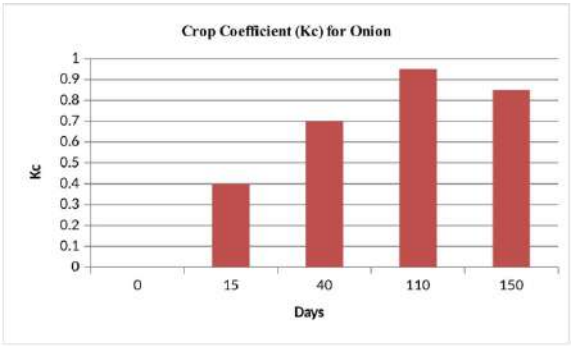
Figure.1: Schematic of Multilevel Break-up Procedure



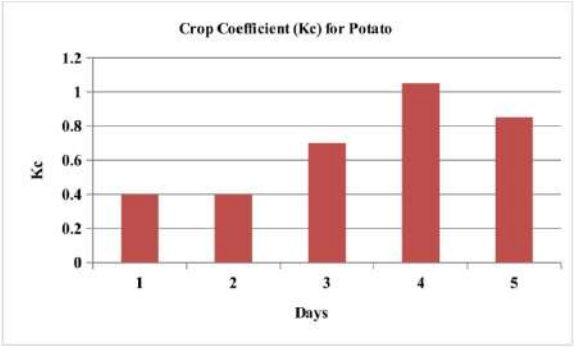
Graph.1: Crop coefficient day wise for wheat crop



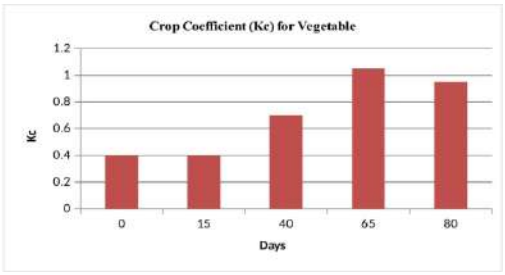
Graph.2: Crop coefficient day wise for gram crop



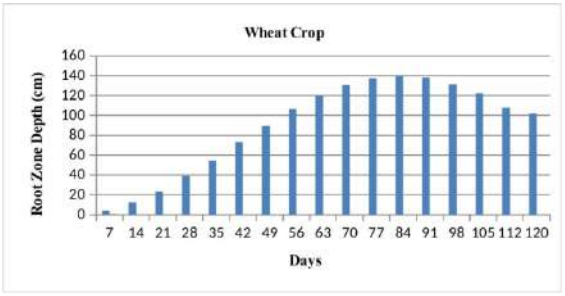
Graph.3: Crop coefficient day wise for onion crop



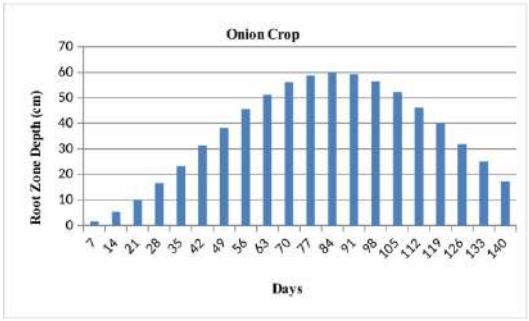
Graph.4: Crop coefficient day wise for potato crop



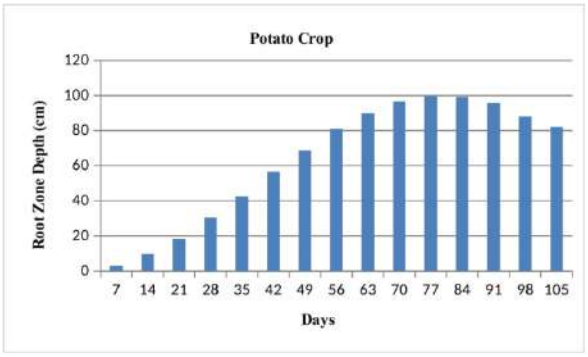
Graph.5: Crop coefficient day wise for vegetable crop



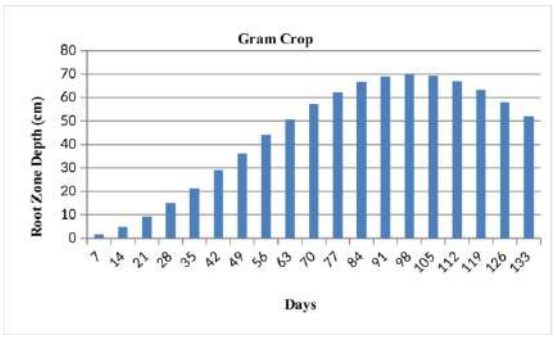
Graph.6: Depth of effective root zone at different time interval after showing for wheat crop



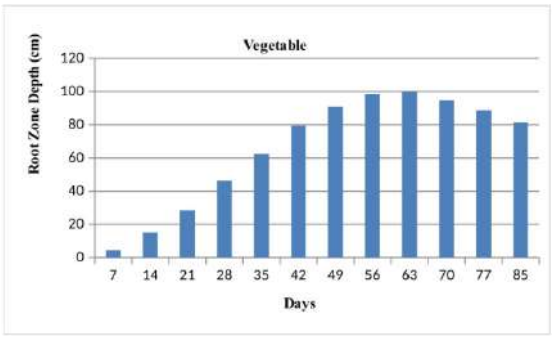
Graph.7: Depth of effective root zone at different time interval after showing for onion



Graph.8: Depth of effective root zone at different time interval after showing for Potato



Graph.9: Depth of effective root zone at different time interval after showing for gram crop



Graph.10: Depth of effective root zone at different time interval after showing for vegetable

RESEARCH ARTICLE

aUniversal Immunization Programme in India

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ABSTRACT

The Universal Immunization Programme (UIP) commenced in India in 1985 as an extension of the Expanded Programme for Immunization (EPI). The objective was to administer recommended vaccines for tuberculosis, polio, and other diseases to all children across the country. The Ministry of Health and Family Welfare oversaw the program, receiving substantial assistance from the global community. India has one of the largest Universal Immunization Programs (UIP) in the world in terms of the quantities of vaccines used, number of beneficiaries covered, geographical spread and human resources involved. Under the UIP, all vaccines are given free of cost to the beneficiaries as per the National Immunization Schedule. While the program has made strides in improving immunization coverage in India, it has encountered significant managerial hurdles and has not fully achieved its goal of providing vaccination coverage to every child as initially intended. Overall, the immunization programme has a profound impact on public health in India, delivering significant results across the nation.

Keywords: Universal Immunization Programme, India, Mission Indradhanush, Challenges

INTRODUCTION

Vaccines represent essential preventive measures in primary healthcare and are integral to a nation's health security. While international organizations like the World Health Organization (WHO) and the United Nations Children's

Fund (UNICEF) advocate for global immunization initiatives and policies, the effectiveness of an immunization program within a specific country is largely influenced by local circumstances and national strategies. This holds particularly true for vast and diverse developing nations like India, characterized by a population exceeding 1 billion and an annual birth rate of 25 million.[1] Furthermore, the National vaccine policy plays a crucial role in guiding decision-making processes to strengthen the UIP. This policy addresses various aspects such as vaccine security, management, regulatory guidelines, research and development, and product development. To facilitate informed decision-making regarding modifications in vaccination schedules or the inclusion of new vaccines, a National Technical Advisory Group on Immunization (NTAGI) has been established. Comprising technical experts, national program leaders and managers, representatives from development partners, and professional bodies, this group reviews and discusses all issues related to the immunization program and vaccines, providing final recommendations.[2] The Universal Immunization Programme (UIP) commenced in India in 1985 as an extension of the Expanded Programme for Immunization (EPI). The objective was to administer recommended vaccines for tuberculosis, polio, and other diseases to all children across the country. The Ministry of Health and Family Welfare oversaw the program, receiving substantial assistance from the global community. While the program has made strides in improving immunization coverage in India, it has encountered significant managerial hurdles and has not fully achieved its goal of providing vaccination coverage to every child as initially intended.[3]Vaccines play a crucial role in primary healthcare by serving as preventive measures against infectious diseases. Hence, achieving self-sufficiency in vaccine production and fostering self-reliance in vaccine technology are critical factors influencing our nation's health security. Immunization is one of the most cost effective public health interventions and largely responsible for reduction of under-5 mortality rate. However, vaccine preventable diseases (VPDs) are still responsible for over 5 lakh deaths annually in India. This underlines the need of further improvement. Today, India is a leading producer and exporter of vaccines. The technology mission started by the Government of India under the Universal Immunization Programme in 1986 yielded some results in improving the number of people covered under the vaccination scheme.

Evolution Of UIP

The Expanded Programme on Immunization (EPI) was launched in India in 1978 with the aim of diminishing morbidity and mortality caused by diphtheria, pertussis, tetanus, poliomyelitis, and childhood tuberculosis. Its goal was to offer immunization services to all eligible children and pregnant women by the year 1990.[4] The technological missions in India were initiated in 1987 by Sri Rajiv Gandhi led Congress government. Following consultations with leading immunization specialists, the initiative opted to initiate nationwide immunization efforts using oral vaccine. Since the oral vaccine comprised live virus components, it necessitated refrigeration for storage. Consequently, a cold chain infrastructure was devised to facilitate the proper handling and distribution of vaccines. Collaborations were established with industrial stakeholders to ensure refrigeration accessibility across all regions of India. The mission also launched India’s polio vaccine production capacity.[5] The Comprehensive Child Survival and Safe Motherhood (CSSM) Program endeavors to provide maternal and child health services comprehensively, addressing the overall requirements of mothers and children across health and illness scenarios. Initiated in 1991, the program was implemented initially in 100 districts across Uttar Pradesh, Bihar, Rajasthan, and Madhya Pradesh, aiming to offer a comprehensive package of services for maternal and child health.[6]The Child Survival and Safe Motherhood (CSSM) program aims to enhance existing infrastructure to deliver Emergency Obstetric Care (EOC), which forms the cornerstone of the Safe Motherhood initiative. In 1997, the Government of India followed up the International recommendation on Reproductive and Child Health (RCH) as a National Programme. It is an expanded version of maternal and child health services within the framework of family welfare, encompassing elements of safe motherhood and child survival initiatives to reduce Maternal Mortality Ratio from 60 (State Report) to 55, to reduce Infant Mortality Rate from 34 (NFHS-3) to 25, to reduce Total Fertility Rate from 2.9 (NFHS-3) to 2.5.

UIP In India

Introduced in 1978, India's Expanded Programme on Immunization (EPI) supplied vaccines to children. The programme was renamed as the Universal Immunization Programme (UIP) in the mid-1980s.

In 1985, UIP started with six antigens diphtheria, pertussis, and tetanus (DPT), poliomyelitis (OPV), tuberculosis [Bacillus Calmette Guerin (BCG)] and typhoid-paratyphoid in the programme and no new antigen was added to the programme for the next 16 years. During this period, globally and in India, a number of new vaccines became licensed and available in the market.[7-9] The total resource requirement of the UIP from 2013 to 2017 was Rupees 34,336 million ($5,282 million).[10] The Hepatitis B vaccination initiative commenced in June 2002, initially targeting 14 metropolitan cities in India. Subsequently, in October 2003, an additional 33 rural districts were incorporated into the vaccination program.[11] Furthermore, the utilization of the Hepatitis B vaccine was extended to encompass all districts within 10 states of the nation during the period of 2007-08. In 2008, it was advised to include the *Haemophilus influenzae* type bHib vaccine in the Universal Immunization Program (UIP). Since December 2011, the combination of the Hib vaccine with diphtheria, pertussis, tetanus, and hepatitis B has been incorporated into the UIP in the states. A detailed technical assessment of Hib diseases and vaccines was published in this journal in 2009. This article offers a recent overview of the global utilization of the Hib vaccine and examines the procedures and measures adopted in India for the introduction of the pentavalent vaccine containing Hib.[12] The live attenuated SA-14-14-2 vaccine for Japanese encephalitis (JE) was incorporated into routine immunization through the Universal Immunization Program 2006 across 181 endemic districts in India. More recently, the Government of India has declared the inclusion of a single dose of JE vaccine for adults residing in endemic districts.[13] In 2016, India became one of the first countries in Asia to introduce an indigenously manufactured rotavirus vaccine. However, any new vaccine introduction needs to be meticulously planned to allow for strengthening of the existing immunization systems instead of burdening them.[14] Within the framework of Mission Indradhanush, all vaccines included in the Universal Immunization Program (UIP) are administered according to the National Immunization Schedule.

Additionally, Mission Indradhanush was recognized as a key initiative within the Gram Swaraj Abhiyan, covering 16,850 villages across 541 districts, as well as the Extended Gram Swaraj Abhiyan, encompassing 48,929 villages across 112 aspirational districts. Mission Indradhanush (MI), a flagship program of the Ministry of Health and Family Welfare (MoHFW), Government of India was launched in December 2014 with the aim to reduce child mortality and accelerate the process of full immunization coverage for children at a rapid pace, ensuring that all children under the age of 2 years and pregnant women are fully immunized with all available vaccines. However, vaccination on demand to children up to 5 years of age will be provided during drives. The government has initiated the Intensified Mission Indradhanush (IMI) 2.0, spanning from December 2019 to March 2020. IMI 2.0 is designed to intensify efforts towards achieving the goal of attaining 90% national immunization coverage throughout India by addressing deficiencies identified in previous phases. This program will be implemented across 271 districts in 27 states and 652 blocks in Uttar Pradesh and Bihar, focusing on reaching underserved and tribal communities.[15-17] To date, ten phases of Mission Indradhanush have been successfully carried out, encompassing 701 districts across the nation. As of April 2021, these various phases of Mission Indradhanush have resulted in the vaccination of a total of 3.86 crore children and 96.8 lakh pregnant women. Notably, the initial two phases of Mission Indradhanush contributed to a 6.7% increase in full immunization coverage within a year. Furthermore, a survey (IMI-CES) conducted across 190 districts as part of the Intensified Mission Indradhanush (the fifth phase of Mission Indradhanush) indicated an 18.5% point rise in full immunization coverage compared to NFHS-4. Continuous efforts to bolster routine immunization and periodic intensification drives have led to significant enhancements in immunization coverage, as evidenced by the latest reports from the National Family Health Survey (2019-21) compared to NFHS-4 (2015-16). Notably, full immunization coverage among children aged 12-23 months has surged from 62% (NFHS-4) to 76.4% (NFHS-5) due to these concerted efforts. In February and March 2021, two phases of Intensified Mission Indradhanush (IMI) 3.0, each lasting 15 days, were carried out to target pregnant women and children who had missed vaccinations through the routine immunization program. These efforts were undertaken across 250 districts spanning 29 states and union territories. During IMI 3.0, approximately 9.5 lakh children and 2.2 lakh pregnant women received vaccinations.[18]

Vaccination Delivery

The ASHAs (Accredited Social Health Activist) were requested to work with the ANMs (Auxiliary Nurse and Midwife) to guarantee that the children on the list who are not inoculated receive their shots. ASHAs provided

information about live births and new pregnancies in their service areas, along with reports of immunizations administered. These updated reports from ASHAs were sent to the field coordinator via the LHSs for distribution at monthly sector meetings.[9] Healthcare workers must verbally remind eligible homes prior to each immunization day, per government regulations. their responsibilities in immunization programme are Planning for Immunization , Managing the Cold chain, On receiving the vaccine carrier and logistics or at the immunization session site, Preparing and conducting the immunization session, Communicating with caregivers, Recording, Reporting and tracking of dropouts , Capacity building of ASHAs and AWWs to perform their roles in UIP, Coordination with ICDS supervisor.[19] Every metropolitan community, especially slums, should have "immunization booths," and board members of local municipalities should be held responsible for their actions. It is possible to assemble sizable and diverse volunteer groups to provide immunization services, such as retired nurses, quacks, pharmacists, chemists, and local registered medical practitioners.[20] For 100% vaccination, government takes action like appropriate legislation should mandate complete immunization in order to get admittance to schools. Families with fully immunized children may be eligible for incentives in the form of cash and kind.

METHODOLOGY

Case-Fatality Ratios

Disease-specific case-fatality ratios, which represent the proportion of deaths among individuals with a specific condition over a defined time frame, were utilized in conjunction with mortality projections from the Lives Saved Tool. This approach helped estimate the potential reduction in vaccine-preventable cases resulting from enhanced immunization rates.[21]

Alternate Vaccine Delivery

As an alternative to injectable vaccines, efforts have been made to enhance antigen stability and enhance overall immunogenicity. Specifically, innovative approaches involving edible or intradermal vaccine formulations have shown promise in eliciting both systemic and mucosal immune responses.[22]These novel vaccination delivery systems offer several benefits compared to injectable preparations, including the potential for self-administration, cost reduction, improved stability, and elimination of the need for a cold chain.

Treatment Costs Averted

To assess the potential savings in treatment costs due to reduced illness from immunization, it was imperative to ascertain the number of cases prevented by vaccination that would have otherwise sought medical care, the sources of care they would have accessed, and the associated expenses. The quantity of prevented cases who would have utilized care from different facilities was subsequently multiplied by the nation-specific expenses of care at each facility, as determined by the World Health Organization.

Challenges And Consideration

Migrant populations with limited access to healthcare services exhibit higher rates of dropout from vaccination programs. Factors such as a transient lifestyle, overcrowding, inadequate sanitation, and poor personal hygiene contribute to increased transmission of vaccine-preventable diseases (VPDs). Research on the determinants of immunization has revealed that nearly one-third of migrant children struggle to complete their vaccination regimen.[23] Vaccine costs were estimated by multiplying doses used (including wastage) by unit prices of vaccines. The primary cost categories considered in this analysis encompassed personnel, vaccines and supplies, travel and transport, training, maintenance and overhead expenses, incentives, and the annual value of capital expenditures. These capital expenses encompassed crucial infrastructure elements such as cold chain facilities, buildings, and vehicles. Financial data were sourced from various reports including financial statements and monthly immunization reports. Additionally, immunization registers detailing vaccines administered, as well as stock and issue registers, were utilized to gather pertinent information. Data collection occurred at different levels of administration, including district, state, and national offices. At the facility level, personnel costs were computed based on the salaries and

allowances allocated to staff directly involved in immunization delivery. This included personnel such as physicians, auxiliary nurse midwives, lady health volunteers, and cold chain handlers, among others. The calculation factored in estimates of time spent on various tasks related to immunization services, including vaccine administration, transportation, record-keeping, and travel to immunization sessions, accounting for 285 days per year.[24]

Economical Benifits

Expanding the coverage of new vaccines can yield numerous advantages, including enhanced economic productivity and heightened societal appreciation for healthy individuals, families, and community members. Recent studies suggest that the worth of a life-year saved in a low- or middle-income nation is estimated to be 1.5 times greater than the country's GDP per capita. We evaluated the potential reduction in the number of deaths achievable through enhanced childhood vaccination coverage.[25]

Global Collaboration Innovation In Vaccine Development

Early efforts focused on development of an aerosolized measles vaccine; however, inhalation devices that had to fit over the nose and mouth created practical logistical challenges for administration in young infants and ultimately a phase 3 clinical trial in 2010 found suboptimal immunogenicity. An alternative vaccine delivery system that simplifies logistics and provides non-inferior immunogenicity compared with the current methods. Specifically, innovative approaches involving edible or intradermal vaccine formulations have shown promise in eliciting both systemic and mucosal immune responses. This significant advantage, combined with the complete elimination of the need for subcutaneous injection using needles and syringes, represents a transformative breakthrough in enhancing vaccination coverage and eradication efforts. By eliminating sharps waste, reducing the requirements for cold chain storage, and simplifying logistics, MAPs enable the administration of vaccines by community volunteers, thereby facilitating routine outreach services and mass vaccination campaigns, including house-to-house vaccination initiatives that are occasionally necessary in areas where conventional systems struggle to reach all individuals. MAPs have been under development for over two decades by numerous academic and biotech laboratories, with at least 31 published randomized controlled trials, including two phase 3 clinical trials (examining parathyroid hormone for osteoporosis and zolmitriptan for acute migraine), assessing MAPs for drug delivery.[26] Novel approaches to vaccination have been put forth. Specifically, oral vaccinations that activate the GALT and intradermal methods that use Langerhans cells can stimulate the immune system on the mucosa as well as the system as a whole. As our understanding of these strategies has grown, so too have several preclinical investigations and a number of encouraging clinical trials. Furthermore, because these vaccination approaches are simple to administer and don't require a lot of antigen processing, they are regarded as safe and economical. Vaccination schedule and protocol[27] are shown in the following tables.

RESULTS

In 2010, India became the final country globally to incorporate the second dose of the measles vaccine into its national immunization program. Some states included the vaccine in the Universal Immunization Program (UIP) as a second booster, while the remaining 14 states administered it through Supplementary Immunization Activities (SIAs). By the conclusion of 2012, measles campaigns had been conducted in 137 districts across nine states, namely Arunachal Pradesh, Assam, Chhattisgarh, Haryana, Jharkhand, Manipur, Meghalaya, Nagaland, and Tripura, reaching nearly 27 million children. In five states (Bihar, Madhya Pradesh, Uttar Pradesh, Rajasthan, and Gujarat) where approximately 110 million children were targeted across 230 districts, a total of 61 districts had completed campaigns, resulting in the vaccination of about 26 million children. The accomplishment of India's immunization effort in the mid-1970s in eliminating smallpox. India's campaign has also been successful in eliminating poliomyelitis. India and the other ten Southeast Asian nations were declared polio-free in 2014. As per UNICEP India's health results have improved dramatically in the past 20 years, especially in the areas of immunisation and child health. 2015 saw the end of maternal and neonatal tetanus in the nation. Over 13 million vaccination sessions

are held countrywide to vaccinate children and pregnant women, with almost 26 million newborns and 34 million pregnant women targeted for immunization each year through UIP.

New vaccinations have been made available across the country, such as the Rotavirus Vaccine (RVV), Pneumococcal Conjugate Vaccine (PCV), and Measles-Rubella. The program's execution was determined to be average, ranging from 53.6% to 63.8%, while the cold chain and logistics for vaccines were found to be fair, ranging from 71.0% to 79.4% across all states.[28]

CONCLUSION

The Universal Immunization Programme (UIP) has played a pivotal role in providing a diverse array of vaccines tailored to target various diseases. This initiative has introduced a range of vaccines to combat the escalating prevalence of diseases in the country. The administration of these vaccines has been carried out through different methods, ultimately leading to a decrease in morbidity rates across India. However, the vaccination programme has not been without its challenges, particularly in dealing with migrant populations, which has resulted in an uptick in the transmission of vaccine preventable diseases. Despite these obstacles, the vaccination programme has yielded evident economic benefits, underscoring its crucial role in improving public health. A structured vaccine schedule has been devised to ensure the timely delivery of recommended doses for individuals of specific ages. Moreover, guidelines detailing the appropriate route, age, and site of vaccine administration for both pregnant women and children of all ages have also been outlined. Overall, the immunization programme has a profound impact on public health in India, delivering significant results across the nation.

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Table 1: Vaccine schedule

Age	Vaccines given
At birth	BCG, OPV , Hep B
At 6 weeks	DPT_1, OPV_1,Hep B_1, $RotaV_1$
At 10 weeks	DPT_2, OPV_2,Hep B_2, $RotaV_2$
At 14 weeks	DPT_3, OPV_3,Hep B_3, $RotaV_3$,IPV
At 9 months(completed)	Measles 1st dose, Vitamin(1 lac IU),JElive attenuated vaccine
Every six months till age of 6 years	Vitamin A (2Lac IU)
16-24 years	DPTB,OPVB,JE live, Measles 2nd dose
At 5-6 years	DPT
At 10years	TT
At 16 years	TT
For pregnant women	TT_1 and TT_2(1 month apart) TT booster if TT_2 doses received in last 3 years

Table 2: Vaccination protocol

Vaccine	Dose	Site	Route
For pregnant women			
TT-1	0.5 ml	Upper Arm	Intra-muscular
TT-2	0.5 ml	Upper Arm	Intra-muscular
TT- booster	0.5 ml	Upper Arm	Intra-muscular
For children			
DPT	0.5 ml	Antero-lateral side of mid-thigh	Intra-muscular
JE-2	0.5 ml	Left upper ARM	Sub-cutaneous
DPT booster -2	0.5 ml	Upper Arm	Intra-muscular
MR 2nd dose	0.5 ml	Right upper Arm	Sub-cutaneous
Vitamin A	2ml	Oral	Oral
OPV Booster	2 drops	oral	Oral
TT	0.5ml	Upper Arm	Intra-muscular

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RESEARCH ARTICLE

Inclusive Development of Fringe Areas in Tier II Metro City: A Step towards Inclusive City Region

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ABSTRACT

Urbanization is a spontaneous process that is increasing at an enormous scale globally. Currently, 56% of the world's population, or 4.4 billion inhabitants, are living in urban areas. This number is expected to increase to 68% by 2050. Population projections show that rural to urban migration and increasing urbanization, along with the growing global population, will add approximately 2.5 billion people to urban areas by 2050. Nearly 80% of the global GDP is generated in urban areas. Due to land availability, increasing land rates, and density saturation in urban areas, people are moving towards fringe areas. Hence, the fringe areas, also known as peri-urban areas, are continuously changing, and dynamic changes are observed in the spatial pattern of the fringe area. Urbanization leads to inclusive growth by enhancing productivity and innovation. As a component of the inclusive planning process, urban areas are saturated, and the potential for economic development of the urban fringes can be utilized through policy introductions related to inclusive development, which enhances sustainability at the regional level. Sustainable Development Goal 11 aims at making settlements and cities inclusive, safe, resilient, and sustainable. The challenge of inclusive development of fringe areas is primarily to overcome the separation of urban and rural planning and functions to achieve multifunctionality. The stimulation of sustainability and inclusiveness in urban fringes contributes to inclusive cities as a whole. Therefore, the analysis depicts a need for planning strategy intervention at the fringe area level that can lead to inclusive development at the regional, local, as well as the fringe area level. This research will justify methods for the inclusive development of fringes, which will eventually lead to inclusive regions with respect to SDG 11.A: Strengthening urban, peri-urban, and rural linkages for strong regional planning. The research aims to analyze the infrastructural parameters of the fringe areas of Lucknow city and provide

recommendations for inclusive development of basic services and infrastructure at the fringe area level, which will lead to strengthening the city-region through the regional planning approach in order to achieve SDG 11.A.

Keywords: Inclusive development, fringe areas, Tier II Indian metro cities, urban-rural disparities, sustainable growth, community well-being,SDG-11

INTRODUCTION

At a global scale , the urban areas are becoming dense and populous, with projections indicating that by 2050, 68% of the world's population will reside in urban areas. This trend is driven by various factors, including rural to urban migration, natural population growth, and economic opportunities concentrated in urban centers. As urban areas expand, they inevitably encroach upon their peripheries, giving rise to what are commonly referred to as fringe areas . The rural-urban fringe has been called 'planning's last frontier', and it is a frontier that is now receiving greater attention from policy makers. (Gallent, 2008)These fringe areas play a crucial role in accommodating the growing urban population, providing space for housing, industries, and infrastructure. Fringe areas of the Tier II metro cities in India have long been neglected, with basic public services and infrastructure lagging behind more affluent central and northern regions . However, these areas provide unique opportunities for inclusive development that can benefit the wider urban economy and society. The Urban area population is increasing all over the World, especially in the Global South where the shift from rural to urban life is still ongoing. (Buondonno, 2020)The importance of fringe areas in the context of urban expansion cannot be overstated. Not only do they serve as a buffer between urban and rural landscapes, but they also serve as hubs of economic activity and innovation. Urbanization has exerted a significant pressure on both Urban and fringe areas, due to the increasing urban population the infrastructural capacity gets outpaced leading to inadequate services . The infrastructure faces frequent breakdowns resulting in inefficient delivery. (Singh, 2005) Against this backdrop, there is a compelling rationale for focusing on inclusive development in fringe areas. Inclusive development seeks to ensure that the benefits of growth and development are shared equitably among all segments of society, including the most vulnerable and marginalized. Figure 1 shows the status of India's population with respect to the global scenario, it further depicts that in April 2023, India has surpassed China to become the world's most populous country. India's population reached approximately 1.428 billion people, Source: (buccholz, 2022) In a nutshell it can be concluded that India is the most populous country globally and hence demands intense attention for inclusive regional development.

Urbanization rate in India , which is the annual percentage change of the urban population share, was 1.34% in 2021, up 1.5% from the previous year which depicts that the urban population grew faster than the total population. Currently 97 number of tier II cities exist in India. Figure 2 depicts urbanization trends in India , India's urban population stands at approximately 461 million people. Source: (The Department of Economic and Social Affairs, 2019) It can be concluded from figure 2 ; that a significant portion of the urban infrastructure projected for 2050 is yet to be constructed, indicating a substantial shortfall in current urban infrastructure investment. This gap is not just a matter of future planning but is already having a negative impact, as it hinders inclusive development. The insufficient infrastructure investment , therefore is a critical barrier to achieving the necessary urban growth and development by 2050.

Major challenges of Urbanization in Uttar Pradesh

Urbanization in Uttar Pradesh currently at crossroads, there is a complete lack of policies to tackle urbanization. Biggest threat to urbanization is lack of employment , housing and Infrastructure. Due to the absence of Urban land policy the process of creating land bank for infrastructure and housing becomes challenging . Due to lack of robust planning framework , the development often occurs in an ad-hoc manner, leading to unplanned organic growth. Government institutions lack capacity to tackle skill and capacity building gaps in Infrastructure that has been

created due to urbanization. This inadequacy of infrastructure leads to poor living conditions . Uttar Pradesh consists of 4 number of tier II metro cities namely; Lucknow , Kanpur , Agra and Meerut . Lucknow being the capital city of Uttar Pradesh is renowned for its rich cultural heritage and rapid development and is also serving as a regional hub for education and economy in the state.

Potential of Tier II Metro cities

The growth of Tier II metro cities has been accompanied by the rapid expansion of their fringe areas, presenting both challenges and opportunities for inclusive development due to the existing disparities. Tier II cities, which function as significant regional hubs, are experiencing substantial population and economic growth due to urbanization and industrialization. As core urban areas become saturated, the expansion of fringe areas transitional zones between urban and rural settings becomes inevitable. Figure 3 depicts the possible parameters for potentiality of Tier II metro cities. These Tier II metro cities serve as centers of economic and Urban development Infrastructure development plays a crucial role in utilising the potential of tier II metro city. Source: (Tier 2 Pioneers: Capitalizing on Emerging Real Estate Trends, 2024) It can be inferred from the figure 3 that infrastructure development plays a vital role in urban growth, economic progress, and investment strategies. The segments suggest that prioritizing infrastructure is crucial for achieving sustainable urban development and maximizing investment returns.

Dynamics of Urbanization and Fringe Area

The dynamics of urbanization and fringe area transformation are shaped by a complex interplay of demographic, economic, and spatial factors. Spatially, urban expansion follows distinct patterns, often characterized by concentric rings of development radiating outward from the city center. Fringe areas are a transition from rural to urban land uses and experiencing rapid changes in land use patterns and spatial organization. This spatial transformation is accompanied by a host of challenges, including environmental degradation, loss of agricultural land, and the proliferation of informal settlements. There are several examples of haphazard growth in the fringe areas of developed towns especially in India. (Howlader, 2020)The urban fringe linkages have a bearing on the livelihood and well being over space and can create regional economies .(Fazal,2014). Figure 4 depicts Peri-urban (fringe) linkages that exist over time, these include the linkages to rural, urban areas ,other peri urban areas and within a peri urban area .Source: (Piorr, 2013) These linkages comprise of forward linkages such as access to services , infrastructure , employments and markets and backward linkages such as ecosystem services , Land based employment , leisure and tourism , Housing development , Commercial development ,Health and educational facilities and transport and infrastructure . This figure further interprets that approaches incorporated at the fringe level can lead to enhancement at the city-region level .In conclusion, infrastructure approaches at the fringe level can lead to significant enhancements at the city-region level by promoting decentralization, improving connectivity, fostering economic diversification, and setting sustainable development standards. These actions help create a more balanced, resilient, and dynamic urban region, with benefits that extend far beyond the fringe areas themselves.

Linkages between Inclusive Development and Inclusive Region-Building

The approach of Inclusive development aims at creating equitable access to infrastructure, opportunities and reduction of disparities whereas an inclusive region is characterized by its efforts to reduce regional inequalities .The linkages between inclusive development and inclusive region- building are fundamental to understanding how targeted interventions in fringe areas of Tier II metro cities can contribute to broader regional development goals. Inclusive region-building extends this concept to the regional level, aiming to create an environment where all areas within a region, including urban cores, peri-urban areas, and rural hinterlands, contribute to and benefit from economic growth, social progress, and environmental sustainability. The linkages between inclusive development and inclusive region-building underscore the importance of holistic and integrated approaches to development that address the needs of all communities within a region. By focusing on inclusive development in fringe areas, policymakers can catalyze broader regional development processes that promote equity, sustainability, and social cohesion across the entire region. The process of evolution of fringe areas in Tier II metro cities is a pivotal step towards fostering inclusive growth and creating a more balanced and equitable region. As these Tier II metro cities serve as regional hubs, these fringe areas play a crucial role in regional balance by reducing urban congestion ,

creating better employment opportunities , improving infrastructure and services and promoting balanced urban development. The following points depicted in Figure 5 elucidate the linkages between inclusive development and inclusive region-building: Source: Generated by Author Each of the above mentioned parameters is vital for achieving a balanced and equitable region ,though infrastructure serves as a foundation that supports and enhances the other elements, such as enabling governance, promoting economic integration, and ensuring environmental sustainability. Hence this research paper will focus on infrastructure aspects only. It will aim to understand how interventions related to enhancement of infrastructure at the fringe level can lead to creation of a inclusive city region through the regional planning approach.

Introduction to the Study Area

The study area is Bakshi ka talaab(BKT) which is a fringe area in the district of Lucknow, Uttar Pradesh. BKT is situated on the North of Lucknow along the Sitapur Road,at a distance of 17 kilometers from city centre or core . Lucknow is the state capital of India's most populous state Uttar Pradesh consists of 5 fringe areas namely Kakori ,Kalli Paschim, Sarsawan , Gosainganj and Bakshi ka talab (these fringes have been delineated in Map 1). The current status of Uttar Pradesh depicts strong regional imbalance between eastern and western parts . Table 1 emphasizes the statistics of fringe areas of Lucknow , Bakshi ka talaab being the largest fringe area in Lucknow in terms of both area and population. Source: Generated by Author using ArcG is Source: Generated by Author

Infrastructure Scenario of the Study Area

The existing Level of service(LOS) of the physical infrastructure scenario of Bakshi ka Talaab has been analyzed with respect to water supply, sanitation, solid waste management and along with social infrastructure like education and health . The Sample size for physical infrastructure is 200.

Water Supply

Over recent years, Bakshi ka talaab area has witnessed growth which has led to increase in infrastructure needs , including water supply. The primary source of water in Bakshi ka talaab comes from groundwater, accessed through bore wells and hand pumps, which cater to the daily needs of the local population. However, with the rapid pace of development, there is an increasing demand for a more reliable and sustainable water supply system. The area faces challenges such as inconsistent water quality, limited access during peak demand periods, and the need for improved distribution networks. The parameters studied for water supply were Sources of water supply ,reasons for lack of access to public water supply , location of Sources of water supply , and average distance travelled to fetch water . Figure 6 depicts the sources of water supply ,only 26.7% are dependant on public ground water sources i.e hand pump and 67.9% households were dependant on bore well with submersible pumps. For water supply Bakshi ka talaab is totally dependant upon the groundwater sources such as submersible pump and hand pump due to absence of a piped water supply delivery system. A major percentage of the households that were surveyed were dependent upon private individual borewells along with submersible pump which depicts limited access to public water systems and vulnerability to water scarcity and fluctuations in ground water levels. Figure 7,the pie-chart represents the possible reasons for lack of access to public water supply in percentage as reported by the households during the survey, the major reason reported by (95% of the sample households was absence of Distribution line
Source: Generated by Author on basis of Survey data The survey results clearly point out that the lack of infrastructure, specifically distribution lines, is the most critical barrier to accessing public water supply in the surveyed area. Figure 8 shows the ease of access to water is has been accessed using the parameter location of water supply source .Through the survey it was concluded that 29% percent of households donot have water supply source available within their house premises whereas 71% households have water supply source inside premises . Source: Generated by Author on basis of Survey data It can be inferred from the Figure 8 that habitants face challenges in accessing clean and safe drinking water and exposed to risk of waterborne diseases and sanitation-related issues . One-third of the households still lack ease of access, highlighting a gap in the water supply infrastructure. Addressing this gap by extending on-premises water supply to these households could enhance overall accessibility, reduce the burden on affected households, and improve their living conditions .

Figure 9 depicts the average distance which is travelled to fetch water . It is depicted via Figure 9 that approximately in 42 % of households people travel more than 10 meters to fetch water It was also stated via the primary survey that 3/4th households the work of fetching water is done by females depicting gender inequality and leading to social issues. Source: Generated by Author on basis of Survey data In a nutshell it can be concluded that there is a physical and time burden on individuals and lack of infrastructure availability at household level also A gender inequality is existent in three-quarters (75%) of the households, the task of fetching water is primarily performed by females. This highlights a significant gender disparity, where women and girls disproportionately bear the burden of water collection. Figure 10 shows that 100% samples have chemical contamination present both in case of borewell and hand pump and 88.2% samples of submersible pumps had bacteriological contamination and 54.5% samples of hand pump had bacterilogical contamination. Source: Generated by Author on basis of Survey data It can be concluded that widespread contamination of groundwater resources is existent .The reason can be due to agricultural runoff, industrial discharge, or improper waste disposal .

Sanitation

Access to safe sanitation has been prioritised in India via Swachh Bharat Mission(SBM) scheme. The parameters analysed for accesing the Sanitation scenario of BKT is functional Status of toilet , typology of toilet available and typology of Sanitation systems . It id depicted via figure 11 revealed via survey that 12.9% of the total households lacked IHHL (Indian Household Latrine) and 87.1 had functional toilets at home. lacks access to basic sanitation facilities and practice of open defecation . Source: Generated by Author on basis of Survey data It is inferred from the above figure that a considerable percentage lacks access to basic sanitation facilities and practice of open defecation .In the figure 12 , it is depicted that 88.5% had Simple containment structure as the toilet type i.e simple holding tanks have not desludged their pits yet. One of the main issues with simple containment structures is that the simple containment structures have their waste outlet into the open drains . Source: Generated by Author on basis of Survey data There is a lack of proper management of faecal waste. There is a major absence of septic tanks ,increasing the risk of groundwater contamination. 3 public toilets and 19 community toilets were present in the area ,whose septic tank was directly connected to the drains. Figure 13 represents the on-site sanitation systems. As there is no functional sewerage network existing, hence the households are dependant upon on site sanitation systems .
Source: (Singh D. , 2020). The presense of On-site sanitation systems have risk of groundwater contamination , Health risks , Issues of maintenance .

Solid Waste Management

The Solid waste Management scenario of Bakshi ka Talaab ,Lucknow is analyzed using Per Capita waste generation , Segregation of Solid waste at source and Waste disposal method .It is depicted in figure 14,majority percentage of waste generated comprises of Bio-Degradable waste i.e 52.8gms per capita whereas 3.5gms is Hazardous waste .
Source: Generated by Author on basis of Survey data The presence of Hazardous and Inert waste requires safe collection, storage, and disposal to mitigate any potential risks. Only 48% of households had segregation of waste at source (Figure 15) reveals a significant gap in waste management practices . Source: Generated by Author on basis of Survey data It can be inferred from figure 15 that more than half of the households does not participate in separating waste at the source, which can lead to inefficiencies in recycling and increased strain on waste management systems. This also depicts lack of community awareness. Figure 16 represents waste disposal methods used depicts 42% of Waste disposed by Landfill ,7.7% of waste to energy and 50.3% of other disposal methods that includes composting Source: Generated by Author on basis of Survey data The landfill site was located at a distance 20kms from the study area due to which major percentage was dependant on other methods of disposal such as composting. Major dependence on composting is due to the percentage of Bio-degradable waste .

Education

Education is foundational to sustainable development. Good educational infrastructure helps equip the local population with the skills and knowledge necessary to participate in and contribute to economic growth. This is essential for peri-urban areas that are increasingly becoming hubs for economic activities and need a skilled workforce . Education scenario of Bakshi ka Talaab has been accessed by two parameters i.e Percentage of Literates

and Availability of Schools . The current Literacy rate of India stands at 77.70%, with literate males at 84.70% and literate females at 70.30% and Literacy rate of Lucknow is 82.50% of which male and female literacy was 86.04% and 78.70% percent. The percentage of literates in Bakshi ka Talaab data is shown in figure 17 ,which reveals the percentage literates along with male and female literate percentages is below the percentage literates of Lucknow..The low percentage is the root cause for social inequality , economic impact, lack of awareness and deficit of infrastructure. Source: Generated by Author on basis of Census Data Figure 18 represents the availability of schools in BKT. As per URDPFI there is a requirement of 20 primary schools , 4 secondary schools , and 7 senior secondary schools . Accessing the current scenario of educational infrastructure there is a shortage of 4 Senior secondary schools . Also in some cases the gap is fulfilled because of private schools but people of BKT are not able to afford the same which is leading to unequal access to education . Also there is lack of government primary schools in BKT, which depicts a gap in access to basic education for children in this region. Source: Generated by Author on basis of Census Data This leads to issues such as educational inequality, leading to lower enrollment rates, poor literacy, and limited opportunities for child.

Health

For assessing the health infrastructure scenario of Bakshi ka Talaab The availability of hospitals and beds has been taken into account . As per URDPFI guidelines there is a need of 3 dispensaries ,1maternity centre with 25-30 beds ,1 Intermediate hospital with about 100 beds and 1 General hospital .Figure 19 depicts , There is a shortage of 2 dispensary in the BKT fringe which cause delays in receiving basic medical attention. There is a shortage of 27 beds in the maternity centre. Similarily a Shortage of 80 beds exists at general and intermediate hospital respectively . These shortages indicate a need for improved health infrastructure in BKT to meet the growing demand and ensure better healthcare delivery. Source: Generated by Author on basis of Census Data

CONCLUSION

A gap exists between the fringe areas and urban areas of Lucknow, characterized by uneven urban growth, infrastructural gaps, and limited availability of services and facilities..The study area, Bakshi ka Talaab lacks the robust infrastructure found in urban areas of Lucknow. Water supply issues such as lack of piped water supply system ,lack of household tap connections and contamination of water sources. Similarily, Sanitation issues exist such as Lack of IHHL at household level, inefficiency in management of faecal waste, absence of septic tanks. Solid waste management scenario of BKT lacks proper segregation of waste and disposal of waste. Households of fringe areas of BKT face hindrances in accessing essential services such as healthcare and education, contributing to a lower quality of life compared to urban areas.Also a lower literacy rate is observed in the fringe of BKT in comparison to literacy rate of Lucknow . Overall a disparity is existing in the urban and fringe areas of Lucknow which is hampering the development of Lucknow city-region . Overall, inclusive development of fringe areas in Tier II metro cities is essential for creating a more balanced, resilient, and cohesive region where all residents have equitable access to opportunities and services .

Recommendations

The basic approach is to strengthen Urban and Peri-Urban (fringes) in a city-region by the development of the basic services and the infrastructure in fringe areas for strengthening the city-Region through the regional planning approach ,in order to make the city-region inclusive. The figure 20 describes the strengthening of the city-region via development of the basic services in the fringe areas .It basically suggests the methodology we will be using to make the region inclusive. Source: Generated by Author The Figure 21 depicts recommendations for development of basic services and Infrastructure in the fringe areas of Bakshi ka talaab that will contribute to strengthening of the city-region along with making the region Inclusive . The integration of the basic services and infrastructure in the fringe areas can contribute to making city-region as a whole

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Table 3: A glimpse of basic statistics of fringe area of Lucknow City Region as per LDA Master plan 2031

S.No	Name	Area (in sq.km)	Population	Distance from Core
1	**Bakshi ka Talaab**	**41.9**	**49166**	**17**
2	Kakori	3	19403	19
3	Kalli Pashchim	14.4	12157	16
4	Sarsawan	6.06	10655	9
5	Gosainganj	5.9	9649	22

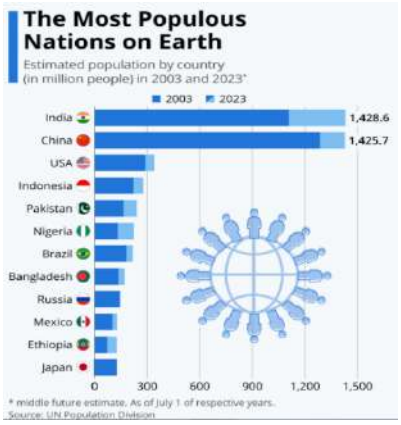

Figure.3: Showing the status of India's Population with respect to the Global scenario.

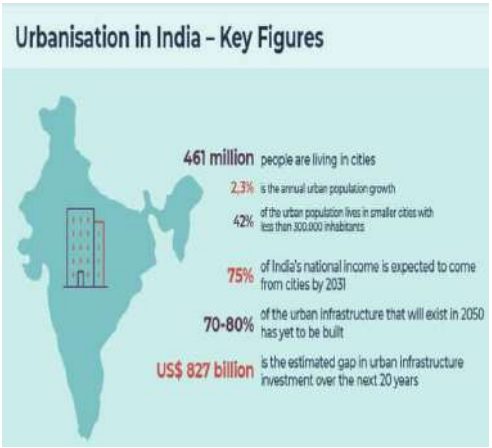

Figure.4:Shows Urbanization trends in India and associated

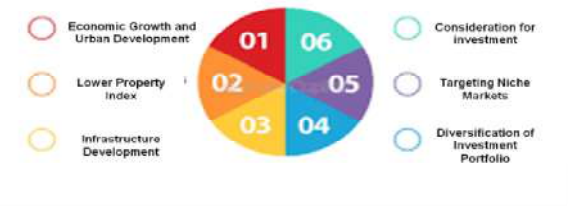

Figure.5:Shows the parameters of potentiality of Tier II metro cities in India

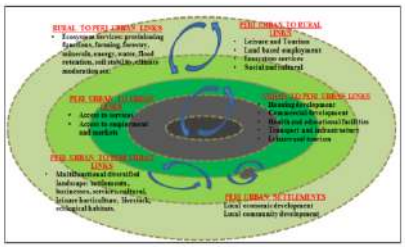

Figure.6:Shows the forward and backward linkages of Peri-urban areas with urban core

Figure 7:Linkage between inclusive development and city-region

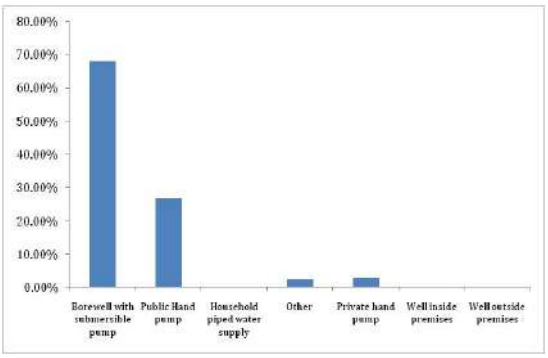

Figure 8 : Sources of water supply

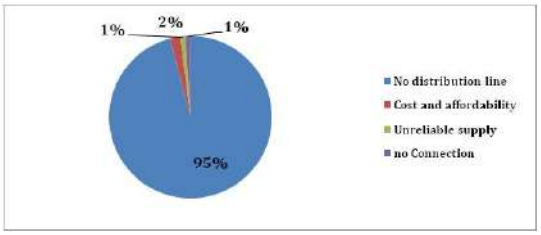

Figure 9 :Reasons for Lack of access to public water supply

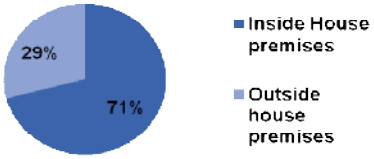

Figure 10 : Location of Sources of Primary Water Supply

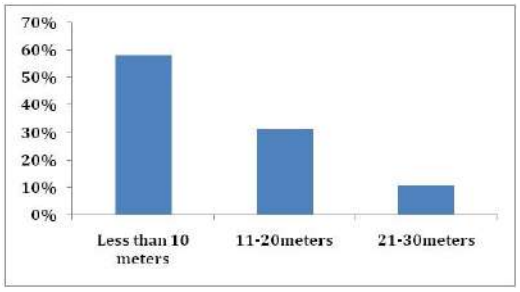

Figure 11: Average Distance travelled to fetch water

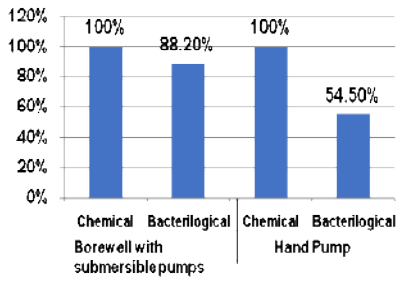

Figure 12 : Contamination levels of water at Source

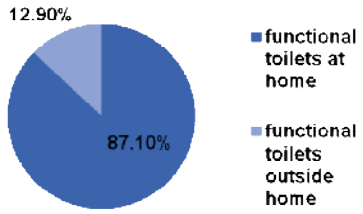

Figure 13 : Status of Functional Toilet

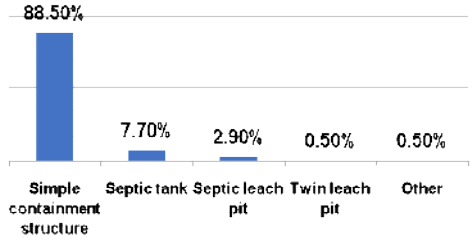

Figure 14 : Typology of toilet available

Figure 15 : Shows On-site sanitation systems in Bakshi ka Talaab

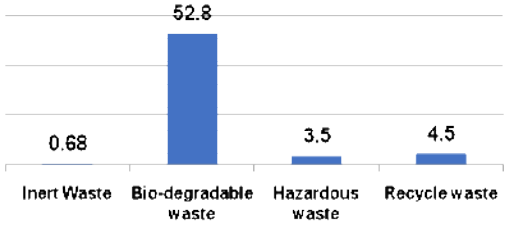

Figure 16:Per Capita waste generation (gms)

Figure 17 : Segregation of Solid waste at source

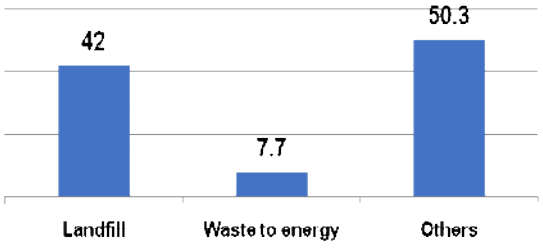

Figure 18: Waste Disposal Method

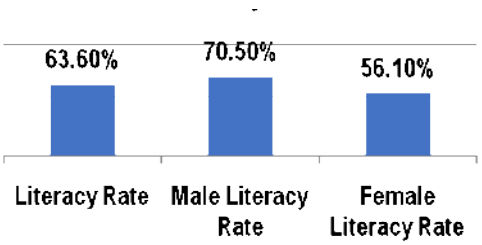

Figure.19:Percentage of Literates in BKT

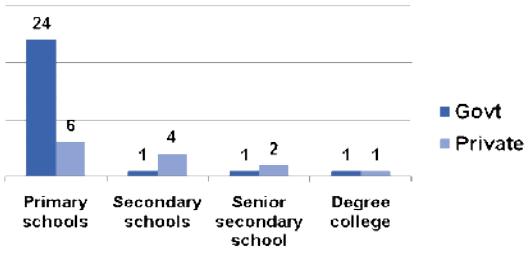

Figure .20:Availability of Schools in BKT

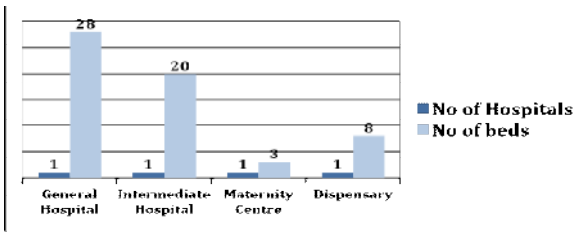

Figure 21: Availability of Health Infrastructure in BKT

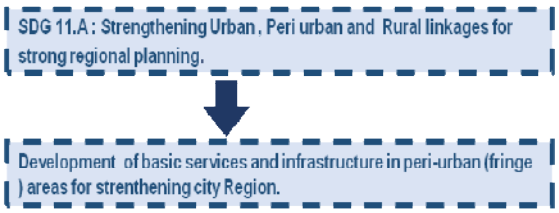

Figure 22: Strengthening Urban-Peri-urban Linkages

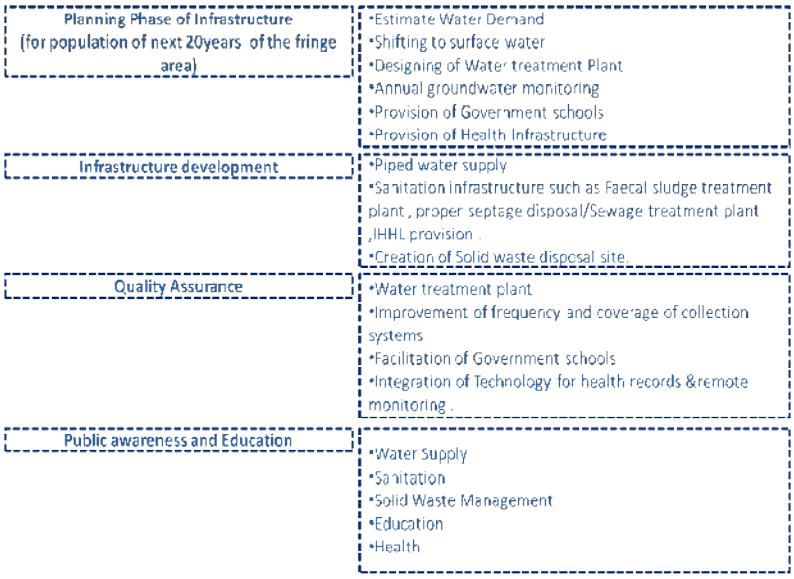

Figure 23: Development of basic services and Infrastructure

RESEARCH ARTICLE

Impact of Obesity on the Efficacy of Different Combined Kinetic Chain Exercise Protocols in Knee Joint Osteoarthritis

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ABSTRACT

Obesity and knee joint osteoarthritis often occur concomitantly. Obesity, a global issue,has been stated as the most robust alterable predisposing factor of knee joint osteoarthritis. Exercise has been found to be the first line of management of knee joint osteoarthritis. But the impact of obesity on exercise treatment protocols has not been studied in literature. To address this gap, in this study, 151 subjects, females, aged 40-65 years with knee osteoarthritis were randomly allocated to either of the three groups all using different combinations of combined kinetic chain exercises: group 1 (Control group: conventional combined kinetic chain exercises), group 2 (Conventional combined kinetic chain exercises and retro walking) or group 3 (Conventional combined kinetic chain exercises and perturbation training). Subjects performed exercises 3 days every week for a period of 6 weeks. Outcome measures utilized were, Numeric Pain Rating Scale (NPRS), Timed Up and Go test (TUG) and Lower Extremity Functional Scale (LEFS). Body Mass Index (BMI) was utilized to assess obesity. SPSS 21.0 version was used for all statistical analysis. Paired t-test was used for comparisons within group and unpaired t-test was used for comparisons between groups. Level of significance was considered as $p<0.05$.Statistically significant improvements in outcome measures were seen within all the three groups at the end of 6 weeks of treatment. Statistically significant better improvements as shown by the outcome measures were observed in non -obese subjects in contrast to obese subjects. Subjects in both the experimental groups exhibited statistically significant improvements than the control group in all outcome measures. It can be

concluded that obesity has a negative impact on the efficacy of all three protocols of combined kinetic chain exercises. Hence, management of obesity is must for the optimum efficacy of combined kinetic chain exercises. Moreover, the comparison of Conventional combined kinetic chain exercises and retro walking versus Conventional combined kinetic chain exercises and perturbation training shows similar efficacy to one another but significantly better efficacy than conventional exercises alone.

Keywords: Knee osteoarthritis (OA), Obesity, Combined Kinetic Chain Exercises (CCE), Retro walking, Perturbation training.

INTRODUCTION

American Rheumatism Association has defined osteoarthritis as "a heterogeneous group of conditions that lead to joint symptoms and signs which are associated with defective integrity of cartilage, in addition to the related changes in underlying bone and at the joint margin"[1]. Osteoarthritis (OA) is categorized to be the 5th highest factor causing years lived with disability amongst people of developed nations, and the 9thleading factor in under developed and developing nations[2]. It is a condition which may involve joints like the knees, hips, hands, feet, and spine. The entire joint may be involved in OA leading to physical impairments like swelling, pain, stiffness etc. and also impairing mental health due to its chronic nature [3]. The knee joint, a key factor in maintaining balance of the human body, is the most commonly affected lower-limb joint [4]. During the last decade, the prevalence of knee osteoarthritis has more than doubled making it the 10th largest contributor to global years lived with disability [5]. As stated bya recent study of 2020, the pooled global prevalence of osteoarthritis of the knee was 22.9% in people aged ≥40 years. The study also reported that there are around 654.1 million people aged 40 years or more with knee OA in 2020 worldwide and the prevalence in Asia was 19.2% [6]. Thus, knee osteoarthritis is an extremely common form of arthritis globally irrespective of whether it is a developed or developing nation. In a community based cross-sectional study of 2020, the universal prevalence of knee OA was recorded as 35.7% with greater prevalence among females (44.5%) [7]. The estimated prevalence of OA knee among women of 40-65 years in Guwahati, Assam, India was found to be 28.3% , hence depicting that the local prevalence as high too [8].

A critical role is played by physiotherapists in the conservative treatment of knee OA and exercise therapy is firmly acknowledged as a significant way of providing physiotherapy treatment for this purpose[9-15].Traditionally different protocols of open kinetic chain(OKC) and closed kinetic chain (CKC) exercises such as straight leg raising exercise, static quadriceps, terminal knee extension, leg press, isometric hip adduction exercise, and semi-squat have been routinely used by clinicians in their practice globally [16]. OKC exercises as progressive resisted exercises can be prescribed in osteoarthritis in various ways e.g. dynamic quadriceps, hip flexion or extension exercises etc. CKC exercises in knee OA can be included in many ways e.g. static quadriceps, squats, retrowalking or agility and perturbation exercises. A fair amount of studies in the literature also reveal that Combined Chain Exercises (CCEs) are better than either OKC or CKC exercises alone for relieving pain in knee OA patients. A blend of OKCs and CKCs in treating osteoarthritis of knee showed promising results[16]. Majority of the cases of osteoarthritis have a clear predisposing factor which makes them vulnerable, such as aging, trauma, obesity, overuse, genetics, occupation, gender and ethnicity, decreased bone density, improper diet etc. yielding the impression that OA portrays a common climax with varied causes [17-18]. Obesity, a global issue, has been stated as the most robust alterable predisposing factor of knee joint osteoarthritis[19]. Literature reveals that the risk of acquiring knee OA multiplies nearly 7-times in people with body mass index above 30 kg/m^2 [20].Despite the high volume of publications on the subject, there are still gaps in our understanding of whether obesity has an impact on the treatment outcomes of osteoarthritis.

There have been a number of studies which have evaluated the efficacy of combined kinetic chain exercises in the management of knee joint osteoarthritis but no study has evaluated whether obesity may have an impact on the

effectiveness of an exercise protocol or not. Hence, the purpose of this study was to analyse if obesity had an impact on the efficacy of combined kinetic chain exercises in the management of knee joint osteoarthritis.

MATERIALS AND METHODS

Study Design

It was an experimental design which utilized balanced, randomized allocation to 3 parallel groups: conventional Combined Kinetic Chain Exercises (CCE), conventional CCE and retro-walking training, or conventional CCE and perturbation exercises. The Declaration of Helsinki and CONSORT guidelines were followed in the study [21].

Sample Design

Purposive Sampling technique depending on inclusion criteria, exclusion criteria and subjects diagnosed as knee OA referred by orthopaedic doctor or physician after thorough examinations and investigations - randomly allocated to one of the 3 groups: Group 1, Group 2 or Group 3.

Source of Data

Knee OA patients referred for physiotherapy by physician or orthopaedic doctor at Physical Medicine and Rehabilitation OPD of Gauhati Medical College and Hospital, Bhangagarh, Guwahati, Assam.

Criteria for Sample Selection

[22-25].

Inclusion criteria

Age group 40-65 years; Females with menopause or menopause related symptoms;Diagnosed as a case of knee OA according to the American College of Rheumatology (ACR) criteria; Patients with unilateral/bilateral involvement**;** Radiographic grade of 2 –3 as per Kellegren-Lawrence; Knee pain for more than 6 weeks

Exclusion criteria

Males ; Patients <40 years of age and >65 years of age**;** Not fulfilling ACR criteria for diagnosis of knee OA**;** Knee pain for less than 6 weeks ; Low back ache; History of any lower limb injury or underlying pathology or surgery; Any spinal surgery ; Any physical / medical problems wherein exercises are contraindicated;Deformity of knee/ hip/ back**;** History of inflammatory joint disease **;** Patients utilizing an assistive device for walking**;** Patients who has undergone physiotherapy treatment or intra-articular injection at knee within a span of last 3 months.**;** Any established mental illness.

Randomization and Blinding

The subjects fulfilling the inclusion criteria were randomly allocated to one of the 3 groups (1, 2 or 3). An on-line tool with a random number generator function was utilized for randomization[26].Physiotherapists assessing outcome measures and statisticians were blinded to group allocation.

Outcome measures

[27-30]

Body Mass Index (BMI)
For assessment of obesity

Numeric Pain Rating Scale (NPRS)
For assessment of the intensity of pain (A reduction of 2 points, or 30%, on the NPRS scores were reported to be to be clinically important)

Timed up and Go Test (TUG)
For assessment of the mobility of the patient (The minimum detectable change MDC, based on measurements by a single ratter and between raters, was 1.10 and 1.14 seconds, respectively) Lower Extremity Functional Scale (LEFS): For assessment of physical function (The MDC for the LEFS is 9 points)

Ethical Clearance
Ethical clearance was obtained from Assam down town University Ethics Committee as well as from Gauhati Medical College and Hospital Institutional Ethical clearance committee (adtu /Ethics /PhD Scholar /2019/008)&(190/2007/Pt-II/Oct-2019/62)

Methodology
Baseline assessments of obesity, pain, mobility, physical function were recorded for all the groups using the outcome measures. After completion of all baseline measurements participants were randomly allocated to one of two intervention groups (Group 2 or Group 3) or the control group (Group 1).
GROUP 1 (control group):
Subjects received conventional combined kinetic chain exercises 3 days per week for 6 weeks.
GROUP 2 (experimental group): Subjects received retro walking training along with conventional combined kinetic chain exercises 3 days per week for 6 weeks.
GROUP 3 (experimental group): Subjects received and perturbation exercises along with conventional combined kinetic chain exercises 3 days per week for 6 weeks.
Subjects were restricted from doing any home exercise or walking program other than the prescribed program. All exercises were performed bilaterally and all the participants received moist heat[31] for 10 minutes around the affected knee joint before exercise.

Conventional Combined Kinetic Chain Exercises: [10, 32-34]
Participants in all the three groups received a supervised conventional combined kinetic chain exercise protocol, a combination of open and closed kinetic chain exercises from previous published studies consisting of Open kinetic chain exercises: Straight leg raising (SLR) and Full-arc extension and closed kinetic chain exercises: Quadriceps setting and Wall slides.

Retro walking:[16, 31]
Warm-up (ankle toe movements, hamstring and calf muscle stretching, and heel raise exercises); Retro walking (The participants underwent a supervised 10 min backward walking training on a flat surface at their comfortable speed and gradually increased the walking time up to 30 min over a period of 6 weeks); Cool down (same exercises as performed in the warm up phase).

Perturbation Exercises:[31, 35]
Double leg foam balance activity, Wobble board (tilt board) balance training, Roller board and platform perturbations. Post-treatment assessment of Pain, Range of Motion, Mobility and Physical Function were recorded after 6 weeks of intervention for all the groups for comparison with the pre-treatment assessment data.

Statistical Analysis

SPSS 21.0 version was used for all statistical calculations. Demographic data and baseline scores of all outcome measures were utilized to appraise the baseline comparability of treatment groups. One way Analysis of variance(ANOVA) was used for significance testing in the mean age of study participants between the three groups. Descriptive data was reported for each group as the mean change in the outcome measures at baseline and at the end of the 6 weeks of treatment. Paired t-test and unpaired t-test were used for within group and between group comparisons respectively. The statistical significance was determined at a significance level of 0.05. For statistical analysis to determine whether obesity had an impact on the effectiveness of the combined kinetic chain exercises across all groups, the participants were classified into two categories in each group of the study according to their BMI. Pertaining to this study, body mass index was considered in a dichotomous format, non-obese (<30) versus obese (≥30).

RESULTS AND DISCUSSION

The subjects who participated in all the three groups of the study were comparable at baseline with regard to age, sex and severity of knee joint osteoarthritis; hence, any consequent difference in outcome measures between them after treatment can be attributed to the difference in the effectiveness of the interventions. Statistically very high significant differences have been observed between pre and post NPRS, pre and post TUG as well as in pre and post LEFS in all the three groups (Table no. 1,2 & 3). This implies that combined kinetic chain exercises, in general, are highly effective in the treatment of OA knee. The significant effects of all the three different protocols of CCEs on pain, mobility and physical function is consistent with reports from a previous study by Olabegi *et al*. in which they reported the superiority of CCEs over OKC and CKC exercises [32]. The main intention of this study was to evaluate the impact of obesity, as measured by BMI, on the efficacy of CCEs in the treatment of knee joint osteoarthritis. According to the established minimal detectable change values for outcome measures, apart from improvement in physical function (as measured by LEFS) for obese participants in Group 1 and Group 3, clinically meaningful improvement was seen across all groups for all outcome measures for non-obese as well as obese participants. On comparative analysis between the obese and non-obese subjects in all the groups, it was found that: In Group 1(CCE alone): Mean improvement was better in all outcome measures in non-obese participants as compared to obese(Table no. 4). Furthermore, improvement in physical function for obese subjects was not clinically meaningful whereas, clinically meaningful improvement was seen across all groups for all outcome measures for non-obese subjects. Improvement seen in non-obese subjects was statistically significantly better as compared to obese subjects in TUG and LEFS ($p<0.001$) though not significant in NPRS ($p=0.255$). In Group 2 (CCE and retro walking): Mean improvement was better in all outcome measures in non-obese subjects as compared to obese(Table no.5). Clinically meaningful improvement was seen across all groups for all outcome measures for non-obese as well as obese subjects. Statistically significant better improvement was observed in non-obese subjects in comparison to obese as depicted by NPRS, TUG and LEFS ($p<0.001$). In Group 3 (CCE and perturbation exercises): Mean improvement was better in all outcome measures in non-obese participants as compared to obese(Table no. 6). Furthermore, according to previous established data [30], improvement in physical function for obese participants was not clinically meaningful whereas, clinically meaningful improvement was seen across all groups for all outcome measures for non-obese participants. Statistically significant better improvement was observed in non-obese participants in contrast to obese as shown by NPRS, TUG and LEFS ($p<0.001$). Thus, the results reveal that combined kinetic chain exercises are effective in knee joint osteoarthritis across all the groups in knee joint osteoarthritis. Furthermore, though improvement is seen in non-obese as well as obese subjects but statistically significant better improvements are seen in non-obese subjects as compared to obese in all outcome measures across all groups, except in improvements of pain scores in Group 1(Table no.4, 5, 6).Hence, these finding support an interrelation between obesity and reduced improvements in treatment outcomes for osteoarthritis whether measured by pain (NPRS), functional mobility(TUG), or physical function(LEFS). In the present study, among the 150 participants, 6.7% had

normal weight, 56% were overweight, 24.7% had stage I obesity, 19 12.6% had stage II/ stage III obesity. The values are comparable to a previous study done by Raud *et al.* ,in which they found the characteristics of their participants as follows: 57.0% were overweight, 28.4% had stage I obesity and 14.6% had stage II/III obesity. It also proves that obesity is a robust factor in the occurrence of osteoarthritis[36]. The connection between obesity and OA has been extensively discussed in published research papers. Studies of knee OA propose obesity to be linked with a diminished quality of life and greater risk of disability[37] and also as affecting knee joint impact rates hence leading to enhanced pain[38]. But as per database search by the author, this is the first study to describe the impact of obesity, as measured by BMI, on the effectiveness of combined kinetic chain exercises in knee joint osteoarthritis.

Rehabilitation or physical activity is globally accepted as one of the first non-pharmacological approach of treatment for knee osteoarthritis and is advocated for all sufferers [39]. The present study demonstrated that obesity decreases the effectiveness of rehabilitation(Table no.4,5,6).Another study concluded thatsincelow BMI was associated with higher physical activity and aided in averting the clinical outcomes of knee OA, hence the plan of action to treat knee OA should vary according to the severity of obesity. Physical activity aids in enhancing function, but when severity of obesity increases, it leads to altered function, thus reducing the amount of physical activity carried out [36].Hence, a mandatory assessment of BMI of each patient before initiation of knee OA rehabilitation may be recommended so that a weight loss program may be included for obese patients to improve the effectiveness of physiotherapy rehabilitation protocols. Research shows patients' efforts towards losing weight can be facilitated by healthcare providers' support and that empathy of clinician motivates patient to engage in activities that lead to weight reduction [40, 41]. Therefore it is important that a compassionate, non-stigmatizing approach is taken by healthcare providers in this matter. Previous research on knee OA has demonstrated that a 5% reduction in body weight resulted in decreased knee joint pain, which is a major reason of prescribing physical activity in knee OA, and a 10% weight reduction correlated with moderate-to-large improvements[42].

In view of this present study, a comparative statistical analysis was also performed which revealed that subjects in the groups 2 and 3(both experimental groups) exhibited statistically significant improvements than Group 1 (control group) in all outcome measures(Table no.7 & 8). Additionally, though Group 2 showed better mean improvements in all outcome measures when compared to group 3 but the differences were not statistically significant. It can be deduced that the comparison of Conventional exercises and retro walking versus Conventional exercises and perturbation training shows similar efficacy to one another but significantly better efficacy than conventional exercises alone.

Improvement seen in Group 1 could be attributed to the strengthening exercises for hip and knee. The principal outcomes of the current study seem to corroborate with the earlier research studies showing reduction in pain and increase in mobility and physical function after strengthening exercises[43, 44]. The improvements in Group 2 may be by virtue of the unique kinematics of retro walking. Various published research have reported the efficacy of walking backwards in knee OA by enhancing mobility [45] pain reduction and better quality of life[46, 47]. Reduced dynamic stability of the knee joint has been recognized as a potential etiologic factor in occurrence of OA knee and further disintegration of articular cartilage amongst knee OA patients [48, 49]. The improvements seen in Group 3 may be attributed to the capacity of perturbation exercises to utilize balance movements to activate, challenge, and adapt the nervous system's proprioceptors thereby decreasing instability of the knee.

CONCLUSION

From the above discussion, it may be concluded that since both retro walking and perturbation exercises combined with conventional CCE showed better improvements than CCE alone, either of the protocols may be opted for the treatment of knee joint osteoarthritis with Grade 2/3 OA as per Kellegren Lawrence scale.. But from the authors' viewpoint, the protocol involving retro walking provides an edge over the perturbation exercise protocol because retro walking doesn't involve any equipment and neither has it required assistance of a physiotherapist in contrast to

perturbation training. Moreover since obesity had a negative effect on the outcome of these exercises, hence assessment of BMI and weight management program along with CCE is recommended for better clinical outcomes.

Limitations and future recommendations

The present study did not assess a long-term follow up. Medications of patients, activities of daily living and recreational activities of patients were not taken into account. Home exercise program was not given. The age group of the participants was restricted to only women aged 40–65 years. Obesity assessment was done but weight management techniques were not incorporated. Future studies should investigate the effects of combined chain exercises along with weight management techniques; effects of CCE on different age group and gender of patients with knee OA may also be investigated. The efficacy of CCEs in osteoarthritis of the hip joint may also be assessed.

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Table.1: Testing the significant difference in the outcome measures between baseline and post 6 weeks' treatment scores for Group 1

	Mean	SD	SE	CI (95%)	T	Df	Sig(2-tailed)
Pre NPRS Post NPRS	2.160	.738	.104	1.950 to 2.370	20.638	49	.000*
Pre TUG	2.59400	.41028	.05802	2.47740 to	44.707	49	.000*

Post TUG				2.71060			
Pre LEFS Post LEFS	-11.040	4.005	.566	-12.178 to -9.902	-19.492	49	.000*

SD: Standard Deviation; SE: Standard Error; CI: Confidence Interval; t: t test value; df: degrees of freedom; Sig: Significance[p]< 0.05 statistically significant; *Statistically significant

Table.2: Testing the significant difference in the outcome measures between baseline and post 6 weeks' treatment scores for Group 2

	Mean	SD	SE	CI (95%)	T	Df	Sig(2-tailed)
Pre NPRS Post NPRS	3.720	.991	.140	3.438 to 4.002	26.555	49	.000*
Pre TUG Post TUG	4.05400	1.15037	.16269	3.72707 to 4.38093	24.919	49	.000*
Pre LEFS Post LEFS	-24.900	10.514	1.487	-27.888 to -21.912	-16.746	49	.000*

SD: Standard Deviation; SE: Standard Error; CI: Confidence Interval; t: t test value; df: degrees of freedom; Sig: Significance[p]< 0.05 statistically significant; *Statistically significant

Table.3: Testing the significant difference in the outcome measures between baseline and post 6 weeks' treatment scores for Group 3

	Mean	SD	SE	CI (95%)	T	Df	Sig(2-tailed)
Pre NPRS Post NPRS	2.880	.940	.133	2.613-3.147	21.669	49	.000*
Pre TUG Post TUG	3.27959	.85440	.12206	3.03418-3.52500	26.869	48	.000*
Pre LEFS Post LEFS	-17.760	7.032	.994	-19.759 to -15.761	-17.858	49	.000*

SD: Standard Deviation; SE: Standard Error; CI: Confidence Interval; t: t test value; df: degrees of freedom; Sig: Significance[p] < 0.05 statistically significant; *Statistically significant

Table.4: Table depicting the significantdifference in improvement in the parameters among obese and non-obese in Group 1(control group): Conventional Combined kinetic Chain Exercises (CCEs)

Outcome measures	BMI	N	Mean Improvement	SD	SE Mean	INDEPENDENT SAMPLES TEST				
						t- test for equality of means				
						T	df	Sig(2-tailed)	Mean difference	SE difference
NPRS	NO	25	2.2800	0.73711	0.14742	1.153	48	0.255	0.24000	0.20817
	OB	25	2.0400	0.73485	0.14697					
TUG	NO	25	2.8440	0.18947	0.03789	5.411	48	0.000*	0.50000	0.09240
	OB	25	2.3440	0.42139	0.08428					
LEFS	NO	25	-14.2000	3.21455	0.64291	-9.144	48	0.000*	-6.32000	0.69118
	OB	25	-7.8800	1.26886	0.25377					

BMI: Body Mass Index; df: degrees of freedom; N O: Non obese; O B: obese; N: Sample size; T: value of t test; SD: Standard deviation; Sig: Significance; p< 0.05 statistically significant; *Statistically significant; SE: Standard Error

Table.5: Table depicting the significant difference in improvement in the parameters among obese and non-obese in Group 2(experimental group): Retro walking and conventional CCEs

Outcome measures	BMI	N	Mean	SD	SE Mean	INDEPENDENT SAMPLES TEST				
						t- test for equality of means				
						T	Df	Sig(2-tailed)	Mean difference	SE difference
NPRS	NO	33	4.2424	0.66287	0.11539	7.674	48	0.000*	1.53654	0.20022
	OB	17	2.7059	0.68599	0.16638					
TUG	NO	33	4.8091	0.48436	0.08432	16.717	48	0.000*	2.22086	0.13285
	OB	17	2.5882	0.35335	0.08570					
LEFS	NO	33	-30.7273	6.22632	1.08386	-8.637	48	0.000*	-17.13904	1.98435
	OB	17	-13.5882	7.41669	1.79881					

BMI: Body Mass Index; df: degrees of freedom; N O: Non obese; O B: obese; N: Sample size; T: value of t test; SD: Standard deviation; Sig: Significance; p< 0.05 statistically significant; *Statistically significant; SE: Standard Error

Table.6: Table depicting the significant difference in improvement in the parameters among obese and non-obese in Group 3(experimental group): Perturbation exercises and conventional CCEs

Outcome measures	BMI	N	Mean	SD	SE Mean	INDEPENDENT SAMPLES TEST				
						t- test for equality of means				
						T	df	Sig(2-tailed)	Mean difference	SE difference
NPRS	NO	35	3.2571	0.78000	0.13184	5.463	48	0.000	1.25714	0.23010
	OB	15	2.0000	0.65465	0.16903					
TUG	NO	35	3.6143	0.71255	0.12044	5.642	48	0.000	1.16095	0.20577
	OB	15	2.4533	0.53966	0.13934					
LEFS	NO	35	-21.6000	4.31277	0.72899	-10.840	48	0.000	-12.80000	1.18087
	OB	15	-8.8000	2.24245	0.57900					

BMI: Body Mass Index; df: degrees of freedom; N O: Non obese; O B: obese; N: Sample size; T: value of t test; SD: Standard deviation; Sig: Significance; p< 0.05 statistically significant; *Statistically significant; SE: Standard Error

Table.7: Testing the significant difference in the outcome measures between Group 2 and Group 1 (control) after 6 weeks of treatment

	T	Df	Sig (2-tailed)	Mean difference	SE difference	CI (95%)
NPRS	-4.519	98	.000*	-1.68000	.37180	-2.41783 to -.94217
TUG	-3.593	98	.001*	-1.91800	.53388	-2.97746 to -.85854
LEFS	4.865	98	.000*	13.94000	2.86561	8.25330 to 19.62670

T: t test value; Df: degrees of freedom; Sig: Significance[p]< 0.05 statistically significant; *Statistically significant; SE: Standard Error; CI: Confidence Interval

Table.8: Testing the significant difference in the outcome measures between Group 3 and Group 1(control) after 6 weeks of treatment

	T	Df	Sig (2-tailed)	Mean difference	SE difference	CI (95%)
NPRS	-2.585	98	.011*	-.98000	.37914	-1.73239 to -.22761
TUG	-2.583	97	.011*	-1.31596	.50944	-2.32706 to -.30486
LEFS	2.889	98	.005*	7.96000	2.75527	2.49226 to 13.42774

T: t test value; Df: degrees of freedom; Sig: Significance[p]< 0.05 statistically significant; *Statistically significant; SE: Standard Error; CI: Confidence Interval

RESEARCH ARTICLE

Hindi Translation, Content Validation and Test-Retest Reliability of the Fugl Meyer Assessment Upper Extremity Scale : A Cross-Sectional Study Protocol

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ABSTRACT

Stroke, a global health concern, causes substantial mortality and disability. The Fugl Meyer Assessment Upper Extremity (FMA-UE) evaluates sensorimotor impairment and rehabilitation progress in poststroke patients and individuals with upper extremity deficits. Currently, there is no existing literature on the translation of the FMA-UE scale into Hindi. This study aims to systematically translate the Fugl-Meyer Assessment Upper Extremity (FMA-UE) into Hindi and evaluate its validity and test-retest reliability. The objective is to ensure that translated version retains its content validity and reliability. A Cross-Sectional Study. Fugl Meyer Assessment Upper Extremity (FMA-UE) is to be translated from English into Hindi language by two translators familiar with medical terminology and two with a non- medical background following the guidelines of Beaton et al. [1] An observer will synthesize the translations to

produce a T1 version of this scale. This version will undergo reverse translation and be reviewed by an expert panel to ensure accuracy. After evaluating content validity, the pre-final form will be tested on patients to confirm its validity. The translated version will be analysed by the ethics committee, and test-retest reliability will be assessed by measuring subjects on two separate occasions and calculating the correlation. In conclusion, the research will ascertain the validity and reliability of the FMA-UE's Hindi version among individuals who have survived stroke.

Keywords: Stroke, Upper Extremity, Translation, Test-Retest Reliability, Cross Sectional Study, English, Hindi, Linguistic Adequacy

INTRODUCTION

Stroke continues to be the world's second-leading cause of death and the third-leading cause of disability.[2] In India, stroke is currently the fifth most common cause of disability and the fourth most common cause of death. Previous studies indicate that between 105 and 152/100,000 people in India experience a stroke annually.[3] Approximately 80% of stroke survivors experience motor impairment in their upper limbs, including reduced dexterity, loss of coordinated movements, abnormal muscle tone, and decreased sensation.[4,5]Common outcome measures for assessing upper extremity function in stroke patients include the Fugl-Meyer Assessment (FMA-UE), Action Research Arm Test (ARAT), Box and Block Test (BBT), Nine-Hole Peg Test (NHPT), Wolf Motor Function Test (WMFT), and the Motor Activity Log (MAL),still (FMA-UE) is the most commonly used measure.[6] The upper-extremity (UE) portion of the Fugl-Meyer Assessment (FMA-UE) is a quantitative instrument originally developed by Fugl–Meyer et al. in 1975, this is the most frequently used outcome scaleto evaluate the extent of sensorimotor impairment and the progress of rehabilitation in stroke patients with upper extremity impairments and track improvements over time.[7,8]Excellent inter and intra-rater reliabilities have been documented for the FMA-UE, indicating that it can be used as a reliable and consistent stroke assessment tool.[9] The original FMA-UE text is lengthy and complex, which has led to varying interpretations in multiple studies. Consequently, the evaluation results can differ depending on how the FMA-UE is understood.[10-12] Therefore, when the FMA-UE is utilised in nations where there are languages other than English, this problem becomes more significant because each clinician may translate it into their own language, which could cause confusion. There are versions of the FMA-UE available for assessment in English, Swedish, Croation, Czech, Danish, Italian, Greek, Korean, Latvian, Norwegian, Persian, Spanish, Romanian, Ukrainian, and Urdu; however, there is currently no Hindi version of the FMA-UE available for the population that speaks and understands Hindi exclusively.[12-17] The aim is to ensure that the FMA-UE can be effectively used by therapists working with Hindi-speaking patients who may not be fluent in English. Since the FMA-UE is an assessment-based scale, therapists need to translate and instruct patients in Hindi during the evaluation. However, this immediate translation process could lead to potential misinterpretations, affecting the accuracy of the assessment.

METHODS

Ethical statement has been granted by the Institutional Ethical Committee(IEC/MMDU/2791), and the study is registered on Clinical Trials (CTRI/2024/03/081350).The study will adhere to the World Medical Associations Helsinki Declaration, CIOMS International Ethical Guidelines, and the Indian Council of Medical Research National Ethical Guidelines. All stroke volunteers will provide signed informed consent before participating

Translation procedure

Beaton et al.'s guidelines served as the foundation for this study.[1]

Stage of forward translation

The scale will be translated from English to Hindi using two forward translations. One translator, FMA-UE T1, will have a medical background and understanding of the principles, while the other, FMA-UE T2, will lack a medical background. The translations provided by the non-medical translator are referred to as "naive"as these translators are more likely to grasp the true meaning of the original scale, using terminology familiar to the target audience with less academic influence, will also flag unclear parts of the original scale.For this step to be successful, both translators must be proficient in Hindi and English. Any discrepancies between translations will be noted, and the translators will discuss them to correct grammatical errors.

Stage of synthesis

The primary goal of this step is to combine the forward translations. The writer will maintain communication with the translators via email or WhatsApp. The principal investigator will work with FMA-UE T1 and T2 to synthesize the FMA T1-2, making contextual adjustments to ensure each item's meaning is accurate. This stage is crucial for reviewing content and modifying words that deviate from the original scale.

Stage of backward translation

The FMA-UE T1-2 will be back-translated into English by FMA-UE BT1 and BT2, who will use the T1-2 version without knowledge of the translation process. This ensures the translated version matches the original and helps identify unclear terminology. An agreement between the back translation and the source version, however, provides consistency, it does not guarantee accuracy, as errors in forward translation may persist. This method, conducted by two English-speaking translators with no medical background, aims to avoid information bias and reveal unexpected interpretations, highlighting any significant errors, increasing the likelihood of identifying flaws.

Content Validation Procedure

Expert committee review

The completion of the FMA-UE translation into Hindi relies on feedback from a review committee using an online Delphi approach. Delphi experts, medical professionals with minimum 5 years of experience working with stroke patients in India, will evaluate the translated scale. If a second Delphi survey is necessary, a new panel will be used. Experts will review the scale via Gmail, rating items as (1) Not relevant; (2) Items needs revision; (3) Relevant but needs minor revision; (4) Very relevant. A four-point rating system is commonly used for content validation. Experts' choices will guide the final documentation and rationale for the Hindi scale. Key questions include: Do the terms have the same meaning? Is there more than one interpretation? Are there grammatical errors or difficulties? [22,23]

Phase of review of the Final Translated (HFMA-UE)

At this stage, the draft of translated HFMA-UE will be assessed in patients to evaluate comprehension and feasibility. Responses to each item will be reviewed to ensure the accuracy of the interpretation in a real-world context.

Transmission of the documented records for submission

The final step involves sending all documents and paperwork to the committee overseeing the translated scale. This ensures that the translation was completed ethically and that all necessary steps were taken. The procedure will be confirmed, with reports accurately reflecting the process. The organisation or committee won't be involved in altering the content; instead, will verify that a fair translation was achieved through the outlined process.

Content validation

Each scale item will be verified and recorded within the Item-level Content Validity Index (ICVI) using a tabular format. The Delphi method will be used for primary validation via email or WhatsApp. Items will be assessed with the Item-level Content Validity Index (I-CVI) and Scale-level Content Validity Index (S-CVI), using the Averaging method (S-CVI/Ave) and Universal Agreement calculation (S-CVI/UA). Based on Lynn's (1986) criteria, for a group of six to ten review experts, the S-CVI/Ave should be at least 0.90 and the minimum I-CVI should be 0.78 for superior

content validity. [17,18] The scale will be revised in the native language until these values are achieved. If necessary, another Delphi round will be conducted, with a new panel if required, until the S-CVI/Ave reaches 0.80.
A new version of the scale will be adjusted in the native language until the predetermined value points are reached. [23]

Reliability
The test-retest reliability will be assessed measuring subjects on two separate occasions and calculating the correlation to ensure consistent results over time. This approach ensures that the scale yields stable and dependable results across different testing periods.

Study participants and setting
To test the reliability of the final translated Hindi FMA-UE, 51 patients with acute, subacute, or chronic ischemic or haemorrhagic stroke will be selected from a tertiary care super specialty hospital in accordance with Beaton's guidelines.[1] The study will include both male and female participants over the age of eighteen who have had a stroke, can understand Hindi, and have the cognitive ability to comprehend the scale. Exclusion criteria will include individuals with neurological or musculoskeletal disorders, uncontrolled comorbidities, dementia, cognitive impairments, or those who cannot follow verbal instructions from the assessor.

STATISTICAL ANALYSIS

Content validity of the translated scale will be evaluated using the Item-level Content Validity Index (I-CVI) and the Scale-level Content Validity Index (S-CVI/Ave). For good to exceptional validity, I-CVI should be at least 0.78, and S-CVI/Ave should approach 0.90 after Delphi surveys with 6-10 experts.[18] Reliability will be assessed using absolute and relative methods. Relative reliability, measuring consistency across multiple observations, will be evaluated with the intra-class correlation coefficient (ICC), Spearman Rank correlation, and Pearson correlation, based on data normality. Internal consistency will be measured with Cronbach's alpha, ranging from 0 (no consistency) to 1 (perfect consistency).Additionally, regression analysis and coefficients will examine predictive consistency, and Bland-Altman plots will assess measurement agreement, identifying any biases or variability.[19-22]

DISCUSSION

Translating, validating, and testing the reliability of the Hindi Fugl-Meyer Assessment Upper Extremity (HFMA-UE) scale will significantly advance stroke rehabilitation for Hindi-speaking individuals. This effort aims to provide more precise assessments and tailored rehabilitation plans, thereby enhancing stroke care for this population. The FMA-UE is recognized for its validation, reliability, and sensitivity to changes in sensorimotor function over time, ensuring consistent evaluation and outcome comparison across different rehabilitation settings. [8] Currently, there is no reliable and accurate Hindi version available for assessing stroke patients, which is why we are translating the FMA-UE to better serve Hindi-speaking communities.

CONCLUSION

In conclusion, this study seeks to assess the content validity and test-retest reliability of the Hindi version of the FMA-UE scale in stroke patients.

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Author contributions
The study design, techniques, and write-up have all been equally contributed to by all authors.

Competing Interests
The authors claim they don't have any competing goals.

Conflict of Interest
The authors don't have any conflict of interest

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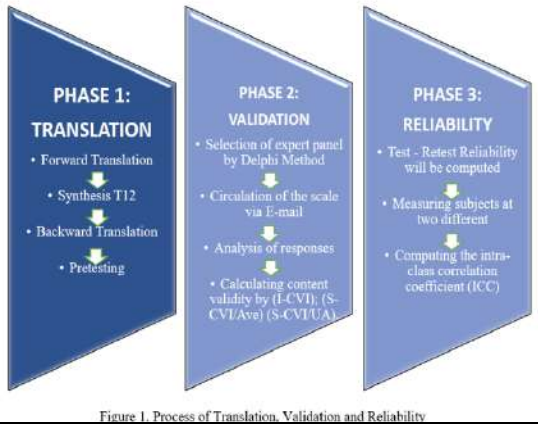

Figure:1 Process of Translation and Reliability

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REVIEW ARTICLE

The Role of Panchakarma in Women's Gynaecological Health : An Evidence - based Review

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ABSTRACT

Panchakarma, an integral component of Ayurveda, offers a holistic approach to women's health, addressing a wide range of conditions from menstrual irregularities and reproductive challenges to mental well-being and menopause management. This evidence-based review explores the efficacy of the five main Panchakarma therapies—Vamana, Virechana, Basti, Nasya, and Raktamokshana—in improving women's health by balancing the body's doshas. Modern scientific research validates the therapeutic potential of these techniques in managing hormonal imbalances, reproductive health disorders, and stress-related conditions. As the demand for complementary and integrative medicine grows, further research is required to fully realize Panchakarma's potential in mainstream healthcare for women.

Keywords: Panchakarma's holistic approach, Menstrual health benefits, Reproductive health , Menopause management , Mental health and stress relief.

INTRODUCTION

Panchakarma is an ancient therapeutic practice rooted in Ayurveda, an Indian holistic system of medicine. Comprising five key cleansing and rejuvenation techniques—Vamana (emesis), Virechana (purgation), Nasya (nasal administration of medicine), Basti (medicated enema), and Raktamokshana (bloodletting)—Panchakarma has been widely applied for its potential health benefits across a range of ailments. In women's health, Panchakarma offers particular promise in managing hormonal imbalances, gynecological disorders, and promoting general well-being. This evidence-based review explores how Panchakarma can influence various aspects of women's health, from menstrual and reproductive health to mental well-being, drawing on both traditional wisdom and modern scientific research. Panchakarma has garnered attention in the context of women's health due to its holistic approach in managing these challenges. By detoxifying the body, balancing hormones, and rejuvenating tissues, Panchakarma is believed to help in managing a variety of disorders such as polycystic ovarian syndrome (PCOS), dysmenorrhea, menorrhagia, endometriosis, infertility, and even psychological conditions like anxiety and depression. The therapies work synergistically to restore hormonal balance, improve reproductive health, and enhance mental well-being, making them suitable for women of all ages, whether in their reproductive years or transitioning through menopause. While Panchakarma has a deeply rooted tradition, modern scientific inquiry into its effectiveness has gained momentum over the past few decades. Research studies have begun to investigate its role in women's health through clinical trials, case studies, and observational reports. For example, several studies have demonstrated the efficacy of Panchakarma, particularly Basti and Virechana, in managing PCOS and infertility. Similarly, Nasya and Shirodhara (another Ayurvedic therapy involving the pouring of oil on the forehead) have been studied for their roles in reducing stress, anxiety, and symptoms of menopause.

Overview of Panchakarma Therapies

Panchakarma involves a preparatory phase (Purva Karma), the main cleansing treatments (Pradhan Karma), and a post-therapeutic phase (Paschat Karma) that focuses on restoring balance and strengthening the body. The therapies target the body's 'doshas'—Vata, Pitta, and Kapha—which are believed to govern physiological functions. Any imbalance in these doshas leads to illness, and Panchakarma is designed to restore equilibrium.

Vamana (Therapeutic Emesis) in Gynaecology

Vamana is primarily used for Kapha-related disorders, but its role in women's health extends to metabolic and hormonal conditions like Polycystic Ovarian Syndrome (PCOS), a condition frequently associated with Kapha imbalance. PCOS is characterized by obesity, irregular periods, and metabolic disturbances, which can be attributed to excess Kapha accumulation in the body. In gynaecological Ayurveda, Vamana helps in clearing excess Kapha, aiding in weight loss, regulating ovulation, and improving metabolic health. This process purifies the body, improves digestion (Agni), and balances the endocrine system, all crucial in managing conditions like PCOS. Furthermore, by expelling toxins from the upper digestive and respiratory tract, it also improves insulin sensitivity, which is critical in managing PCOS-associated metabolic syndrome.

Virechana (Purgation Therapy) in Gynaecology

Virechana is considered one of the most beneficial therapies for Pitta disorders and is widely used in Ayurveda to treat inflammatory and hormonal disorders. In women's health, Pitta dosha plays a significant role in regulating menstruation, fertility, and skin health. Imbalances in Pitta can lead to conditions like heavy menstrual bleeding (menorrhagia), endometriosis, dysmenorrhea (painful menstruation), and skin issues such as acne, which are often aggravated by hormonal fluctuations. In Ayurveda, Virechana helps in detoxifying the liver and intestines, which are responsible for metabolizing hormones like estrogen. By purging the body of excess Pitta and toxins (Ama), Virechana can regulate menstrual cycles, alleviate excessive bleeding, and reduce inflammation in conditions like endometriosis and fibroids. This therapy is especially beneficial for women with Pitta-related skin conditions like acne and melasma, which often accompany hormonal imbalances during menstruation or pregnancy.

Basti (Medicated Enema) in Gynaecology

Basti is highly regarded in Ayurveda for managing Vata-related disorders, making it one of the most powerful Panchakarma therapies for gynaecological health. Vata governs movement in the body, including the menstrual cycle, ovulation, and the function of the reproductive system. Imbalances in Vata can manifest as irregular periods, infertility, painful menstruation (dysmenorrhea), and menopausal symptoms like hot flashes and insomnia. Basti therapy is especially effective for conditions like infertility, where nourishing medicated oils and herbal decoctions are administered via the rectum to directly target the reproductive organs. Ayurvedic texts praise Basti for improving fertility by enhancing uterine health, balancing the menstrual cycle, and supporting hormonal equilibrium. It also helps alleviate symptoms of menopause by nourishing the tissues and reducing dryness, anxiety, and fatigue, which are common during the menopausal transition. For women experiencing conditions like fibroids, PCOS, or endometriosis, Basti helps in reducing inflammation, balancing hormones, and detoxifying the reproductive system. The therapy also enhances ovarian health, improves egg quality, and increases the chances of conception.

Nasya (Nasal Administration) in Gynaecology

Nasya, or the administration of medicated oils or powders through the nasal passages, is particularly effective in treating Vata and Kapha-related disorders affecting the head, neck, and neurological functions. In the context of gynaecology, Nasya is invaluable for managing stress, anxiety, and mental fatigue, which are often associated with hormonal changes, menstruation, pregnancy, and menopause. Stress and anxiety can exacerbate many gynaecological conditions, including PCOS, menstrual irregularities, and fertility challenges. In Ayurveda, Nasya is believed to calm the nervous system by balancing Prana Vata, which governs mental clarity, emotional stability, and the body's stress response. By administering medicated oils that travel through the nasal cavity to reach the brain and nervous system, Nasya therapy can help reduce symptoms of migraines, headaches, and emotional disturbances, which are often linked to menstrual cycles or hormonal imbalances. Additionally, Nasya is helpful during menopause when women experience cognitive issues like brain fog, memory loss, or insomnia. By balancing the nervous system and regulating hormonal communication through the hypothalamic-pituitary-ovarian axis, Nasya can alleviate mental health symptoms that accompany reproductive changes.

Raktamokshana (Bloodletting) in Gynaecology

Raktamokshana, though less frequently practiced today, holds importance in Ayurvedic gynaecology for managing blood-related disorders. Pitta dosha, which governs blood and heat in the body, can become imbalanced, leading to inflammatory conditions like acne, boils, or heavy menstrual bleeding. In Ayurveda, Raktamokshana helps reduce the excess Pitta and purifies the blood, which is beneficial for conditions like menorrhagia (excessive menstrual bleeding), endometriosis, and skin disorders associated with menstruation or hormonal imbalances. It is also used to treat varicose veins and other circulatory disorders that can arise from hormonal changes during pregnancy or menopause. For women suffering from chronic inflammatory skin conditions such as eczema or acne, especially during hormonal shifts, Raktamokshana can help by cleansing the blood and reducing heat in the system. While it is not commonly used today, its historical significance in treating gynaecological conditions cannot be overlooked, and it continues to hold therapeutic potential in specific cases of blood disorders.

Menstrual Health

Panchakarma has been applied to manage a variety of menstrual disorders, including dysmenorrhea (painful menstruation), menorrhagia (heavy bleeding), and amenorrhea (absence of menstruation). Virechana and Basti therapies are particularly effective in these cases. Modern studies have shown that Virechana can help regulate hormonal imbalances by cleansing the digestive tract and supporting liver detoxification, which is critical in estrogen metabolism.

Case Study: Panchakarma in PCOS Treatment

In a 2016 randomized controlled trial, women with PCOS undergoing Virechana therapy showed significant improvements in menstrual regularity, weight reduction, and hormonal balance compared to the control group. The trial highlighted the detoxifying effects of Virechana in managing insulin resistance, a key feature of PCOS.

Reproductive Health

Panchakarma therapies have a long history in treating infertility and enhancing reproductive health. Basti therapy, in particular, has been studied for its potential in improving uterine health and balancing Vata dosha, which is critical in reproductive functions. Ayurvedic practitioners have used Basti in combination with herbal preparations to enhance fertility and support conception.

Menopause Management

Menopause brings several physiological changes that can significantly affect a woman's quality of life. Hot flashes, mood swings, insomnia, and osteoporosis are some of the common symptoms. Panchakarma, particularly Basti and Nasya, has been explored for its role in managing menopausal symptoms by balancing the Vata dosha, which becomes dominant in the post-reproductive phase of life.

Mental Health and Stress Management

Women are often more prone to stress and anxiety due to hormonal fluctuations, particularly during menstruation, pregnancy, and menopause. Panchakarma therapies like Nasya and Shirodhara (a technique where medicated oil is poured on the forehead) have been studied for their calming and rejuvenating effects on the nervous system.

Scientific Validation and Modern Evidence

While Panchakarma has a long-standing tradition in Ayurvedic medicine, modern scientific research is increasingly validating its effectiveness. Studies have employed randomized controlled trials, biochemical markers, and patient-reported outcomes to demonstrate the benefits of Panchakarma in women's health.

DISCUSSION

The Impact of Panchakarma on Women's Health

The evidence supporting the effectiveness of Panchakarma therapies in managing women's health conditions is growing. Vamana (therapeutic emesis) and Virechana (therapeutic purgation), for example, have demonstrated benefits in addressing metabolic and hormonal disorders like polycystic ovarian syndrome (PCOS), where detoxification helps reduce insulin resistance and improve menstrual regularity. Similarly, Basti (medicated enema) has been particularly effective for Vata-related reproductive issues such as menstrual irregularities, infertility, and menopause-related symptoms. These therapies support hormonal regulation, uterine health, and mental well-being, making them suitable for a wide spectrum of gynecological and reproductive health concerns. Studies have highlighted the role of Virechana in regulating estrogen metabolism by improving liver function, which is crucial for hormonal balance. Likewise, Basti's impact on the reproductive organs through Vata regulation shows promise in managing infertility and alleviating conditions such as endometriosis and painful menstruation. Given the importance of Vata dosha in reproductive health, the application of Basti in menopausal care has been noteworthy, as it can alleviate symptoms like hot flashes, mood swings, and insomnia.

A Discussion on Scientific Validation and Modern Evidence

Panchakarma, despite its origins in ancient Ayurvedic traditions, has begun to receive increasing attention from modern scientific research. This shift is driven by the growing interest in integrative and holistic healthcare, where traditional practices like Panchakarma are being studied and validated through the lens of modern medical science. The use of randomized controlled trials (RCTs), biochemical markers, and patient-reported outcomes has helped bridge the gap between ancient wisdom and contemporary scientific standards, providing valuable insights into the efficacy of Panchakarma in women's health.

Biochemical Markers

One of the most compelling ways modern science is validating Panchakarma is through the measurement of biochemical markers. These markers allow researchers to objectively assess the physiological changes that occur

before, during, and after Panchakarma therapies. For instance, studies measuring hormonal levels in women undergoing Virechana or Basti therapies have shown improvements in estrogen and progesterone balance, which are crucial for managing conditions like PCOS and menstrual irregularities. Similarly, reductions in insulin resistance—a key factor in metabolic disorders associated with PCOS—have been documented in women receiving Panchakarma treatments, providing biochemical evidence of the therapies' benefits. Inflammatory markers such as C-reactive protein (CRP) and interleukins have also been studied in patients receiving Panchakarma, particularly in the context of conditions like endometriosis and chronic inflammation. These studies have shown a reduction in inflammation, supporting the Ayurvedic understanding that Panchakarma helps to balance Pitta dosha, which is often associated with heat and inflammation in the body. The ability to track such changes using biochemical markers provides a concrete, measurable way to evaluate the impact of Panchakarma and offers scientific validation for its detoxifying and anti-inflammatory effects.

CONCLUSION

Panchakarma offers a range of therapies that hold promise for managing various aspects of women's health, from menstrual disorders and reproductive health to mental well-being and menopause. The traditional wisdom of Panchakarma, combined with emerging scientific evidence, suggests its potential as a complementary therapy for modern women's health challenges. While the evidence base is growing, further research is necessary to integrate Panchakarma into mainstream healthcare practices and explore its full potential in improving women's health outcomes.

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RESEARCH ARTICLE

To Compare the Effect of Long Wave Diathermy versus Ultrasound Therapy for Pain and Dysfunction in Upper Trapezitis in College Going Students:- A Comparative Study

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ABSTRACT

Trapezitis is defined as an 'inflammation of trapezius muscle'. The upper trapezius muscle designed as postural muscle and its highly susceptible to overuse. From the site of primary inflammation, the pain may refer to other areas causing pain at rest and during activity. Amongst antagonistic muscle due to pain passive range of motion may be painful and restricted. The aim of the present study was to compare and determine the effect of LWD versus US on pain and dysfunction in upper trapezitis students. A comparative study design, selected students with upper trapezitis was randomized into two groups (A & B). Total 60 students, 30 students in each group, data was collected who completed the study. Group A received long wave diathermy with trapezius muscle stretching and Group B ultrasound therapy with trapezius muscle stretching for 5 weeks/day for 1 week. Outcome measurements such as Numerical Pain Rating Scale, Neck Disability Index and cervical Range of Motion were measured. Statistical analysis and result shows that intervention of LWD is more significant than US modality by reducing upper trapezitis, trigger point and reducing pain. Present study concluded that LWD is more effective in decreasing trigger point and pain in upper trapezitis.

Keywords: Upper trapezitis, long wave diathermy, ultrasound therapy, NPRS, NDI, ROM, neck pain, trigger point, muscle pain, stretching.

INTRODUCTION

Trapezitis is defined as inflammation of trapezius muscle. The upper trapezius muscle is located at the neck and causes raises of head and shrugging shoulders. Upper trapezius is highly suspectable to overuse and brings on strong neck spasm.[1] Neck pain affects over two-thirds of people at some point in their lives[2]. Its prevalence is maximum in females with middle age and less common in males with is fluctuating with mean point prevalence of 13%and neck pain occurs usually in upper trapezius muscle. Mechanical neck pain has a life time prevalence of 30-50% in general world population8.The prevalence of neck pain has been reported as 48- 78%[3]. For healing of soft tissues lesions and managing pain, therapeutic ultrasound is consider as an complementary treatment in physical therapy regimens. The treatment exerts therapeutic effects through thermal (continuous US) and non-thermal (pulsed US) modalities via a variety of application parameters (i.e., intensity, wavelength, duty cycle, and frequency). Continuous US achieves the thermal effect and is proposed to produce analgesia through temperature elevation, which increases capillary permeability and tissue metabolism, thereby enhancing fibrous tissue extensibility and pain thresholds. Non-thermal effects are achieved by modulating cell membrane permeability, increasing protein synthesis, and activating immune response near the injury site, which may stimulate regeneration of damaged tissue[4]. Long Wave Diathermy (LWD), or capacitive and resistive electric transfer therapy, is a type of heating electrotherapeutic modality which produces heat and improves the metabolic flow and microcirculation of the superficial and deep tissues. Long wave diathermy works at a frequency range of 0.3-1 MHZ and wavelength of 300m. The penetration range of the long wave diathermy is as deep as two inches. Long wave diathermy generates oscillating electromagnetic fields (EMF), comprising both magnetic and electric fields. These fields lead to production of heat in the tissues due to rapid alternating movements of ions. At the molecular level, the LWD causes heating of the blood vessels and the muscles. The heat which is generated gets retained due to the insulating properties of the fat tissues. The physiological effects of LWD includes reduction of pain, increased metabolic functions, increased temperature of the deep tissues, improved range of motion, decreased stiffness of the tissues and relaxation of muscle spasm. LWD specific cream acts as an coupling media between affected part and treatment head.. The LWD is most commonly indicated to treat conditions like osteoarthritis, rheumatoid arthritis, tendinitis, bursitis, capsulitis, and other conditions. However, it is contraindicated in the areas of anaesthesia, pus enclosed areas, arteriosclerosis, and in malignancy cases etc. For the generation of heat, diathermy uses high frequency currents of 1,000,000 to 3,000,000 cycle per second[5]. So, the purpose of the study is to find out the effectiveness of LWD vs US amongst on upper trapezitis students.

MATERIALS AND METHODS

Study Design – An Comparative Study.
Source Of Data – Students Were Selected From Mahatma Gandhi Physiotherapy College, Ahmedabad, Gujarat.
Sample Design – Simple Random Sampling (Odd-Even Method)
Sample Size – 60 Students
Study Population – College Going Students With Upper Trapezitis
Duration Of Study – 6 Months
Materials Used For The Study -- Consent Form, NPRS, NDI, Case Record Form, Pen, Plinth, Table, Chair, Pillow.

Criterias For Selection
Inclusion Criteria
Patient Willing to participate in the study
Gender: male and female
Age group – 18 - 25 years
student diagnosed with trapezitis

Exclusion Criteria
Pt's not cooperative
cervical radiculopathy
Upper extremity fracture.
taken steroids for last 6 month

Procedure
Using Simple Random Sampling (Odd-Even Method): (30 students were allotted to group A and 30 students to group B) 60 students with upper trapezitis were selected on the basis of inclusion and exclusion criteria. Informed consent was obtained from all the students. All students were undergone Tender point assessment by therapist and the pain andfunctionalactivitywasmeasuredinNumericalPainRatingScale(NPRS)andNeck Disability Index Scale (NDI). Group A: - (n=30) Long Wave Diathermy: - students were made to sit in a wall support chair and then lean forward in comfortable manner. His\her head and arms were supported with pillow. LWD was given on the trapezius Tender point 5 days/week for one week. Pre and post intervention NPRS, NDI and Cervical side flexion range was Measured. Group B: - (n= 30) Ultrasound Therapy: - students were made to sit in a wall supported chairs and lean forward in a comfortable manner. His/her head and arms were supported with pillow. Ultrasound Therapy was given on the trapezius Tender point 5 days/week for one week. Pre and post intervention NPRS, NDI and Cervical side flexion range was Measured.

RESULT

Statistical analysis was done using SPSS version 20, was used to generate tables and graphs. Mean was calculated as a measure of central tendency for NPRS-R, NPRS-A, ROM, And NDI. Standard deviation was calculated as measure of dispersion. Level of significance was kept at 5% with confidence interval (CI) at 95% (P value=0.05). Shapiro wilk test was performed taking pre-outcome measure and p value was<0.05forNPRS- R, NPRS-A, ROM, And NDI, this showed that this following outcome measure in both groups was not normally distributed. So, NPRS-R,NPRS-A,ROM, And NDI, non parametric test was used. In both within group comparison and group analysis after 5session of intervention for NPRS-R, NPRS-A, ROM, And NDI was done using Wilcoxon signed ranks test used and In between group comparison of data Mann-whitney U test was applied. Hence, the null hypothesis was rejected and alternate hypothesis was accepted for the between group comparison. Above results shows that LWD was found to be more effective in reducing pain, improving ROM and functional activity of patients as compared to US as the mean difference of LWD was less in NPRS-A, NPRS-R and NDI and more in range of motion while comparing with US. So LWD was more effective than US modality.

DISCUSSION

Trapezitis is an inflammation of the trapezius muscles, muscle spasm occurs early after inflammation this makes a since that tightness in the muscle in painful when basic injury is not treated, spasm causes formation of muscle knots form because, the spasm keeps the muscle continuously under tension muscle are not designed for this continuous walk, our a period of time the muscle get overload and forms that knots. As a result, treatment of the spasm is necessary to reduce this problem in the study, the subjects were chosen from 15-25 years. The result of the study reveals that there was reduction in trigger point and decrease in pain by NPRS in both groups A and B after the respective protocol. The reduction in pain and trigger point in group-A which received LWD was more significant than group-B which received US. Hence, the result of this study proves that, there will be beneficial effect of LWD in treatment of upper trapezitis. Usha Panihar, *et al,* in 2022 further supported our study which shows that after application of long wave diathermy amongst 30 patients with the age group of 20-26 years. The participants were divided into 2 groups. in experimental group, LWD was given along with home exercise and in control group simple home based exercise protocol was given for 3 times/week for 2 week. As an outcome measure Visual analogue scale (VAS), neck disability index (NDI), and Neck range of motion were assessed at baseline, at 2weeks, and follow-up

after 2 weeks. Result shows that there was a significant improvement in pain, disability, and ROM post-intervention in the control group and experimental. Parameters were continuous mode, 1 MHz frequency and duration 10 minutes/session. This study and present study LWD parameters almost same. Study concluded that in patients with neck pain, LWD along with neck exercises was found to be an effective therapeutic intervention for improving pain, neck disability, and neck range of motion. They gave LWD and in present study focused on LWD, there is additional effect on pain and function and range. So, this result support and justify the result of the present study. which justify that Heat produced by LWD also causes vasodilatation efflux from the affected tissue of chemical implicated as the mediator of pain such as bradykinin, serotonin and the prostaglandins. The heat also leads to the increased microcirculation and metabolism. The reduction of pain further contributes to decreased neck disability and improved functions.[6]

Another study done by Brite Sagaya Raina, Dr Arvind Manhas et al1, 2021 on Comparison of Ultrasound Therapy &Transcutaneous Electrical Nerve Stimulation in the Treatment of Upper Trapezitis. In this study thirty samples with upper trapezitis was selected based on inclusion and exclusion criteria. All participants undergo trigger point assessment by ultra-sonogram and their pain was measured by Numerical pain rating scale (NPRS). Participants was assigned into two groups 15 numbers in each randomly. Statistical Analysis shows that for reducing Upper trapezius trigger point and reducing pain, intervention of Ultrasound Therapy in more significant than Transcutaneous Electrical Nerve Stimulation. Study conclude that ultrasound therapy are more effective than Transcutaneous Electrical Nerve Stimulation in decreasing pain and trigger point. They used US protocol Frequency - 3 MHZ, Intensity - 1.0 W cm2, Duration - 10 minutes, but present study protocol was, Frequency – 1 MHZ, Intensity – 1.0 W/cm2, Duration - 10 minutes different, from this study. So, it could be the reason for difference in the result contrast to present study.[7] Limitation of the present study is Male / Female ratio was unequal , Study duration was short, Onset and severity of the disease was not taken into account. Future recommendation study can be done on acute, sub-acute, chronic and chronic conditions by upper trapezitis, study can be done on large sample size, study can be done on different population by applying same protocol, study can be done comparing and controlling group.

CONCLUSION

On the basis of present study, Group A received LWD with upper trapezius stretching and Group B Received US with upper trapezius stretching and both the group shows reduction in pain and improve cervical side flexion range and Functional activity of the students with upper trapezitis. So, it concluded that LWD is more effective than US in reduction of pain and improving cervical side flexion range and Functional activity of the students with upper trapezitis.

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Table 1: Parameters

Parameters	**GROUP-A**	**GROUP-B**
Modality	LWD+ upper trapezius stretching	US+ upper trapezius stretching
Sample size	30	30
Frequency	1 MHz	1 MHz
Intensity	Ptstolerancelevel	1W/Cm²
Treatment duration	10 minutes	10 minutes
5Days/ weekfor1week		

Table: 2 Age And Outcomes Distribution In Two Groups

	Group	**N**	**Mean±SD**	**P value**
AGE	1	30	21.80±0.76	0.00
	2	30	22.33±0.95	0.00
PREREST	1	30	3.80±1.56	0.16
	2	30	2.83±1.26	0.06
PREACTIVITY	1	30	4.90±1.44	0.05
	2	30	4.17±1.26	0.01
ROM	1	30	37.70±2.61	0.06
	2	30	36.27±3.09	0.00
NDI	1	30	22.20±5.18	0.00
	2	30	22.53±5.71	0.00

Table3: Group: A within Group Comparison

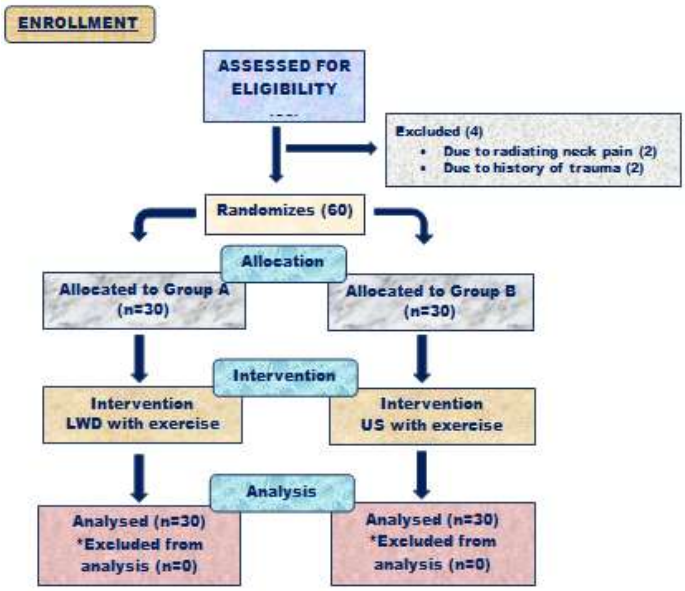
Parameter	Pre(mean ± SD)	Post(mean ±SD)	z value	P value	Significance
NPRS-R	3.80±1.56	1.23±1.13	-4.76	0.00	SIGNIFICANT
NPRS-A	4.90±1.44	2.07±1.23	-4.74	0.00	SIGNIFICANT
ROM	37.70±2.61	42.07±2.19	-4.82	0.00	SIGNIFICANT
NDI	22.20±5.18	14.33±3.14	-4.79	0.00	SIGNIFICANT

Table 4: Group: B within Group Comparison

Parameter	Pre(mean ±SD)	Post(mean ±SD)	z value	P value	Significance
NPRS-R	2.83±1.26	1.97±1.18	-4.52	0.00	SIGNIFICANT
NPRS-A	4.17±1.26	2.87±1.16	-4.27	0.00	SIGNIFICANT
ROM	36.27±3.09	39.37±3.05	-4.73	0.00	SIGNIFICANT
NDI	22.53±5.71	17.00±4.20	-3.94	0.00	SIGNIFICANT

Table 5: Between Group Comparison Of Group: A & Group: B

PARAMETERS	z value	p value	DIFFRENCE
NPRS-R	-2.17	0.03	SIGNIFICANT
NPRS-A	-2.31	0.02	SIGNIFICANT
ROM	-3.50	0.00	SIGNIFICANT
NDI	-2.48	0.01	SIGNIFICANT


ENROLLMENT
ASSESSED FOR ELIGIBILITY
Excluded (4)
Due to radiating neck pain (2)
Due to history of trauma (2)
Randomizes (60)
Allocation
Allocated to Group A (n=30)
Allocated to Group B (n=30)
Intervention
Intervention LWD with exercise
Intervention US with exercise
Analysis
Analysed (n=30) *Excluded from analysis (n=0)
Analysed (n=30) *Excluded from analysis (n=0)

Flow Chart

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RESEARCH ARTICLE

On Vertex Minimal Dominating Fuzzy Graph of a Fuzzy Graph

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ABSTRACT

The concepts of connectedness and vertex connectivity are fundamental to fuzzy graph theory. We introduced a novel class of intersecting fuzzy graph in the context of fuzzy dominance theory. Applying strong arcs to calculate the strength of connectivity between the two nodes. Strong arcs were utilized to provide an explanation for the dominance in the fuzzy graph. Characterizations for fuzzy graphs with a connected and complete dominating fuzzy graph are presented in this study. In addition, we establish the bounds on order, size, diameter and vertex connectivity of vertex minimal dominating fuzzy graph. We present a new class of dominating fuzzy graphs in this paper, called Vertex minimal dominating fuzzy graph of a fuzzy graph. The vertex minimal dominating fuzzy graph of a fuzzy graph is denoted by$M_vDF(G)$: $(\sigma_v, \mu_v)$and is defined to be the intersection graph on the minimal dominating sets of vertices in Fuzzy Graph.

Keywords: Vertex connectivity, Connectedness, Minimal dominating set, Strength of connectivity, Vertex minimal dominating fuzzy graph.
2010 Mathematics Subject Classification: 03E72, 05C72.

INTRODUCTION

The fundamental characteristics of systems with finite components can be modelled quite effectively using graph theory. Communication issues, traffic networks, railroad networks, phone networks, and other networks are represented graphically. On occasion, graph theoretic models might offer a helpful framework for the application of analytical methods. Another way to express a relationship between a given collection of things is via a graph. Every object is represented by a vertex, and the relationship between them is represented by a directed edge in the case of an ordered relation between the objects, and by an edge if the relationship is unordered. The criteria for defining a relationship between items need not always be exact; fuzziness emerges when we consider vague concepts. Through the publication of a seminar paper, L.A. Zadeh introduced a mathematical framework in 1965 to explain the concept of uncertainty in real life. By accurately indicating the degree of relationship between the objects in a given set, A. Rosenfeld's fuzzy graph, which uses fuzzy relations, represents the relationship between the objects. In addition, he developed a number of hazy analogous graph theoretic terms, including bridge, cut vertex, and tree. There are numerous uses for fuzzy graphs in the modelling of real-time systems where the system's intrinsic information varies with varying degrees of precision. Strong arcs were used by Nagoor Gani and Chandrasekaran to discuss domination in fuzzy graphs. In the field of domination theory, V.R. Kulli et al. introduced a variety of types of graph valued functions known as dominating graphs. In the field of domination theory, B. Basavanagoud and S.M. Hosamani introduced a new class of intersection graphs. Within the context of fuzzy domination theory, we present a novel kind of fuzzy graph in this paper.

RESULT AND DISCUSSION

Definition: The Vertex Minimal Dominating Fuzzy Graph

Give a fuzzy graph $G = (\sigma, \mu)$ and an underlying crisp graph $G^* = (\sigma^*, \mu^*)$. Let S be the collection of every minimal dominating set of G, Let G^* be (V, E).$M_vDF(G)$: (σ_v, μ_v) is represent the vertex minimal dominating fuzzy graph of G with node set the disjoint union of $V \cup S$, where

$\sigma_v(u) = \sigma(u)$ if $u \in \sigma^*$

$= \mu^{\infty}(u, v)$ if $u, v \in e_i$ and $\forall\, e_i \in S = 0$ *otherwise*

$\mu_v(v_i, v_j) = \sigma_v(v_i) \wedge \sigma_v(v_j)$ if $v_i, v_j \in \sigma^*$

$\mu_v(v_i, e_j) = \sigma_v(v_i) \wedge \sigma_v(e_j)$ if $v_i \in \sigma^*$, $e_j \in \mu^* = 0$ *otherwise*

Since$\sigma_v$can only be defined by the values of σ & μ,

$\sigma_v: V \cup E \rightarrow [0,1]$ is a well- defined fuzzy subset on $V \cup E$. Furthermore,μ_v is a fuzzy relation on σ_v&

$\mu_v(u, v) \leq \sigma_v(u) \wedge \sigma_v(v) \forall\, u, v$ in $V \cup E$.

Example

Figure:1. Figure:2

Observations

(i) $M_vDF(G)$is a strong fuzzy graph.

(ii) For any connected fuzzy graph G,

$|V(MDF(G))| < |V(M_vDF(G))|$& $|E(MDF(G))| < |E(M_vDF(G))|$

&$|V(DF(G))| = |V(M_vDF(G))|$& $|E(DF(G))| < |E(M_vDF(G))|$.

where the dominating fuzzy graph is represented by DF(G) and the minimal dominating fuzzy graph by MDF(G).

(iii)Each edge functions as an effective edge in $M_vDF(G)$.

(iv)The vertex minimal dominating fuzzy graph $M_vDF(G)$ of G is complete if and only if G is K_1.

Theorem:1

$M_vDF(G)$ is a connected fuzzy graph for any given fuzzy graph G.

Proof

Every vertex in $M_vDF(G)$ is not an isolated vertex because for each vertex $v \in V$, a minimal dominating set with$v$ in it exists. However, since $M_vDF(G)$ is a disconnected fuzzy graph, G_1&G_2 are at least two components of the vertex minimal dominating fuzzy graph. Afterwards, two nonadjacent vertices $u, v \in V$exist such that $v \in V(G_2)$ &$u \in V(G_1)$. This suggests that G does not have a minimal dominating set that contains bothu and v; consequently,$M_vDF(G)$ is connected.

Theorem:2

diam (M_vDF(G)) ≤ 3,for any connected fuzzy graph G.

Proof

Suppose that G has a minimum of two vertices. In that case,$M_vDF(G)$ has three vertices or more.

Assume that$x, y \in V$. The following instances are taken into consideration:

Case 1: let's say that$x, y \in V$.$d(x, y) \leq 2$ in $M_vDF(G)$ thereafter.

Case 2: Assume $y \notin V$ &$x \in V$. Consequently, a minimal dominating set of G is y = D.In$M_vDF(G)$, $d(x, y) = 1$ if $x \in D$. If $x \notin D$, then there exists a vertex $z \in D$ strong neighbour to x and hence in $M_vDF(G)$, $d(x, y) = d(x, z) + d(z, y) = 2$.

Case 3: Assume $x, y \notin V$. In that case, G has two minimal dominating sets, $x = D$ & $y = D'$. Every vertex $z \in D$ is strong neighbour to some vertex $w \in D'$if D & D' are disjoint sets, and vice versa. This suggests that$d(x, y) = d(x, z) + d(z, w) + d(w, y) = 3$ in$M_vDF(G)$. In $M_vDF(G)$,$d(x, y) = d(x, z) + d(z, y) = 2$ if D & D' are non-disjoint sets. We thus have $diam\ (M_vDF(G)) \leq 3$from Theorem 1 and above all three cases.

Theorem 3

In any connected fuzzy graph G, M_vDF(G) is a tree if and only if $G = \overline{K}_p\ or\ K_2$.

Proof

Assume that$M_vDF(G)$ is a tree. Then G doesn't have a cycle. Conversely, let us assume that$G \neq \overline{K}_p\ or\ K_2$. We are now going to look at these two cases:

Case 1: G is a star, if $\Delta(G) = p - 1, p \geq 3$.

Thus, there is a contradiction in$M_vDF(G)$because it contains a cycle.

Case 2: If$\Delta(G) \leq p - 2$, then there exist three vertices x, y & $z \in V(G)$ such that x & y are strong neighbour and z is not strong neighbour to both x& y. This implies that x & y are connected by at least two paths in $M_vDF(G)$, which is contradictory. Resulting from the two cases mentioned above, $G = \overline{K}_p\ or\ K_2$. On the other hand, it is evident that $M_vDF(G)$ is a tree if $G = \overline{K}_p\ or\ K_2$.

Theorem 4

The bounds on the order of M_vDF(G) for any connected fuzzy graph G are as follows:

$p + d(G) \leq \left|V\left(M_vDF(G)\right)\right| \leq \frac{p(p+1)}{2}$.

Additionally, the upper bound can only be reached if and only if G is (p − 2) regular, and the lower bound can only be reached if and only if

$G = K_p\ or\ \overline{K}_p\ or\ K_{1,p-1}$.

Theorem 5

The bounds on the size of M_vDF(G) for any connected fuzzy graph G are as follows:

$p + q \leq \left|E\left(M_vDF(G)\right)\right| \leq p(p-1)$.

Additionally, the upper bound can be reached if and only if G is (p − 2) regular and the lower bound can be reached if and only if every vertex of G is in exactly one minimal dominating set of G.

Theorem 6

M_vDF(G) is bipartite for any connected fuzzy graph G if and only if

$G = \overline{K}_p\ or\ K_{1,p-1}$.

Proof

Assuming that$M_vDF(G)$ is bipartite, we must demonstrate that $G = \overline{K}_p$ *or* $K_{1,p-1}$. In contrast, there exists a non-trivial component G_1 of G if $G \neq \overline{K}_p$. This leads to the obvious contradiction that $M_vDF(G)$ contains a cycle of length five. Thus, $G = \overline{K}_p$. Assume that if $G \neq K_{1,p-1}$, then$G$ contains a cycle. Since, G is a subgraph of $M_vDF(G)$, which suggests that $M_vDF(G)$ has a cycle of odd length, which is contradicted once more.$G = K_{1,p-1}$ follows. On the other hand, if$G = \overline{K}_p$, then it is evident from Theorem 3 that $M_vDF(G)$ is tree, which means that$M_vDF(G)$ is bipartite. If $G = K_{1,p-1}$, then$D$ *and* D' are the only two minimal dominating sets that exist.D' has the $V(G) - x$ vertices of degree one, while$D$includes the vertex x of degree $(p-1)$. It is evident that the bipartite graph is obtained by the definition of $M_vDF(G)$.

Theorem 7

In any connected fuzzy graph G, the vertex connectivity of the vertex minimal dominating fuzzy graph is,

$\kappa(M_vDF(G)) = min\left\{min\left\{deg_{M_vDF_{1\leq j\leq p(G)}}(V_j)\right\}, min\left\{deg_{M_vDF_{1\leq i\leq n(G)}}(S_i)\right\}\right\}$.

Proof

The following cases are taken into consideration:

Case 1: Among all the vertices of $M_vDF(G)$, let z be a vertex that corresponds to the vertex of G and has the minimum degree .A disconnected graph is then produced by removing vertices that are strong neighbours of z. Which implies, $\kappa(M_vDF(G)) = min\left\{deg_{M_vDF_{1\leq j\leq p(G)}}(V_j)\right\}$

Case 2: Assume x is a vertex of $M_vDF(G)$ that represent the minimal dominating set of G and has the minimum degree of all the vertices in $M_vDF(G)$. A disconnected graph can be created by removing the vertices that strongly neighbour x. Which implies, $\kappa(M_vDF(G)) = min\left\{deg_{M_vDF_{1\leq i\leq n(G)}}(S_i)\right\}$. The minimum of these two cases is hence the vertex connectivity of $M_vDF(G)$.

Theorem 8

In any connected fuzzy graph G, the edge connectivity of the vertex minimal dominating fuzzy graph is,

$\lambda(M_vDF(G)) = min\left\{min\left\{deg_{M_vDF_{1\leq j\leq p(G)}}(V_j)\right\}, min\left\{deg_{M_vDF_{1\leq i\leq n(G)}}(S_i)\right\}\right\}$.

Proof

The following cases are taken into consideration:

Case 1: Among all the vertices of $M_vDF(G)$, let z be a vertex that corresponds to the vertex of G and has the minimum degree . A disconnected graph is then produced by removing edges that are strong neighbours of z.

Which implies, $\lambda(M_vDF(G)) = min\left\{deg_{M_vDF_{1\leq j\leq p(G)}}(V_j)\right\}$

Case 2: Assume x is a vertex of $M_vDF(G)$ that represent the minimal dominating set of G and has the minimum degree of all the vertices in $M_vDF(G)$. A disconnected graph can be created by removing the edges that strongly neighbour x. Which implies, $\lambda(M_vDF(G)) = min\left\{deg_{M_vDF_{1\leq i\leq n(G)}}(S_i)\right\}$. Hence the edge connectivity of $M_vDF(G)$ is the minimum of these two cases.

Theorem 9

$\gamma(M_vDF(G)) = p$ for any connected fuzzy graph G *if and only if* $G = K_p$.

Proof

Assume that$\gamma(M_vDF(G)) = p$. In contrast, there must be at least two non-strong neighbour vertices x& y in G, if $G \neq K_p$. It is obvious that every vertex $z \in V(G)$ except for$x$& y forms a minimal dominating set of G. The set $\{x, y\}$ also constitutes a minimal dominating set of G. Consequently, there is a contradiction$\gamma(M_vDF(G)) = (p-1)$. Thus,$G = K_p$. On the other hand, if$G = K_p$, then every$\{x\} \subseteq V(G)$ represents a minimal dominating set of G. Since every vertex is a strong neighbour of precisely one minimal dominating set according to the definition, therefore, $\gamma(M_vDF(G)) = p$.

Theorem 10

For any connected fuzzy graph G, $d(M_vDF(G)) = 2$ if and only if $G = \overline{K}_p$ *or* K_2.

Proof

Assumed$(M_vDF(G)) = 2.M_vDF(G)$ is clearly a tree in that case. we obtain$G = \overline{K}_p$ *or* $K_2$by Theorem 3. On the other hand, let$G = \overline{K}_p$ *or* K_2. According to Theorem 3, $M_vDF(G)$ is a tree. Indicating that$d(M_vDF(G)) = 2$.

CONCLUSION

We identified a vertex minimal dominating fuzzy graph of a fuzzy graph. Several properties of the vertex minimal dominating fuzzy graph have been provided. Additional research in the area of fuzzy dominating theory will specify a few more characteristics of the dominating fuzzy graph and present a substitute class of intersecting graphs. To provide some practical applications for the dominating fuzzy graph as well.

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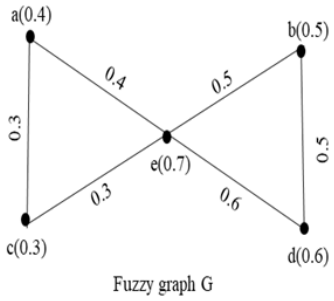

Figure.1: Fuzzy Graph G

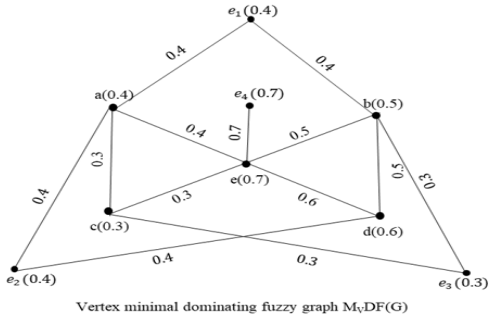

Figure.2: vertex minimal dominating Fuzzy graph $M_vDF(D)$

REVIEW ARTICLE

A Review Article on Urinary Tract Infection Among Pregnant Women's

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ABSTRACT

Urinary Tract Infection (UTI) in general can be termed as the symptomatic presence of microbial pathogens in the urinary tract i.e., kidney, ureters, bladder, and urethra. The common cause of UTI can be both Community acquired, and Hospital acquired. The common causative agents of UTI include Gram positive and Gram-negative bacteria. For example, few bacteria like *Escherichia coli, Klebsiellapneumoniae, Staphylococcus aureus, Enterobacterspp, Staphylococcus saprophyticus, Proteus mirabilis, Enterococcusfaecalis.* During pregnancyUTI is considered as a prevalent infection worldwide and can lead to poor perinatal and maternal outcomes. It causes various harmful impacts on both the fetus and the mother. These infections range from bacteriuria, which is asymptomatic, to acute cystitis, which is symptomatic, and pyelonephritis, which is termed as the deadliest. Preterm delivery rates and low birth weight are among the unfavourable pregnancy outcomes that have been associated with the occurrence of UTIs. This study intends to ascertain the prevalence of UTIs during pregnancy, the most common microorganism responsible for UTIs, and the effects of such infections on the outcomes of both the mother and foetuses.

Keywords: Pregnancy, Asymptomatic, Preterm delivery.

INTRODUCTION

Urinary Tract Infection (UTI) is considered as one of the most prevalent bacterial infections. About 150 million people are affected each year all around the world. Urinary tract infection (UTI) is a condition where bacteria develop and cause inflammation in the urinary tract **(Glaser *et al.,* 2015).**It is a pathological condition characterized by the proliferation of microorganisms within the urinary tract, resulting in the occurrence of inflammation. The urinary system experiences a few anatomical, hormonal, and functional changes during pregnancy .**(Matuszkiewicz*et al.,*2015).**These infections are caused by the rise in urine stasis and the ascent of urine that has been contaminated by microorganisms presentfrom the bladder and into the ureters. It encompasses various vital organs, including the kidneys, bladder, ureters, and urethra. Urinary tract infection, which is considered one of the most common infectious diseases, is frequently observed across all age groups. However, certain populations exhibit a greater susceptibility to UTIs. Diabetic patients are considered for instance to be at a heightened risk of developing UTIs . Moreover, females possess a fourteen-fold higher likelihood of acquiring UTIs compared to males. These disparities can be attributed to the involvement of various factors. For example, women possess a shorter urethra in comparison to men, which opens in closer proximity to the anus.

Consequently, the lower third of the urethra is consistently exposed to pathogens from the vagina and rectum.**(OM *et al,.* 2015)** Additionally, women tend to not fully empty their bladder, unlike men. Every other woman is expected to have experienced a UTI at least once in her lifetime,**(Geerlings*et al.,*2016)** with 10–60% of all women reporting symptoms of a UTI at some point. As one ages, the chance of infection rises. UTI manifests in two distinct forms, namely asymptomatic infection, and symptomatic infection**.(Czajkowski*et al,.*2021)**.UTI denotes the continual presence of bacteria within the female urinary tract, without the manifestation of any clinical signs or symptoms. **(Salari*et al.,*2023).** Symptomatic UTIs are further categorized into lower and upper infections. Urinary tract consists of the kidney, urinary bladder, ureters, and urethra. **(Muthulakshmi*et al.,*2017)**. UTI has the potential to manifest in individuals indiscriminately, albeit its prevalence is predominantly observed in the female demographic. It has been considered that approximately 33% of adult women receive a UTI diagnosis prior to reaching the age of 24. The incidence of UTI has been documented to afflict 20% of expectant mothers and stands as the primary catalyst for admission into obstetrical wards **(Navarro *et al.,*2019)**. The term "UTI" in pregnancy frequently refers to both symptomatic and asymptomatic bacteriuria or it can also bereferred to as the presence of bacteria in the urine without any symptoms. The phrase "urinary tract infection" is broad and includes both symptomatic infections characterized by urinary tract inflammation and microbial invasion as well as silent bacteriuria.

(Muthulakshmi*et al.,*2017).It is also known as asymptomatic bacteriuria, is the recognition of a quantitative measurement of ≥10,000 CFU/mL of more than one bacterial species in a urine sample, regardless of the presence of pyuria. **(Belete*et al.,* 2020)**. Whereas, the determination of symptomatic lower urinary tract infection (UTI) is established through clinical observations of dysuria, urgency, frequency, hematuria, suprapubic pain, and uterine contractions, in conjunction with the presence of bacteriuria exceeding a count of 10,000 colony-forming units per milliliter (CFU/mL). **(Ansaldi*et al.,*2023)**. UTIs are commonly caused by ascending movement of bacteria that colonize the lower gastrointestinal and genitourinary tract **(Johnson *et al.,*2021)**. In pregnant females, there are alterations in both the physiological and anatomical aspects of the urinary tract, in addition to modifications in the immune system during gestation. Pregnancy is accompanied by structural, physiological, and functional alterations in the urinary system, which primarily lead to the rise of pathogens into the urinary bladder, causing (UTIs). Within the general population, pregnant women exhibit a higher occurrence of UTIs compared to other women in good health. Symptomatic as well as asymptomatic UTIs are prevalent in pregnant women and can have negative consequences linked on the mother, fetus, and newborn. These changes contribute to an elevated prevalence of asymptomatic bacteriuria (ASB) and occasionally result in symptomatic infection. The consequences of such infections pose considerable risks for both the expectant mother and on the developing fetus. Furthermore, advanced maternal age, parity, diabetes, sickle cell anemia, past occurenceof (UTI), urinary tract disorders, and immune

deficiencies may serve as potential factors that increase the vulnerability of pregnant expectant mothers to UTIs**. (Azami*et al.,*2019)**. The primary goal of managing asymptomatic bacteriuria in a pregnant woman is to avert its advancement to pyelonephritis, which poses exceptional hazards during gestation. Pyelonephritis occurring in pregnancy has the potential to induce premature labour, anaemia, septicaemia, respiratory insufficiency, and in rare cases, maternal mortality. Furthermore, UTI during pregnancy are linked with the development of pre-eclampsia and congenital anomalies. The causative agents of urinary tract infections (UTIs) in females, regardless of their reproductive status, are members of the same taxonomic group and share the same virulence characteristics. *Escherichia coli, Klebsiellapneumoniae, Proteus species, Acinetobacter species, Staphylococcus saprophyticus, Group B Streptococcus (GBS), and Pseudomonas aeruginosa* are among the bacteria that are commonly seen. Pregnant women are known to be significantly predisposed to urinary tract infections (UTIs) by a number of factors, including advanced maternal age, multiparity, sexual activity, diabetes, sickle cell anemia, immunodeficiency, and urinary tract abnormalities. Pregnancy-related UTIs are often recognized as a contributing cause to poor maternal and perinatal outcome**s.(Balachandran *et al,*.2022).** The signs and symptoms connected with urinary tract infection (UTI) include discomfort or agony during urination, frequent urination, a sense of urgency, presence of blood or mucus in the urine, cramps or ache in the lower abdominal, discomfort during sexual intercourse, and pain, pressure, or tenderness in the bladder area. In cases where bacteria spread to the kidneys, patients may experience back pain, chills, fever, nausea, and vomiting**.(Ranjan*et al,*. 2017).**

Classification

The classification of UTI during pregnancy involves categorizing them into symptomatic and asymptomatic bacteriuria. Asymptomatic bacteriuria refers to the presence of true bacteriuria (>100,000/ml) without any specific symptoms of acute UTIs. On the other hand, symptomatic bacteriuria can be further divided into lower tract (cystitis) and upper tract (pyelonephritis) infections.

Asymptomatic bacteriuria ASB, is a bacterial UTI that occurs without any noticeable symptoms. It is worth noting that a significant percentage of expecting mothers who have asymptomatic, untreated bacteriuria, around 20-30%, may develop symptomatic UTIs such as cystitis or pyelonephritis. These UTIs pose a significant risk to both the foetus and mother. There is substantial evidence suggesting a link between UTIs and the onset of preterm labor. Therefore, it is advisable to conduct a urinalysis test at each prenatal diagnosis and monitor urine characteristics throughout the pregnancy.

Urethritis: It describes an infection of the urethra brought on by viruses, bacteria, protozoa, or fungi. This happens when these organisms get access to the entire female urethra as well as the periurethral glands in the male urethra**.(Ansaldi *et al.*,2023).** Several sexually transmitted Urinary tract infections in both sexes are frequently caused by pathogens such as *Neisseria gonorrhoeae, Trichomonas vaginalis, Chlamydia trachomatis*, and herpes simplex virus..

Cystitis: Women are more likely than males to get a bladder infection. Sexual activity frequently occurs before simple cystitis in female patients. When symptoms like dysuria, urgency, frequency, nocturia, hematuria, and suprapubic discomfort are present, it can be differentiated from asymptomatic bacteriuria. It is characterized by substantial bacteriuria with invasion of the bladder mucosa. These indicators are seen in women who are afebrile and do not exhibit any systemic disease symptoms. (**Kustrimovic*et al* ,.2024).**

Pyelonephritis: It is a condition suspected in the presence of systemic illness when a midstream MSSU culture finds at least 100,000 bacteria/mL of a single uropathogen, together with inflammation of the renal parenchyma, calices, and pelvis. Pyelonephritis can lead to early birth, preterm labor, and maternal sepsis if treatment is not received. Pyelonephritis symptoms include nausea, vomiting, chills, pyrexia, rigidity, flank or renal angle pain, andhip pain. Lo**w**er tract infection symptoms, like frequent urination and lack of thirst, may or may not be present**.(Zagaglia*et al,*. 2022).**

Pathogenesis

Urinary tract infections (UTIs) are caused by gut-resident uropathogens that colonize the urethra and subsequently the bladder through the action of certain adhesins. In the event that the host's inflammatory response is insufficient to destroy the bacteria, they begin to proliferate and produce toxins and enzymes that help them survive. Bacteremia may develop if the pathogen colonizes the kidneys and then passes through the kidney epithelial barrier. (**McLellan *et al*,.2016).** The pathogenicity of Urinary tract infection involves the invasion of the urethra by uropathogens, followed by their invasion of the bladder by means of certain adhesins. Upon evading the defense mechanism, these bacteria undergo multiplication, leading to the development of biofilms. Bacteria could rise from the lower urinary tract and reach the kidney, which may lead to bacteremia developing. Uropathogens usually attach themselves to the catheter and grow by using biofilm as protection when a complex UTI occurs. Bacteremia and pyelonephritis could develop from the infection if treatment is not received. If the bacteria survive and multiply, they create poisons and enzymes that help them survive, in case the host's inflammatory response is insufficient to erase them. Consequently, the identification of pathogenicity factors and the cultivation of bacteria that are uropathogenic and are advocated for the appropriate management of pyelonephritis. **(Lewis *et al*., 2016).** The infection and contamination do not appear to possess a notably severe nature, particularly during its initial phases; however, it has the potential to deteriorate significantly when complicated factors are present. Factors that complicate the progression of UTI encompass microbial, urinary retention resulting from barrier, and the utilization of catheters. Urinary tract infections comprise a wide range of clinical conditions that exhibit variations regarding their etiology and severeness of their conditions.

Etiology

UTI primarily results from the presence of numerous species, such as fungus, bacteria, viruses, and parasites. The majority of UTI's stem from both gram-positive and gram-negative bacteria that inhabit the large bowel or large intestine, such as *Enterococcus faecalis, Escherichia coli, Klebsiellapneumoniae and Proteus mirabilis*. Additional agents accountable for UTIs encompass *Pseudomonas aeruginosa, Staphylococcus saprophyticus, Group B Streptococcus (GBS)*. (**Manusco*et al* ., 2023)**.Uropathogenic E. coli represents the most prevalent pathogens. While bacteria stand as a prominent cause of UTI's,other microorganisms, such as viruses and fungus involved, are rather infrequent. Fungi, like *Candida albicans* stands as the most prevalent fungal species instigating UTIs. Notable viral causes of UTIs encompass human papillomavirus, cytomegalovirus, herpes simplex virus and type 1 human Polyomavirus. (**Tia *et al*. 2016).**

Agents causing Urinary Tract Infection

Clinical Manifestation

The UTI's clinical signs rely on their age, stage of infection, host response and type of bacteria causing the infection. The main symptoms of UTI during pregnancy are sensation of pain or a burning feeling during the process of urination ,increased frequency of the urge to urinate compared to usual urination occurring prior to reaching the toilet (referred to as 'leaking' or incontinence) sensation of the bladder being full, even after completion of urination urine that appears cloudy, has a presence of blood, or emits a strong odor pain experienced in the lower abdomen or above the pubic bone presence of a fever If the kidneys are now affected by the infection, symptoms may also include a high fever, back pain, and vomiting.

Treatment

Guidelines regarding treatment of UTIs have been disseminated, although there is inadequate adherence to these guidelines in terms of antibiotic preference, dosage, and duration. Noncompliance with these guidelines has the potential to yield diminished antibiotic efficacy (because of resistance development) and augmented healthcare expenditures. (**Chu*etal* ., 2018). Since**uropathogens may develop multidrug resistance, the treatment must be determined by testing for antibiotic susceptibility. Greater than or equivalent to 100,000 CFU/mL of bacteria is thought to be indicative of the infection (UTI), yet this number frequently produces false negatives, failing to identify many pertinent infections.**(Bader *et al*.,2020).**For both symptomatic and asymptomatic urinary tract infections (UTIs) during pregnancy, antibiotics are the usual course of treatment**(Kot*et al*.,2019)**. On the other hand, overuse of them can lead to antibiotic resistance (AMR) and expose the foetus to medications that could harm its development.

Currently, the greatest way to lower the frequency of UTIs and should refrain from taking antibiotics while expecting is to adopt preventative behaviours. **(Ghouri*et al.,* 2019).** However, excessive utilization of antibiotics may induce enduring alterations in the normal microbiota of the vaginal and gastrointestinal tracts, which may consequently result in hepatic and renal impairments, an imbalance in the flora, and various other complications. (**Gupta *et al.*,2017).** For first-line therapy, nitrofurantoin, trimethoprim-sulfamethoxazole (TMP-SMX), pivmecillinam, and Fosfomycintromethamine are the four indicated medicines. It is also advised to use two different agents: Both fluoroquinolones and β-lactams. (**Mueller *et al.*,2017.** Alternatives for Urinary Tract Infection treatment (**Kashif*et al.*,2019)** caused by multidrug resistant (MDR) Pseudomonas species include fluoroquinolones, ceftazidime, cefepime, piperacillin-tazobactam, carbapenems such as imipenem-cilastatin/relebactam, meropenem, and fosfomycin, ceftolozane-tazobactam, ceftazidime-avibactam, aminoglycosides including plazomicin, aztreonam, and ceftazidime-avibactam, cefiderocol, and colistin (**Radha*et al* ., 2016).** It is crucial to utilize these new antimicrobial agents wisely when treating UTIs caused by MDR organisms to prevent the development of resistance. (**Bader *et al.*, 2019).** Selection of antibacterial drugs is based on the susceptibility and resistance patterns specific to each individual and local area. However, it is advisable to consider the following options as initial empiric choices: - Cephalexin - Nitrofurantoin - Trim ethoprim/sulfamethoxazole**.(Holm *et al.*,2019).**

It'scrucial to remember that pregnant women having UTI should not take nitrofurantoin who are at term, in labor and delivery, or about to go into labor due to the potential risk of hemolytic anemia in the newborn**.(Zhou *et al.*,2023).**Expectant mothers who have G6PD deficiency should also avoid taking nitrofurantoin. Additionally, utilizing nitrofurantoin during the last 30 days (about 4 and a half weeks) of pregnancy may make neonatal jaundice more common. If no other options are available, nitrofurantoin should only be taken during 1 to 12 weeks (about 3 months) of pregnancy. (**Shallcross*et al.*,2020).** Trimethoprim/sulfamethoxazole (TMP/SMX) can lead to congenital malformations, such as neural tube defects, and kernicterus in newborns. The risk of some congenital malformations may be reduced with folic acid supplementation. (**Mireles *et al.*,2015).** TMP/SMX should only be used during the first trimester when no other options are available. After treatment, it is necessary to conduct proof-of-cure cultures. (**Johnson *et al.*,2017).** Women who have pyelonephritis or have experienced urinary tract infections on several occasions may require suppressive therapy throughout the remainder of their pregnancy. Typically, this involves the use of TMP/SMX (prior to 34 weeks) or nitrofurantoin. (**Klein *et al.,* 2020).** For women with bacteriuria, with or without a urinary tract infection or pyelonephritis, monthly urine cultures should be performed. (**Gharbi*et al,*.2019).**

CONCLUSION

Pregnant women are found to be more prone to UTI, which can be extremely stressful and anxiety-inducing. Their main worry is about the potential effects of the infection or the antibiotics on their unborn child**.(Luu*et al.*,2022**). While some women raise concerns about the safety of antibiotics, many women employ a risk assessment method that leads them to view antibiotics as necessary and safe to use during pregnancy if they exhibit any suspected UTI symptoms**.(Klein *et al* ., 2020)**.

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Table.1: List of microbes causing UTI

Bacteria's	Viruses	Fungi	Parasites
•*Escherichia coli*: the most common cause. •*Klebsiellapneumoniae* •*Proteus mirabilis* •*Enterobacter spp.* •*Pseudomonas aeruginosa* •*Acinetobacter spp.* •*Serratiaspp* *Enterococcus spp.* •*Staphylococcus saprophyticus* •*Staphylococcus aureus* •*Staphylococcus epidermidis* •*Streptococcus agalactiae* •*Mycobacterium tuberculosis*	•Adenovirus •Cytomegalovirus •Human polyoma virus	•*Candida albicans*	•*Schistosomahaematobium* •*Enterobiusvermacularis* •*Trichomonas vaginalis*

RESEARCH ARTICLE

Fibonacci Prime Labeling of Franklin Graph

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ABSTRACT

Let $G = (V, E)$ be a graph with p vertices and q edges. A bijection $f: V(G) \to \{1,2,3, \dots, p\}$ is said to be prime labeling if for each edge $e = uv$, the labels assigned to u and v are relatively prime. A prime labeling is said to be a Fibonacci prime labeling if, $i. f: V(G) \to \{f_2, f_3, \dots, f_{n+1}\}$,Where f_n is the n^{th} Fibonacci number. $ii. f^*: E(G) \to N$ defined by $f^*(uv) = gcd\{f(u), f(v)\} = 1$, $\forall uv \in E(G)$. A graph G admits a Fibonacci prime labeling and is called a Fibonacci prime graph. In this paper we apply duplication of vertex, switching of vertex and path union in FG and FG admits Fibonacci prime graphs.

Keywords: Franklin graph, graph labeling, Fibonacci prime labeling, duplication, switching, and path union.

INTRODUCTION

All graphs considered here are finite, simple, undirected, connected and non-trivial graph. Vertex set $V = V(G)$ and edge set $E = E(G)$ of the graph G. The order of the graph was defined by the number of elements of V, written as $|V|$, and its size was defined by the number of elements of E, denoted as $|E|$. For terminology and notation, we cite J.A. Bondy and U.S.R. Murthy [1]. Roger Entringer introduced the term "prime labeling" and Tout.A[9] explored it in a study. "Prime labeling of split graph of Star$K_{1,n}$" by Dr. V. Ganesan et al. Dr. V. Ganesan demonstrated "prime labeling of split graph of cycle C_n" in [4]. According to S.K.Vaidhya and K.K. Kanmani's proof in [10], networks created by identifying any two vertices, duplicating any arbitrary vertex, and switching any vertex in cycle C_n are prime labeling-admitting. Prabhakaran proved the Franklin graph's prime labeling in [7]. "Fibonacci prime labeling of graphs" was introduced by C. Sekar and S. Chandrakala in [8]. We'll provide a succinct review of terminology and other details that are related to the work at hand.

Preliminary Definitions

Definition 1.1
The Fibonacci number f_n is defined recursively by the equations $f_1 = 1, f_2 = 1, f_{n+1} = f_n + f_{n-1} (n \geq 2)$. Then $g.c.d\ (f_n, f_{n+1}) = 1, for\ all\ n \geq 1$.
Definition 1.2
A prime labeling of a graph G is an injective function $f: V(G) \rightarrow \{1,2, \dots, |V(G)|\}$ such that for every pair of adjacent vertices u and v, $gud\{f(u), f(v)\} = 1$.A graph which admits a prime labeling is called a prime labeling.
Definition 1.3
The Franklin graph is a 3-regular graph with 12 vertices and 18 edges.
Definition1.4
Duplication of a vertex v_k of a graph G produces a new graph G_1 by adding a vertex v_k with $v_k = N(v_k)$.
In other words a vertex $v_k{}'$ is said to be a duplication of v_k if all the vertices which are adjacent to v_k are now adjacent to $v_k{}'$
Definition1.5
A vertex switching G_v of a graph G is obtained by taking a vertex v of G, removing the entire edges incident with v and adding edges joining v to every vertex which are not adjacent to v in G.
Definition1.6
Let $G_1, G_2, G_3, \dots, G_n$ be n copies of a fixed graph G. The graph obtained by adding an edge between G_i and G_{i+1} for $i = 1,2, \dots, n-1$ is called the path union of G.

MAIN RESULTS

Definition 2.1
A Fibonacci prime labeling of a graph $G = (V, E)$ with $|V(G)| = n$ is an injective function $g: V(G) \rightarrow \{f_2, f_3, \dots f_{n+1}\}$, where f_n is the n^{th} Fibonacci number, that induces a function $h^*: E(G) \rightarrow N$ defined by $g^*(uv) = gcd\{g(u), g(v)\} = 1\ \forall uv \in E(G)$.
Theorem 2.2
Franklin graph is a Fibonacci prime graph.
Proof
Let G be a Franklin graph with 12 vertices and 18 edges.
$V[G] = \{v_1, v_2, v_3, \dots, v_{12}\}$
$E[G] = \{v_i v_{i+1}\ /1 \leq i \leq 11\} \cup \{v_{12} v_1\} \cup \{v_i v_{9-i}\ /1 \leq i \leq 2\} \cup \{v_i v_{13-i}\ /3 \leq i \leq 4\} \cup \{v_i v_{17-i}\ /5 \leq i \leq 6\}$
$|V(G)| = |n| = 12, |E(G)| = 18$
Define $g: V(G) \rightarrow \{f_2, f_3, \dots, f_{n+1}\}\ as\ g(v_i) = f_{i+1}, 1 \leq i \leq n\ \forall v_i \in V(G)$.
The induced function $g^*: E(G) \rightarrow N$ is defined by
$g^*(uv) = gcd\{g(u), g(v)\}, \forall uv \in E(G)$
$gcd\{f(v_i), f(v_{i+1})\} = gcd\{f_{i+1}, f_{i+2}\} = 1\ \ for\ 1 \leq i \leq 11$
$gcd\{f(v_{12}), f(v_1)\} = gcd\{f_{13}, f_2\} = 1$
$gcd\{f(v_i), f(v_{9-i})\} = gcd\{f_{i+1}, f_{10-i}\} = 1\ \ for\ 1 \leq i \leq 2$
$gcd\{f(v_i), f(v_{13-i})\} = gcd\{f_{i+1}, f_{14-i}\} = 1\ \ for\ 3 \leq i \leq 4$
$gcd\{f(v_i), f(v_{17-i})\} = gcd\{f_{i+1}, f_{18-i}\} = 1\ \ for\ 5 \leq i \leq 6$
Example Figure 2.1 Franklin graph admits Fibonacci prime labeling
As result, f meets the Fibonacci prime labeling condition FG accept Fibonacci prime labeling.
As a result, FG is a Fibonacci prime labeling.
Theorem 2.3
Franklin graph, which allows Fibonacci prime graph when any vertex of degree three is duplicated.
Proof
Consider the FG, which has 12 vertices and 18 edges. Let g be the graph generated by duplicating any vertex of degree three in the Franklin graph from FG. We can consider v_1 to be duplicating vertex, and let $v_1{}'$ be the duplication vertex of v_1.
$V(G) = \{v_1{}', v_1, v_2, \dots, v_{12}\}$

$E(G) = \{v_i v_{i+1} / 1 \le i \le 11\} \cup \{v_{12} v_1\} \cup \{v_i v_{9-i} / 1 \le i \le 2\} \cup \{v_i v_{13-i} / 3 \le i \le 4\} \cup \{v_i v_{17-i} / 5 \le i \le 6\} \cup \{v_2 v_1'\} \cup \{v_{12} v_1'\} \cup \{v_8 v_1'\}$
$|V(G)| = |n| = 13, |E(G)| = 21$
Define $g: V(G) \to \{f_2, f_3, \dots, f_{n+1}\}$ *as*
$g(v_i) = f_{i+1}, 1 \le i \le n \; \forall v_i \in V(G)$.
The induced function $g^*: E(G) \to N$ is defined by
$g^*(uv) = gcd\{g(u), g(v)\}, \forall uv \in E(G)$
$gcd\{f(v_i), f(v_{i+1})\} = gcd\{f_{i+1}, f_{i+2}\} = 1 \;\; for \;\; 1 \le i \le 11$
$gcd\{f(v_{12}), f(v_1)\} = gcd\{f_{13}, f_2\} = 1$
$gcd\{f(v_i), f(v_{9-i})\} = gcd\{f_{i+1}, f_{10-i}\} = 1 \;\; for \;\; 1 \le i \le 2$
$gcd\{f(v_i), f(v_{13-i})\} = gcd\{f_{i+1}, f_{14-i}\} = 1 \;\; for \;\; 3 \le i \le 4$
$gcd\{f(v_i), f(v_{17-i})\} = gcd\{f_{i+1}, f_{18-i}\} = 1 \;\; for \;\; 5 \le i \le 6$
$gcd\{f(v_2), f(v_1')\} = gcd\{f_3, f_{14}\} = 1$
$gcd\{f(v_{11}), f(v_1')\} = gcd\{f_{12}, f_{14}\} = 1$
$gcd\{f(v_{12}), f(v_1')\} = gcd\{f_{13}, f_{14}\} = 1$
f fulfil the prime labeling condition.
As a result, G admits prime labeling.
Hence G is a prime graph.

Example Figure 2.2 Duplication of the vertex $v1$ in Franklin graph and its Fibonacci prime labeling

Theorem 2.4
The graph obtained by switching of a vertex v_1 in a FG admits Fibonacci prime graph.
Proof
Let FG be the franklin graph with 12 vertices and 18 edges. $H_\alpha$denotes the graph obtained by vertex switching of FG with respect to the vertex v_1.
$V(H_\alpha) = \{v_1, v_2, \dots, v_{12}\}$
$E(H_\alpha) = \{v_i v_{i+1} / 2 \le i \le 11\} \cup \{v_2 v_7\} \cup \{v_i v_{13-i} / 3 \le i \le 4\} \cup \{v_i v_{17-i} / 5 \le i \le 6\} \cup \{v_1 v_{2+i} / 1 \le i \le 5\}$
$\cup \{v_1 v_{8+i} / 1 \le i \le 4\}$
$|V(H_\alpha)| = |n| = 12, |E(H_\alpha)| = 23$
Define $g: V(G) \to \{f_2, f_3, \dots, f_{n+1}\}$ *as*
$g(v_i) = f_{i+1}, 1 \le i \le n \; \forall v_i \in V(G)$.
The induced function $g^*: E(G) \to N$ is defined by
$g^*(uv) = gcd\{g(u), g(v)\}, \forall uv \in E(G)$
$gcd\{f(v_i), f(v_{i+1})\} = gcd\{f_{i+1}, f_{i+2}\} = 1 \;\; for \;\; 2 \le i \le 11$
$gcd\{f(v_2), f(v_7)\} = gcd\{f_3, f_8\} = 1$
$gcd\{f(v_i), f(v_{13-i})\} = gcd\{f_{i+1}, f_{14-i}\} = 1 \;\; for \;\; 3 \le i \le 4$
$gcd\{f(v_i), f(v_{17-i})\} = gcd\{f_{i+1}, f_{18-i}\} = 1 \;\; for \;\; 5 \le i \le 6$
$gcd\{f(v_{11}), f(v_{2+i})\} = gcd\{f_2, f_{3+i}\} = 1 \; for \;\; 1 \le i \le 5$
$gcd\{f(v_{12}), f(v_{8+i})\} = gcd\{f_2, f_{9+i}\} = 1 \; for \;\; 1 \le i \le 3$
Thus f is a prime labeling and consequently Gu is a prime graph
Therefore the switching of a vertex $v1$ in a Franklin graph admits prime labeling.
Example Figure 2.3 Switching **of the vertex $v1$ in Franklin graph admits Fibonacci prime labeling**

Theorem 2.5
The Fibonacci prime graph is admissible in the graph created by the path union of two pieces of FG.
Proof
Consider two copies of Franklin graph FG and FG^* respectively.
$V[G] = \{v_1, v_2, v_3, \dots, v_{12}\}$
$E[G] = \{v_i v_{i+1} / 1 \le i \le 11\} \cup \{v_{12} v_1\} \cup \{v_i v_{9-i} / 1 \le i \le 2\} \cup \{v_i v_{13-i} / 3 \le i \le 4\} \cup \{v_i v_{17-i} / 5 \le i \le 6\}$
$V(H_\beta) = V(FG) \cup V(FG^*)$
$E(H_\beta) = E(FG) \cup E(FG^*) \cup \{v_1 u_1\}$
$|V(G)| = |n| = 24, |E(G)| = 37$

Define $g: V(G) \to \{f_2, f_3, \dots, f_{n+1}\}$ *as*

$g(v_i) = f_{i+1}, 1 \le i \le 12\ \forall v_i \in V(G)$.

$g(u_i) = f_{i3+1}, 1 \le i \le 12\ \forall v_i \in V(G)$.

The induced function $g^*: E(G) \to N$ is defined by

$g^*(uv) = gcd\{g(u), g(v)\}, \forall uv \in E(G)$

$gcd\{f(v_i), f(v_{i+1})\} = gcd\{f_{i+1}, f_{i+2}\} = 1 \quad for\ 1 \le i \le 11$

$gcd\{f(v_{12}), f(v_1)\} = gcd\{f_{13}, f_2\} = 1$

$gcd\{f(v_i), f(v_{9-i})\} = gcd\{f_{i+1}, f_{10-i}\} = 1 \quad for\ 1 \le i \le 2$

$gcd\{f(v_i), f(v_{13-i})\} = gcd\{f_{i+1}, f_{14-i}\} = 1 \quad for\ 3 \le i \le 4$

$gcd\{f(v_i), f(v_{17-i})\} = gcd\{f_{i+1}, f_{18-i}\} = 1 \quad for\ 5 \le i \le 6$

$gcd\{f(u_i), f(u_{i+1})\} = gcd\{f_{i+13}, f_{i+14}\} = 1 \quad for\ 1 \le i \le 11$

$gcd\{f(u_{12}), f(u_1)\} = gcd\{f_{14}, f_{25}\} = 1$

$gcd\{f(u_i), f(u_{9-i})\} = gcd\{f_{i+13}, f_{22-i}\} = 1 \quad for\ 1 \le i \le 2$

$gcd\{f(u_i), f(u_{13-i})\} = gcd\{f_{i+13}, f_{25-i}\} = 1 \quad for\ 3 \le i \le 4$

$gcd\{f(u_i), f(u_{17-i})\} = gcd\{f_{i+13}, f_{29-i}\} = 1 \quad for\ 5 \le i \le 6$

Thus f admits a Fibonacci prime labeling.

Hence G_β is a Fibonacci prime labeling.

Example Figure 2.4 Path union of Franklin graph admits Fibonacci prime labeling

Application Of Graph Labelling

Numerous applications are mentioned here. Depending on the problem scenario, a certain type of graph is used for each application type to depict the issue. The issue is solved by applying an appropriate labeling to that graph.

- Measuring the effectiveness of sensor network communication
- Making algorithms in compression networks less complicated
- Communication-Related Graph Labeling for Adhoc Networks
- Secure Communication in Graph
- Short Label Names for Routing Algorithm Identification
- Automatic Routing with labeling
- Security while utilizing labeling scheme to reduce packet size
- Radio labeling-based quick communication in sensor networks.

CONCLUSION

We look into a few Fibonacci prime labeling findings. Similar conclusions may be drawn when applying the stated condition to additional graph families and various graph labeling issues. As mentioned before, labeling is a strong tool that facilitates communication in a variety of networking sectors.

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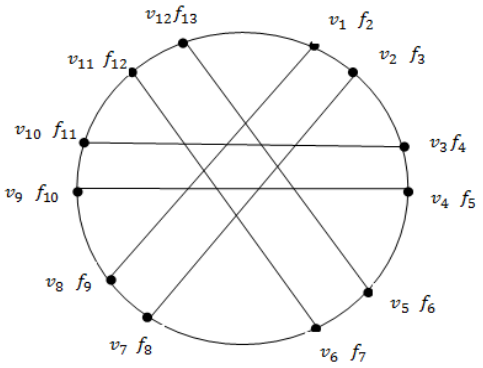

Figure 2.1 Franklin graph admits Fibonacci prime labeling

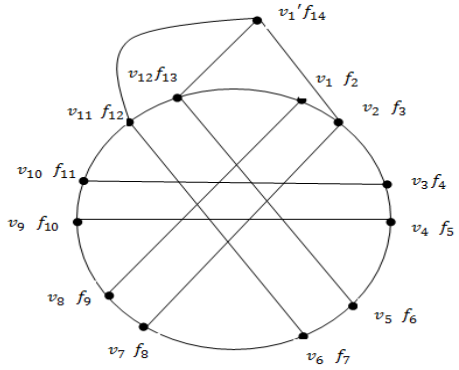

Figure 2.2 Duplication of the vertex $v1$ in Franklin graph and its Fibonacci prime labeling

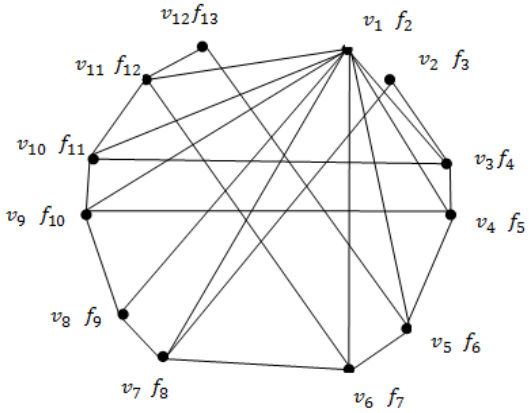

Figure 2.3 Switching **of the vertex $v1$ in Franklin graph admits Fibonacci prime labeling**

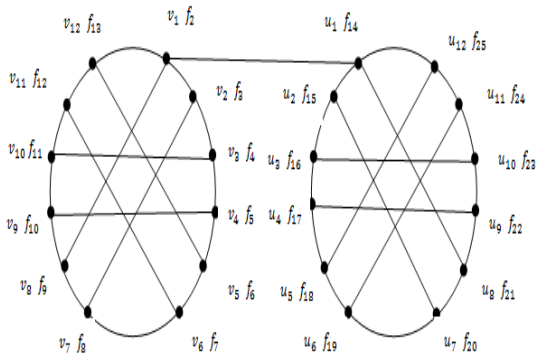

Figure 2.4 Path union of Franklin graph admits Fibonacci prime labeling

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RESEARCH ARTICLE

Effect of Blended Learning on Professional Development of Teachers

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ABSTRACT

This study addressed the multifaced approach of Blended Learning. As the innovative approach provides an opportunity to students to learn through face to face mode as well as digital mode. The given study focuses not merely on the effect of Blended Learning on students but also focuses on the effect of Blended Learning on teachers effectiveness. Blended Learning provides an opportunity to the learner to learn according to their own pace. There is no boundation of time and place. Blended Learning also provides an opportunity to the teacher so that a teacher can take the break from keep on rushing after the syllabus. Teacher gets extra time after the physical class, they can provide digital classes based on activities related to the content taught in the class so that students can get to know the depth of the content. The aim of the study is to determine the effect of Blended Learning on teacher's effectiveness, taking into consideration teacher's satisfaction, technical aspect of teachers, student teacher interaction and professional development of teachers in Blended Learning environment.

Keywords: **Blended Learning** According to **Grahem (2006)***"Blended Learning system combines face to face instruction with computer mediated instruction."*

Technophile
According to **Wikipedia** *"Techno philia refers generally to a strong enthusiasm for technology, especially new technologies such as personal computers, the internet mobile phones."*

Technophobia
According to **Wikipedia** *"Technophobia also known as techno fear. is the fear or dislike of advanced technology or complex devices, especially computer."*

Teacher Effectiveness
The term Teacher Effectiveness refers to the quality of a teacher who teaches and communicates knowledge or skills to the leaner being successful in producing a projected result. Teacher effectiveness is the measure of success of teacher in carrying out institutional and other specified duties demanded by the nature of his her position.

Teacher effectiveness includes effectiveness in strategies of instruction, student and classroom management, inter personal relations, evaluation and feedback.

According to **Umme Kulsum** *"Teacher effectiveness means that teachers have attained the needed competence in their roles and functions, namely preparation and planning, classroom management, knowledge of subject matter, teacher characteristics and inter personal relations. Also these excel in their other personality characteristics. They are said to be the best teachers."*

Medley terms teacher effectiveness as *"The possession of knowledge and skills that falls under the headings of teacher performance and use of knowledge and skills in the classroom as teacher performance with the accomplishment of teacher goals."*

INTRODUCTION

As we know effectiveness of teachers is perquisite for making teaching and learning process interesting, so that the children enjoys learning and whatever they learn remains in their memory for long. Teacher effectiveness, is basically all about the type of strategies used by teacher during class ,the kind of behaviour teacher shows in the classroom ,which later on adopted by children. as children spends most of their time in school. Effective teacher ,when enters into the classroom he/she is ready with teaching plan, objectives which he set for the class, he discuss the objectives with the class, use different strategies, try to make class more interesting ,so that his students fully involved in the class. Education is a lifelong process. Teaching and learning is the integral part of education. Teaching and Learning is the process which continues throughout one's life. Every little thing teaches us something and we learn, which enhance our horizon of knowledge and our experiences are based on that only. Teacher and learner are the two integral part of any education system. Effectiveness of both are prerequisite. Effective teachers and their teaching strategies are the back bone of any education system. It is the teacher who helps in shaping the whole personality of the learner and inculcates a sense of discipline, discipline in respect of behaviour as well as discipline in the way learner study , gain knowledge and apply the gained knowledge. For the proper functioning of teaching and learning process effectiveness of teachers is very important. Applying new and innovative teaching strategies is very important and crucial skill for teachers. Using innovative teaching strategies enhances student's learning as well as keeps them motivated for learning. Experimenting with strategies keep the student accelerated for learning. In this changing scenario it is very much important for student that they themselves take the responsibility of their learning. They should be able to gather information, analyse information, retain and also able to find out the solution of their problem. For all that they need the atmosphere in which they will be able to develop their critical thinking and reasoning ability with the use of new and innovative teaching strategies. A teacher can create such environment for students where a student gets varied experiences and they learn by doing things which results fruit full learning outcomes. Effective teachers keep on changing their way of teaching according to the interest of their students.

They choose those strategies which cater the need of each and every student. Gone are the days when students set passionately and listen whatever taught by the teacher. Today a child likes to explore each and every thing. Today's child is mor active fickle and playful, he needs novelty in his classroom also. So for that teachers must prepare themselves with the handful of teaching strategies with proper planning. In the present scenario teachers need to be enthusiastic about modern gadgets because they are the only who have to implement the various strategies in the classroom and new modern gadgets are now becoming the part of those strategies, which are planned by the teachers for their students. Becoming an effective teacher is not a simple task, a teacher must be proficient and techie also, techie here means one who has positive attitude towards use of modern gadgets, one who is enthusiastic and curious for the use of new technology and implementation of those technologies in the classroom as a teaching strategy so that the students get varied experiences in the classroom, which not only helps students to understand the concept but makes the learning long lasting. As we know that use of proper teaching-learning tools and strategies help in griping the attention of students. As we all know that today's era is the era of technological advancement and technology proves itself in every field or we can say that it affects almost every field of our life weather we talk about healthcare, transportation, better communication, easy and faster access to information, globalization, socialization and now it proves far more beneficial in the field of education. In the 21st centaury children are far more different from the children in earlier. Earlier children used to set in one place and listen whatever taught by the teacher at that

time the main focus is on the rote memorization but now this is the era of active learning, engaging students is a big task. Technology has proved itself in this field also now a days the focus of education system is shifted from mere lecture method, providing notes towards the use of innovative educational strategies by the teacher which not only helps in learning but also ensure the engagement of students, which is a big challenge for the teachers as student engagement in learning is prerequisite for their achievements as well as for healthy classroom environment, student's eagerness as well as interest in learning is also one of the most important factor which most of the time depends on the teacher's own enthusiasm and interest in teaching as well as the teacher's positive attitude towards the teaching strategies which they employ for their students. Here positive attitude of teachers towards use of teaching strategies not mere focus on the use of those strategies while teaching it means teachers themselves use those strategies with all their interest. They themselves feel confident while using them. Use of technology as a teaching strategies is the need of the hour because it not only helps in students engagement whereas also provides a fun while learning, which afterwards helps in the skill development of students. This is also applicable for teachers. As we all know that most of the times it has been seen that teachers abstain themselves from the use of new modern gadgets and technology as they are not technophile, they are technophobic and if they there-self do not take interest in the use of the technology how can they make their students to use technology while learning, whereas we all know very valuable words those have been around since time immemorial.

Gur Brahma Guru Vishnu,
Guru Devo Maheshwaraha,
Guru Saakshaat Parabrahma,
Tasmai Sri Gurave Namaha.

Teachers are the backbone of any education system, he/she can do everything that is for the betterment of his/her students. Teacher employs various innovative teaching strategies in his/her classroom which results focused and curious students, curiosity to know more and more, curiosity to explore each and everything for the attainment of knowledge. The various innovating teaching methods used by teachers are project based learning, e-learning whereas one method which is the combination rather we can say which is the blend of all those methods are Blended Learning. Blended Learning is the combination of face to face learning as well as online learning where students can learn on their own pace, they get more and more opportunities to go through the content or to understand the concept from both medium face to face as well as on digitally. According to **Colis and Moonen (2001)**, blended learning is a hybrid of traditional face-to-face and online learning so that instruction occurs both in the classroom and online, and where the online component becomes a natural extension of traditional classroom learning.

As we all know that the concept of Blended Learning employed mostly by teachers after COVID pandemic, when everything was shut down completely whereas we could not stop school education completely as children's education would suffer a lot. At that time, studies started from online mode and Blended Learning mode. Online learning takes place online using new technologies such as computer, smartphone or tablets whereas Blended Learning is the combination of both online learning as well as traditional method. Students can learn according to their pace. They get double opportunity to understand the concept fully. There is no boundary of knowledge student can take knowledge from anywhere whether he/she is sitting at home or school. Blended Learning provides such environment where student will always find him/her-self resourceful, student can understand the concept whenever he/she wants, wherever he wants, for that he/she does not need school like before and he/she does not even need to sit on the tuition like before, the concept he/she did not understand in school, student can understand the same concept at home which is provided by teacher in digital form. Blended Learning provides and uninterrupted learning platform to the students in which teacher plays a very important role. As we know in the present scenario, teacher is not just a guide for students, he/she is a friend, philosopher as well as mentor of his/her students, who is now present physically as well as virtually to mentor his/her students whenever they require. Blended Learning also provides an opportunity to the teacher to be up-skill and re-skill which is essential in the changing technological scenario to be revolutionized for the betterment of the whole teaching and learning process. Emphasizing technology does not mean traditional classroom teaching is less effective, for the holistic development of students which means physical, social, emotional, mental and intellectual growth. It is very important for children to go to school and spend time there with their classmates, participate in various curricular and extra co-curricular activities, ensure all round

development of the student. So Blended Learning is an instructional strategy which ensures both types of learning on-line learning where student can learn in its own pace, students can refer to the learning material as required and then move forward when they feel ready, and traditional learning where students get face to face learning experience. Blended Learning ensures both types of learning including technology as resource in education system is the call of time. Including technology in education system mere not solve the purpose whereas it is far most important that teachers as well as students should have expertise in technology. Incorporating Blended Learning as a method of instruction would definitely solve the purpose as it employ regular use of technology by teachers as well as by students and make them technophile. A teacher uses LMS (Learning Management System) for course creation, monitor learner presence and their performance. LMS is software tool used to provide learning material and content, student go through the content provided by the teachers, assignment according to their own pace. LMS facilitate centralized learning. All learning material is saved into LMS due to which learner get all the learning material in one place, it is also easy to use which makes it a great to learn tool.

The concept of Blended Learning evolves a new scenario of teaching and learning where student gets experience and both e-learning as well as traditional learning. There are various models of Blended Learning. Blended Learning provides the opportunity to the students as well as the teachers to take the whole process of teaching and learning, outside the four walls of classroom making it possible for students to access knowledge both online as well as offline. It is beneficial for all types of learner one who is benefited more from traditional teaching and one who is benefited more from digital learning. Blended Learning offers self-paced learning where learning videos, materials, quizzes are provided to the students through different LMS system. Various kinds of LMS are google classroom, canva, Microsoft team, all information is provided to the students in the learner's home page in a LMS. Now a days various types of pre application and software are being introduced to facilitate online learning. Blended Learning provides a new teaching and learning platform with full of creativity and enthusiasm for both teachers and students. Blended Learning provides an productive atmosphere to the children where they can involve in their studies according to their need and interest. They are free to satisfy their learning needs at any time no boundation of place as well. If a child has curiosity or if a child is facing any problem regarding understanding of content, he/she can take the help of online resources if a teacher is not available at the very moment.

The policy document on education, Nep 2026, highlights the major objective of Blended Learning is to make the process of learning not only impactful but also engaging, encouraging, interesting and challenging for learners." Nep 2020, also emphasis that, while promoting digital learning, face-to-face learning should be given full recognition. Blended Learning provides a platform to learner as well as teachers where they can move towards the digitalization of education without harming traditional way of teaching and learning where emphasis is given to teaching by the teachers. Digitalization of education provides an opportunity to the learner, learner who is curious to understand the certain content which he/she fails to understand in the class that concept can later be understood by the student by various learning apps as well as they go through the videos which were sent by teachers in L.M.S. The proper use of technology in education requires proper digital infrastructure as well as teacher's own technological acceptance which means at what extent a teacher is competent to use technology and what are the ways and means by which a teacher use technology to fulfil the learning needs of their students including Blended Learning methodology nt only helps students to fulfil their needs and cater individual differences whereas also helpful n the part of teacher as teacher becomes more resourceful. They have variety of things in their hands to make their teaching more objective. Blended Learning helps learner to be aware and vigilant towards their learning as they have many things to explore regarding their subject matter. They can follow their own style of learning whether he/she is auditory learner, whether they are visual learner, any of them can take benefit. Blended Learning makes the learning not only long lasting but easy to achievable like with the help of technology can easily access to virtual libraries, communicate with the scholars of respective subject, records lesson. Those who are high achievers can enhance their knowledge, go deep into the subject matter where other can go through the content repeatedly, revise the content and get feedback from their teachers and develop better understanding of the subject matter and eradicate the problems they are facing. Blended Learning is a flexible approach which provides an opportunity to the teacher to cater individual difference because each and every learner has their own set of interests, preferences and hurdles which a teacher has

to eradicate. So teachers must prepare themselves to create a Blended Learning environment which suit the learning need of every learner. For that a teacher must know in advance about his/her learner which results an effective learning experience. Knowing your learner will help you to formulate objectives, plan activities and assessment according to the need of your children which inculcate a sense of responsibility towards studies, sense of belongingness motivation, which is helpful in maintaining a good self-esteem. Blended Learning helps in nourishing teacher effectiveness, it provides an opportunity to the teacher that a teacher can provide variety of options to their learner according to the need and interest of learner side a teacher can provide. Instruction either using videos, audios and by text according to the different learning style and learner, a teacher can provide different activities and assessment quizzes, projects, presentations to the students. Blended Learning provides autonomy to the learner which means a learner has freedom and control over their learning but for better outcome. Learner needs to be more responsible. He/she has to manage his/her time and learning strategies very wisely, he/she must know the ways and means which best suit their learning style. Blended Learning is not an alternate of school teaching, but it compliments school teaching where a teacher gets a chance to make his/her teaching more effective, teacher has an autonomy how effectively he/she explains the content to his/her student by using various tools, gather online. Information shows them videos, conducts quizzes which provide an innovative learning environment to the learner, where student learn independently. Student gets varied chances to understand a concept until the concept is fully understood by him/her, which certainly improves his learning, which certainly improves his/her learning which is one of the most important criteria for measuring effectiveness of a good teacher that how he/she provides best to his/her students. Most of the time it has been seen that student himself enjoys online learning where he can go through various videos, solving online puzzles, interact with other students outside the class, digitally establish good repo with teacher also.

One more practical aspect of Blended Learning was realized when the DM ordered the closure of all schools due to rain whereas schools those who have Blended Learning concept have ordered conducting the online classes which saved the time of the students as well as helped in completing syllabus. In Blended Learning student has autonomy to choose the methodology which best suits his/her interest. Blended Learning provides an opportunity of timely assessment of student learning which is prerequisite for any teaching learning process to know how much student understood the concept delivered by the teacher. One of the most important advantage of both face-to-face and online learning is that a teacher can also take care of his/her weak student by first explaining the concept to him physically and then if required he can conduct the online class for his student to make the concept more clear. Blended Learning approach proves really beneficial when a teacher establish proper balance between physical and digital learning for that before conducting class. Teacher must know in advance what to taught and how will it proceed. Which certainly emphasis on proper planning done by teacher before conducting the class what activities will be done online and which one will be done offline, which creates a balance between two approaches. When we compare E-learning and online learning we find that E-learning also arrange fruitful learning, in which there is time and place boundation but still it cannot replace the traditional teaching. Therefor Blended Learning is more preferable which includes both online learning as well as traditional learning where students learn under the shadow of his teacher.

History of Blended learning:

The idea of blended learning has grounded in the 1960's when technology became available to support conventional learning. Blended Learning actually has its origin from remote leaning. Sir Issac Pitman invented shorthand and established his training company in 1837. He developed a distanced learning programme that allowed people to learn shorthand from anywhere without travel to classes and this became the early example of diverting the attention from mere setting in the classroom and accumulating knowledge towards gaining knowledge from anywhere without attending the physical classes. According to **(Garrison and Kanuka, 2004)**Blended has the potential to radically transform the design and dynamic of teaching and learning in education. **(Grid and Lane,2015)** further emphasis that this is enabled by the availability of information and communication technology, including the digital resources and technologies, utilized in the provision of teaching, learning and assessment. **Thorn (2003)** describes blended learning as a way of meeting the challenges of tailoring learning and development to the needs of individuals by integrating the innovative and technological advances offe3red with best of traditional leaning.

Tailoring learning is all about personalizing learning of each learner. Teacher changes his style of teaching which suits each type of learner for the better outcomes. In the same way, North American council for online learning (NACOL) an international Association, defines blended learning as combining online delivery of educational content with the best features of classroom interation and live instruction to personalize learning, allow thoughtful reflection and differentiate instruction from student to student across a diverse group of learners.

Status of Recent Research in National Level

1. **Sanjukta Sahoo, Regional Institute of Education, NCERT, Bhubaneswar, India and Dipak Bhattacharya, DukhulalNibarn Chandra College, West Bengal (2021)** studies the different models in blended teaching and learning process. In their study they concluded that blended teaching – learning strategy is a creative and technical development in a creative and technical development in online education that incorporates the engagement and involvement of conventional instruction. But they also point out that some students still facing difficulties in online components because of various socio-economic backgrounds or because of the lack of IT knowledge.
2. **SupriyaDahiya, MaharshiDayanand University, Rohtak (2015)** studies teacher effectiveness among secondary school teachers in relation to job stress, work motivation and use of information and communication technology. In this study researcher use descriptive survey method. The result of the study confirms that increase the teacher effectiveness of teachers, their job stress must be controlled and a positive correlation is found between work motivation and teacher's effectiveness as well as between use of ICT and teacher's effectiveness.
3. **Deviam M. (The Gandhigram Rural Institute (2018)** studies the effectiveness of blended learning in enhancing the B. Ed. Trainees achievement at psychology. Researcher use the pre-test and post-test equivalent group experimental design. The experimental group was taught using blended learning whereas the control group was taught using conventional teaching methods. The result of the study confirm that the Blended Learning is effective, interesting and offers better satisfaction to the learner.
4. **SonuShekhar Hindustan University (2020)** researcher investigate an expert mental study on blended learning approach to teach presentation skills to tertiary level engineering students. The study follower quasi experimental design. The researcher has collected data in two phases, before and after the intervention of the program. The result of the study classifies the efficiency of the Blended Learning system had a very substantial impact on the students of the experimental group. The result obtained clearly point out the improvement in speaking skills due to the introduction of the blended learning.
5. **Sonia Sharma &Piyali Sarkar, Lovely Professional University Punjab, 2020,** researchers investigate the "Efficiency of Blended Learning in Reduction of Anxiety with Special Reference to High School Students". Researchers use survey based study. An online survey was conducted through survey monkey software. Blended Learning Strategies: Role in fighting anxiety questionnaire' was prepared. Researchers proved that for the reduction of anxiety blended learning can be the remediation for teaching and learning process in India.

Status of Recent Research at International Level

1. **Abdulrahman M. Alfahadi, Abdulrahman A. Alsalhi and Abdullah S. Alshammari, (Tabuk University, Tabuk, KSA) 2015**. Researcher investigate the EFL secondary school teachers views on Blended Learning. Researcher also investigate the teacher's views on blended learning, learning content and process and how blended learning is effective in developing teacher's performance. Researcher collected quantitative data using questionnaire instruments. The result obtained indicates that the teachers views towards blended learning were highly optimistic about how blended learning would help them in improving their performance and how it would motivate their students to learn English. There is no significant differences between teachers responses to the content and process of blended learning with regards to qualification, experience and the amount of training done.
2. **Ibrahim Yildirim (Harran University) and SevilayCirak Kurt (Adiyaman University), 2018** conducted a research. The purpose of these study was to reveal student's perception on blended learning through Q method. The research data was compiled through the Q-sort and the judgemental statement created by the researcher

from 31 students. The finding of the study shows that the students are satisfied with the blended learning process.

3. **Melinda S. Payton, Concordia University, Portland, 2019.** Researcher studied *"Secondary Teacher's Description of Blended Learning and Professional Development: A case study."* Researcher used qualitative, descriptive single case study. The results of this study described the teacher saw technology as a necessary tool for students to live in a digital world, they saw technology as a tool to build good relationships and make content more interesting. Teachers wanted more district opportunities to have professional development.
4. **Osamah (Mohammad Ameen) AldalalahJodara University, Jorden, FeuasShatat Emirates College of Technology (ECT), Abu Dhabi, UAE. Zyad Waleed Abahneh, Ministry of Education, UAE** conducted study *"The impact of Blended Learning on the Development of the Cognitive and Metacognitive thinking Skills in Mathematics of the ECT Students."* They investigated the extent to which ECT students acquire cognitive and metacognitive skills with blended learning. Researchers applied the descriptive analytical method to develop the inventory of cognitive and metacognitive skill. Quantitatively the researchers used quasi-experimental design to identify how effective was blended learning on acquisition of cognitive and metacognitive thinking skills. The finding of the study reveal that the use of blended learning has positive effects in the student's metacognitive thinking skills in maths such that planning, organisation and evaluation. Blended learning has also shown an effective role in developing the low achievement students to acquire cognitive and metacognitive thinking skills in math.
5. **Mugenyi Justice Kintu, Changzhu and Edmond Kagambe (UniversitatOberta De Catalunya, Colombia)** researcher conducted the study to investigate the effectiveness of a blended learning environment through analysing the relationship between student characteristics, background design features and learning outcomes. Result showed that blended learning design features and student characteristics predict student satisfaction as an outcome.
6. **Nisreen Saleh Khader (2016)** researcher conducted the study. The effectiveness of blended learning in improving student's achievement in third grade's science in BaniKenana. The study sample consisted of 108 male and female students who were divided into two groups, experimental and control. An achievement test was developed in the mentioned units of the science course to measure the achievement which had a sufficient validity and reliability. The result indicated the presence of statistically significant differences in the post achievement due to the teaching method in favour of the experimental group.

Blended learning as a pedagogical strategy

Blended learning can be considered as the combination of traditional teaching and online teaching. Online teaching here refers to the use of technology. Technology in its self a wide field which include internet, CD-ROMs and interactive white board. Blended learning as a pedagogical strategy provides a wide variety of learning experiences to the learner, provides them self-paced learning, caters their individual needs. Students are free to choose their learning style, work on their weakness with the support of the teacher, as blended learning provides an opportunity to the teacher that they act as a 'Mentor' who gives continuous support and guidance to their students. Teacher themselves take into consideration the differentiated learning need of students. Thus, differentiated instruction are very much possible and it is required also in the present scenario of teaching and learning. Differentiated instruction is the process of tailoring the content according to the interest and need of each student, which helps teacher to personalize learning. Blended learning as a pedagogical strategy provides an opportunity of systematic and strategic use of technology which supplements the face to face leaning or we can say class room learning. Blended learning provides discretion to students in terms of time and place, high attention is given to students learning and pedagogical needs, diversity among students learning needs are given high priority. According to **(Eduviews,2009)** The blended learning model are so flexible and adaptive that teachers can create instructional activities that gives students the opportunities to work collaboratively, tapping their interests and abilities in social learning. According to **Dziuban, Hartman and Moskal (2004)** Blended learning should be viewed as a pedagogical approach that combines the effectiveness and socialization opportunities of the classroom with technologically enhanced active learning possibilities of the online environment, rather than a ratio of delivery modalities. Blended learning is basically a shift from mere 'lecture' to 'student centered instruction.' Which enables more and more interaction between student-instructor ,student-student, student-content ,student outside resources. According to **Babusha**

Arti Dangwal

Yagnik (Social science and Economics teacher National public school Rajajinagar ,Bengaluru, Karnataka ,India) 2015 Blended learning is need of the hour, earlier face to face teaching is popular among pupils but with the passage of time inclusion of technology in different domains leads to the introduction of technology in education as well. Research says, blended learning is the most engaging and effective model of teaching and learning. Let us see how Blended learning has become the crying need for the educational institutions: Education only cannot be left out: Big billion sale; ease in booking tickets; quick order of food; fast delivery of products/ services, all in all the market is all set to allure you to the fastest, simplest and cheapest services and this is only possible through technology. When technology has captured such a huge area of the society then why should only education be left behind. Hence in order to stay connected to the world it becomes important to include the use of technology along with face-to-face teaching in the education.

Differential Learning can be followed

Learner's needs and circumstances are different for each individual, hence teaching methods should also be different. Whereas with the incremental size of the class, it becomes difficult for teachers to cater to the needs of each individual. By using technology, a teacher can provide different learning aids as per the needs of individual students. Teacher can share videos/worksheets/links as per the student's requirements. Teacher can also provide more scaffolding to the students needing additional support to get them on the same level where others are. This will maintain the pace in the classroom and provide the required assistance to the students.

Lengthy syllabus

Lengthy syllabus is the main culprit for teachers running over the course to complete it on time. With the use of technology, the teacher can continue their process of teaching even through the press of button. Through technology, teacher can provide more resources to students, which can be accessible at their own time and convenience. Hence teacher would never run pout of time in completing their syllabus.

Flexibility with choice and use of content

Students studying now don't know what and how many will be the career options available to them. With globalization, the adoption of new things/patterns/ways is increasing and it has become mandatory to be updated with the global trends, new research, new methods, new assessment which assists teacher in providing best teaching to students and prepare students for the upcoming challenges. Needless to say, it is only possible through the integration of technology. In a nutshell, to be in the race of growing educational institutions, which are most adaptive and flexible as per the learner's needs, teachers have to use technology.

Models in Blended Teaching and Learning Strategy

The Blended Learning programme provides an independent and autonomous environment to the students where they enhance their knowledge as well as creativity. The Blended Learning Models are assisted by adaptive study systems and resources that allow teachers to fit the right student with the correct material in due course **(Powell et al., 2015)**. Adaptive study system means a type of learning environment where students are given various resources and activities according to their need and interest. There are four methods of Blended Learning **(Staker & Horn, 2012)**. These are Rotation Model, Flex Model, Self-Blend Model and Enriched-virtual Model. The Rotation Model can also be divided into four sub model: Station Rotation Model, Lab Rotation Model, Flipped-Classroom Model and Individual Rotation Model **(Staker & Horn, 2012)**.

Rotation Model

A Rotation Model shows the rotation of students between different learning stations, either according to the teacher's discretion or on a fixed schedule. Students are divided into groups when one group is engaged in independent online learning, the teacher involves another group of students in small group activities, projects, individual tutoring. It includes four models.

Station Rotation Model

In this model students rotate on a fixed schedule among various learning stations in a classroom. The three learning stations are : 1) Face to face instruction. 2) Online learning. 3) Group projects. Station rotation is a best option when you have limited access to technology.

Lab Rotation Model

In Lab Rotation Model students rotate to a separate computer lab for the online learning. It is the other option which works when you do not have a full set and computers in classroom. In station rotation and lab rotation models teachers are able to maximize learning with limited technology.

Flipped Classroom Model

It is a kind of model in which students receive instruction and content online (student have an autonomy to select the location in which they want online study) initially according to their own pace and place. After that, the experience is reinforced in the classroom. Students finish the lower level of cognitive work before class and when they come to class they can involve in higher level of cognitive work.

Individual Rotation Model

In Individual Rotation Model, students move through different learning modalities according to its needs rather than scheduled by teacher. No need for student to move through every modality. Some students primarily receive direct guidance from teacher and then sent to an online study lab whereas some students are sent directly to the online lab.

Flex Model

In Flex Model students complete most of their work online under the assistance of teacher. Most of the contents are provided online. It allows students to work on their own pace. In this model students can set their deadlines in consultation with their instructor. If students are facing a difficulty in concept, they can slow down their pace, once they complete that content, they may follow their regular work schedule.

Self-Blend Model

In this type of model students take online classes in addition to traditional classes. It helps students to supplement their learning. Online classes can be taken by students on the school campus or at home. It also solves the problem of the course which are not provided by the school.

Enriched Virtual Model

In this type of model main focus is on digital learning. Student may have face to face classes occasionally with their teacher. Main interaction between teacher and student take place through online platform.

Advantages of Blended learning

Blended learning proves to be a effective approach which embrace all diversities present in children. Diversities in term of their needs, interest, their learning experience which ,if not effectively addressed can create gap in learning.

Here are some advantages of blended learning

- It provides flexibility to both teacher as well as the students . In term of teacher, a teacher is free to decide, how he present learning material and in terms of students, students can learn according to their own pace, interest and strength.
- Blended learning comprises of multiple methods of instruction which give freedom to students that they can learn from the method which best suits their understanding. There are learner who learn better when they visualize the concept, where as other types of leaner are auditory and kinaesthetic. With help of blended learning teacher plan their instruction to help all different types of learners and provide personalize learning experience.
- Blended Learning is a new concept of pedagogy which increases student engagement in learning.

- Enhances student teacher interaction.
- Blended Learning also benefits the teacher, it shifts from knowledge provider to a coach and mentor.
- It is student centred, bottom-up and customized.
- Blended Learning is against traditional classroom which is teacher centred, top-down and one size fit all approach.

Challenges in Blended Learning Strategy

In spite of so many advantages, the successful implementation of Blended Learning is not yet possible because of the following:

1. One of the important major challenge of Blended Learning strategy is lack of infrastructure. Learning with the help of technology needs proper hardware, software and high bandwidth network connection.
2. For the proper implementation of Blended Learning in addition to infrastructure, skill full trained staff to help the user and maintain the system is prerequisite.
3. In today's scenario, technology equips and provides more resources and tools to the teacher so that by using those tools a teacher can provide better understanding of the subject material to his/her students whereas for that positive attitude of teachers towards technology is very much required. There are many teachers who are not technophile rather they like to use pen and pencil method of teaching which is a great hurdle for the implementation of Blended Learning.

CONCLUSION

Innovative teaching is basically the implementation and introduction of new teaching strategies into the classroom, which not only helps in the knowledge enhancement of student whereas also helps in inculcating creative thinking, decision making ability and works in collaboration among students. According to **Albert Einstein** "I never teach my pupils, I only attempt to provide the condition in which they can learn." The phrase "Provide the condition" as mentioned by Albert Einstein, these words or proper implementation of these words is very much important rather prerequisite for whole teaching and learning process. As we all know and also it is widely accepted that teaching should be such that learning is long lasting. For that a teacher should select teaching strategies very wisely and use of Blended Learning is one such strategy where students get face to face experience as well as virtual experience, which not only broaden the horizon of their knowledge but also provides the atmosphere where they can access to learning from any place. Blended Learning is a very innovative concept which is adopted by many educational institutes especially after COVID-19. This approach definitely cater learning need and interest of each and every learner. However teacher's perception about Blended Learning is also very important because he/she is the one who will be the introducer of technology in classroom. For that a teacher must accept the scenario of technology. Most of the times it has been observed that teachers himself or herself not ready to accept the change, they are more willingly to use the old instructional strategies. As we know that teachers and students spend most of their time in teaching and learning, wouldn't it be better if we bring technology into their studies? By always using new technology teachers as well as students will become assimilated to it and they gradually accept new technology and will start feeling confidence in using new technology. Blended Learning is an instructional strategy that combines face to face as well as online learning which not only provides different learning experiences to students whereas also provides an opportunity to teachers to enhance their teaching skills. For the proper implementation of Blended Learning teacher must enjoy technology, plan different instructional strategies for their students. Teacher can use videos, puzzles, online quizzes for their students whereas for that a teacher has to be tech-savvy than only he/she promotes a positive environment in classroom because if a teacher enjoys his/her teaching than only students enjoy their learning. So proper technical training must be provided to teachers those who are technophobic as well as those who are technophile. However wouldn't it be better if we implement Blended Learning workshops for B.Ed. trainees as they are the future educator.

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RESEARCH ARTICLE

Critical Analysis of the Effects of Nasya Karma and Neti Karma in the Management of Ardhavbhedaka W.S.R to Migraine: A Pilot Study

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ABSTRACT

Migraine is an intricate neurological condition characterized by recurring headaches, nausea, vomiting, sensitivity to light or sound, and visual disturbances such as tunnel vision or loss of vision in one eye. Additionally, individuals may experience difficulty speaking and intense pain typically concentrated on one side of the head. Commonly prescribed modern medications for managing migraine symptoms include nonspecific abortive therapies like Aspirin, Paracetamol, Ibuprofen, and Diclofenac, as well as specific medicaments such as Ergot derivatives and 5-HT receptor agonists. These medications are often recommended to alleviate symptoms and diminish the frequency and severity of migraine attacks. Ayurvedic texts have proposed several treatments for migraine, among which nasya therapy holds significant importance. According to yogic literature, neti is an important shatkriya that plays a crucial role in managing urdhavjatrugatavikara. Ardhavbhedaka is the disease of urdhwajatrugata. Jalaneti functions by purifying the nasal passages through saline water irrigation, eliminating gathered mucus, allergens, and pathogens commonly linked with migraines. This study attempted to use brihatdashmoola Taila as mentioned in shiroroga Chikitsa. This is an open-label randomized comparative clinical trial conducted on patients diagnosed with ardhavbhedaka. These patients were divided into two groups: Group A with 5 patients given Abhyanga Nadi Swedana followed by Nasya with Brihat Dashmoola

Taila, and Group B with 5 patients given Jala neti for 7 days. The study aims to explore the benefits of Nasya Karma and Neti Karma based on the principles outlined in Ayurvedic texts and Yogic teachings.

Keywords: Ardhavbhedaka, Nasya, Neti karma, Brihat Dashmoolataila, Migraine

INTRODUCTION

Ardhavbhedaka is one of the Shirorogas mentioned in Ayurvedic literature. According to Acharya Charaka, there are five types of Shirorogas in Sutrasthana: Vataja, Pittaja, Kaphaja, Sannipataja, and Krimija. He also mentioned four additional Shirorogas: Shankhaka, Ardhavbhedaka, Suryavarta, and Anantvata in Siddhisthana [1]. According to Acharya Sushruta, there are eleven types of Shirorogas: Vatika, Paittika, Kaphaja, Sannipatika, Raktaja, Kshayaja, Krimija, Suryavarta, Anantvata, Ardhavbhedaka, and Shankhaka [2]. Ardhavbhedaka is made up of two words: Ardha and Avabhedaka. Ardha means half or half side, while Avabhedaka means breaking through, perforating, or bursting out type of pain. Chakrapani explained Ardhavabhedaka as "Ardha Mastaka Vedana" [3]. Acharya Sushruta mentioned the involvement of tridoshas, while Acharya Charaka mentioned only Vata-Kapha involvement, and AcharayaVagbhatta described the involvement of Vata dosha only [4]. The vitiated Doshas mix with Ama in Amashaya, leading to Sroto-Dushti in Shirogata Rasa-RaktavahaSrotas (can be correlated with blood vessels) [5].

In cases of Ardhavbhedaka, typical symptoms include Shirahshoola (Headache), Shirobhrama (Confusion), Prakash-ashishnuta (Sensitivity to light), ShiraJala (Pulsating vessels), Netra hani (Loss of Vision), and Anorexia (Aruchi). These symptoms are characteristic manifestations of Ardhavbhedaka. Migraine is a complex condition marked by recurring headache episodes triggered by spasms in the blood vessels of the brain. It is now understood as a chronic condition rather than a mere headache disorder. Migraine represents the most common form of vascular headache characterized by abnormalities in blood vessel function that lead to constriction and dilation in the head [6]. "Migraine affects more women than men and is most common between the ages of 20 and 30. It was ranked as the 3rd most prevalent disorder and the 7th highest specific cause of disability worldwide [7]. In contemporary science, treatment encompasses non-pharmacological approaches like identifying triggers, meditation, relaxation training, and psychotherapy, as well as pharmacotherapy for abortive and preventive purposes. Aspirin, Paracetamol, Ibuprofen, Diclofenac, etc., represent nonspecific abortive therapies, while Ergot and 5-HT receptor agonists are specific abortive treatments. Preventive therapies include Triptans and Anti-convulsants[8]. However, these treatments may be associated with various side effects, such as tingling, numbness, nausea, and dizziness in about 40% of patients. Additionally, there is a risk of drug dependence and withdrawal, with a risk of rebound headaches[9].

Ardhavbhedaka is best treated with Ghrita, Taila, and Majja Shiro Virechana, Kaya Virechana, Nadisveda, Niruha and Anuvasana Basti, Upanaha, and Shiro Basti. Nasya therapy is regarded in Ayurveda as the master key to all Urdhvajatrugatavikaras. Special indications have been made by Sushruta for Nasya with Sirishphala, Dashmooladyavpidana, Madhukadhyavapidan, and Madhuradinasya. In a clinical study, the effect of Dashamoola in the management of sensory and motor disorders related to sympathetic and parasympathetic outflow amongst patients presenting with primary neurological disorders has shown significant improvement in nerve conduction velocity[10]. Therefore, BrihatDashamoola Taila was chosen for Nasya therapy. In the second group, we are practicing Shatkarmas. The Shatkarmas described in Hatha Yoga and Gheranda Samhita are highly effective, serving as both preventive and curative practices. Among these, the six types of Neti—Jala Neti, Dugdha Neti, Vyukrama Neti, Sitakarma Neti, Sutra Neti, and Madhu Neti—are emphasized[3]. These purificatory procedures play a crucial role in cleansing the body and mind, facilitating the opening of blocked channels and energy pathways known as Nadis. Neti, particularly Jala Neti, focuses on cleansing the nasal passages, aiming to purify the respiratory tract from the neck to the nostrils, essentially the region above the chest. This process aids in opening both the Nadis and the body-mind circuits, promoting overall well-being[11].

Aim
To evaluate the efficacy of Nasya with Brihat Dashmoola Taila and Jala Neti in the management of Ardhavbhedaka.

Objectives
Primary Objective: To observe the efficacy of Nasya using BrihatDashmoola Taila in Ardhavbhedaka.
Secondary Objective: To observe the efficacy of Jala Neti using Ushna Jala in Ardhavbhedaka.

MATERIALS AND METHODS

Study Approval
IEC Approval: No. PU/PIA/IECHR/2023/36 (Date: 17/04/2022)
CTRI No.: CTRI/2023/06/054576

Sources of Data
Patients diagnosed with Ardhavbhedaka from the OPD and IPD of Parul Ayurved Hospital, Waghodia, Vadodara, were selected for the study based on inclusion and exclusion criteria[12].

Method of Data Collection
Study Type: Open-labeled clinical trial.
Sampling Method: Simple randomized sampling procedure.
Sample Size: 10 patients (5 patients in each group).
Selection Criteria: Patients were selected based on diagnostic criteria of Ardhavbhedaka[13].

Study Design

Group	Drug	Dose	Duration	Route of Administration	Follow Up
A	Brihat Dashmoola Taila	2 Bindu	7 days	Nasal	8th & 14th day
B	Sukhoshan Jala + Saindhav Lavana	500 ML + 2.5 GM Saindhav Lavana	7 days	Nasal	8th & 14th day

Sample Source
Patients suffering from Ardhavbhedaka were selected from the OPD and IPD of Parul Ayurved Hospital and Khemdas Ayurved Hospital in Waghodia, Vadodara [14].

Drug Source
BrihatDashmoola Taila and Sukhoshana Jala were taken from Bhaisajya Ratnavali and Gherand Samhita, respectively, and prepared according to Taila Paka Vidhi described in the classics at GMP Certified Parul Ayurved Pharmacy, Vadodara, Gujarat [15].

Diagnostic Criteria
Individuals were selected as per the classical Lakshanas (symptoms) of Ardhavbhedaka such as Shirashoola (Pain on half side), Shirah Bhrama (Confusion), Prakash Ashishnuta (Photophobia), Netrarihani (Visual disturbance), and Anorexia (Aruchi).

Inclusion Criteria
- Age: 20–60 years
- Patients diagnosed with Ardhavbhedaka as per the diagnostic criteria
- Willingness to participate and give written informed consent

- Complaints persisting for more than six months

Exclusion Criteria

- Pregnant and lactating women
- Patients with uncontrolled systemic disorders
- Individuals on any specific medications or treatments known to interfere with study results
- Those with any severe systemic illness or condition contraindicating the trial medication

Investigations

Relevant investigations were carried out to exclude other conditions.

Assessment Parameters

Subjective Parameters

- Ardhashirashoola
- Manyashoola
- Bhrama
- Prakash-Sabda Ashahisnuta
- Chhardi
- Hrillas

Objective Parameters

Symptom	Scoring Pattern
Duration of Headache	0 = Nil 1 = 1-3 hours/day (Mild) 2 = 3-6 hours/day (Moderate) 3 = 6-12 hours/day (Severe)
Nausea (Hrillas)	0 = Nil 1 = Occasionally 2 = Moderate, does not disturb routine work 3 = Severe, disturbing work
Vomiting (Chhardi)	0 = Nil 1 = Only if headache does not subside 2 = Vomiting 1-2 times 3 = Vomiting 2-3 times
Photophobia/Phonophobia	0 = No symptoms 1 = Mild (can do work) 2 = Moderate (forced to stop work) 3 = Severe (Forced to medicate)
Vertigo (Bhrama)	0 = Nil 1 = Feeling of giddiness 2 = Feels everything is revolving 3 = Revolving signs + blackouts
Cervical Pain (Manyashoola)	0 = No 1 = Yes

Intervention

Group A: Nasya Karma with Brihat Dashmoola Taila

Procedure: Administered as per classical Nasya Karma protocol.

Materials Required: Nasya table, Nasya Yantra, dressing room, spittoon, etc.

Group B: Jala Neti with Ushna Jala and Saindhav Lavana

Procedure: Performed as per classical Jala Neti protocol.
Materials Required: Neti pot, salt, and lukewarm water.
Duration of Treatment
7 days, with follow-up assessments on the 8th and 14th days.

RESULTS

Clinical Observations and Assessments
Show the Table.1
Group A: BrihatDashmoola Taila Nasya

Patient No.	Ardhshira Shoola	Manyashoola	Bhrama	Hrillas	Chhardi	Prakash Ashahisnuta	Sabda Ashahisnuta
1	BT: 2, AT: 1	BT: 1, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 2, AT: 1	BT: 2, AT: 1
2	BT: 2, AT: 0	BT: 1, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 2, AT: 0	BT: 2, AT: 0
3	BT: 1, AT: 0	BT: 1, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 1, AT: 0
4	BT: 2, AT: 0	BT: 1, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 1, AT: 1	BT: 2, AT: 1	BT: 2, AT: 0
5	BT: 1, AT: 0	BT: 1, AT: 1	BT: 0, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 1, AT: 0

BT = Before Treatment, AT = After Treatment

Group B: Jala Neti

Patient No.	Ardhshira Shoola	Manyashoola	Bhrama	Hrillas	Chhardi	Prakash Ashahisnuta	Sabda Ashahisnuta
1	BT: 2, AT: 1	BT: 1, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 2, AT: 1	BT: 2, AT: 1
2	BT: 2, AT: 0	BT: 1, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 2, AT: 0	BT: 2, AT: 0
3	BT: 1, AT: 0	BT: 1, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 1, AT: 0
4	BT: 2, AT: 0	BT: 1, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 1, AT: 1	BT: 2, AT: 1	BT: 2, AT: 0
5	BT: 1, AT: 0	BT: 1, AT: 1	BT: 0, AT: 0	BT: 0, AT: 0	BT: 0, AT: 0	BT: 1, AT: 0	BT: 1, AT: 0

Assessment of Nasya Karma
Patient Symptom Tracking (Group A: Nasya with Brihat Dashmoola Taila)

Sr No.	Lakshana (Symptoms)	1st Day	2nd Day	3rd Day	4th Day	5th Day	6th Day	7th Day
1	**Shiro Laghava (Lightness of Head)**	+,+,+,-,+ (4/5)	+,-,+,-,+ (3/5)	+,-,+,-,+ (3/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)
2	**Sukha Swapna (Sound Sleep)**	+,-,+,-,+ (3/5)	+,-,+,-,+ (3/5)	+,-,+,-,+ (3/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,+,+ (5/5)
3	**Sukha Prabodha (Ease of Waking)**	+,+,+,+,+ (5/5)	+,+,+,+,+ (5/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,+,+ (5/5)	+,+,+,5,+ (5/5)
4	**Vikaro Pashama**	+,-,+,-,+	+,-,+,-,+	+,+,+,-,+	+,+,+,-,+	+,+,+,-,+	+,+,+,-,+	+,+,+,-,+

	(Symptom Relief)	(3/5)	(3/5)	(4/5)	(4/5)	(4/5)	(4/5)	(4/5)
5	**IndriyaShudhi (Sense Purification)**	+,+,+,-,+ (4/5)	+,-,+,-,+ (3/5)	+,-,-,-,+ (2/5)	+,-,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)

Summary of Results for Nasya (Group A)
1st Day: 19/25 (76%)
7th Day: 22/25 (88%)
Assessment of Jala Neti

Sr No.	**Lakshana (Symptoms)**	**1st Day**	**2nd Day**	**3rd Day**	**4th Day**	**5th Day**	**6th Day**	**7th Day**
1	**Lightness of the Head**	+,+,+,-,+ (4/5)	+,-,+,-,- (2/5)	+,-,+,-,- (3/5)	+,+,-,-,+ (3/5)	+,+,-,-,+ (3/5)	+,+,-,-,+ (3/5)	+,+,-,+,+ (4/5)
2	**Cleanses the Nasal Passage**	+,-,+,-,+ (3/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,-,-,+ (3/5)	+,+,-,-,+ (3/5)	+,+,-,+,+ (4/5)
3	**Easy Breathing**	+,-,+,-,+ (3/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)	+,+,+,-,+ (4/5)

Summary of Results for Jala Neti (Group B)
1st Day: 10/15 (66%)
7th Day: 12/15 (80%)

DISCUSSION

Ardhavabhedaka, an Ayurvedic condition analogous to migraine, is addressed through therapies that balance the body's doshas (Vata, Pitta, Kapha) and detoxify (Ama). Nasya Karma, recommended by Acharya Sushruta for head and neck disorders (UrdhvajatrugataVikaras), involves administering medicated oils into the nasal passage, which helps balance Vata and Kaphadoshas, clear nasal congestion, and improve circulation.

Group A: Nasya with Brihat Dashmoola Taila
Brihat Dashmoola Taila, particularly effective in pacifying Vata and Kaphadoshas, was selected for Nasya in this study. Dashmoola, a combination of ten roots, is known for its anti-inflammatory, analgesic, and dosha-balancing properties. The therapy's mechanism involves reaching the Shringataka Marma and distributing the medicine through the head, eyes, ears, and throat. The results showed a significant reduction in the intensity and frequency of headaches, along with improvements in associated symptoms such as nausea and sensitivity to light and sound. This can be attributed to the Vata-pacifying effects of the Dashmoola formulation, which is crucial in managing Ardhavabhedaka.

Group B: Jala Neti
Jala Neti, a traditional yogic practice, is highly effective in cleansing the nasal passages and sinuses, thereby alleviating congestion and associated headaches. Regular practice of Jala Neti has been shown to reduce the frequency and severity of headaches by clearing irritants and mucus from the nasal passages, which is particularly beneficial in conditions like Ardhavabhedaka. The practice also improves overall nasal health, reducing sensitivity to environmental triggers and contributing to a general sense of well-being. Over the course of seven days, patients reported a marked improvement in symptoms, including lighter head sensations and easier breathing.

Ardhavbhedaka, comparable to migraine in modern medicine, significantly impacts an individual's quality of life due to its severe symptoms. The results of this pilot study suggest that Nasya with BrihatDashmoola Taila shows promising outcomes in reducing the frequency and severity of migraine attacks, improving patients' overall well-being more effectively than Jala Neti. This observation aligns with Ayurvedic principles, which emphasize the significance of Nasya in treating UrdhvajatrugataVikara. Furthermore, the cleansing action of Jala Neti also

demonstrated beneficial effects, particularly in enhancing respiratory function and reducing nasal congestion, though it was less effective than Nasya in alleviating migraine symptoms.

CONCLUSION

This pilot study highlights the potential efficacy of Nasya with BrihatDashmoola Taila in managing Ardhavbhedaka. Both treatments were well tolerated by patients, and no adverse effects were reported. Both **Nasya with Brihat Dashmoola Taila** and **Jala Neti** showed marked improvements in managing Ardhavabhedaka, particularly in reducing headache intensity, frequency, and associated symptoms like nausea and congestion.

Nasya Therapy: Demonstrated an 88% effectiveness by the seventh day, making it a potent treatment for Vata-predominant disorders. **Jala Neti:** Improved overall nasal health and reduced headache severity, with a 14% improvement observed over seven days.

Further research with larger sample sizes and longer follow-up periods is recommended to validate these findings and explore the underlying mechanisms.

Conflict of Interest: None

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Table 1: Baseline Characteristics of Patients

Characteristic	Group A (n=5)	Group B (n=5)
Age (years)	35 ± 5	34 ± 6
Gender (M/F)	3/2	2/3
Duration of Migraine (years)	7 ± 2	6 ± 3
Frequency of Attacks (per month)	5 ± 1	6 ± 2
Visual Disturbances (%)	60%	50%

RESEARCH ARTICLE

Evaluating the Impact of Pilates on Non-Specific Low Back Pain in Postmenopausal Women : A Comparative Study

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ABSTRACT

Post-menopausal women, especially among the Indian population, are susceptible to experience non-specific low back pain which refers to pain or discomfort in the lower back region without a clear underlying structural cause or specific pathology. Pilates can help with the low back pain through a combination of strengthening, flexibility, postural improvement, and body awareness. Pilates reduces the pain by core strengthening, improving spinal alignment, balanced muscle development, dynamic stretching and controlled movements, encouraging mindfulness and awareness of movement patterns, specific breathing techniques, mind-body connection approach. Quantitative true experimental study was conducted among eighty Post menopausal women with non specific low back pain by simple random samplings. The experimental group were provided with Pilates training program and the control group were given with conventional exercise program for three times per week and for 8 weeks after assessing their pain, flexibility and endurance. Pretest and post test scores of experimental and control group were analyzed statistically. There was reduction of pain, improvement of flexibility and endurance of the post menopausal women of the experimental group (Pilates group) compared to the control group (conventional group). In spite of under regular conservative treatment of non specific low back pain among post menopausal women the Pilates training program has gained recognition for its beneficial effects on various aspects of physical health and well-being thereby improving the pain, flexibility and endurance among post menopausal women.

Keywords: Post menopausal women, Pilates, Non specific low back pain, flexibility, endurance.

INTRODUCTION

The majority of back pain is non – specific and idiopathic. It is estimated that 30 -70 % of Postmenopausal report episode of back pain between the age of 50 – 55 years. According to Yi Xiang J. Wang [1] Menopause as a potential cause for higher prevalence of low back pain in women than in age-matched men. This non specific low back pain restricts the flexibility and mobility of the postmenopausal women.[2] As the age increases, the present day women live a third of their life in menopause [3]. Low back pain is more prevalent in women than in men, and it increases as her age increases [4, 5,6]. According to Whelan *et al* even 80% of women suffer from various symptoms (including pain) in the postmenopausal period [7] Pilates exercise, in conjunction with our breath, it is a system of exercise designed to enhance the body's potential by correcting muscular imbalances finding optimal alignment and creating efficient movement pattern. A convenient Pilates exercise intervention can significantly improve muscle strength and trunk flexibility in women and decrease the Changes in Postmenopausal symptoms of vasomotor, mental and physical symptoms [8]. The present study had been undertaken with the aim of reducing the low back pain, improving the flexibility and endurance of the postmenopausal women with the help of Pilates exercise program.

MATERIALS AND METHODOLOGY

The research was commenced after the approval of Institutional Ethics committee of K.A.P.Viswanatham Government Medical College Tiruchirapalli – 620001 (Ref No: KAPV/IEC/221104001).Quantitative research approach was implemented with true experimental research design. The rationale for the number of people taken for study was done by the Convenience non probability sampling method, which suggested to select postmenopausal women with non specific low back pain samples with forty in experimental and forty in control group.

Inclusive Criteria

Females of age group between 45 to 57 years diagnosed with Menopause. Post menopausal women experiencing non specific low back pain without specific identifiable cause duration of three months, with severity of pain more than 5 as assessed in Numerical pain rating scale. Post Menopausal with functional limitation and decreased ability to perform the work due to low back pain as assessed by Oswetry Disability Index score less than 24 and decreased quality of life due to low back pain as assessed by MENQOL Questionnaire score more than 40.

Exclusion criteria

Age more than 57 Pre Menopausal women. Women with psychological pain Menopause Women diagnosed with Lumbar fractures Menopause women who have undergone any Lumbar Surgery Stroke, spinal cord pathology. Inflammatory joint disease. Lumbar spine infection Marked osteoporosis, Lumbar spine cancer Congestive heart failure, uncontrolled hypertension ,pacemaker, internalized metal stent

Outcome measures

Quality of life measured with MENQOL- Questionnaire Improved range of motion measured with goniometer Decreased intensity of pain through Numeric Pain scale Reduction in the disability level measured by Oswetry disability scale.

Experimental and interventional procedure

After getting proper informed consent, the participants who are coming under the inclusion criteria are asked to complete the Oswetry Disability Index Questionnaire and how it affected their ability to manage everyday life. The scores of the Oswestry Disability Index (ODI) range from 0 to 50, with higher scores indicating higher levels of disability. The scores are calculated based on the answers given to the 10 questions on the questionnaire, and each answer is given a score of 0 to 5. The scores are then added together to give a total score, which is then used to determine the level of disability experienced by the patient. A score of 0-20 is considered minimal disability, 21-40 moderate disability, and 41-50 severe disability [9]. Pilates [10, 11] advocates tout the core-strengthening benefits of

the method to improve posture and balance. Pilates targets the "powerhouse" muscles, which includes the glutei, hips, pelvic floor, and lower back. The MENQOL is self-administered and consists of a total of 29 items in a Likert-scale format. Each item assesses the impact of one of four domains of menopausal symptoms, as experienced over the last month: vasomotor (items 1–3), psychosocial (items 4–10), physical (items 11–26), and sexual (items 27–29) [12, 13].The answers to the questions are scored and used to calculate a total score, which provides a summary of the woman's Quality of life pre and post test. The Pilates exercise program was given to the experimental group, the treatment was administered for 8 weeks, 3 days in a week, with a 40 minutes session and the conventional exercise program was given to the control group for 8 weeks, 3 days in a week for 40 minutes. The post test survey questionnaire was conducted after 8 weeks and the findings of the participants were recorded in the coding sheet. The final analysis was done by descriptive and inferential statistics.

DISCUSSION

Quantitative data difference between experiment and control was analyzed using non parametric Mann Whitney U Test. A p value of ≤ 0.05 was considered statistically significant and two tailed test was used for significance testing. The table 1 shows the comparison of lumbar flexion, extension of the pre and post test of the experimental group shows significance with a p value of 0.00652, and 0.00168 respectively. The outcome measures of the experimental group the Numerical pain rating scale for pain, Oswetry disability scale for flexibility and MENQOL score for quality of life shows significance of p value of 0.00024, 0.00018,0.00022 respectively less than 0.05. The table 2 shows the comparison of lumbar flexion, extension of the pre and post test of the control group shows significance with a p value of 0.0161, and 0.0236 respectively. The outcome measures of the experimental group the Numerical pain rating scale for pain, Oswetry disability scale for flexibility and MENQOL score for quality of life shows significance of p value of 0.0285, 0.030, 0.0081 respectively less than 0.05 The table 3 shows the comparison of lumbar flexion, extension of the post test of the experimental and control group shows significance with a p value of 0.042, and 0.045 respectively. The outcome measures of the experimental group the Numerical pain rating scale for pain, Oswetry disability scale for flexibility and MENQOL score for quality of life shows significance of p value of 0.004, 0.007, 0.001 respectively less than 0.05 The effectiveness of the Pilates exercise program in reducing the low back pain was ascertained by comparing the pretest and post test of the experimental and control group is portrayed in figure – 1. Figure 2 depicts the comparison of pretest and Post test among the control group explaining the lumbar flexion, extension, the low back pain measure using the NRI, the ODI score and the MENQOL score. From the figure 1 and 2 we could see that the experimental group is much more effective in pointing out that there is a decrease in symptoms of pain, increase in flexibility and improvement in the quality of life of the post menopausal women with non specific low back pain compared to the control group.

Importance of Pilates training

According to many authors rehabilitating a spine musculature both in strength and flexibility with non specific low back pain is very essential to restore the function and prevent reoccurrence [14]. The study was conducted to assess the effectiveness of Pilates exercise program on selected postmenopausal women with non specific low back pain. The primary objective was to evaluate the effectiveness of Pilates training program among the experimental group. The study findings revealed that there was reduction of the pain, improvement of the flexibility and quality of life of the post menopausal women among the experimental group. The decrease in pain is measured by the numeric pain scale questionaire, the decrease in the disability is done by the Oswetry disability scale index, the flexibility measured by Universal goniometer, the quality of life improved was identified with the MENQOL Questionaire. The control group who were undergone with the normal conservative exercises did not have significant changes from the pretest and the post test. Pilates is a mind / body exercise that requires core stability, strength and flexibility and attention to muscle control, posture and breathing. Pilates have positive effects on personal autonomy, static balance and quality of life in the elderly females [15] The Pilates method using functional exercises improves the muscular strength and endurance.[16,17] The practicing level of these exercises increases week after week and finally helps in improving

the good postural control improvement. Pilates exercise program is more effective in decreasing pain and increasing lumbar strength and flexibility [18]

CONCLUSION

The research findings revealed that the Pilates exercise program is more effective in reducing the non specific low back pain by increasing the flexibility, strength and improving the Quality of life of the post menopausal women compared to the conventional exercise. The post menopausal women should take care of her health and live a happy and peaceful life by overcoming the postmenopausal symptoms by increasing her physical activity with the help of Pilates exercise Program.

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Conflicts of Interest
There are no conflicts of interest

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Table.1: Comparison among experimental group

Physical assessment						
	Mean	**SD**	**Mean**	**SD**	**Mean difference**	**Mann whitney U Test**
Lumbar flexion of spine	27.5	9.8	27	3.16	0	z =- 2.7213 p=0.00652
Lumbar extension spine	13.1	2.02	18	2.5	4.9	z =- 3.1371 p=0.00168
Pain	6.7	0.94	3.8	0.78	2.9	z =- - 3.666 p=0.00024
ODI Score	24.9	3.47	23.8	2.8	0.1	z =- 3.741 p=0.00018
MENQOL Score	51	10.3	34.3	3.5	16.7	z = 3.704 p=0.00022

Table.2: Comparison among control group

Physical assessment	**Pre test**		**Post test**			
	Mean	**SD**	**Mean**	**SD**	**Mean difference**	**Mann witney U test**
Lumbar flexion of spine	24.8	3.79	27	3.8	0.2	z= - 1.398 p=0.01615
Lumbar extension spine	12.8	2.14	15	2.74	2.2	z= - 1.927 p=0.0236
Pain	6.8	1.1	5.7	0.48	1.1	z=- 2.192 p=0.02852
ODI Score	26	3.8	23.8	2.8	2.2	z= 1.020 p=0.03077
MENQOL Score	48.2	8.6	43.3	6.01	3.9	z=- 1.738 p=0.00818

Table.3:Comparison between the experimental and control group

Physical assessment	**Group**					
	Experimental(n=10)		**Control (n = 10)**			
	Mean	**SD**	**Mean**	**SD**	**Mean difference**	**Mann Whitney U Test**
Lumbar flexion of spine	29	3.16	27	3.88	2	z =.7937 p=0.04295
Lumbar extension spine	18	2.58	15	2.74	3	z =.2.0032 p=0.04551
Pain	3.8	0.78	5.7	0.48	1.9	z =.- 3.515 p=0.0044
ODI Score	18.6	1.57	23.8	2.85	5.2	z =.- 3.363 p=0.0078

MENQOL Score	34.3	3.5	43.3	6.01	9	z =.- 3.212 p=0.00132

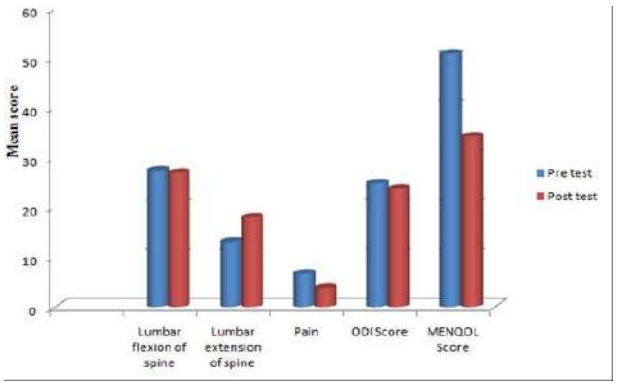

Figure.1:Comparison of pretest and post test among experimental group

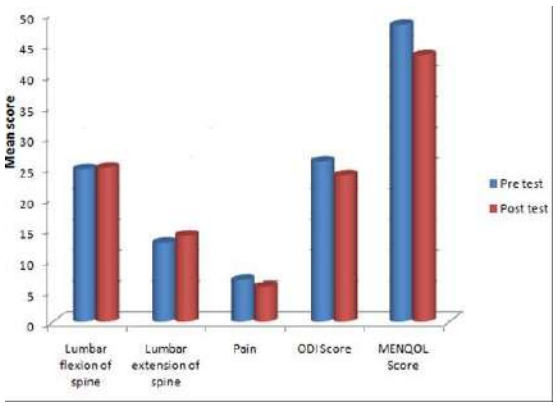

Figure.2:Comparison of pretest and post test among control group

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REVIEW ARTICLE

Machine Learning Integrated with Data Envelopment Analysis (DEA) and it's Applications : A Comprehensive Review

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ABSTRACT

This paper reviews the integration of machine learning (ML) techniques with data envelopment analysis (DEA) in various fields like manufacturing, banking, education, health services etc. The reviewed study demonstrate the effectiveness of combining DEA with ML algorithms to predict efficiency, evaluate performance, and address challenges like variable selection and model optimization. The research frameworks presented offer valuable insights into the application of ML-DEA methodologies, highlighting the potential for enhancing decision-making processes and resource allocation. The integration of machine learning with DEA represents a significant advancement in efficiency measurement techniques, providing promising avenues for future research and practical implementation across diverse industries.

Keywords: Efficiency; Data envelopment analysis; Decision making units (DMUs); Machine learning**.**

INTRODUCTION

Data envelopment analysis (DEA) is a non-parametric approach to assess relative efficiency of decision making units (DMUs). Since its original development in the late 1970s by Charnes, Cooper, and Rhodes[2], it has become more and more well-liked in a number of disciplines, including operations research, economics, management science, and healthcare. Analysts can evaluate the effectiveness of several DMUs that has multiple inputs to make multiple

outputs using this non-parametric approach. DEA is especially useful in scenarios when the production function is unknown or difficult to represent, as it does not necessitate precise functional forms or assumptions about the underlying production process, in contrast to standard parametric techniques. The primary objective of DEA is to identify the most efficient DMUs, which are those that achieve the highest level of outputs relative to their inputs, or equivalently, those that use the fewest inputs to produce a given level of outputs. Inefficiencies are measured by comparing each DMU's performance to that of the most efficient units, providing insights into potential areas for improvement. One of the key strengths of DEA is its flexibility in handling multiple inputs and outputs, as well as its ability to incorporate both quantitative and qualitative factors into the analysis. Additionally, DEA can handle various forms of data, including ratio data, interval data, and ordinal data, making it applicable to a wide range of real-world scenarios. DEA has some drawback and that can be overcome by integrating machine learning with DEA. However, if a new DMU is introduced while the organization is being evaluated, its efficiency score must be known; in order to do this, the DEA analysis must be repeated. Particularly in the present day, as big data is developing so swiftly, DMU datasets are expanding rapidly in the actual world. As a result, the DEA model would need to be rerun, requiring a significant amount of memory and CPU time on computers that have already been used to calculate the efficiency scores of a large number of DMUs. For this reason, we try to suggest a method based on machine learning (ML) algorithms for predicting the efficiency score [20]. We can forecast whether or not an organization may be classified as efficient with a sufficient correct classification rate by combining the DEA with machine learning methods.

The purpose of this review paper is introducing ML together with DEA and how ML techniques can enhance the efficiency of DEA model. Using ML in DEA we can select input and output variables also we can predict the efficiency score of new DMU. The four main types of machine learning are intense learning, semi-supervised learning, supervised learning, and unsupervised learning. Every strategy has particular advantages and disadvantages. One of the most popular machine learning algorithms, supervised learning, has two main tasks: classification and regression. Machines are trained to classify a group into discrete groups throughout the classification process. One simple example of classification is the spam filter on an email account. The filter examines emails that have already been reported as spam and contrasts them with fresh ones. These fresh communications will be tagged as spam and directed to the relevant folder if their proportion matches. Unrelated emails are categorized as regular and delivered to the mailbox [19]. Regression involves the computer making predictions about the future based on past (marked) data. Apps for the weather are a prime illustration of a return. The mobile weather application (APP) is able to examine current weather conditions and forecast future weather based on past data on weather events (such as humidity, average temperature, and precipitation)[19]. Without being specifically programmed to carry out the task, machine learning (ML) algorithms create a mathematical model of sample data, or "training data," in order to generate predictions or judgments. It is applied while utilizing DEA to assess organizational performance. For example, Delimiro Visbal -Cadavid *et al. (*2019) [8] proposed a DEA-ANN hybrid model to predict efficiency of Colombian higher education institutions. AnirbanNandy *et al.* (2020) [4] employ a hybrid strategy combining data envelopment analysis and machine learning to estimate farm efficiency. Nan Zhu *et al.* (2020) [19] used a combined machine learning algorithms and DEA method for measuring and predicting the efficiency of Chinese manufacturing listed companies. Anup Kumar et al. (2021) [3] measure performance of Indian banks using DEA and machine learning. Nadia M. Guerrero *et al*. (2022) [18] proposed "Data Envelopment Analysis-based Machines (DEAM)". The proposed approach prevents overfitting in the corresponding technology estimate by controlling the model's generalization error. Nor FaezahMohamadRazi *et al.* (2022) [17]proposed a machine learning predictive model of academic achievement efficiency based on Data Envelopment Analysis. Toni Duras *et al*. (2023) [22] used machine learning to select variables in DEA. Raul Moragues *et al*. (2023) [20] introduce an unsupervised machine learning method for production frontier estimation.

Review Of Papers

In the paper, "Prediction of efficiency in Colombian higher education institutions with data envelopment analysis and neural networks", author apply the CCR model [2] of the Data Envelopment Analysis (DEA), to determine efficiency of an HEI, and followed by neural networks to predict whether a new observation (HEI) can be classified

as efficient. The information utilized in this study was gathered from the Ministry of National Education of Colombia's database and matched the management indicators of public universities in that country from 2011 to 2013. Within the Colombian Public University System, they have gathered data on thirty-two universities. The constant return to scale (CRS) model, also referred to as the CCR model, states that each change in inputs should result in a corresponding change in output. Number of academic personnel overall, spending by administrative staff, financial resources, and physical resources are examples of input variables. Number of UG and PG degrees enrolled, Results Saber PRO, Indexed journal, Research publication, and Professor Mobility are the output variables. First they applied DEA-CCR-O (output oriented) model to get efficient and inefficient observations (96 observations), forty of the 96 observations are regarded as efficient, whereas 56 are not. The 96 observations were split into 72 for training (train) and 24 for validation (test) in order to model the neural network. The R software's caret and net packages were utilized to model the neural network. The caret package determines the optimal Size and Decay parameters for the neural network. The resulting model is an artificial neural network (ANN) with 10 inputs, 3 hidden neurons, and 1 output, or (10, 3, 1). The ten variables from the previously mentioned DEA model are the inputs used in the ANN. The findings demonstrate that applying the DEA in conjunction with neural networks enables us to forecast whether or not a HEI can be classified as efficient, with a sufficient rate of accurate classification. The results show that 50% of the created models exhibit accurate classification rates of 64.58% and 58.33% for training and validation data, respectively, indicating that this methodology has the potential to produce superior resource allocations [8].

In the paper, "Farm efficiency estimation using a hybrid approach of machine learning and data envelopment analysis: Evidence from rural eastern India", author investigates farm efficiency in rural eastern India by utilizing a hybrid model combining data envelopment analysis (DEA) and machine learning, specifically the Random Forest (RF) algorithm. The study collected primary data from 450 paddy growers in West Bengal and analyzed inputs such as human labor, machinery, and outputs like yield value. Environmental variables like age, education, and ownership were also considered. The RF method showed high prediction accuracy, outperforming traditional logistic regression. Key factors influencing farm efficiency were identified as land ownership, K is an Credit Card availability, education, and farming experience. The study suggests that improving these factors can enhance farm productivity and alleviate poverty in rural areas [4]. In the paper, "A combined machine learning algorithms and DEA method for measuring and predicting the efficiency of Chinese manufacturing listed companies", author proposes a novel approach that combines Data Envelopment Analysis with 4 Machine Learning algorithms to predict the efficiency of Decision Making Units in Chinese manufacturing listed companies. The study discusses the historical development of ML, highlighting its resurgence in the late 1970s with advancements in AI and data mining. Previous research on the hybrid ML-DEA methodology is reviewed, emphasizing the need for combined models to predict efficiency and compare results with single models. The research framework involves explaining the DEA method and the four ML algorithms, followed by measuring and predicting the performances of Chinese manufacturing listed companies in 2016. According to the empirical data, the ML-DEA algorithms GANN-DEA, BPNN-DEA, ISVM-DEA, and SVM-DEA are ranked from good to poor, with an average accuracy of projected efficiency of about 94%. Future research directions include collecting larger datasets, optimizing DEA methods with ML algorithms, comparing computational complexities, and addressing technical issues like activation function selection and model optimization.

Overall, the paper contributes to the field by demonstrating the effectiveness of combining DEA with ML algorithms for efficiency prediction in the manufacturing sector, providing insights for future studies and improvements in efficiency measurement techniques [19]. In the paper, "Performance evaluation of Indian banks using feature selection data envelopment analysis: A machine learning perspective", author presents a new "feature selection-based data envelopment analysis" (FSDEA) model that combines machine learning techniques with traditional data envelopment analysis to calculate the efficiencies and predict stress of Indian banks. The DEA ranks, bank success and failure rates, and other comparable decision-making units (DMUs) are all mapped out in the model. Additionally, it aids in the resolution of issues pertaining to the right selection of input and output features as well as time-dependent data points, all of which typically have a lag. The FSDEA approach, which combines a nonparametric frontier decision model with a machine learning technique, is unique in its sort. By choosing

input/output characteristics and turning time-series data into point data using a relief algorithm, it does away with the lag issue that plagues classical DEA. A total of 100 features are obtained by applying the model to a dataset consisting of 25 features collected over a period of four years. As a result, banks that failed in the past four years have lower efficiency than those that survived. The FSDEA model can be effectively used to test the stress of banks by fixing a cut-off efficiency for high stress, low stress, and no stress. It may also be applicable in ranking and examining the financial stress of firms in general. This study provides a way to find the ranks of the firm based on financial information, providing an early signal of potential failure for various stakeholders, such as management personnel, lenders, and shareholders. However, the model is only applicable when appropriate samples of past data are available regarding DMU performance [3]. In the paper, "Combining Data Envelopment Analysis and Machine Learning", author introduces a novel approach called "Data Envelopment Analysis-based Machines" (DEAM) that integrates non-parametric frontier analysis with machine learning techniques. DEAM aims to balance empirical and generalization errors in estimating production frontiers, addressing the over fitting issue associated with traditional DEA methods. Through computational simulations, DEAM is shown to outperform DEA in terms of bias and mean squared error, leading to more robust estimates of production technologies. The study emphasizes the flexibility and efficiency of DEAM in generating production possibility sets that adhere to microeconomic postulates while deviating from the minimal extrapolation axiom. Overall, the paper contributes to the field of efficiency assessment by offering a new methodology that combines the strengths of DEA and machine learning for improved technical efficiency analysis [18].

In the paper, "Machine Learning Predictive Model of Academic Achievement Efficiency based on Data Envelopment Analysis", author discusses a new research framework that aims to measure academic achievement efficiency using Data Envelopment Analysis (DEA) and machine learning. The authors emphasize the need to focus on multiple determinants, such as student attitude and digital skills, to predict academic success rather than solely relying on grades. They highlight the potential of DEA in evaluating academic efficiency and the challenges in selecting input and output variables for the analysis. They also introduced the integration of machine learning with DEA to expedite the process and improve accuracy. The authors propose a four-phase research framework involving variable selection, efficiency analysis using DEA, development of academic achievement efficiency prediction models, and evaluation of the predictive model. They emphasize the significance of this research framework in contributing fundamental knowledge to decision science and education performance measurement. The authors stress the potential of Auto-ML in machine learning and its role in accelerating model design and implementation. This research framework is positioned to contribute to decision science and education performance measurement by addressing current gaps in academic achievement evaluation. In conclusion, the document provides a well-structured and insightful overview of the proposed research framework, emphasizing the importance of a holistic approach to measuring academic achievement efficiency. It offers a detailed analysis of the potential contributions of the research framework and the significance of integrating DEA with machine learning. The document effectively conveys the authors' research objectives, the gaps they aim to address, and the potential impact of their proposed framework on decision science and education performance measurement [17].

In the paper, "Using machine learning to select variables in data envelopment analysis: Simulations and application using electricity distribution data", author addresses the challenge of variable selection in DEA models and explores the potential of machine learning techniques to improve this process. By introducing the ALASSO method and a two-step analytical approach, the authors aim to enhance the accuracy and efficiency of DEA models used in the regulation of electricity distribution systems. The authors obtained data from the Swedish Energy Markets Inspectorate (SEMI) on all Swedish distribution system operators (DSOs) for the year 2018. They used existing data sources and previous studies to investigate multicollinearity issues and select candidate variables for the analysis. The ALASSO method was applied for variable selection, and a DEA model estimated using the SCNLS framework was used to calculate firm-level efficiencies. The study demonstrates that the ALASSO method is effective in selecting relevant input variables for DEA models, particularly in the presence of multicollinearity. The two-step analytical approach provides a robust framework for calculating firm-level efficiencies in electricity distribution systems. The paper highlights the importance of incorporating machine learning techniques in variable selection to

improve the accuracy of DEA models. The findings of this study have significant implications for regulators and policymakers in the electricity distribution sector. By utilizing machine learning-based variable selection techniques, regulators can enhance the efficiency and effectiveness of DEA models used for regulatory purposes. The ALASSO method offers a promising approach to address multicollinearity issues and improve the selection of input variables in DEA models [22]. In the paper, "An unsupervised learning-based generalization of Data Envelopment Analysis", author presents a cutting-edge unsupervised learning-based technique that extends the capabilities of DEA in measuring technical inefficiency and optimizing production processes. By incorporating principles of machine learning, the method offers a fresh perspective on efficiency analysis and performance measurement in diverse industries. The unsupervised method in DEA utilizes a directional distance function to estimate production frontiers without the need for labeled data. This departure from traditional supervised approaches allows for a more robust and flexible analysis of efficiency scores. The methodology is meticulously explained, highlighting its advantages over conventional DEA models. The implications of the unsupervised method in DEA are far-reaching, offering researchers and practitioners a powerful tool for enhancing productivity and performance measurement. Future research directions could include applying the technique to multi-output databases and exploring its applicability in different empirical contexts. In conclusion, the unsupervised method in Data Envelopment Analysis represents a significant advancement in the field of efficiency analysis and production frontier estimation. By combining the principles of machine learning with traditional DEA concepts, the method provides a promising framework for improving decision-making processes and optimizing resource allocation in various industries [20].

CONCLUSION

The reviewed papers highlight the growing significance of integrating machine learning techniques with data envelopment analysis (DEA) to enhance efficiency prediction and decision-making processes in various sectors. The studies demonstrate the effectiveness of combining DEA with machine learning algorithms to predict efficiency, evaluate performance, and address challenges such as variable selection and model optimization. The research frameworks presented in the paper offer valuable insights into the applications of ML-DEA methodologies in fields like manufacturing, banking, education, health services etc. By leveraging the strengths of both DEA and machine learning, these studies contribute to advancing efficiency measurement techniques and offer promising avenues for future research and practical implementation. The integration of machine learning with DEA represents a significant advancement in the field, providing researchers and practitioners with powerful tools to improve decision-making, optimize resource allocation, and enhance productivity across diverse industries. The future scope of ML-DEA research includes exploring multi-output databases, diverse empirical contexts, optimizing DEA methods with ML algorithms, conducting comparative studies, analyzing large-scale datasets, addressing technical challenges, and developing advanced algorithms for forecasting continuous efficiency values. These avenues offer opportunities to enhance efficiency prediction accuracy, scalability, and applicability across industries, driving innovation in decision-making processes and resource optimization.

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CONFLICT OF INTEREST:

The author declare no competing interests.

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RESEARCH ARTICLE

Implementing Ashta Ahara Vidhi Vishesh Ayatana in Contemporary Life : An Ayurvedic Perspective on Health

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ABSTRACT

Ayurveda, one of the world's oldest health care systems, emphasizes the role of *Ahara* (food) in maintaining health and preventing disease. *Ahara*, *Nidra* (sleep), and *Brahmacharya* (celibacy or balanced sexual conduct) are the foundational pillars of health, with *Ahara* being paramount. The *Ashta Ahara Vidhi Vishesh Ayatana* outlined by *AcharyaCharak*, presents eight factors crucial for dietary practices, including*Prakriti*(nature of food),*Karana*(preparation methods), *Samyoga* (food combination), *Rashi*(quantity),*Desha*(habitat),*Kala*(time),Upyogasamstha(eating rules), and Upyokta(individual habits). These factors offer guidance for aligning diet with individual constitution (*Prakriti*), seasonal variations (*Ritucharya*), and digestive capacity (*Agni*), which is essential for preventing lifestyle disorders.In modern dietary contexts, processed and fast foods, irregular meal timing, and imbalanced diets contribute to widespread health issues. By applying Ayurvedic principles, particularly the *Ashta Ahara Vidhi Vishesh Ayatana*, individuals can improve nutrient absorption, enhance gut health, and optimize metabolism. The integration of these guidelines into contemporary eating habits offers a holistic approach to preventing chronic diseases, promoting well-being, and addressing the challenges posed by modern food practices. This review emphasizes the need for a critical reassessment of current eating patterns, encouraging the reintegration of Ayurvedic food guidelines for sustainable health.

Keywords: *Ayurveda, Ashta Ahara Vidhi Vishesh Ayatana, Prakriti*, diet, lifestyle disorders, modern nutrition

INTRODUCTION

Ayurveda, the ancient Indian system of medicine, places significant emphasis on promoting health and preventing illness through a comprehensive and balanced approach to living. This is encapsulated in the guiding principle, "Swasthasya Swasthya Rakshanam Aturasya Vikara Prashamanam Cha," which translates tothe preservation of health in the healthy and the mitigation of disease in the sick.[1] Among the foundational elements of good health-*Ahara* (diet), *Nidra* (sleep), and *Brahmacharya* (regulated sexual behaviour)-diet is regarded as the most important.[2] In *Ayurveda, Ahara* is so highly esteemed that it is referred to as "*Mahabhaishajya*," or the supreme medicine.[3]Due to its critical role in maintaining well-being and managing diseases. Improper dietary habits are considered a major contributor to various diseases, underscoring the pivotal role food plays in both the promotion of health and the onset of illness. In today's world, where fast foods, erratic meal patterns, and nutritionally imbalanced diets have become the norm, the principles of *Ashta Ahara Vidhi Vishesh Ayatana* offer a holistic and scientifically grounded framework for nutrition. These principles take into account not only the individual's constitution but also environmental factors, thus presenting a well-rounded dietary approach. The application of these guidelines is especially relevant in modern times, as the neglect of these dietary principles is closely linked to the rise of lifestyle disorders, which are increasingly prevalent due to contemporary dietary and lifestyle habits.

MATERIALS AND METHODS

A conceptual study involves reviewing and analysing existing literature on a specific concept. This includes examining classical texts, scientific journals, dissertations, and research papers related to the concept. The study focuses on collecting and evaluating literary data to gain insights into the concept under investigation.

Review of Literature

Aahar Vishesha- Special Effects of Food.
Vidhi Vishesha-Specific Method or Arrangement of Eating.
Ayatana- Sustenance
1. Prakriti -Food's natural state
2. Karana- Food preparation process
3. Samyoga- Combination of various food
4. Rashi- Food quantum
5. Desha- Food habitat
6. Kala- Time-Age, seasons, region
7. Upyogasamstha-Food consumption guidelines
8. Upyokta- Individual a pattern of conduct [4]

Prakriti

The natural qualities inherent in food substances (*Ahara Dravya*) are known as their Prakriti. These qualities, like Guru (heavy) and Laghu (light), are present from the time of their origin and define their unique characteristics. For example, Mung beans are considered *Laghu* (light), while Urad dal is *Guru* (heavy) in nature. Each food and medicinal substance has its own inherent qualities—some are naturally hot or cold, and others might have cooling effects even in a warm environment or vice versa. These characteristics determine how the substance interacts with the body. It is crucial for a physician to prescribe remedies based on these qualities to effectively address specific diseases and complications.[5]

Karana

Karan refers to the process or transformation that food undergoes, which changes its original properties. This transformation, known as *samskara*, can occur through various methods such as cooking (*Agnisanskaran*), mixing with

water (*Jalasamyog*), cleaning, and churning (*Manthana*). Many foods are not suitable for direct consumption in their raw form and need to undergo these processes to become digestible and beneficial to the body. For example, raw rice is considered *Guru* (heavy), but when cooked, it becomes *Laghu* (light) and easier to digest. Similarly, while raw rice is cooling in nature, boiling transforms it into a warming food. Processing can also enhance or alter the qualities of food—for example, brown (unpolished) rice is considered more nutritious than polished rice, which loses some of its beneficial properties during refinement.[6]

Samyoga

When two or more substances are combined, this mixture is referred to as *Samyoga*. The combination can lead to the development of new qualities that weren't present in the individual components. Sometimes, however, this can result in harmful effects. For example, while ghee and honey are safe and beneficial on their own, combining them in equal parts can create a toxic effect. Similarly, combining foods like honey, fish, and milk can lead to health issues like *KushtaRoga* (skin disorders), even though these foods are harmless when consumed separately. On the other hand, some combinations, such as rice and lentils (dal), complement each other nutritionally and are beneficial when eaten together. Thus, the effects of food combinations can vary widely, and it's important to be mindful of what is mixed together for safe and beneficial consumption.[7]

Rashi

Rashi refers to measuring both the total quantity of food and its ingredients to assess proper dosages. Food should be consumed according to one's digestive capacity (*Agni*), with half the stomach filled with solid food, one-quarter with liquids, and one-quarter left empty to allow *Vata* flow. Guru foods (heavy) should be eaten in moderation, while Laghu foods (light) are easier to digest but still require balance. Eating too much (*Ati Matra*) or too little (*Heena Matra*) disrupts digestion and overall health.[8]

Desha

The climate of a region influences the nature of the food produced there. Foods that grow in hot climates tend to have a warming effect on the body, while those from colder regions are naturally cooling. This connection between climate and food helps explain why certain foods thrive in different temperatures, reflecting the environment they come from.[9]

Kala

In *Ayurveda*, two key aspects of *Kala* (time) are recognized: *Nityaga Kala* and *Avasthika Kala*, both of which hold significant importance in relation to diet (*Ahara*). *Nityaga Kala* pertains to the routine timing of meals, which should be adjusted according to the natural daily cycle and seasonal variations. For instance, meal times may vary based on the season, and appropriate foods are consumed accordingly. On the other hand, *Avasthika Kala* refers to the timing of food intake during different stages of a disease.[10]

Upyogasamstha

It refers to dietary guidelines that are based on digestive symptoms. Consuming food before the previous meal has not been fully digested can disturb all three Doshas, potentially leading to severe health issues. Dietary guidelines emphasize eating hot, unctuous food in proper amounts, only after digestion of the previous meal. Avoid incompatible foods, eat in a suitable environment, without distraction, and with proper attention.[11]

Upyokta

The individual consuming food is responsible for its healthfulness through the habitual intake of substances suited to their constitution, known as *Oka Satmya*. It is essential for one to evaluate and reflect upon their unique physiological constitution and adjust their dietary choices accordingly.[12]

DISCUSSION

The integration of *Aṣṭāahāra Vidhi* principles into daily life is crucial for preventing lifestyle-related disorders and promoting overall health. By adhering to these dietary guidelines, individuals can make informed food choices tailored to their unique constitutions (*Prakriti*) and health requirements. This discussion examines the impact of neglecting *Aṣṭāahāra Vidhi* through the lens of prevalent lifestyle disorders, including metabolic syndrome, cardiovascular diseases, and gastrointestinal disturbances. Modern food processing methods, the proliferation of processed foods, and fast-paced lifestyles are critiqued in light of *Ayurvedic* principles.

Prakriti

Contemporary diets often consist of processed and fast foods, such as chips, carbonated drinks, and frozen meals, which are typically heavy, oily, and dry. These characteristics can disrupt internal balance, particularly aggravating *Vata*,*Pitta* and *Kapha* doshas. The consumption of processed foods contributes to inflammation, digestive disorders, and a general disturbance of the body's natural homeostasis. Ayurveda emphasizes understanding the inherent qualities of food—whether hot, cold, light, or heavy to make better dietary choices, encouraging the consumption of fresh, whole foods such as fruits and vegetables, which are more aligned with individual constitutions.

Karana

The widespread availability of packaged snacks and ready-made meals, storaged items has increased reliance on food preparation techniques such as deep-frying and microwaving, which drastically alter the natural properties of food, rendering them harder to digest. Highly processed foods lose essential nutrients, contributing to the development of health conditions such as obesity and diabetes. *Ayurveda,* in contrast, advocates for simpler cooking methods, such as steaming or boiling, to preserve nutrient content and enhance digestion.

Samyoga

Certain modern food combinations, such as fruit-based milkshakes or pizza topped with cheese and meats, are considered incompatible (*Viruddha Ahara*) in Ayurveda. These combinations can lead to digestive discomfort, including bloating, and contribute to the formation of toxins (*Ama*). Ayurveda advises avoiding such imbalanced food pairings, instead promoting simpler and more harmonious combinations that support efficient digestion and overall health.

Rashi

The trend of consuming large portion sizes, often seen in "all-you-can-eat" buffets, has led to overeating becoming a common problem. Even nutrient-dense foods, when consumed in excess, can contribute to health issues such as weight gain and metabolic disorders. Overeating taxes the digestive system and can lead to conditions like indigestion and obesity. Ayurveda emphasizes mindful eating and portion control to prevent overeating, thus addressing modern health concerns like type 2 diabetes.

Desha

Globalization has facilitated the consumption of foods grown far from their native environments, such as the consumption of tropical fruits in cold climates. Ayurveda teaches that locally grown and seasonal foods are better suited to an individual's constitution and help maintain optimal digestion and health. Consuming foods that are aligned with the local environment supports the body's adaptation to surrounding conditions.

Kala

Irregular eating patterns have become increasingly common due to busy modern lifestyles, such as late-night dinners, night shift job or snacking at odd hours. Additionally, seasonal eating patterns have been disrupted by the year-round availability of produce. Such irregular habits disrupt the body's natural circadian rhythms and contribute

to digestive disturbances like acid reflux and weight gain. Ayurveda underscores the importance of eating in alignment with natural cycles, both daily and seasonal, to support digestion and metabolic balance.

Upayoga samstha

Skipping meals or eating at irregular intervals, such as skipping breakfast or consuming late-night snacks, disrupts the digestive process and metabolic balance. Ayurveda advises maintaining regular meal times and eating only when genuinely hungry. Irregular eating habits, such as meal skipping, can lead to indigestion and metabolic issues, including insulin resistance. Consistent meal patterns support healthy digestion and metabolic function.

Upyokta

Eating while multitasking, such as watching TV or working, has become the norm, often leading to overeating or poor digestion and child obesity. Ayurveda advocates mindful eating, encouraging individuals to sit in a calm environment, chew thoroughly, and avoid distractions while eating. This practice enhances digestion, improves nutrient absorption, and prevents overeating, counteracting the negative effects of stress-related eating.

CONCLUSION

In the context of modern dietary practices, following the guidelines for consuming *Ahara Dravya* is crucial for maintaining overall health. The *Ashta Ahara Vidhi Vishesh Ayatana* offers scientifically grounded principles that align with contemporary nutrition needs, promoting balance and well-being. These *Ayurvedic* guidelines take into account factors such as an individual's constitution (*Prakriti*), seasonal variations (*Ritucharya*), and digestive capacity (*Agni*), which can help address modern lifestyle-related conditions like obesity, diabetes, and cardiovascular diseases.By aligning food choices with these principles, individuals can enhance nutrient absorption, support gut health, and improve metabolic efficiency. Given the rise of fast food, processed meals, and irregular eating habits, it is essential to reassess current eating patterns. Integrating Ayurvedic dietary wisdom into modern food practices can help counteract the negative impact of unhealthy diets, restore balance, and prevent the onset of chronic diseases, ultimately fostering holistic well-being tailored to individual needs and environmental factors.

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REVIEW ARTICLE

Phytochemistry and Pharmacological aspects of Polyalthia longifolia - A Review

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ABSTRACT

Tall and attractive, *Polyalthia longifolia* (PL) is an evergreen tree of the Annonaceae family. It is available throughout many tropical nations, including all of India. Because of how well it reduces noise pollution, it is frequently utilized as an ornamental street tree.Many substances have been identified in plant extracts from the leaves, stem, bark, roots, fruits, and seeds. This plant contains a variety of compounds that are used in traditional medicine to treat fever, skin conditions, diabetes, heart issues, helminthiasis, and other conditions. These compounds include steroids, alkaloids, terpenoids, phenols, fatty acids, flavonoids, glycosides, saponins, tannins, resins, carbohydrates, and essential oils. Anti-microbial, hypotensive, antioxidant,anti-inflammatory, anti-cancer, hepatoprotective, anti-hyperglycimic, anti-fungal, anti-leishmanial, anti-ulcer, anti-malarial, and termicidal action are only a few of the important biological and pharmacological properties of *Polyalthia longifolia.* Thus, it is more than simply a decorative tree; it is also regarded as a plant with potential therapeutic use and a good source of secondary metabolites. In an effort to offer guidance for future research, this review attempts to gather comprehensive investigation of all the phytochemical and pharmacological features of *P. longifolia* that are currently known.

Keywords: *Polyalthia longifolia,* Phytochemistry, Pharmacology, Group compounds.

INTRODUCTION

Medicinal herbs are essential to human existence. There is a significant interaction between humans and herbs. Since the dawn of human civilization, plants have been utilized to treat and manage a variety of illnesses. Due to the fact that about 80% of people in underdeveloped nations rely on plants for their main healthcare, medicinal plants continue to play significant roles in society even in the face of huge technological advancements. In addition to being a keystay of conventional medical practices, plant-based therapy is the primary source of inspiration for a number of significant pharmaceutical products used in the fight against a wide range of illnesses. Due to their ease of use, safety, and efficacy, medicinal plants are in high demand in both developed and developing nations. Due to these factors, medicinal plants are a traditional medical practitioner's first choice for daily practice. Of the roughly 120 species in the genus *Polyalthia* (Annonaceae), only 14 are native to India(Dixit et al.,). The Greek word *polyalthia* means "many cure," while the Latin word *longifolia* describes the length of the leaves. The plant is primarily found in India's hot regions. *Polyalthia longifolia (P. longifolia)* was mentioned in the earliest documented description of the use of plantwood by Troup RS and Chopra RN as a medicine for the treatment of gonorrhea, as well as for snake bites and scorpion stings. The plant's bark can be extracted aqueously to lower heart rate and blood pressure. Chopra RN also claimed that the bark can be utilized as a febrifuge.Due to its ability to effectively reduce noise pollution, one such plant is *Polyalthia longifolia* (Order: Magnoliales ; Family: Annonaceae). This evergreen species is frequently employed as an ornamental street tree. Other names for *Polyalthia longifolia* include Green Champa, Buddha Tree, Indian Mast Tree, Indian Fire Tree, and False Ashoka. It grows in a symmetrical pyramidal form, with long, narrow lanceolate leaves that have undulate borders and willowy, weeping pendulous branches. The tree can reach a height of more than thirty feet. Different herbal formulations are used in traditional medicine to treat duodenal ulcers. The herb has been used to treat helminthiasis, fever, skin conditions, diabetes, and hypertension in traditional medicine.

The plant has yielded several chemicals that are physiologically active (Wu Y.C et al.,). The plant's aromatic leaves are typically used for adornment, but in India, the bark is utilized as a traditional remedy for pyrexia and other bleeding diseases.From an ethanomed perspective The adaptable plant *Polyalthia longifolia* is used to cure a variety of conditions, including helminthiasis, diabetes, skin conditions, menorrhagia, rheumatism, and scorpion stings. The custard apple family, or Annonaceae, is the one to which the mast tree belongs. Plants in the Annonaceae family are widely used in literature as traditional medicine. These plants are used to cure cancer, hepatomegaly, hepatosplenomegaly, coughing, diarrhea, and septic infections. Because of its exceptional contract of young golden and coppery brown leaves over old dark green leaves, it is the tree of choice for landscape design. Another name for *P. longifolia* is the Buddha tree. It is made up of a lightweight, straight trunk. It is known as the mast tree because it was formerly used to prepare masts for sailing ships. The majority of its applications are in the production of little items as pencil boxes. The plant's stem bark is commonly substituted for or utilized as an adulterant in place of *Saraca indica* bark.*P. longifolia* exhibits good metal-adsorbent properties. The plant is beneficial for managing industrial waste water and effluent due to this action. Moreover, the plant demonstrates a strong ability to prevent corrosion.

PHARMACOLOGICAL ACTIVITIES OF *POLYALTHIA LONGIFOLIA*

Hepatoprotective activity

Using both in vitro and in vivo techniques, the methanolic extract of *Polyalthiya longifolia* fruits was studied as a powerful hepatoprotective agent. Freshly obtained rat primary hepatocytes and HepG2 cells were subjected to CCl4 in conjunction with or without different amounts of methanolic extract (125, 250, and 500 Hg/kg) in an in vitro investigation. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, and total proteins were measured in the in vivo investigations using the CCl4 intoxication method, and the results were corroborated by histological investigations. When tested at 300, 600, and 900 mg/kg doses, the methanolic leaf extract of *Polyalthiya longifolia* had a notable hepatoprotective action, indicating its potential as a hepatoprotective agent against diclofenac sodium as the toxicant (Jain et al.,).

Anti-diabetic activity

Polyalthia longifolia extracts in ethanol and chloroform demonstrated the two enzymes' inhibitory action in vitro (η-amylase and η-glucosidase) as well as their anti-diabetic activity in vivo (against streptozotocin-induced type 1 diabetes mellitus in rats). It was discovered that the ethanolic extract's IC50 for ·-amylase was 154.3±2.42 Hg/ml, while the IC50 for chloroform was 180.3± 1.35 ×g/ml. The ethanol's IC50 values for η-glucosidase inhibition were discovered to be 208.7±2.54 Hg/ml, whereas the chloroform value was 271.6±0.85 ×g/ml.Studies on acute toxicity revealed that the extracts at 2000 mg/kg b.w. were safe. The aberrant alterations seen in untreated diabetic rats were reversed by both extracts in a dose-dependent manner, with the ethanol extract having a marginally stronger impact than the chloroform extract. When given orally to rabbits in an alloxan-induced diabetes paradigm, the petroleum ether extract from *Polyalthia longifolia* leaves (50, 100, 200, and 300 mg/kg) significantly reduced blood glucose levels. *Polyalthia longifolia* bark extracts in n-hexane, ethyl acetate, and methanolic solvents significantly enhanced the rats' ability to tolerate glucose in alloxan-induced diabetes in comparison to the normal control group, and these extracts at 300 mg/kg dose demonstrated a decrease in glucose levels. Rats with alloxan-induced experimental diabetes were used to test the hypoglycemic and antihyperglycemic effects of different solvent extracts of *Polyalthia longifolia var. pendula* leaf extracts. The powder and extracts of *Polyalthia longifolia* shown glucose-lowering action. Nonetheless, none of the biochemical parameters were appreciably altered by the extracts (Nair et al.,).

Analgesic activity

Mature *P. longifolia* leaves exhibited analgesic efficacy in the methanol, ethyl acetate, and benzene extracts. Ethyl and benzene extracts were shown to exhibit a weaker analgesic effect than the methanol extract. Moniruzzaman et al. evaluated the ethanolic extract of *P. longifolia* stem bark for its antinociceptive properties, or its ability to prevent the perception of a painful stimulus. The study employed thermal and chemical models of nociception, including licking tests generated by glutamate and formalin, tail-immersion and hot-plate tests, and writhing tests induced by acetic acid. In a dose-dependent manner, the extract exhibited good antinociceptive efficacy(Moniruzzaman et al.,).

Anti-pyretic activity

Utilizing an LPS-induced antipyretic activity model, the antipyretic properties of *Polyalthia longifolia* methanolic extracts of the leaves, stem bark, and root were evaluated at doses of 30, 100, and 300 mg/kg body weight. Significant dose-dependent antipyretic efficacy was demonstrated by all extracts. All extracts showed more activity at 300 mg/kg than Acetylsalicyclic acid (Aspirin), which had an 86% percentage suppression of pyrexia. With a percentage inhibition of 127.5%, the root extract was the most active, followed by the leaf extract (123.0%) and the stem bark extract (99.2%) (Annan et al.,).

Anti-inflammatory activity

With IC50 values of 3.06±0.20 and 3.30±0.48 ×M, respectively, a clerodane diterpenoid 16-hydroxycleroda3,13(14)E-dien-15-oic acid from *P. longifolia* significantly inhibited the release of elastase in formyl L-methionyl-L-leucyl-L-phenylalanine (FMLP) activated human neutrophils in a concentration-dependent manner. Using Cotton pellet granuloma, a sub-acute anti-inflammatory model, the anti-inflammatory activity of ethanolic and aqueous extracts of *P. longifolia* leaf in albino wister rats was assessed. The weight of the cotton pellet decreased significantly when compared to the illness, indicating that all of the extracts significantly reduced the granuloma tissue. The anti-inflammatory properties of both the ethanolic and aqueous leaf extracts were comparable to those of indomethacin, and the highest anti-inflammatory activity was seen at a dosage of 300 mg/kg. At a dosage of 200 mg/kg body weight, the aqueous extracts, as opposed to the ethanolic extracts, had superior anti-inflammatory action. Acute inflammatory experiments in Wistar albino rats were used to assess the anti-inflammatory properties of several solvent extracts (petroleum ether, hexane, toluene, chloroform, acetone, and methanol) of *P. longifolia* leaf. Three doses of methanolic extract (300, 600, and 900 mg/kg) were utilized to assess the extract's potential as an anti-inflammatory agent because it showed the greatest promise. The anti-inflammatory properties of the three methanolic extract dosages were equivalent to those of the reference drug, diclofenac sodium(Tanna et al.,).

Antioxidant activity

Rat liver homogenate was used to test the *Polyalthia longifolia* seeds' ethanolic extract's antioxidant properties. Significant free radical scavenging activity was demonstrated by nitric oxide, ferrous sulphate, and carbon tetrachloride-induced lipid scavenging activities. A dose-dependent rise was observed in the percentage reduction of peroxide production. Using well-established in vitro models such as ferric reducing antioxidant power (FRAP), 2,2-diphenyl-1-picryl-hydrazyl (DPPH), hydroxyl radical (OH), nitric oxide radical (NO) scavenging, metal chelating, and antilipidperoxidation activities, methanolic leaf extracts from *Polyalthia longifolia* were assessed for in vitro antioxidant activity and free radical scavenging capacity. The concentration-dependent antiradical activity of *P. longifolia's* methanolic extracts was demonstrated by their ability to inhibit the DPPH radical, with inhibitory concentration 50% (IC50) values of 2.721 ± 0.116 mg/mL. The ethanolic extract of *P. Longifolia* leaves contained active ingredients such as quercetin, quecetin-3-O-fl-glucopyranoside, and rutin. These constituents demonstrated their antioxidant capacity by scavenging the ABTS+ radical cation, which was expressed using Trolox Equivalent Antioxidant Capacity (TEAC) assays(Sashidhara et al.,).

Anti-cancer activity

The stem bark ethanolic extract of *Polyalthia longifolia* was tested for antitumor activity both in vitro and in vivo. The extract demonstrated concentration-dependent cytotoxicity in HeLa, MCF-7, Dalton's ascites lymphoma (DLA), and Ehrlich's ascites carcinoma (EAC) cells, with IC50 values of 45.77 and 52.52, 25.24, and 50.49 ×g/ml, respectively. The two novel clerodane diterpenes, 16·-hydroxy-cleroda3,13(14)Z-diene-15,16-olide and polyalthialdoic acid, were extracted from *Polyalthia longifolia* leaves and tested for their ability to induce cell death in human leukemia HL-60 cells. These substances, with IC50 values of 21.8 and 13.7 μM, respectively, suppressed cell growth (Sari et al.,). After being separated from the ethanolic extract of *Polyalthia longifolia* leaves, the uncommon bisclerodane imides Longimide A and Longimide B were tested for their cytotoxic effects against four human cancer cell lines. It was discovered that they were most effective against cervical carcinoma cell lines, with IC50 values of 10.03 and 4.12 lg/ml, respectively.

Anti-bacterial activity

Dsorbitol and *Polyalthia longifolia* leaf extract were used to create silver nanoparticles. In tests against the bacterial pathogens Pseudomonas aeruginosa (Gram negative), Escherichia coli (Gram positive), and Staphylococcus aureus (Gram positive), these silver nanoparticles demonstrated excellent antibacterial activity . This suggests that the synthesized silver nanoparticles have better antibacterial action against Gram-positive organisms than Gram-negative organisms.Due to their smaller size, silver nanoparticles produced at 60°C (8 mm-16.4 mm) had a greater effect of antibacterial activity against test organisms (Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus) than those synthesized at 25°C (7.3-14 mm), according to the results. Using the agar disc diffusion method and MIC determination test, leaf extracts of *Polyalthia longiflia* (Debdaru) treated with various solvents such as hexane, methanol, and chloroform were subjected to an in vitro determination of antibacterial activity against six tested pathogenic bacteria: Bacillus subtilis, Sarcina lutea, Xanthomonas compestris, Escherichia coli, Klebsiella pneumonia, and Pseudomonas sp.It was discovered that the zone of inhibition against the studied microorganisms ranged from 21.00 to 44.20 mm. At 500Ïg/10Ïl, the *Polyalthia longiflia* extracts produced the maximum zone of inhibition against pathogenic bacteria, specifically Sarcina lutea, measuring 41.80mm, 44.20mm, and 43.50mm, respectively. MIC values for all extracts were almost 15.625 ×g/ 10Ïl against six tested bacteria. Extracts from the stem bark of *Polyalthia longifolia var.angustifolia* were tested against six major pathogenic bacteria: Salmonella typhi, Bacillus subtilis, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Klebsiella sp., and Staphylococcus aureus.Using a Soxhlet apparatus, the powdered stem bark extracts were progressively extracted using petroleum ether, chloroform, methanol, and water. Both the serial dilution and agar well diffusion methods were used to carry out the antibacterial activity investigation. It was discovered that the petroleum ether extract had the greatest effectiveness against every tested bacterium(Ghosh et al.,).

Wound healing property

Rats with excision wound models were used to test the ethanolic leaf extract of *P. longifolia's* ability to promote wound healing. The antero-dorsal side of the rats' skin was evaluated for up to 14 days during the investigation. When applied topically, the extract demonstrated wound contraction as a means of healing. The notable wound healing effect was caused by *P. longifolia* bark extract in several solvents, including methanolic, n-hexane, and ethyl acetate for the separation of active components. It demonstrated healing activity and accelerated myofibroblast contraction and epithelization (Lakshmi et al.,).

Anti-leishmanial Activity:

The long-term survival (>6 months) of treated mice suggested that 16a-Hydroxycleroda3,13(14)Z-dien-15,16-olide, a clerodane diterpene, from *Polyalthia longifolia*, was a possible antileishmanial and non-cytotoxic agent. Compound 1 caused a very quick and dose-dependent mortality at doses ranging from 2 to 50 mg/ml. When compared to the reference medication miltefosine, the IC50 was determined to be 8.04 mg/mL. The methanolic extract from *P. longifolia* leaves was tested for its in vitro antileishmanial activity against Leismania donovani promastigotes using the 3-4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide promastigote cell toxicity assay. The extract showed an IC50 value of 4.18 µg/ml and significantly reduced the growth of L.donovani promastigotes in vitro in a dose-dependent manner(Pal et al.,).

Anti-microbial Activity

Using both in vitro and in vivo tests, *Polyalthia longifolia* yielded the previously described clerodane diterpene (16·-hydroxycleroda-3, 13 (14) Z-dien-15, 16-olide) that was effective against methicillin-resistant S. aureus. This compound's minimum inhibitory concentration (MIC) against the reference strain demonstrated notable antibacterial activity (15.625 31.25 mg/ml). The antibacterial and antifungal properties of methanol extracts of *Polyalthia longifolia var. pendula's* leaves, stem, twigs, green berries, flowers, roots, root-wood, and rootbark were examined. The methanol extract of leaves and berries, with MIC values ranging from 7.8 to 500 ×g/ml, exhibits potential antibacterial activity. Bioassay monitored isolation work was conducted on this extract. The antibacterial activity of various *P. longifolia* leaf extracts, including 1, 4-dioxan, methanol, and acetone extracts, was examined at two different doses against 91 clinically significant microbial strains. At a 500 ×g/disc concentration, all three extracts demonstrated efficacy against 95% of the gram-positive bacterial strains tested. 1, 4-Dioxan extract shown activity against 18.18% of the total gram-negative bacterial strains, whereas acetone and methanolic extracts demonstrated activity against 12.72% of the strains(Chanda et al.,).

Anti-fungal Activity

Polyalthia longifolia was extracted using various solvents, including petroleum ether, benzene, chloroform, methanol, and ethanol. The antifungal activity of the petroleum ether extract was found to be much higher than that of the other extracts. Ten rice seed-borne fungus (Oryza sativa L.) were investigated in vitro for the antifungal activity of aqueous (10–50%) *Polyalthia longifolia*. In comparison to synthetic fungicides such as Dithane M-45, Captan, Benlate, Thiram, and Bavistin at 2% recommended dosage, the fungus strain A. alternata recorded a maximum inhibition of 92.88%, followed by F. solani (87.10%), F. moniliforme (86.40%), D. Halodes (86.07%), F. oxysporum (85.14%), C. lunata (83.33%), and D. tetramera (83.02%) at 50% concentration. The inhibitory effect of *P. longifolia's* leaf and pericarp aqueous extracts against Pythium aphanidermatum and Fusarium oxysporium, which were isolated from ginger rhizome rot specimens, was evaluated in vitro. It was discovered that the extract exhibited dose-dependent antifungal activity (Dileep et al.,).

Anti-ulcer activity

The anti-ulcer activity of P*olyalthia longifolia's* ethanolic extract was tested against aspirin plus pylorous ligation-induced gastric ulcers in rats, ethanol-induced ulcers in mice caused by HCl, and ulcers caused by water immersion stress at 300 mg/kg body weight. The results demonstrated a significant decrease in gastric volume, free acidity, and ulcer index when compared to the control group. Additionally, it demonstrated 89.71 percent and 95.3% inhibition, respectively, in ulcer protection index in stress-induced ulcers and HCl-ethanol-induced ulcers(Malairajan et al.,). At

270 mg/kg and 540 mg/kg body weight, the methanolic extract of *Polyalthia longifolia* demonstrated gastroprotective activity on ethanol and ethanol/HCl caused ulcers. It was discovered that the decrease in ulcer index among treated animals was statistically significant when compared to control animals.

Termiticidal activity

At different concentrations (0.5%-5% solution), *Polyalthia longifolia* shown termiticidal action in relation to their respective solvent extract, namely chloroform, methanol, ethyl acetate, n-hexane, and distilled water. Strong termiticidal activity was demonstrated by methanolic extract. Along with Samanea saman, Cassia siamea, Pithecellobium dulce, and Eucalyptus camaldulensis, at different concentrations—75, 75, 55, 50, and 45% death occurred, respectively—a notable mortality rate was noted with 5% chloroform extract of *Polyalthia longifolia(* Muhammad et al.,*)*.

Anti-plasmodial activity

The in vivo antimalarial effects of *P. longifolia* leaf aqueous extract were assessed in a strain of Plasmodium berghei (ANKA) that was resistant to chloroquine. It demonstrated the inhibition of parasite growth(Bankole et al.,).
Strong antimalarial effects were demonstrated by the ethanolic extract of *P. longifolia* stem bark against drug-resistant Plasmodium falciparum infections(Gbedema et al.,).

Anti-viral effect as a laxative and an Immunomodulator agent

Research on *P. longifolia* leaf methanolic extract revealed antiviral properties. The suppression of viral entrance and budding prevents the spread of viruses(Yadav et al.,). Balamuruganvelu et al. used wistar albino rats to investigate the plant's laxative properties. Oral administration of *P. longifolia* bark extract in ethanolic form demonstrated a laxative effect akin to sodium picosulfate, the medication of reference (Balamuruganvelu et al.,). The ethanolic extract of *P. longifolia* leaves was used to treat and prevent immunodeficiency disorders because it has an immunostimulatory effect on T and β cells (Doshi et al.,).

Anti-hyperuricemic activity

The hydroxylation process of hypoxanthine to xanthine was performed by the enzyme xanthine oxidase. Uric acid was produced by further converting xanthine. The body's ability to metabolize glucose was compromised by the rise in uric acid levels(Nan et al.,) . Many illnesses, including gout, hypertension, and renal injury, can cause hyperuricemi. *P. longifolia* leaf chloroform extracts notably shown an in vitro inhibitory effect on xanthine oxidase(Sivashanmugam et al.,).

Nephroprotective Activity

Using both curative and protective models, the nephroprotective efficacy of an ethanolic root extract of *Polyalthia Longifolia* (PL) on vancomycin-induced nephrotoxicity was investigated. These results show that the *Polyalthia longifolia* root extract only modestly protected nephrons, which need selenium support to avoid vancomycin-induced kidney damage, whether it is delivered before or after renal damage is induced(Kuntal Das et al.,).

TOXICOLOGICAL ASSESSMENT

The acute oral toxicity of *P. longifolia* leaf extract in Wistar albino rats was recently reported by Chanda et al. Following oral drug administration of the extract (540, 1080, 2160, and 3240 mg/kg body weight), the parameters they assessed daily included mortality, symptoms of toxicity, feed and water consumption, and changes in body weight up to a 14-day period. On the fifteenth day, the effects of varying extract dosages on organ weight, biochemical, and hematological parameters were also assessed. They discovered that the rats tolerated the *P. longifolia* leaf methanol extract well, and that it had no adverse effects or fatalities up to a dose level of 3240 mg/kg body weight. Additionally, they stated that the extract had no effect on feed, water, or body weight. Animals of both sexes did not exhibit any dose-dependent alterations in any of the parameters tested in the organ weight, biochemical, or hematological analyses. They came to the conclusion that a single dose of the acute oral administration of *P. longifolia* leaf methanolic extract was safe and nontoxic (Chanda et al.,)]. The animals were given five different dose levels of *P.*

longifolia leaf extract orally (p.o.). The following five dose levels were examined: 800 mg, 1200 mg, 1600 mg, 3200 mg/kg, and 400 mg. All extracts caused modest to moderate hypoactivity and showed some analgesic activity, according to safety evaluation in acute conditions and gross behavioral investigations. They came to the conclusion that *P. longifolia* leaf extracts and crude powder are safe to use up to 3.2 g/kg of dose in acute conditions. (Shazid et al.,). Additionally documented the toxicity of a 90% ethanol extract from *P. longifolia* barks using the mortality assay of brine shrimp. According to the researcher, *P. longifolia* bark extract had a very low level of general toxicity in the lethality test for brine shrimp, with an LC50 of 20 μg/ml and an LC90 value of 70.80 μg/ml.

PHTYTOCHEMICAL STUDY OF *POLYALTHIA LONGIFOLIA*

The plant *Polyalthia longifolia* is highly adaptable because of its chemical components, which are in charge of its diverse range of pharmacological effects. A literature review of a few phytochemical screening tests conducted on this plant reveals that the main phytochemical constituents of the plant are saponins, polysaccharides, alkaloids, tannins, resins, steroids, glycosides, and flavonoids.Its leaves, bark, roots, fruit, and seeds have all been the subject of previous research, which has identified a variety of diterpenoids and alkaloids with a wide range of biological activities, including cytotoxic, antihypertensive, anti-inflammatory, and antibacterial properties.

Chemical constituents extracted from the leaves

Successful identification and isolation of clerodane diterpenoids, namely 16(R and S)-hydroxy-cleroda3,13(14)Z-dien-15,16-olide-2-one, (4→2)-abeo-16(R and S)-hydroxy-cleroda-2,13(14)Z-dien-15,16-olide-3- al, 3β,16α-dihydroxy-cleroda-4(18),13(14)Z-dien15,16-olide, methyl-16-oxo-cleroda-3,13(14)E-dien15-oate, 2-oxo-kolavenic acid, 16-oxo-cleroda3,13(14)E-dien-15-oic acid, and 16(R and S)-hydroxy-cleroda-3,13(14)Z-dien-15,16-olide were performed from the methanolic extract of leaves and berries of the plant. These diterpenes were further subjected for an antimicrobial activity analysis (Faizi et al.,). Afolabi et al. isolated tetranorditerpene as 1-naphthalene acetic-7-oxo-1,2,3,4,4a,7,8,8aoctahydro1,2,4a,5-tetramethyl acid from *P. longifolia* leaves. These terpenoids were evaluated for cytotoxicity toward human leukemia HL-60 cells(Afolabi et al.,). *P.longifolia* leaves when extracted with ethyl acetate, indicated the presence of carbohydrates, flavonoids, steroids, glycosides, and tannins. A diterpene, called 16α-hydroxycleroda-3,13(14)Z-dien15,16-olide, had been extracted from the leaves of the plant(Bhattacharya et al.,). Numerous pharmacological activity indicators were demonstrated by this diterpene, primarily antibacterial, antileishmanial, antifeedant, antifungal, cytotoxic and antiulcerative qualities(Edmond et al.,). From the methanolic extract of *P. longifolia* leaves, three aporphine N-oxide alkaloids were isolated: (+)-O-methyl bulbocapnine-β-Noxide, (+)-O-methyl bulbocapnine-α-N-oxide, and (+)-Nmethyl nandigerine-β-N-oxide. Additionally, an azaflurene alkaloid was identified as polylongine (5-hydroxy-6-methoxy-l-methyl -4-azafluoren-9-ol).

From the ethanolic extract of *P. longifolia* leaves, Sashidhara et al. identified rare bisclerodane imides, namely longimide A and longimide B, and a cytotoxic cycloartanetriterpene called longitriol(Sashidhara et al.,). (-)-14,15-bisnor-3,11E-kolavadien-13-one, (-)-16- oxocleroda-3,13(14)E-dien-15-oic acid, (-)-3β,16αdihydroxycleroda-4(18),13(14) are the seven clerodane diterpenoids.E-kolavadien-15-oic acid-16-al, (-)-3,12 E-dien-15,16-olide, (+)-(4→2)-abeo-16(R/S)-2,13 Z-kolavadien-15,16-olide-3-al, (-)-labd-13 E-en-8-ol-15-oic acid, (-)-16α-hydroxycleroda3,13(14).The ethanolic extract of *P. longifolia* leaves yielded Z-dien-15,16-olide and five alkaloids: liriodenine, (-)-anonaine, (+)-isoboldine, (-)-asimilobine, and hordenine (Sashidhara et al.,). Doshi et al. estimated the amount of rutin in plant leaves. High-performance liquid and thin-layer chromatography methods were used to estimate its amount, and the results showed that it was 11.60% w/w and 4.03% w/v, respectively(Doshi et al.,). From the methanolic extract of *P. longifoliavar. pendula* leaves, twenty recognized chemicals were identified and extracted, along with a new oxo-protoberberine alkaloid, (-)-8-oxopolyalthiaine, and a new halimane diterpene, 3β,5β,16α-trihydroxy halima-13(14)-en-15,16-olide(Chen et al.,). The *P. longifolia* leaf extract included heavy metals, such as lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg)(Jothy et al.,) and the concentration was well within the acceptable daily consumption limits. Essential oils high in sesquiterpenes are found in *P. longifolia.* About 70 chemicals were found in the leaf oil, according to an investigation. These included 2 acyclic compounds, 11 monoterpenes, 53 sesquiterpenes, 3 fatty acids, and 1 diterpene acid. A larger portion of the volatile oil was made up of sesquiterpene hydrocarbons (83.1%). With α-selinene (2.8%), β-selinene (2.5%), trans-β-bergamotene (1.9%), trans-

α-bergamotene (1.7%), α-copaene (1.3%), and δ-cadinene (1.2%), the main constituents were (E)-β-caryophyllene (27.5%), α-zingiberene (11.9%), allo-aromadendrene (14.1%), and α-humulene (8.3%). α-pinene (1.6%) and (E)-β-ocimene (0.6%) were among the monoterpene hydrocarbons (2.6%) together with camphene, myrcene, and limonene. Among the 0.5% of oxygenated monoterpenes were α-terpineol, thymol, and linalool. At trace quantities, two oxygenated acyclic non-terpene chemicals were found: 2-nonanone and 2-methylnonanal. There were also some minor sesquiterpene hydrocarbons present, such as α-ylangene, isocaryophyllene, γ-cadinene, and calamenene, as well as several stereoisomers such as trans-α-bergamotene, (E)-β-farnesene, trans-β-bergamotene, ar-curcumene, γ-muurolene and β-humulene, β-sesquiphellandrene, and δ-cadinene. Sesquicineole, palustrol, caryophylla-4(14),8(15)-dien-5α-ol, caryophyllenol II,1-epi-cubenol, τ-cadinol, τ-muurolol, cubenol, selin-11-en-4α-ol, α-cadinol, caryolan-4-ol, β-bisabolol, and α-bisabolol were also found to be 2.4% of oxygenated sesquiterpenes. Additionally, it contains the following: bornyl formate, bornyl acetate, geranyl acetate, 4,8-α-epoxycaryophyllane, 4,8-β-epoxycaryophyllane, 5,8-cyclocaryophyllan-4-ol, caryolan-8-ol, 4-formyl-5-nor-β-caryophyllene, 5,11-epoxycadin-1(10)-ene, humulene oxide I, zingiberenol I, muurola-4,10(14)-dien-1β-ol, zingiberenol II, torreyol, caryophyllenol I, bisabola-2,10-dien-1-ol, trans-β-sesquiphellandrol phytone, oleic acid, linoleic acid, linolenic acid, and kovaleic acid(Ouattara et al.,).
Based on a dry weight basis, the *P. longifolia* sample produced a bright yellow hue and 0.15% v/w of volatile oil [49]. It was also found that gallic acid was present in the ethanolic extract of *P. longifolia* leaves (Sampath et al.,).

Chemical constituents extracted from seeds and fruits

The percentage of moisture (5.0 g), crude oil (7.5 g), crude protein (14.0 g), crude fiber (7.3 g), and total carbohydrates (65.3 g) were found in each 100 g sample of *P. longifolia* seeds. Numerous minerals, including potassium, magnesium, calcium, iron, sodium, manganese, copper, zinc, nickel, cobalt, lead, and chromium, as well as macro- and micronutrients were present in the seeds(Oyedeji et al.,). Atolani et al. investigated the plant's seed oil, which was extracted using the Soxhlet method. From the seeds of *P. longifolia*, fatty acids were extracted in the following primary proportions: oleic acid (30.31%), linoleic acid (19.27%), palmitic acid (15.11%), and small amounts of tricosylic acid (6.10%) and stearic acid (5.56%) (Atolani et al.,). Paper chromatography was used to identify the amino acids found in the seeds of *P. longifolia*. According to the findings, proline, l-glutamic acid, glycine, dl-isoleucine, dl-threonine, l-tyrosine, dl-methionine, l-hydroxy-proline, and others were present(Mundhe et al.,). Powdered ripe and unripe pericarps have been shown to contain a variety of minerals, including calcium, potassium, sodium, and magnesium. There were additional reports of a few trace elements, including zinc, manganese, iron, nickel, chromium, lithium, and copper(Prashith Kekuda et al.,).

Chemical constituents extracted from stems and stem bark

P. longifolia stems and stem bark were used to isolate three azafluorene alkaloids (darienine, polyfothine, and isooncodine) and three aporphine alkaloids (liriodenine, noroliveroline-β, and oliveroline-β-N-oxide)(Wu et al.,). α-copaene and α-muurolol (8.7%), β-selinene (8.6%), viridiflorene (8.1%), α-guaiene (7.8%), allo-aromadendrene (7.4%), and δ-cadinene (7.0%) were found in an analysis of essential oils from *P. longifolia* stem bark. Two monoterpenoids, camphene and α-pinene, were missing(Ogunbinu et al.,). Four new protoberberine alkaloids, namely (-)-8-oxo-10-hydroxy-2,3,9-trimethoxyberberine, (-)-8-oxo-11-hydroxy-2,3,9,10-tetramethoxyberberine, (-)-8-oxo-2,11-dihydroxy-3,10-dimethoxyberberine, and (-)-8-oxo-2,10-dihydroxy-3,9,11-trimethoxyberberine, were also isolated from the methanolic extract of *P. longifolia* stem, namely 4α,18β-epoxy-16-hydroxyclerod-13-en-15-oic acid, 6α,16-dihydroxycleroda-4(18),13-dien-15-oic acid, and 6α,16-dihydroxycleroda-3,13-dien-15-oic acid (Lee et al.,). An antibacterial lactone, (3S, 4R)-3,4,5-trihydroxypentanoic acid-1,4-lactone, is present in the stems' ethanol extract (Faizi et al.,). Clerodane diterpenes were extracted from *P. longifolia's* stem bark and included cleroda-3-ene pyrrole-15,16-dione, cleroda-3-ene pyrrolidine-15,16-dione(4), cleroda3,13(14)E-diene-15,16-diamide, and cleroda-3-ene15,16-diamide. These diterpenes may have anti-plasmodial properties(Annan et al.,). The hexane extract of the plant's stem bark revealed the presence of clerodone diterpenes, such as 16-oxocleroda-4(18),13 E-dien-15-oic acid, cleroda-4(18),13-dien-16,15-olide, and 16-hydroxycleroda-4(18),13-dien-16,15-olide, and ent-halimane diterpenes, such as 16-oxo-ent-halima5(10),13E-dien-15-oic acid, ent-halima-5(10),13-dien-16,15-olide, and 16-oxo-ent-halima-5(10),13 E-dien-15-oic acid, ent-halima-l(10),13E-dien-16,15-olide, and ent-halima-5(10),13E-dien-16,15-olide (Hara et al.,). γ-methoxy butenolide clerodane diterpene was detected in the *P. longifolia* bark petroleum ether extract(Chakrabarty et

al.,). In addition to one steroid, beta-stigmasterol, and two alkaloids, darienine and stepholidine, the ethanolic extract of the stem bark of *P. longifolia* produced three clerodone diterpenes: 16-hydroxy-cleroda-3,13-dien-16,15-olide, 3,16-dihydroxycleroda-4(18),13(14)Z-dien-15,16-olide, and 16-oxocleroda-3,13E-dien-15-oic acid(Gbedema et al.,).

Chemical constituents extracted from root

Pendulamine A, B, penduline containing stigmasterol 3-O-β-D-glucoside, allantoin, kolavenic acid, and the azafluorene alkaloid isoursuline were detected in *P. longifolia* root extract (Faizi et al.,). From the defatted extract of the *P. longifolia* root bark, kolavenic acid, liriodenine, bisclerodane imide with its four olefinic isomers, clerodane diterpene with its four olefinic isomers, and lysicamine were extracted(Saleem et al.,). The plant's root wood yielded two clerodone diterpenoids, solidagonal acid and kolavenic acid (Faizi et al.,).

CONCLUSION

We made an effort to compile the phytochemical and pharmacological data on *Polyalthiya longifolia* in this review. *Polyalthiya longifolia* is an important plant in traditional medicine and an old treatment that may have new uses in the future. *Polyalthia longifolia* is a significant medicinal plant with a broad range of pharmacological and phytochemical properties, according to a thorough review of the literature. Numerous chemical components found in the plant, including steroids, alkaloids, terpenoids, phenolics, and flavonoids, are linked to a number of pharmacological and medicinal characteristics, including the ability to treat inflammation, cancer, ulcers, gonorrhea, hyperuricemia, diabetes, liver damage, and a host of other infectious diseases.On the other hand, *Polyalthia longifolia* has to be evaluated in order to investigate its hidden regions and potential therapeutic uses for the benefit of humankind.

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RESEARCH ARTICLE

Secondary k-Kernel Symmetric Neutrosophic Fuzzy Matrices

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ABSTRACT

The secondary k- kernel symmetric Neutrosophic fuzzy matrices are described in this study as well as examples. The links between the s- k- kernel Symmetric Neutrosophic Fuzzy Matrix, s- kernel Symmetric Neutrosophic Fuzzy Matrix, and K- kernel Symmetric Neutrosophic Fuzzy Matrix are discussed with example. There are necessary and sufficient conditions that must be met for a matrix to qualify as a Neutrosophic fuzzy matrix with an s-k kernel symmetric.

Keywords: Neutrosophic fuzzy matrix, Kernel symmetric Neutrosophic fuzzy matrix, s - symmetric Neutrosophic fuzzy matrix, s-kernel symmetric Neutrosophic fuzzy matrix, s-k- kernel symmetric Neutrosophic fuzzy matrix.

INTRODUCTION

A Neutrosophic fuzzy matrix P is a range symmetric Neutrosophic fuzzy matrix if $R(P) = R(P^T)$, and a kernel symmetric Neutrosophic fuzzy matrix if $K(P) = K(P^T)$. The notions of range and kernel symmetry are well known to be applicable to complex matrices. This fails for a Neutrosophic fuzzy matrix. This inspired us to research s-k kernel

symmetric Neutrosophic fuzzy matrices. Lee [1] has studied Secondary Symmetric, Secondary Skew Symmetric, Secondary Orthogonal Matrices. Antonio and Paul [2] have discussed Properties of the eigen vectors of persymmetric matrices with applications to communication theory. Hill and Waters [3] have studied on k-Real and k-Hermitian matrices. Meenakshi and Jayashree [5] have focused on k-kernel symmetric matrices. Meenakshi [4] has studied Fuzzy Matrix: Theory and Applications. Meenakshi and Krishanmoorthy [6] have introduced on Secondary k-Hermitian matrices. Meenakshi, S.Krishnamoorthy and G.Ramesh [7] have studied on s-k-EP matrices. Meenakshi and Jayashree [8] have characterized on k -range symmetric matrices. Jaya shree [9] has introduced Secondary κ-Kernel Symmetric Fuzzy Matrices. Anandhkumar [10] has studied Pseudo Similarity of Neutrosophic Fuzzy matrices and on various Inverse of Neutrosophic Fuzzy Matrices. Anandhkumar [11] has special Kernal and k-kernal Intuitionistic Fuzzy matrices. Punithavalli and Anandhkumar [13] have studied Reverse Sharp and Left-T and Right-T Partial Ordering on Intuitionistic fuzzy matrices. As mentioned in the above introduction section, Meenakshi and Jaya shree introduced the concept of k-kernel symmetric matrices and Jaya shree introduced Secondary κ-Kernel Symmetric Fuzzy Matrices. Here, we have applied the concept of Secondaryk-Kernel Symmetric Neutrosophic Fuzzy Matrices. Both these concepts plays a significant role in hybrid fuzzy structure and we have applied Secondaryk-Kernel Symmetric Neutrosophic Fuzzy Matrices and studied some of the results in detail. First we present equivalent characterizations of a Secondaryk - Kernel Symmetric Neutrosophic Fuzzy Matrices and then, derive equivalent conditions for a Neutrosophic fuzzy matrices. Also, using the g- inverses, we discuss some theorems and examples for the Secondaryk - Kernel Symmetric Neutrosophic Fuzzy Matrices**.**

1.1 NOTATIONS

(i) P^T = Transpose of P
(ii) NFM = Neutrosophic fuzzy matrix
(iii)P^+ = Moore penrose inverse of P
(iv)K(P) = Null space of P
(v) KS = Kernal symmetric

2.Preliminaries and Definitions

Let the function be defined $M(x) = (x_{m[1]}, x_{m[2]}, x_{m[3]},\ldots, x_{m[s]}) \in F_{s\times 1}$ for $x = (x_1, x_2,..,x_s) \in F_{[1\times s]}$, where M is involuntary, the following are satisfied the associated permutation matrix where M and N are permutation matrix.

($P_{2.1}$) $MM^T = M^TM = I_n$, $K = K^T$, $K^2 = I$
($P_{2.2}$) By definition of N, $N = N^T$, $NN^T = N^TN = I_n$ and $N^2 = I$
($P_{2.3}$) K(P) = K(PN),K(P) = K(PK)
($P_{2.4}$) $(PN)^T = NP^T$, $(NP)^T = P^TN$
If P^+ exists,then
($P_{2.5}$) $(PN)^+ = NP^+$, $(NP)^+ = P^+N$

Definition2.1. Neutrosophic fuzzy matrix PisKS Neutrosophic fuzzy matrixiffK(P) = K(P^T).

Lemma2.1. For $P \in (NF)_n$ and a permutation Neutrosophic fuzzy matrix A, null space of P equal to null space of Q iffK(APA^T)=K(AQA^T).

Lemma2.2. Neutrosophicfuzzymatrix P = MP^{T}M iffMP = (MP)(MP)^T(MP),Neutrosophic fuzzymatrix iff PM = (PM)(PM)^T(PM)Neutrosophic fuzzymatrix

3. Secondaryk-kernel symmetric Neutrosophic fuzzy matrices

Definition3.1. ForNeutrosophic fuzzymatrix $P \in (NF)_n$ iss -symmetric Neutrosophicfuzzymatrixiff P = NP^{T}N.

Definition3.2. ForNeutrosophic fuzzymatrix $P \in (NF)_n$ iss- KS Neutrosophic fuzzymatrix ifK(P) = K(NP^{T}N)

Definition3.3. Neutrosophic fuzzymatrix $P \in (NF)_n$ iss-k- KS Neutrosophic fuzzymatrixifK(P)=K(MNP^{T}NM).

Lemma3.1.ANeutrosophic fuzzymatrix $P \in (NF)_n$ iss-KS Neutrosophic fuzzymatrix iff PN isKS Neutrosophic fuzzy matrix iff NPis KS Neutrosophic fuzzy matrix.

Proof.

P iss-KS Neutrosophic fuzzy matrix iffK(P)= K(NP^{T}N) [ByDefinition3.2]

⇔K(PN) = K((PN)^T) [ByP.2.2]

⇔K(NPNN^T) = K(NNP^{T}N)

⇔K(NP) = K((NP)^T)

⇔NP is KS.

3.The following examples gives relation between symmetric NFM,κ–symmetric Neutrosophic,s-κ- KS NFM , s-κ –symmetric NFM.

$$P = \begin{bmatrix} (0.7,0.3,0.4> & (0.5,0.3,0.4) \\ (0.5,0.3,0.4) & (0.4,0.3,0.5) \end{bmatrix},$$

Example3.1. Form=(1,2),

$$V = \begin{bmatrix} <0,0,0> & <1,1,0> \\ <1,1,0> & <0,0,0> \end{bmatrix}, \quad M = \begin{bmatrix} <1,1,0> & <0,0,0> \\ <0,0,0> & <1,1,0> \end{bmatrix},$$

$$KVP^TVK = \begin{bmatrix} <1,1,0> & <0,0,0> \\ <0,0,0> & <1,1,0> \end{bmatrix}\begin{bmatrix} <0,0,0> & <1,1,0> \\ <1,1,0> & <0,0,0> \end{bmatrix}\begin{bmatrix} (0.7,0.3,0.4> & (0.5,0.3,0.4) \\ (0.5,0.3,0.4) & (0.4,0.3,0.5) \end{bmatrix}$$
$$\begin{bmatrix} <0,0,0> & <1,1,0> \\ <1,1,0> & <0,0,0> \end{bmatrix}\begin{bmatrix} <1,1,0> & <0,0,0> \\ <0,0,0> & <1,1,0> \end{bmatrix}$$

$$KVP^TVK \neq P$$

Here P= KP^{T}K

Therefore P is symmetric NFM, κ–symmetric Neutrosophic, s-κ-KS NFM but not s-κ –symmetric NFM.

$$= \begin{bmatrix} <0,0,0> & <1,1,0> \\ <1,1,0> & <0,0,0> \end{bmatrix},$$

Example2.2 . Let us consider NFM,V

$$P = \begin{bmatrix} <0.7,0.3,0.4> & <0.5,0.3,0.4> \\ <0.5,0.3,0.4> & <0.7,0.3,0.5> \end{bmatrix}, \quad K = \begin{bmatrix} <1,1,0> & <0,0,0> \\ <0,0,0> & <1,1,0> \end{bmatrix},$$

$$KVP^TVK = \begin{bmatrix} <1,1,0> & <0,0,0> \\ <0,0,0> & <1,1,0> \end{bmatrix}\begin{bmatrix} <0,0,0> & <1,1,0> \\ <1,1,0> & <0,0,0> \end{bmatrix}\begin{bmatrix} <0.7,0.3,0.4> & <0.5,0.3,0.4> \\ <0.5,0.3,0.4> & <0.7,0.3,0.5> \end{bmatrix}$$
$$\begin{bmatrix} <0,0,0> & <1,1,0> \\ <1,1,0> & <0,0,0> \end{bmatrix}\begin{bmatrix} <1,1,0> & <0,0,0> \\ <0,0,0> & <1,1,0> \end{bmatrix}$$

$$KVP^TVK = \begin{bmatrix} <0.7,0.3,0.4> & <0.5,0.3,0.4> \\ <0.5,0.3,0.4> & <0.7,0.3,0.5> \end{bmatrix} = P$$

P is symmetric, s-κ-symmetric and hence therefore s-k-KS.

Example2.3. Let us consider NFM

$$K=\begin{bmatrix} <0,0,0> & <1,1,0> & <0,0,0> \\ <1,1,0> & <0,0,0> & <0,0,0> \\ <0,0,0> & <0,0,0> & <1,1,0> \end{bmatrix}, V=\begin{bmatrix} <0,0,0> & <0,0,0> & <1,1,0> \\ <0,0,0> & <1,1,0> & <0,0,0> \\ <1,1,0> & <0,0,0> & <0,0,0> \end{bmatrix}$$

$K \neq V, K \neq I$ and $KV \neq VK$

$$P=\begin{bmatrix} <0,0,0> & <0,0,0> & <1,1,0> \\ <0.5,0.3,0.4> & <1,1,0> & <0,0,0> \\ <0.4,0.2,0.6> & <0.5,0.3,0.4> & <0,0,0> \end{bmatrix}$$

$$KV=\begin{bmatrix} <0,0,0> & <1,1,0> & <0,0,0> \\ <1,1,0> & <0,0,0> & <0,0,0> \\ <0,0,0> & <0,0,0> & <1,1,0> \end{bmatrix}\begin{bmatrix} <0,0,0> & <0,0,0> & <1,1,0> \\ <0,0,0> & <1,1,0> & <0,0,0> \\ <1,1,0> & <0,0,0> & <0,0,0> \end{bmatrix}$$

$$KV=\begin{bmatrix} <0,1,0> & <0,1,0> & <0,1,0> \\ <0,1,0> & <0,1,0> & <1,1,0> \\ <1,1,0> & <0,1,0> & <0,1,0> \end{bmatrix}$$

$$VK=\begin{bmatrix} <0,0,0> & <0,0,0> & <1,1,0> \\ <0,0,0> & <1,1,0> & <0,0,0> \\ <1,1,0> & <0,0,0> & <0,0,0> \end{bmatrix}\begin{bmatrix} <0,0,0> & <1,1,0> & <0,0,0> \\ <1,1,0> & <0,0,0> & <0,0,0> \\ <0,0,0> & <0,0,0> & <1,1,0> \end{bmatrix}$$

$$VK=\begin{bmatrix} <0,1,0> & <0,1,0> & <1,1,0> \\ <1,1,0> & <0,1,0> & <0,1,0> \\ <0,1,0> & <1,1,0> & <0,1,0> \end{bmatrix}$$

$$P^TVK=\begin{bmatrix} <0.5,0.8,0.4> & <0.4,0.8,0.6> & <0,0,0.4> \\ <0,0.7,0> & <0.5,0.7,0> & <0,0.7,0> \\ <0,0,0> & <0,0,0> & <1,0,0> \end{bmatrix}$$

$$KVP^TVK=\begin{bmatrix} <0,1,0> & <0,1,0> & <0,1,0> \\ <0,1,0> & <0,1,0> & <1,1,0> \\ <1,1,0> & <0,1,0> & <0,1,0> \end{bmatrix}\begin{bmatrix} <0.5,0.8,0.4> & <0.4,0.8,0.6> & <0,0,0.4> \\ <0,0.7,0> & <0.5,0.7,0> & <0,0.7,0> \\ <0,0,0> & <0,0,0> & <1,0,0> \end{bmatrix}$$

$$KVP^TVK=\begin{bmatrix} <0,0,0> & <0,0.2,0> & <0,0,0> \\ <0,0,0> & <0,0,0> & <1,0,0> \\ <0.5,0,0> & <0.4,0,0> & <0,0,0> \end{bmatrix} \neq P$$

$P \neq MNP^TNM$

Hence P is not s-k-symmetric. But s-k- KS.

i.e) N(P)=N(KVP^{T}VK)= <0,0,0>

Theorem3.1. For NFM $P \in (NF)_n$ the following are equivalent

i) K(P) = K(MNP^{T}NM)

ii) K(MNA) = N((MNA)^T)
iii) K(PMN) = K((PMN)^T)
iv) K(PNM) = K((PNM)^T)
v) K(NMP) = K((NMP)^T)
vi) K(NP) = K(M(NP)^{T}M)
vii) K(PN) = K(M(PN)^{T}M)
viii) K(PM) = K(N(PM)^{T}N)
ix) K(MP) = K(N(MP)^{T}N)
x) K(P^T) = K(MNP)
xi) K(P) = K(MNP^T)

Proof: Let K(P) = K(MNP^{T}NM)
⇔ K(P) = K(MNP^T) Definition 3.2)
⇔ K(PNM) = N((PNM)^T) (By $P_{2.3}$)
⇔PNM is KS
⇔ (NM)(ANM)(NM)^T (KS Lemma 2.1)
⇔ NMP is KS
⇔ MP (s- KS)
Therefore , (i)iff (iv)iff (v) iff (ix) holds
(ii) iff (vi)
⇔K(MNP) = N((MNP)^T)
⇔K(M^{T}MNP) = N((M^{T}MNP)^T)
⇔ K(NP) = K(NP)^T)
⇔K(NP) = K(M(NP)^{T}M)

Therefore, NP is K KS
(ii) iff (vi) holds
(ii) iff (x)
⇔K(MNP) = K((MNP)^T)
⇔N(MNP) = N(P^T) (By P. 2.3)
Thus(ii) iff(x)hold.
(iv) iff (xi)
⇔ K(PNM) = N((PNM)^T)
⇔ K(P) = K(MNP^T) (By P. 2.3)
(iv) iff (xi) hold
(i) iff (iv) iff (vii)
⇔K(P) = K(MNP^{T}NM)
⇔K(P) = K((PNM)^T)
⇔K(PNM) = K((PNM)^T) (PNM is KS)
⇔K(PNMM^T) = N((PNMM^T)^T)
⇔N(PN) = N((PN)^T)
⇔N(PN) = N(M(PN)^{T}M) (PN is k- KS)
(i) iff (iv) iff (vii) hold
(iii) iff (viii)
⇔K(PMN) = K((PNM)^T)
⇔K(PM) = N(N(PM)^{T}N)
(iii) iff (viii) holds
Hence the Theorem

Corollary3.1. For NFM $P \in (NF)_n$ the following are equivalent

i) K(P) = K(NP^{T}N)
ii) K(NP) = K((NP)^T)
iii) K(PN) = K((PN)^T
iv) K(P^T) = K(NP)
v) K(P) = K(NP^T)

Proof: (i) implies (ii)
⇔K(P) = K(NP^{T}N)
⇔K(NP)=K(NNP^{T}N)
⇔K(NP)=K(N ^{2}P^{T}N)
⇔K(NP) = K((NP)^T)
(i) implies (ii) hold
(i) implies (iii)
⇔ K(P) = K(NP^{T}N)
⇔K(PN) = K(NP^{T}NN)
⇔K(PN) = K(NP^{T}N^2) ⇔K(PN) = K(PN)^T
(i) implies (iii) hold
(i) implies (iv)
K(P^T) = K((NP^{T}N)^T)
N(P^T) = N((NP^{T}N)^T)
N(P^T) = N(NP)
(i) implies (iv) holds
(i) implies (v) easily verified
implies (i) easily verified
Hence the Theorem

Lemma3.2. For NFM $P \in (NF)_n$,if (NMP)$^+$exists⇔(MP)$^+$exists ⇔ P$^+$ exists.

Proof: (NMP)$^+$exists iff $(\mathrm{NMP})^{\mathrm{T}} \in (\mathrm{NMP})\{1\}$

$\text{iff } \mathrm{NMP}=\mathrm{NMP}(\mathrm{NMP})^{\mathrm{T}}\mathrm{NMP}$

$\text{iff } \mathrm{NMP}=\mathrm{NMP}(\mathrm{MP})^{\mathrm{T}}\mathrm{NN}(\mathrm{MP})$

$\text{iff } \mathrm{MP}=\mathrm{MP}(\mathrm{MP})^{\mathrm{T}}(\mathrm{MP})$

$\text{iff } (MP)^{+} \text{ exists iff } P^{+} \text{ exists}$. [Lemma3.4in[8]]

Lemma3.3 For NFM $P \in (NF)_n$ if (MNP)$^+$exists⇔ P$^+$ exists.

Proof:(P)$^+$exists iff (NP)$^+$ exist
iff NP = (NP)(NP)$^+$(NP)
iff NMP = M(NP)(NP)$^+$(NP)
iff MNP = M(NP)(NP)$^+$MM(NP)
iff MNP = (MNP)(MNP)$^+$(MNP)
iff $(\mathrm{MNP})^{T} \in (\mathrm{MNP})\{1\}$
Therefore , (MNP)$^+$ exist.

Theorem3.2.Let $P \in (NF)_n$ .Then any two of the following condition simply the other one.
(i) K(P) = K(MP^{T}M)

(ii) K(P)= K(MNP^{T}NM).
(iii)K(P^T) = K((MPN)^T)

Proof: (i)&(ii)⇒(iii)
ByTheorem3.1
K(P)=K(MNP^{T}NM) implies K(P) = K((PNM)^T)
K(MPM)= K(NP^{T}M) (Lemma 2.1)
K(P)= K(MP^{T}M)
K(MPM)= K(P^T) (Lemma 2.1)
K(P^T) = K((MPN)^T)
Therefore, (iii) hold
(i) & (iii) ⇒ (ii)
K(P) = K(MP^{T}M) implies K(MPM) = K(P^T)
Hence (i) and (iii) K(MPM) = K((MPN)^T)
K(P) = K(MNP^T) (Lemma 2.1)
P is s-k KS [Theorem 3.1]
Therefore (ii) holds.
(ii) & (iii) ⇒ (i)
P is s-k KS
K(P) = K(MNP^T)
K(MPM) = K((NP^{T}M)^T)
Hence (ii) and (iii)
K(MPM) = K(P^T)
N(P) = K(MP^{T}M)
Therefore (i) hold.
Hence the Theorem.

4. s- k-Kernel Symmetric Regular Fuzzy Matrices

The existence of numerous generalized inverses of the NFM in (NF_n) has been demonstrated in this section. Generalized inverses belonging to the sets P {1, 2}, P {1, 2, 3} and P {1, 2, 4} of s-k- KS NFM P are characterized.

Definition:4.1 The NFM $P \in (NF)_n$ is said to be Moore-Penrose inverse if there exists another NFM, $Z \in (NF)_n$ its satisfies the following four conditions.

(iv) PZP = P (Regular or g-Inverse)
(v) ZPZ = Z (2-inverse)
(vi) (PZ)^T = PZ (Least square generalized inverse)
(vii) (ZP)^T = ZP (Minimum norm generalized inverse)

Theorem 4.1: Let $P \in (NF)_n$, $Z \in P$ {1,2} and PZ, ZP, are s- κ- KS NFM. Then P is s- κ - KS NFM ⇔ Z is s- κ – KS NFM.

Proof: K(MNP) = K(MNPZP) ⊆ K(ZP) [since P = PZP]
= K(ZNNP) = K(ZNMMNP) ⊆ K (MNP)
Hence, K(MNP) = K(ZP)
= K(MN(ZP)^{T}NM) [ZP is s- κ- KS NFM]
= K(P^T Z^T NM)
= K(Z^T NM)
= K((MNZ)^T)
K((MNP)^T) = K(P^{T}NM)

= K($Z^T P^T$ NM)
= K((MNPZ)^T)
= K(MNPZ)
= K(MNZ)
MNZ is KS ⇔ K(MNZ) = K((MNZ)^T)
⇔ K((MNZ)^T) = K(MNZ)
⇔ MNZ is KS
⇔ Z is s- κ- KS.

Theorem 4.2: Let $P \in (NF)_n$, Z∈ P {1,2,3}, K(MNP) = K((MNZ)^T).Then P is s-κ- KS NFM ⇔ Z is s- κ - KS NFM.

Proof: Since Z belongs to P {1,2,3} .

We have PZP = P, ZPZ =Z, (PZ)^T = PZ

K((MNP)^T) = K($Z^T P^T$ NM) [By using P = PZP]
= K(MN(PZ)^T)
= K((PZ)^T) [By $P_{2.3}$]
= K(PZ) [(PZ)^T = PZ]
= K(Z) [By using Z = ZPZ]
= K(MNZ) [By $P_{2.3}$]

MNP is KS NFM⇔ K(MNP) = K((MNP)^T)
⇔ K((MNZ)^T) = K(MNZ)
⇔ MNZ is KS
⇔ Z is s- κ – KS.

Theorem 4.3: Let $P \in (NF)_n$, Z∈ P {1,2,4}, K((MNP)^T) = K(MNZ) . Then P is s- κ- KS NFM ⇔ X is s- κ- KS NFM.

Proof: Since Z ∈ P {1, 2, 4}, we have PZP = P , ZPZ = Z, (ZP)^T= ZP

K(MNP) = K(P) [By P. 2.3]
= K(ZP) [ZPZ = Z, PZP = P] [(XA)^T = XA]
= K((ZP)^T)
= K(P ^{T}Z^T)
= K (Z^T)
= K((MNZ) ^{T}). [P.2.3]

MNP is KS NFM ⇔ K(MNP) = K((MNP)^T
⇔ K((MNP) ^{T}) = K(MNZ)
⇔ MNZ is KS NFM
⇔ Z is s- κ – KS NFM.

In particular for M = I , the above Theorems reduces to equivalent conditions for various g-inverses of a s- KS NFM to be secondary KS NFM.

Corollary 4.1: Let $P \in (NF)_n$, $Z \in P$ {1,2} and PZ, ZP are s- KS NFM. Then P is s- KS NFM ⇔ Z is s- KS NFM.

Corollary 4.2: Let $P \in (NF)_n$, $Z \in P\{1,2,3\}$, K(MNP) = K((NZ)^T) . Then P is s- KS NFM ⇔ N is s- KS NFM.

Corollary 4.3: Let $P \in (NF)_n$, $Z \in P\{1,2,4\}$,K((NP)^T) = N(NZ) . Then P is s- KS NFM ⇔ Z is s- KS NFM.

CONCLUSION

We introduced the concept of Secondaryk - Kernel Symmetric NFM with suitable examples. In addition, we have investigated equivalent relation between symmetric NFM,κ–symmetric NFM,s-κ- KS NFM,s-κ –symmetric NFM with examples. There are necessary and sufficient conditions that must be met for a matrix to qualify as a NFM with an s-k kernel symmetric. The existence of numerous generalized inverses of the NFM is demonstrated. In future, we shall prove some related properties of Secondaryk - Kernel Symmetric NFM.

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RESEARCH ARTICLE

Evaluation of Membrane Stabilising Activity of *Moringa oleifera* Flower Extract on Erythrocytes of *Gallus gallus*

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ABSTRACT

The *in vitro* membrane stabilising activity of hydro alcoholic extract of *Moringa oleifera* flower were evaluated by heat induced and hypotonic solution induced haemolysis method. The membrane stabilisation of the flower extract was measured spectrophotometrically at 540 nm. Aspirin (100µg/ml) was used as a standard drug. In heat induced haemolysis method 200 µg/ml and 400 µg/ml concentrations of the extract inhibited25.59±2.32% and 59.39±1.44% haemolysis of erythrocytes membrane respectively in cold condition whereas in heated condition 37.35±2.11% and 62.77±2.06% haemolysis respectively. Standard drug aspirin inhibited 89.75±1.04 % and 89.48±1.16% haemolysis of erythrocytes membrane in cold and heated conditions respectively. In hypotonic solution induced method both the concentrations of the extract inhibited44.11±2.44% and 74.38±1.3% haemolysis of erythrocytes membrane respectively, while aspirin inhibited 82.62±1.58% haemolysis. In all the methods the hydroalcoholic extract of *Moringa oleifera* flower has shown significant membrane stabilisation.

Keywords: Membrane, stabilisation, erythrocyte, haemolysis, heat, hypotonic.

INTRODUCTION

Cell membranes are composed of lipid bilayer and proteins are embedded within the lipid layer and play a critical role in maintaining the integrity of the cell, regulating the permeability of molecule through cell, and transmitting signals between cells. Several factors can cause damage to cell membranes, including physical stress, chemical toxins, and microbial infections. The process involved in preventing or minimizing damage of cell membranes in several stress conditions and maintaining the cellular organelles' integrity and functions is referred as membrane stabilisation [1]. It involves the use of various compounds or techniques which protect the membrane from damage and maintain its function. Examples of compounds that can stabilise cell membranes include antioxidants such as vitamin E and N-acetylcysteine which protect cell membranes from oxidative stress [2], and phospholipids, which can rebuild damaged cell membranes [3]. In addition to chemical compounds, various techniques can be used to stabilise cell membranes, e.g. cooling can prevent damage of membranes in cells that are sensitive to temperature changes, such as red blood cells[4]. Similarly, the addition of certain sugars can stabilise membranes by reducing water loss from cells[5]. Several drugs can be used to stabilise cell membranes, depending on the specific condition being treated. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and aspirin show membrane stabilising effect by reducing inflammation and oxidative stress [6]. *Moringa oleifera,* commonly known as drumstick tree, is a fast growing, drought resistant plant belonging to the family Moringaceae and indigenous to the Indian subcontinent. It can grow up to 10-12 meters tall with a trunk diameter of up to 46 cm. The tree has whitish-gray bark, feathery tripinnate leaves, fragrant yellowish-white flowers, and long, brown capsules containing dark brown seeds [7]. It thrives in tropical and subtropical climates and is known for its rapid growth. Moringa flowers have a range of therapeutic actions. They are known to act as a cholagogue, which helps to enhance bile flow, and as a stimulant, tonic, and diuretic [8]. These flowers also have antibacterial properties [9] and can aid in the preparation of heart circulatory tonics [10]. Additionally, they are beneficial for the eyes, skin, brain, and liver, and act as a blood erythropoietin-stimulating agent [11, 12, 13, 14]. Moringa flowers also exhibit anti-inflammatory, antioxidant, and enzyme inhibitory properties [15]. They contain various bioactive compounds that contribute to these effects, making them useful in traditional medicine for treating a variety of health conditions. Due to its high polyphenolic content and all beneficial properties on damage protection, *Moringa oleifera* flower was evaluated in this study for its membrane stabilising activity.

MATERIALS AND METHODS

Preparation of Extract

Fresh flowers of *Moringa oleifera* were collected from local area of Netaji Subhas Chandra Bose Institute of Pharmacy. The flowers were washed with clean water and taken for the maceration extraction process by using 70% ethanol for 72 hours. The extract was collected, filtered and kept inside a vacuum desiccator for evaporation. The dried extract was kept at 4°C temperature in a refrigerator.

Drugs and Chemicals Used

Aspirin (Anant Pharmaceuticals Pvt. Ltd.), Ethanol (LobaChemiePvt. Ltd.), EDTA (S.N. Chemicals), distilled water.

Preliminary Phytochemical Investigations of the Extract

Hydroalcoholic extract of *Moringa oleifera* flower was evaluated for the phytochemical investigation [16] to check the presence of various phytoconstituents such as alkaloid, carbohydrates, saponin, flavonoids, glycosides, sterols, proteins etc.

Blood Collection

2 ml of blood was collected from brachial wing vein of chicken (*Gallus gallus*) under standard settings of temperature (23±2°C) and relative humidity (55±10%). The collected blood was kept in a test tube with an anticoagulant ethylenediaminete traacetic acid (EDTA).

Preparation of Erythrocyte Suspension

Erythrocyte suspension was prepared by the method described by Niraimathi*et al.*(2011)with some modification [17]. The collected 2 ml of blood was centrifuged using a centrifugal machine for 10 minutes at 3000 rpm and then the sediment was washed three times using isotonic buffer solution (pH 7.4). The volume of sediment was measured and reconstituted as a 2% v/v suspension with isotonic buffer solution (pH 7.4).The isotonic buffer was prepared by dissolving NaH_2PO_4. $2H_2O$ (0.26 g); Na_2HPO_4(1.15 g); NaCl (9 g) in up to 1000 ml distilled water.

Dose Preparation

For this study aspirin was used as standard drug and100 µg/ml dose was prepared. 200µg/ml and 400µg/ml dose of *Moringa oleifera*flowers extract were prepared and named as *Moringa oleifera* low dose (MOLD) and *Moringa oleifera*high dose(MOHD) respectively.

Heat Induced Haemolysis

This test was performed by the method described by Umapathy*et al.* (2009)with some modification [18].5 ml aliquots of the isotonic buffer containing100 µg/ml aspirin, 200µg/ml and 400µg/ml of the extract were taken in three pairs of centrifuge tubes (one pair for each concentration). In another pair of centrifuge tube 5 ml of vehicle was taken as control group. In each tube 100 µl erythrocyte suspension was added and gently mixed by inversion. A water bath was used to incubate one set of tubes at 54°C for 20 minutes. The second set was kept at 0-5^{0}C in an ice bath. After that the reaction mixtures were centrifuged at 2000 rpm for 5minutes and the absorbance of the supernatant was measured at 540 nm using UV-Vis spectrophotometer. The percentage inhibition of haemolysis was calculated using the following equation:

% Inhibition of haemolysis = 100 × (OD1-OD2/OD1)

Where,

OD1=Optical density of control

OD2= Optical density of test sample

Hypotonic Solution Induced Haemolysis

This test was performed by the method described by Umapathy*et al.* (2009) with some modification [18]. 5 ml aliquots of hypotonic solution (0.2%) containing 100 µg/ml aspirin, 200µg/ml and 400µg/ml of the extract were taken in different centrifuge tubes (one tube for each concentration). In another centrifuge tube 5 ml of hypotonic solution was taken as control group. In each tube 500 µl erythrocyte suspension was added and gently mixed. After incubating for 10 minutes at room temperature, all the mixtures were centrifuged at 2000 rpm for 5minutes and the absorbance of the supernatant was measured at 540 nm using UV-Vis spectrophotometer. The percentage inhibition of haemolysis was calculated using the following equation:

% Inhibition of haemolysis = 100 × (OD1-OD2/OD1)

Where,

OD1= Optical density of control

OD2= Optical density of test sample

RESULTS

Preliminary Phytochemical Investigation

The extract obtained from the *Moringa oleifera* flowers was subjected to preliminary phytochemical investigation and the following observations were found(Table 1).

Effect of the Extract on Heat Induced Haemolysis

The results showed that the extracts at concentration of 200 µg/ml (MOLD) and 400 µg/ml(MOHD) were significantly ($p<0.01$) potent on chicken erythrocyte and adequately protecting them againstheat induced haemolysis, when comparing it to the standard drug aspirin (100 µg/ml). Control sample showed no inhibition compared to the test and

standard samples. In cooled condition and heat induced condition, MOLD inhibited 25.59±2.32 %,37.35±2.11 % and MOHD were found to inhibit 59.39±1.44 %, 62.77±2.06% haemolysis of erythrocytes membrane respectively, while in the same condition, standard drug aspirin inhibited 89.75±1.04% and 89.48±1.16% haemolysis of erythrocytes (Table 2).

Effect of the Extract on Hypotonic Solution InducedHaemolysis

The obtained results showed that the extracts at concentration 200µg/ml(MOLD) and 400µg/ml(MOHD) were significantly ($p<0.01$) potent on chicken erythrocyte and was adequately protecting them against hypotonic solution induced lysis, when comparing it to the standard drug aspirin (100 µg/ml). Control sample showed no inhibition compared to the test and standard samples. Both of MOLD and MOHD were found to inhibit 44.11±2.44% and 74.38±1.31%haemolysis of erythrocytes membrane respectively, while in the same conditions, standard drug aspirin inhibited 82.62±1.58%haemolysis of erythrocytes (Table 3).

DISCUSSION

Cell's strength depends on the structural integrity of its membranes. In case of inflammation cellular infiltration happens due to leukocytes for their defensive role. During inflammation they release lysosomal contents like bactericidal enzymes and protease which is responsible for tissue damage. Cell membranes also can destabilize through free radicals generated by lipid peroxidation [19]. In this assessment RBC membrane was subjected to hemolysis by heat induced and hypotonic solution induced method to show membrane stabilizing activity of *Moringa oleifera* flower extract. The flower extract contains large amount of phenolic compounds and flavonoids, which play a significant role in membrane stabilizing activity due to their antioxidant properties.Phenolic compounds, including polyphenols, can scavenge free radicals and lower oxidative stress, they can reduce lipid peroxidation and preserve the integrity of cell membranes [20]. Flavonoids, a diverse group of polyphenolic compound salso can donate electrons to stabilize the free radicals and integrate into lipid bilayers for reducing the oxidative stress and protecting the membrane against lipid peroxidation. Under stress condition flavonoids inhibit the enzymes that promote inflammation and maintain the membrane integrity [21]. The result of the study showed that the extract at a concentration of 200µg/ml and 400µg/ml readily protected the lysis of erythrocyte membrane in heat induced and hypotonic solution induced haemolysis methods compared to the standard aspirin (100 µg/ml). Thus, it is cleared that *Moringa oleifera* flowers extract possess good membrane stabilizing activity.

CONCLUSION

This study was performed to evaluate whether the chemical constituents of *Moringa oleifera* flowers can promote membrane stabilisation. The observation implicated that *Moringa oleifera* flower may be used for the treatment of inflammation in near future. Though several types of medication are already available as membrane stabiliser still *Moringa oleifera* flower can produce a new era in the treatment of inflammation which may be easily available and affordable. Further investigation is required for the exact molecule which is responsible for membrane stabilising activity.

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Table.1: A preliminary phytochemical investigation of *Moringa oleifera* flower extract

SL. NO.	TEST NAME	RESULT
1	Test for alkaloids	Positive
2	Test for Carbohydrates	Positive
3	Test for Glycosides	Positive
4	Test for Protein and Amino acids	Negative
5	test for Flavonoids	Positive
6	Test for Saponins	Negative
7	Test for Steroids	Positive
8	Test for Lipid or Fat	Negative

Table.2: Effect of *Moringa oleifera* flower extract on heat induced haemolysis model

Treatment	% Inhibition of haemolysis	
	Sample cooled	Sample heated
Control	-	-
Aspirin	89.75±1.04 %*	89.48±1.16 %*
MOLD	25.59±2.32 %*	37.35±2.11 %*
MOHD	59.39±1.44 %*	62.77±2.06 %*

All values are shown as mean ±SEM, n=5. *p<0.01 was considered statistically significant compared to control

Table.3: Effect of *Moringa oleifera* flower extract on hypotonic solution induced haemolysis model

Treatment	% Inhibition of haemolysis
Control	-
Aspirin	82.62±1.58 %*
MOLD	44.11±2.44 %*
MOHD	74.38±1.31 %*

All values are shown as mean ±SEM, n=5. *p<0.01 was considered statistically significant compared to control

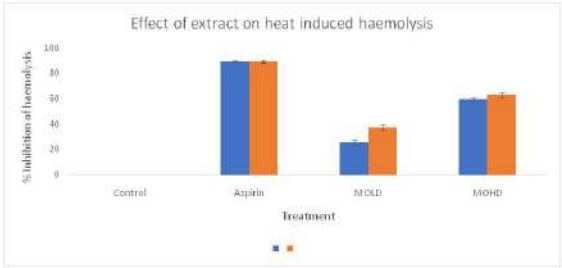

Figure 1: Effects of control, aspirin and different concentrations of the extract on heat induced haemolysis

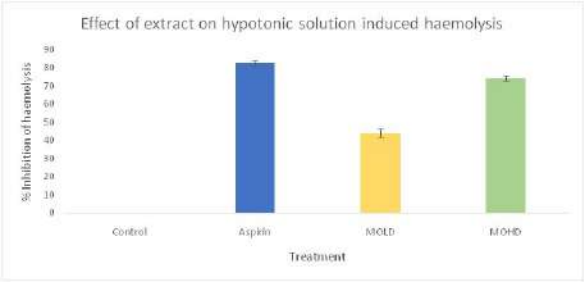

Figure 2: Effects of control, aspirin and different concentrations of the extract on hypotonic solution induced haemolysis

RESEARCH ARTICLE

Comparison of Median Nerve Conduction Parameters between Male Elite Badminton Players and Normal Healthy Controls: A Cross-Sectional Study

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ABSTRACT

Badminton players have typical biomechanics and sport specific repetitive movement of upper extremity joints can lead to overuse injuries of muscles and nerves. This study is aimed at finding out the influence of regular and intense practice of badminton on the median nerve conduction in elite players.2 groups of total 30 asymptomatic male subjects, between 20-40 years age, were created where one group included elite badminton players (n=15), and another included subjects who have not participated in any of the sports activities (n=15). Motor and sensory nerve conduction studies (MNCV and SNCV) of themedian nerve were conducted for subjects in both groups, including conduction velocities (CV) and distal latencies (DL) for subjects in both groups.The descriptive statistics was calculated using mean and standard deviation and comparison was done using 2-way ANOVA test.Distal motor and sensory latencies for median nerve suggested significant delays in non-badminton players when compared to elite players ($p<0.05$). Comparison of sensory conduction velocities formedian nerve between badminton players and normal subjects showed significant difference ($p<0.05$). The findings support role of regular and intense practice of badminton on median nerve of elite players when compared to age matched normal subjects.

Keywords: Badminton, median nerve, nerve conduction, repetitive overuse, upper limb.

INTRODUCTION

Nerve conduction studies (NCS) are an objective, quantitative and reproducible measure of peripheral nerve function, especially the ability of electrical conduction, of the motor and sensory nerves of the human body, and are widely used in diagnosis of nerve related disorders.[1-3] Repetitive force application during day-to-day activities can lead to compression neuropathies where several factors such as, (a) a low force present for a long time; (b) an acute focal application of a large external force or (c) repetitive application of brief large forces, can also play major role along with combination of stretching, shearing and/or compressive force application.[4] Factors such as high repetition of motions, high muscular forces and extreme elbow positions creates excessive physiological demands on the peripheral nerves of upper extremity especially in athletes. Overuse related injuries are very common in the sport involving use of racquets[5]. Rapid and repetitive movements of wrist are used by badminton players in variety of postural positions along with lunges, jumps, lunges, rapid changes in direction and rapid arm movements[6]. Literature supporting prevalence of upper limb neuropathies among badminton players is sparse, but majority of available studies report injuries to be more severe in intensity[7].

MATERIALS AND METHODS

In this study total 30 male subjects were included in the study using purposive sampling through invitation. Out of those, 15 were elite badminton players and 15 were age matched control subjects between age group of 20-40 years. The elite badminton players who were training for minimum of 1 hour per day for at least four days a week were recruited from Dakshin Kannada Badminton Association. The age matched asymptomatic control individuals who did not participate in any of the sports activities on regular basis were included. The subjects having significant history, signs or symptoms of peripheral neuropathy or compression syndrome of upper extremities were excluded. Informed written consent was received from all the participants after explanation of the details and purpose of the study. Nerve conduction parameters (i.e., conduction velocities and distal latencies) were evaluated using Neuro Care™- 2000, manufactured by Bio-Tech™, India. Motor and sensory nerve conduction studies for median nerve were performed using standard techniques of supramaximal percutaneous stimulation with a constant current stimulator and surface electrode recording on both extremities of each subject[9].

DATA ANALYSIS AND RESULTS

Statistical analysis of the data was carried out using SPSS 20.0 by IBM. The mean and standard deviation was calculated for descriptive statistics. Two-way ANOVA was used to compare latencies and conduction velocities of median nerve among elite badminton players and age matched control subjects ($p<0.05$). Comparison of baseline characteristics showed significant difference for age, whereas weight, height and BMI showed no significant difference at $p<0.05$ (table-1). Comparison of means and standard deviations for baseline nerve conduction characteristics showed no significant difference for subjects in both groups at $p<0.05$ (table-2).Table-3 shows the between group comparison of values of nerve conduction parameters using two-way ANOVA. Statistically significant differences were seen in motor and sensory latencies and sensory nerve conduction velocities ($p<0.05$). There was no significant difference seen in nerve conduction parameters for dominant and non-dominant extremity of players and control subjects ($p<0.05$).

DISCUSSION

Sport induced repetitive stress on dominant extremity of players is usually responsible for physiological and pathological changes in musculoskeletal system. Injuries to the components of nervous system such as peripheral nerves may remain subclinical and are not identified before damage is irreversible.[4,5] Many of the players may be

pre-symptomatic or asymptomatic, despite of having abnormal nerve conduction tests indicative of subclinical neuropathy[5]. Badminton is an individual non-contact sport requiring jumps, lunges, quick changes in direction and rapid arm movements from a wide variety of wrist and hand postures along with rapid and repetitive wrist movement[6]. Detection of nerve pathology secondary to such repetitive strains in asymptomatic badminton players may help to prevent further deterioration by early intervention. The results of this study suggest that there is a delay in sensory and motor conduction and reduction of sensory conduction velocities for median nerve in badminton players when compared with control age matched individuals. While comparing the sensory and motor conduction velocities of the radial and ulnar nerves in tennis players, Colak T et. al. (2004) reported a significant delay in conduction in the dominant arms of tennis players compared with their non-dominant arm and normal subjects[5]. The findings of present study are also in coherence with above mentioned study. But, as this study was conducted only on elite male badminton players between age of 20-40 years, the results of this study cannot be generalized for the whole athletic population. Additionally, the sample size for this study was less when two group comparisons were made, in future the study may be replicated in a larger sample and a wider age range. A longitudinal study can be done to find out clinical signs and symptoms in badminton players in later life who were initially asymptomatic with altered findings in nerve conduction parameters. In conclusion, we can say that regular, intense practice of badminton affects nerve functions in upper extremities of elite badminton players when compared to age matched normal subjects. It is also suggested that asymptomatic elite badminton players may have subclinical pathology in dominant upper extremity nerves which affects nerve conduction functions. On the basis of this study, a preventive conditioning program can be designed, for training of badminton players including modification strategies to optimize biomechanics scientifically and to imply neuro-dynamics based pre-rehabilitation.

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Declaration of interest statement

The authors report there are no competing interests to declare.

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Table1: Comparison of baseline characteristics of subjects (n=30)

	Control Group (n=20)		Elite Players (n=20)		T	Sig.
	Mean	**SD**	**Mean**	**SD**		
Age (years)	24.60	0.70	23.20	1.03	3.55	***0.002**
Weight(kg)	60.80	6.90	66.70	5.70	-2.086	0.051
Height (cm)	170.30	4.72	171.40	6.55	-0.431	0.672
BMI(Kg/m^2)	20.87	1.74	22.80	2.77	-1.865	0.079
Note: *2-tailed t-test was done with level of significance set at p<0.05						

Table 2: Comparison of baseline nerve conduction parameters of subjects (n=30)

Parameters	Normal (n=15)		Players (n=15)	
	Dominant	Non-dominant	Dominant	Non-dominant
ML (ms)	2.889 (0.378)	2.989 (0.281)	3.109 (0.508)	3.448 (0.521)
MNCV (m/s)	57.730 (5.972)	59.026 (2.499)	57.967 (1.927)	59.363 (1.968)
SL (ms)	2.289 (0.200)	2.156 (0.175)	2.431 (0.261)	2.463 (0.271)
SNCV (m/s)	54.159 (3.440)	57.459 (4.127)	48.182 (3.934)	47.023 (5.277)

Table 3: Comparison of differences between two groups using 2-way ANOVA(n=30)

Parameters	**Group**			**Dominance**		
	Sum of Squares	**F**	**Sig.**	**Sum of Squares**	**F**	**Sig.**
ML (ms)	1.153	6.121	***0.018**	0.482	2.558	0.118
MNCV (m/s)	0.824	0.067	0.798	18.117	1.464	0.234
SL (ms)	0.504	9.475	***0.004**	0.026	0.479	0.493
SNCV (m/s)	673.466	37.306	***<0.001**	11.46	0.635	0.431
Note: *2-tailed t-test was done with level of significance set at p<0.05						

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RESEARCH ARTICLE

E- Mental Health: AI and the Future of Mental Health Workforce

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ABSTRACT

This article aims to provide a general overview of AI in mental health care, its benefits, and limitations, with ethics and future considerations in application. The global mental health crisis touches over a billion people each year; the need for innovative improvements in diagnosis, treatment, and continued care underlines the need for effective solutions in this regard. Artificial intelligence holds the promise of addressing gaps in mental health care delivery and improving outcomes so that mental health services become even more accessible. AI-based interventions, including the Woebotchat bot, have been proved to provide the effective CBT model to the users and the consequent symptom reduction rate in depression and anxiety of more than 50 % (Fitzpatrick et al., 2017). However, despite all these promises, several challenges still deter AI's large-scale employment in mental health care. These concerns are data privacy, possible algorithmic bias, and the ethical issues related to decision-making driven by algorithms. The quality and representativeness of data used in training AI models will also affect generalizability and the fairness of the AI systems. Furthermore, the complexities of human emotion and the psychological conditions provide limitations against full replacement and complementarity with traditional clinical judgment. Regulations are still quite immature; proper validation and testing processes must be strictly followed in ensuring the safety and effectiveness of AI applications. This paper discusses the opportunities and challenges that center on the potential of AI in transforming mental health, while discussing the obstacles to be addressed in its integration into healthcare systems.

Keywords: E-Mental health, Artificial intelligence, Therapeutic Interventions, Virtual Reality

INTRODUCTION

Artificial Intelligence has emerged as a transformative force in various sectors, and its impact on healthcare, particularly mental health, is proving to be groundbreaking. AI technologies, from machine learning algorithms to natural language processing and predictive analytics, are reshaping the way mental health professionals diagnose, monitor, and treat mental health conditions. By using vast amounts of patient data, AI systems can find patterns and trends that might not be immediately visible to clinicians, thus enhancing diagnostic accuracy and enabling early intervention(Olawade et al., 2024).. These advancements promise to revolutionize traditional mental health care, making it more accessible, personalized, and efficient. From virtual assistants that carry out cognitive behavioral therapy (CBT) to AI-enabled speech and behavior analysis of patients for signs of disorders in mental health, these possibilities are endless and more emergent (Ghosh, S. (2024). But just like the promise, introducing AI into mental health practice poses its own set of challenges and ethical concerns as well. This creates room for debate on issues regarding AI in healthcare, including its privacy, data security risks, and the dangers of algorithmic bias. Indeed, while AI is set to enhance clinical decision making, it cannot substitute elements of empathy, compassion, and subtle understanding necessary to mental health care. In ensuring these technologies are used to supplement and augment human care rather than substitute it, balancing innovation with ethical responsibility will become very important as AI tools develop. The present review covers the current state of AI in mental health, how far-reaching its potential may be to transform the field, and the ethical considerations which need to be worked on as these technologies develop further.

Defining E-Mental Health

E-mental health refers to the application of digital technologies, such as internet-based services, mobile apps, and other online platforms, in order to provide mental health services, support, and resources (Lal, S., & Adair, C. E. 2014). This ranges over a variety of tools including tele-therapy, online counseling, self-help applications, and mental health websites for better access, affordability, and quality of mental health care. E-mental health has rapidly become an integral part of any health care system, primarily on issues of limited access to classic face-to-face mental services, long waiting periods before access, and geographical or location barriers. E-mental health also offers its customers anonymity and convenience of choice as a means of minimizing mental illness stigma (Lehr, D. et al., 2016).

Evolution of E-Mental Health

E-mental health has been transformative, led by technological advancements and a growing need for accessible mental health care. E-mental health is the application of digital platforms and technologies, such as apps, online therapy, and tele-health services, to support and treat mental health issues. Initially, e-mental health services started as basic online resources such as self-help websites and discussion forums. These resources were basic mental health information, but now with the growth of mobile technology and the internet, these services have really expanded. Online therapy platforms and telemedicine enable individuals to consult with therapists and counselors remotely, which has really made mental health care accessible, especially for those who are far away or from underserved areas. In recent years, the development of AI-driven mental health apps and virtual therapy programs has advanced the field further by offering personalized support and real-time tracking of mental health conditions. These tools provide users with resources like mood tracking, guided meditation, and cognitive behavioral therapy (CBT) exercises, improving self-management of mental health. The COVID-19 pandemic has further hastened the adoption of e-mental health as most traditional in-person therapies were pushed to digital formats due to social distancing measures. As the field continues to grow, e-mental health shows promise in reducing stigma, increasing accessibility, and offering cost-effective mental health care solutions. (Ellis, L. A., et al 2021).

AI based technological Interventions in Mental Health care sector

AI is transforming mental health care with multiple innovative applications. In diagnosis and assessment, AI makes use of machine learning, NLP, and chatbots for analyzing responses from mental health screenings to identify depression, anxiety, and PTSD. NLP helps decode patient language, while the presence of chatbots guarantees

constant and unbiased results. (Nazi, Z. A., &Peng, W. 2024) Artificial Intelligence (AI) in healthcare refers to the use of advanced algorithms and machine learning models to analyze complex medical data, assist in decision-making, and improve patient outcomes. AI can be applied across various areas, including diagnostics, treatment planning, personalized medicine, and administrative tasks. Some of the most important applications include medical imaging, where AI systems can analyze X-rays, MRIs, and other scans to detect abnormalities such as tumors or fractures with high accuracy. AI also helps in predicting patient outcomes, identifying risk factors, and recommending personalized treatment plans based on a patient's medical history and genetic information (D'Alfonso, S. 2020). AI-based technologies can help physicians make the right decisions, providing immediate insights from extensive medical literature and patient information. In drug discovery and clinical trials, AI technologies help accelerate new treatments. Additional advantages AI brings include streamlining most administrative work like scheduling and patient triaging; helping manage EHRs thus providing a way of curving the burden healthcare personnel usually face.AI in health care is full of vast possibilities, but the area also poses challenges on the lines of data privacy and regulatory aspects and ensuring that such systems are transparent and ethical. Still, AI does march ahead, offering tremendous scope for efficiency, quality of care, and better costs. AI is powering virtual therapists that deliver accessible platforms for CBT as well as other treatments and apps providing personalized cognitive exercises along with relaxation techniques (Olukayode, S. M., 2024). Another area of real-time therapy is emotion recognition technology for adaptive therapy based on facial expression and voice tone. AI is also improving monitoring and support by tracking vital signs, sleep patterns, emotional states, and early warning signs through wearable devices and mobile applications (Graham, S., 2019). Finally, through predictive analytics, AI works with large datasets to track mental health trends and provide insights into at-risk groups, helping plan resources better and target interventions for the emerging needs.

Impact on the Mental Health Workforce

This, in turn, will help shift the roles of mental health professionals from those of a robot, tasked with conducting assessments and monitoring, freeing psychologists, psychiatrists, counselors, and therapists to focus more on the complexities and interpersonal nuances of care (Rebelo et al. 2023). AI might be good at diagnosis or treatment planning, but people will continue to be good at that which is very personal. The debate is biased towards the notion that AI will complement human practitioners more than replace them. Here, AI will complement in analyzing data, making diagnosis, and delivering treatment to the patient, while leaving human empathy, judgment, and expertise to play vital roles in therapeutic settings (Cross et al. (2024). To adapt to this change, mental health professionals will need to acquire knowledge in AI and technology so that they can use such tools effectively and ethically without compromising patient care (Beck et al. 2018). There are also new jobs to be created, like AI ethics officers, mental health tech developers, and data scientists, who will work in developing AI tools, ensure their ethical use, and manage the huge amounts of data in mental health treatment.

Challenges and Ethical Considerations:

The use of artificial intelligence in mental health care involves both significant opportunities and some complex challenges, particularly around ethics, privacy, and effectiveness. The primary area of concern is the ethical usage of AI systems, since they often require access to sensitive personal data, thus causing questions regarding data privacy and security.(Stahl, B. C., & Wright, D. 2018). Additionally, implementing AI in diagnosing or treating mental health conditions raises a concern over dehumanizing care, as automated systems may replace necessary human empathy and understanding in therapeutic environments. The lack of transparency in AI decision-making processes has been termed as the "black-box" problem and poses a challenge to clinicians and patients as they might not know how such decisions are made, which goes on to affect trust and adoption (Wachter et al., 2017). Another concern is whether AI-driven diagnoses are always accurate and reliable, mainly when the conditions are complicated and nuanced in mental health, with high dependence on subjective human experience. This requires careful regulation and oversight to ensure that AI tools are tested, validated, and implemented under strict guidelines (Shimada, K. (2023). The impact on the mental health workforce is also a concern, as there is a fear that AI may replace professionals or contribute to job displacement, creating tensions within the field (Lomis, K., et al., 2021). Despite these challenges, AI has the potential to improve accessibility and efficiency in mental health care if implemented cautiously. It requires a

balanced approach that ensures ethical practices, equitable outcomes, and collaboration between AI systems and human clinicians.

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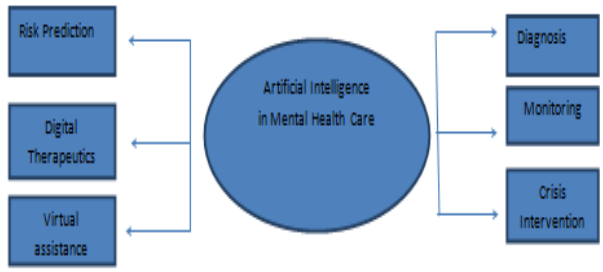

Fig:1 AI based technological Interventions in Mental Health care sector

Fig:2 Impact on the Mental Health Workforce

RESEARCH ARTICLE

Prevalence of Rounded Shoulder Syndrome Due to Physical and Psychosocial Factors among Young Females: A Cross-Sectional Survey Study

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ABSTRACT

Rounded shoulder syndrome is a common postural disorder of the shoulder joint, characterised by elevated and protracted outward scapula. Females are more prone to develop rounded shoulders. It can be caused by either physical, psychological, biological, or social factors. This cross-sectional survey study was thus planned to determine the prevalence of rounded shoulder syndrome due to physical and psychological factors among young females. The survey was conducted among a population of young females (undergraduate, postgraduate, or working in the university) using a self-administered online questionnaire within a duration of 9 months from August 2022 to April 2023.Subjects were chosen according to the predefined selection criteria. The survey questionnaire developed in Google Forms was then distributed to the selected population through social media and email. In the end, all the responses from individuals were collected and analyzed. A total of 270 responses were recorded, of which mostly were undergraduates, followed by post-graduates and individuals working in the university. The findings suggested a high prevalence of carrying heavy backpacks on the back, a sedentary lifestyle, and sitting in a slouched posture among young females with rounded shoulder syndrome. Similarly, higher prevalence was also noted for psychological factors like having stress of any kind and having negative thoughts about oneself. Most of the participants complained of pain around the shoulder followed by upper back, neck, and arm along with tightness of muscles around the region. This study concludes that the high prevalence of physical and psychological factors among the female population with rounded

shoulders is suggestive of the fact that these factors can influence the incidence of rounded shoulder posture.

Keywords: Rounded shoulder syndrome, Shoulder pain, Physical factor, Psychological factor, Female

INTRODUCTION

Rounded shoulder syndrome is a frequent postural condition that affects students and workers who work on computers at a table and chair setup.[1]This results in a stooping posture marked by scapular elevation, protraction, downward rotation, and anterior tilt.[2,3] Because of the adaptive aberrant posture and misalignment in the shoulder joint induced by changes in the position of the scapula, the muscles and ligaments surrounding the shoulder joint are subjected to a great deal of stress, resulting in discomfort and impairment. Complications include inadequate scapulohumeral rhythm, shoulder discomfort, tendinitis, bursitis, impingement, instability, and muscle imbalance.[4] Muscular imbalance occurs when the frontal shoulder muscles, such as the serratus anterior, pectoralis major and minor, shorten and the muscles in the back of the shoulders, such as the rhomboids, middle, and lower trapezius, lengthen, altering their functions and how they work.[5] According to studies, more than 80% of people with myofascial pain syndrome had rounded shoulders. [1,2] According to reports, 73% of healthy people aged 20 to 50 have rounded shoulders on the right and 66% on the left.[2] Its prevalence among people who participate in upper-arm sports such as basketball, badminton, gymnastics, swimming, squash, table tennis, volleyball, and field events is quite evident and such individuals are more likely to have rounded shoulders.[5] According to prior research, certain psychological factors and emotional responses might influence muscle function, body posture, and movement. It indicates that such elements might gradually deteriorate a person's physical posture, attitude, emotions, and feelings. It is believed that the lower a person's self-esteem, the greater the likelihood of having a flexed posture, which is defined by a rounder shoulder.[6] Thus, in addition to the other causes of rounded shoulders, emotional and psychological variables play an important role. People with thoracic hyper kyphosis exhibit anatomical abnormalities in the alignment of the shoulder joint, causing protraction and anterior tilting, resulting in a rounded shoulder posture.[7] Furthermore, rounded shoulder posture has been linked to a variety of disorders, including temporomandibular joint dysfunction syndrome, thoracic outlet syndrome, chronic neck discomfort, shoulder overuse injuries, and even cardiorespiratory deficiencies.[8] Females with macromastia or breast hypertrophy, which is characterized by an uneven rise in breast size in contrast to body size, may also have rounded shoulder posture.[9]It may cause the body's centre of gravity to shift anteriorly, resulting in increased thoracic kyphosis and compensatory changes in the cervical and lumbar spines.[10,11] It is frequently related to social and psychological problems such as low self-esteem and a poor quality of life, which exacerbates the rounded shoulder position.[9]Similar changes in posture are also evident in individuals carrying heavy objects like bags.[12] Most prior research only showed the prevalence of round shoulders after any anatomical alterations. In contrast, the current study focuses on two factors: physical and psychological, all of which may be associated with round shoulder. It also focuses on determining the impact and interference of such posture on pain and activities of daily living. As females are assumed to be more prone to developing rounded shoulder postures the current study aims to find the prevalence of rounded shoulder syndrome due to physical and psychosocial factors among young females.

METHODS

Study Design

A cross-sectional online survey study was conducted at Maharishi Markandeshwar deemed to be University (MMDU), Mullana, Ambala, Haryana, India between August 2022 to April 2023. Being a non-interventional study, no ethical clearance was acquired.

Study Sample

The sample size was determined using the formula $N = \frac{(Z)^2 P(1-P)}{d^2}$, with an expected prevalence (P) of 80%,[13] levels of precision (d) at 5%, by considering a 95% confidence interval, thus Z set at 1.96.The minimum sample size was estimated to be 245. Considering for 20% dropout, the final sample size was calculated to be 270. The convenient sampling technique was used to recruit the participants through social media and email.

Selection Criteria

Young females pursuing undergraduate and post-graduate studies from any of the departments at the MMDU or working in the university, with abnormal rounded shoulder syndrome were a part of this study. The persons with abnormal postures were identified by generalized observation and thorough postural evaluation for the alignment of the body parts.[14] Only females aged between 18 to 26 years were selected as participants for the study. Males were not part of this study. Also, females who were not willing to participate were not a part of this study.

Study Tool

The survey was conducted using a self-administered, structured questionnaire developed by the authors on a Google form. It consisted of twenty questions with three different sections. Each question was assigned a value of 0-3. The first section aimed to identify the physical factors like carrying bags or attainment of abnormal posture that could be causing the rounded shoulder posture, and once found, the second section sought to determine the psychological impact of such postural impairment. The final section sought to determine whether the participant complained of any pain and whether such atypical posture impairs activities of daily living.

Procedure

The study concept was presented to female university students and workers who met the selection criteria, and informed consent was obtained from those who agreed to participate. The created questionnaire was then distributed to students who agreed to participate via various online social media platforms and applications. Any questionnaire-related queries were answered directly through the social media site. The principal author participated in data collection while being supervised by fellow authors. The supervisor trained the data collector, which helped to maintain data quality. All completed questionnaires were evaluated for completeness, clarity, and consistency. Any missing or incomplete data was immediately updated during the data collection period. The completed questionnaires were received on the same day, and a combined analysis was performed later.

Data Processing and Analysis

The data was analysed based on the responses to the Google form. The participant responses were collected using an Excel chart linked to a Google form and assessed programmatically using the most recent version of MS Excel for Windows 11.The normality of the age distribution was analysed using the Kolmogorov-Smirnov test in SPSS v.26. The findings were documented and illustrated via pie charts and tables.

RESULTS

A total of 270 respondents participated with a response rate of 100%. They were aged between 18 to 26 years, with a mean age of 21.16 ± 2.92. The age of the participants was normally distributed with a p-value of 0.2. Out of these 270 participants, 208 (77%) were undergraduate students, 50 (18.5%) were post-graduate students, and the rest 12 (4.5%) were office workers at the university. The result of this present study showed that around 31% of respondents carry large bags regularly, whereas 40.5% lift them on occasion. The majority of them (73.3%) carry big backpacks, followed by laptop bags (16.3%) and cross body bags (10.3%). Approximately 57.4% of these respondents carry bags weighing between 1 and 5 kg, followed by 36% carrying between 5 and 10 kg and 6.6% carrying more than 10 kg. 53.7% of respondents carry their luggage for an average of 1-3 hours, 36.7% for 3-5 hours, and 9.6% for more than 5 hours. The majority of responders (81.8%) carry their bags on their backs.

The majority of respondents, 53.3%, do not prefer to go to the gym or conduct any physical activity. Approximately 46% of participants prefer to sit in a slouched posture. A large proportion of these participants engage in any task that requires holding the body in a prolonged forward position the majority of the time (24.1%) and occasionally (24.4%).

DISCUSSION

To identify the physical and psychosocial factors that possibly lead to rounded shoulder syndrome, the female population between the ages of 18 and 26 were only considered. For evaluating the round shoulder, a trimodal approach was used, that is generalized observation for any abnormality in posture, detailed postural evaluation, and lastly evaluation for tightness of shoulder protractors and weakness of the shoulder retractors. Then the developed self-administered questionnaire using Google Forms was shared via social media platforms like WhatsApp, Facebook, Instagram or email among the identified participants. A total of 270 individuals completed the survey.

Impact of carrying a heavy bag

In the current study, the survey questionnaire included questions related to how much weight a person lifts, how long it takes them to hoist a big bag, and their preferred method of bag carrying, such as front-back or cross body. According to findings, 31.1% of the population responded positively to the survey question about carrying a heavy bag with a yes and 40.4% of the population indicated that they occasionally carry a large bag on their shoulder. Such a prevalence of using heavy bags, mostly ranging between 1 to 5 kg, regularly or occasionally for at least 1-3 hours on the back can thus be considered as a precipitating cause of the rounded shoulder syndrome. A previous study conducted to assess students' cervical and shoulder posture concerning the effects of the backpack concluded that carrying a backpack weighing 15% or more of the body weight affects the shoulder posture as it changes craniovertebral angle and anterior head alignment.[13]In another study exploring the relationship between a forward-facing head, a round shoulder, and thoracic kyphosis, described a lot of factors that can be linked with a round shoulder and one of them was a heavy backpack carriage.[15] The findings of the current research are consistent with these studies. The other physical factors like the high prevalence of individuals not preferring to go to the gym or perform any physical activity, as well as of individuals preferring to sit in a slouched posture can also be considered as the precipitating factors. Such findings were earlier demonstrated, where rounded shoulder posture was linked with long study hours that require sitting for a prolonged period.[15]

Impact of low self-esteem

The aspects of psychological factors that can affect a person's self-esteem were explored in the current survey. It included the prevalence of any sort of stress, any self-defeating thoughts, and how one perceives one's body and others. 44% of people were positive about experiencing stress of any kind. Such findings make it more likely to be a precipitating factor for rounded shoulder syndrome. An article published in the year 2011 had previously demonstrated a link between low self-worth and rounded shoulders. It stated that the lower the self-esteem more will be the chances of having a round shoulder. Any type of stress will affect a person's body language, and if it persists for a long time, it can result in such anatomical changes.[6]In another study conducted to study the influence of breast enlargement on patient posture demonstrated similar findings that females with macromastia are prone to psychological and social complaints that lower their self-esteem which may lead to rounded shoulder posture.11

Pain with rounded shoulder syndrome

To determine which body part of a person with rounded shoulders is affected the most, a pain-based section of the questionnaire was developed to support the research. As a result, 34% of the population reported having shoulder discomfort, 30% complained of neck pain, 32% had upper back pain, and 37% of the population positively responded that they felt muscle stiffness in their upper back, shoulder, and neck regions. A previous study conducted on how sedentary workers' rounded and stooped shoulder positions affected myometric measurements of muscle suggests that rounded shoulders are associated with myofascial pain, decreased pectoralis tone, and increased deltoid

stiffness.[1] Another previously documented study on upper crossed syndrome among medical students stated that muscle imbalance due to rounded shoulder posture can cause pain in the upper back, neck, or arms.[16] A study on the link between thoracic kyphosis, forward head posture, and the round shoulder also supports the findings of the current research by revealing that such posture could cause a muscle imbalance by shortening the muscles in the front of the shoulder, including the pectoralis minor and major, serratus anterior, and upper trapezius, and lengthening the muscles in the back, including the rhomboids and middle and lower trapezius. This muscular imbalance alters the scapular and glenohumeral alignment and kinematics, which raises the possibility of neck, shoulder, and generalised arm pain.[15]

Limitations and Future Recommendations

Even though the findings of this study support the fact that the incidence of rounded shoulder syndrome is higher among females with physical and psychological factors, it does not establish a correlation between them and thus does not establish them as the cause. It also doesn't consider the biological and social factors that could lead to rounded shoulder syndrome. So a future study with a cohort or case-control design to determine all the biological, physical, psychological, and social factors possibly causing rounded shoulder syndrome is recommended.

CONCLUSION

This study concludes that the high prevalence of physical and psychological factors among the female population with rounded shoulder syndromeis suggestive of the fact that these factors can influence the incidence of rounded shoulder posture. Physical factors can include factors like lifting heavy bags, attaining abnormal posture and having a more sedentary lifestyle. Psychological factors include stress and lowered self-esteem of a person.

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CONFLICT OF INTEREST

All authors declare that there is no conflict of interest.

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Table.1: Participants' responses on possible physical factors leading to Rounded Shoulder

	Response	Frequency
Prefer going to the gym or performing any physical activities.	a. Yes b. No c. Sometimes	64 (23.7%) 144 (53.3%) 62 (23%)
Indulged in any task that requires holding the body in a prolonged forward position.	a. Yes b. No c. Sometimes	65 (24.1%) 139 (51.5%) 66 (24.4%)
Preferred sitting posture.	a. Back straight b. Slouched c. Forward head	79 (29%) 124 (46%) 67 (25%)

Table.2: Participants' responses on possible psychological factors leading to Rounded Shoulder

	Response	Frequency
Having stress of any form.	a. Yes b. No c. Sometimes	119 (44.1%) 90 (33.3%)61 (22.6%)
Having any negative thoughts about own selves.	a. Yes b. No c. Sometimes	100 (37%) 101 (37.4%) 69 (25.6%)
Perception of the own body makes one feel less confident.	a. Yes b. No c. Sometimes	87 (32.2%) 118 (43.7%) 65 (24.1%)
Get influenced by others.	a. Yes b. No c. Sometimes	72 (26.7%) 123 (45.5%) 75 (27.8%)

Confident about own abilities.	a. Yes b. No c. Sometimes	121 (44.8%) 74 (27.4%) 75 (27.8%)

Table.3: Participants' responses on the impact and interference of Rounded Shoulder on Pain and Activities of Daily Living

	Response	Frequency
Pain around the shoulder region.	a. Yes b. No c. Sometimes	91 (33.7%) 101 (37.4%) 78 (28.9%)
Pain around the neck.	a. Yes b. No c. Sometimes	82 (30.4%) 110 (40.7%) 78 (28.9%)
Pain around the upper back.	a. Yes b. No c. Sometimes	87 (32.2%) 112 (41.5%) 71 (26.3%)
Pain while raising the arm.	a. Yes b. No c. Sometimes	56 (20.7%) 151 (56%) 63 (23.3)
Tightness of muscle around the upper back, shoulder and neck.	a. Yes b. No c. Sometimes	100 (37%) 92 (34.1%) 78 (28.9%)
Discomfort in standing or sitting for a prolonged time.	a. Yes b. No c. Sometimes	118 (43.7%) 87 (32.2%) 65 (24.1 %)
Difficulty while combing hair or doing overhead activities.	a. Yes b .No c. Sometimes	55 (20.4%) 170 (63%) 45 (16.7%)

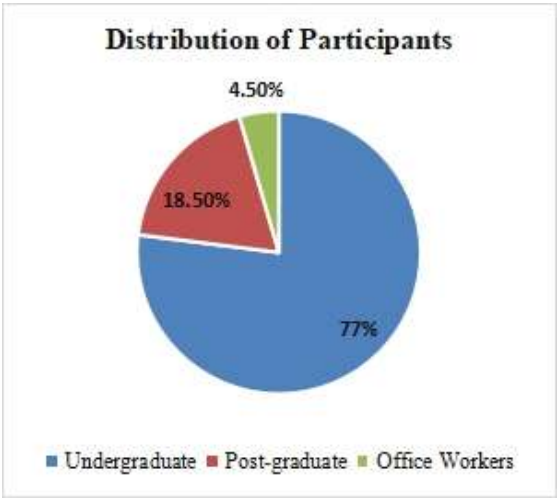

Figure.1: Distribution of Participants

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RESEARCH ARTICLE

Evaluating the Effectiveness of Classical Shodhana Therapies in Treating Sheetapitta with a Focus on Urticaria : A Case Study

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ABSTRACT

The skin, the largest organ in the human body, plays a crucial role in various physiological functions. It serves as a protective barrier against external threats, helps regulate body temperature, and is involved in sensory perception. This integumentary system, which includes the skin, hair, nails, and various glands, is essential for maintaining homeostasis. The skin also serves as a means of communication with the external world, reflecting emotions, responding to stimuli, and providing valuable information about overall health. Changes in skin color, texture, or temperature can indicate underlying health issues. Lifestyle factors such as irregular bowel habits, consumption of junk food, late-night sleep, and excessive use of air conditioning can lead to the development of skin diseases. Sheetapitta, described in Ayurvedic texts as a tridoshaja vyadhi, involves an imbalance of all three doshas. The characteristic symptoms of Sheetapitta include rashes resembling a wasp bite, excessive itching, vomiting, fever, and a burning sensation. Although there are many treatments available for this disease, its recurrent nature makes it challenging to manage with modern medical approaches alone. In a modern context, Sheetapitta can be correlated with urticaria, which also poses significant treatment challenges. In the present case study, classical Ayurvedic treatments, including Vamana (therapeutic emesis), Raktamokshana (bloodletting), and Virechana (purgation), were implemented. Post-treatment, a significant reduction in the signs and symptoms of Sheetapitta was observed. This case study highlights the efficacy of classical Shodhana therapies such as Vamana, Raktamokshana, and Virechana in managing Sheetapitta.

Keywords: Shodhan Chikitsa, Vamana, Raktamokshana, Sheetapitta, Urticaria, Ayurveda, Skin Diseases, Tridosha, Homeostasis

INTRODUCTION

In Ayurveda, Urticaria is referred to as Sheetapitta, derived from "sheeta" meaning cold and "pitta" meaning hot. According to the Brhatatrayi, Sheetapitta arises when Vata and Kapha doshas are aggravated due to exposure to a cold breeze. These aggravated doshas mix with Pitta Dosha, leading to the manifestation of red skin rashes. The primary tissues affected are rasa dhatu (plasma or lymph) and rakta dhatu (blood) [1]. Environmental factors, poor dietary habits such as excessive consumption of spicy, oily, or processed/junk foods, can disturb the dosha balance, contributing to the onset of Sheetapitta. Sheetapitta is characterized by symptoms such as Shoth (swelling), red patches or rashes on the skin, itching (Kandu), pain (Toda), vomiting (Chardi), fever (Jwara), loss of appetite (Aruchi), nausea (Hrullas), heaviness in the body (Angagauravta), and a burning sensation (Daha). Urticaria, commonly known as hives, is a skin condition marked by the sudden appearance of raised, red, and itchy welts or wheals on the skin. These typically last for a few days and do not cause long-lasting skin changes. However, the condition often recurs, with fewer than 5% of cases persisting for more than six weeks. It is estimated that 15% to 23% of adults have experienced at least one episode of acute urticaria in their lifetime, with the prevalence of chronic urticaria in adults estimated to be around 0.5% to 5% [2]. Modern medical treatments for urticaria often do not provide a permanent cure, necessitating lifelong medication use, which can have unwanted side effects. Ayurveda, the holistic science of life, offers a range of therapies, both external and internal, with purificatory therapies (Shodhana) being particularly prominent. Ayurvedic texts recommend Vamana (therapeutic emesis), Raktamokshana (bloodletting), and Virechana (purgation) for managing Sheetapitta effectively.

Case Presentation

Patient Information

A 32-year-old male patient presented to the PIA Hospital outpatient department (O.P.D no. 21020506) on 09/12/2021 with the chief complaint of large, red, itchy rashes covering his entire body. The patient reported that he had been well until two years prior when the symptoms first appeared. The symptoms progressively worsened, particularly in the evening, at night, and upon exposure to cold climates and wind.

Medical History

The patient had a history of using allopathic medicines for four months without satisfactory relief. Consequently, he sought treatment at Parul Ayurved Hospital and was admitted to the Panchakarma IPD ward (I.P.D. no. 213614) for better management. The case was diagnosed as Sheetapitta based on clinical presentation, etiological, and relieving factors.

Associated Complaints

Irregular evacuation of stools

Past History

No significant past illnesses

Family History

No family history of similar illness

Medication History

Use of steroids, both topical and oral

Surgical History
No surgical procedures to date

Allergies
No known allergies to any medications

General Examination
Pulse Rate: 78/min
Blood Pressure: 130/90 mm Hg
Respiratory Rate: 17/min
Heart Rate: 70/min

Systemic Examination
Respiratory System: Normal chest shape and size, bilateral equal air entry, no crepitations
Cardiovascular System: S1 and S2 heart sounds normal, no murmurs or abnormal sounds
Central Nervous System: Patient conscious, well-oriented, good memory
Gastrointestinal Tract: Abdomen soft and non-tender

Astha-vidh Pariksha (Eightfold Examination)
Nadi (Pulse): Vata-Pitta-Kaphaj
Mala (Stool): Prakrita (normal)
Mutra (Urine): Prakrita (normal)
Jihva (Tongue): Alipita (clear)
Sabda (Voice): Prakrita (normal)
Sparsh (Touch): Mrdu (soft)
Drk (Eyes): Prakrita (normal)
Akriti (Body Build): Madhyam (moderate)

Samprapti Ghatak (Pathogenesis Components)
Dosha: Tridosha (Vata, Pitta, Kapha)
Agni: Manda (low digestive fire)
Doshagati: Vriddhi (aggravation), Tiryak (lateral movement)
Shakha Vyadhi Marga: Bahya (external pathway)
Dushya: Rasa (plasma), Rakta (blood)
Srotas: Rasavaha (plasma channels), Raktavaha (blood channels)
Srotodushti Prakara: Vimargagamana (improper flow)
Udbhava Sthana: Aamashaya (stomach)
Vyakti Sthana: Tvak (skin)
Svabhava: Ashukari (acute onset)

Assessment Criteria
Treatment Protocol

DISCUSSION

Following a detailed history and physical examination, the patient's condition was diagnosed as Sheetapitta. In Ayurveda, Sheetapitta is characterized by symptoms such as varati (erythema), damstavata (urticaria), shotha (swelling), and kandu (itching) due to the vitiation of Kapha dosha; shula (pain) due to Vata dosha; and daha (burning sensation) due to Pitta dosha.[4] Additional symptoms include chardi (vomiting), hrullas (nausea), aruchi

(loss of appetite), dehasada (body ache), angagauravta (heaviness in the body), jwara (fever), and vidaha (burning sensation) .

Treatment Approach

In Ayurvedic classics, the treatment of Sheetapitta involves both shodhana (purification) and shamana (palliative) therapies. Shodhana therapies aim at eliminating the imbalanced doshas and toxins from the body, while shamana therapies focus on alleviating symptoms and restoring balance without purification procedures. Sheetapitta involves the vitiation of all three doshas: Vata, Pitta, and Kapha. According to Yogratnakar, the treatment approach involves shodhana chikitsa, which includes Vamana (therapeutic vomiting), Raktamokshana (bloodletting), and Virechana (purgation) [5].

Vamana

Vamana is one of the Panchakarma procedures that aims to eliminate vitiated doshas from the body. Classical texts highlight the involvement of Kapha in Sheetapitta and the use of Vamana in addressing Kapha disorders, especially when associated with Pitta and Vata .[6] Initially, deepana-pachana treatment was administered for aama pachana .[7] Panchtikta ghrita was chosen for snehapana due to its properties like Vishaghna (anti-allergic action), Kandughna (pacifying itching), Kushthaghn (removing skin disorders), and purifying effects on the skin and blood.[8] The ghrita ingredients are primarily Tikta rasatmak, Madhur vipaki, and Ushna viryatmak, which have an affinity towards Rasa dhatu and, eventually, the skin .Vamak drugs like Madanphala bypass normal digestion due to their vyavayi guna, reach the body's minute channels due to their suksma guna, and act immediately before being expelled from the body due to their prabhava [9]. Vamana resulted in a significant reduction in major symptoms such as kandu (itching), shoth (swelling), and shyavata, with improvements in gastrointestinal function and a general feeling of lightness throughout the body. Samsarjana Krama was then followed for seven days.

Shamana Therapy

After Samsarjana Karma, shamana drugs were prescribed for seven days, focusing on pitta-vata shamaka and raktashodhak properties for better outcomes. Arogyavardhini Kashaya, Panchatikta Kashaya, and Patoladi Kashaya Vati were advised, along with Nimba Taila for local application.

Raktamokshana

Given the raktavaha srota dushti and the predominance of rakta and pitta in Sheetapitta, Raktamokshana (siravedha or bloodletting) was planned after completing shamana chikitsa on the 7th, 14th, and 21st days. Raktamokshana helps remove dushit rakta along with remnant doshas, reducing symptoms like vidaha (burning sensation) and promoting raktaprasadana (purification of blood)[10] .

Virechana

Virechana, a treatment for Pitta dosha as per Charaka, was selected to address persistent symptoms like rashes, itching, burning sensation, and sweating. Virechana helps pacify Vata and Pitta and expel the vitiated doshas from the body, effectively addressing the tridosha imbalance seen in Sheetapitta and the derangement of Rasavaha, Raktavaha, and Swedavaha Srotas[11] . Trivrutta is considered an excellent drug for Virechana due to its Vyavayi, Vikasi, and Sookshma Guna, which help it reach the body's minute channels. Its Ushna and Teekshna Guna help liquefy and separate compacted morbid doshas[12]. Acharya Sushruta mentions Trivrutta in Adhobhaghar Gana, indicating its effectiveness in treating Pitta and Kapha dosha with properties like Tikta, Katu rasa, Laghu, Ruksha, and Tikshna Guna, Katu Vipak, Ushna Virya, and Adhobhaghar Prabhav . Trivrutta Avelaha was used as the Virechana drug, leading to relief signs such as a reduction in the size and number of lesions.

CONCLUSION

This case study highlights the successful management of Sheetapitta/Urticaria using Ayurvedic treatment modalities, including both sodhana and shamana chikitsa. The combined effect of therapies such as Vamana, Raktamokshana, and Virechana proved to be more effective than shamana chikitsa alone. Significant reductions were observed in symptoms like Varati dansh sansthana (pricking pain resembling a wasp bite), Shoth (swelling), Kandu (itching), and Vidaha (burning sensation). The current course of remedy shows promise in revolutionizing the treatment of Urticaria. Panchakarma therapies aim to restore doshic balance, addressing the root cause of the disease. By bringing the doshas back to their natural equilibrium, the likelihood of disease recurrence diminishes. This single case study demonstrates the efficacy of Ayurvedic treatment in managing Sheetapitta/Urticaria. However, further research with larger sample sizes is needed to standardize Panchakarma treatment protocols for the management of Sheetapitta/Urticaria.

Conflict of Interest: None

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Table.1: Gradation Scale [3]

Symptoms	Grade 0	Grade 1	Grade 2	Grade 3
Varati Dansh Samsthan Shoth	Absent	In specific area	Present on some part of body	All over body
Kandu (Itching)	Absent	Occasionally	Disturbing sleep	Disturbing

				sleep and normal day
Vidahi (Burning Sensation)	Absent	Occasionally	Disturbing sleep	Disturbing sleep and normal day
Duration of Wheals	Absent	< 1 hour	1-12 hours	> 12 hours
Frequency of Appearance of Wheals	Absent	Once a week	2-3 times/week	Daily
Frequency of Antihistamine Use	Absent	Once a week	2-3 times/week	Daily

Table.2: Assessment of Symptoms

Symptoms	Before Treatment	After Treatment
Varati Dansh Samsthan Shoth	2	0
Kandu (Itching)	2	0
Vidahi (Burning Sensation)	1	0
Duration of Wheals	2	0
Frequency of Appearance of Wheals	1	0
Frequency of Antihistamine Use	1	0

Table.3: Vamana Karma

Date	Name of Treatment	Medicines Used	Duration	Remarks
12/03/2021 14/03/2021	Deepana Pachana	Sankh Vati (1 TID after food), Sutshekar Ras (1 TID after food), Aam Pachak (2 TID after food)	3 days	Until nir-ama avastha
15/03/2021 18/03/2021	Snehapana	Panchtikt Ghrita (D1=30ml, D2=70ml, D3=110ml, D4=140ml)	4 days	Samayak Snigdh Lakshan
19/03/2021	Vishram Kala	Abhyanga with Mahanarayan Taila followed by Basapa Sweda	1 day	
20/03/2021	Vamana Karma	Madhanphala Pippali Yoga	1 day	7 Vegas
21/03/2021 26/03/2021	Samsarjana Karma	Peyadi	5 days	Prakruti Prapta Purusha Lakshana

Table.4: Shamanaushadi (Shamana Therapy)

Date	Medicines Used	For
21/04/2021 -	Panchtikt Kashaya, Arogyavardhini Kashaya, GP-500, Patoladi	External and Internal
27/04/2021	Kashaya Vati, Nimba Taila	Medication

Table.5: Raktamokshana

Date	Method	Quantity	Frequency	Remarks
28/04/2021	Siravyada	80 ml	Once a week	Samyak Raktamokshan Lakshan
05/05/2021	Siravyada	100 ml	Once a week	
12/05/2021	Siravyada	60 ml	Once a week	

Table.6: Virechana Karma

Date	Name of Treatment	Medicines Used	Duration	Remarks
26/05/2021 - 28/05/2021	Deepana Pachana	Sankh Vati (1 TID after food), Sutshekar Ras (1 TID after food), Aam Pachak (2 TID after food)	3 days	Until nir-ama avastha
29/05/2021 - 01/06/2021	Snehapana	Panchtikta Ghrita (D1=30ml, D2=70ml, D3=110ml, D4=140ml)	4 days	Samayak Snigdh Lakshan
02/06/2021	Vishram Kala	Abhyanga with Murchit Tila Taila and Bashpa Sveda	1 day	
03/06/2021	Virechana Karma	Trivrutta Avleha + Dashmoola Decoction	1 day	23 Vegas
04/06/2021 - 09/06/2021	Samsarjana Karma	Peyadi Karma	5 days	Prakruti Prapta Purusha Lakshana

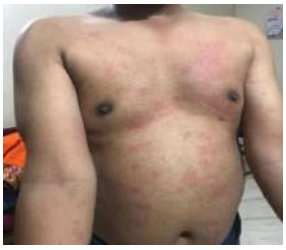

Figure.1:

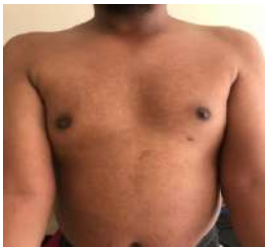

Figure.2:

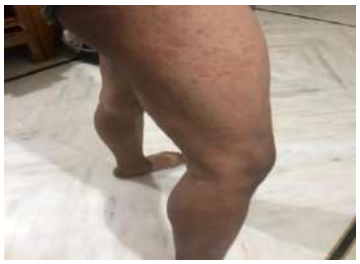

Figure.3:

Figure.4:

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RESEARCH ARTICLE

Development of an *Annona squamosa* based Topical Gel for the Treatment of Psoriasis

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ABSTRACT

Development of an *Annona squamosa* based topical gel for the treatment of psoriasis. This study set out to develop and asses a topical gel that would be used to treat psoriasis, using extract *Annona squamosa* extract as the active component for the treatment of psoriasis. *Annona squamosa*as the active ingredient, while Carbopol 940 was served as the basis. The produced gel was characterized by physical-chemical properties, *in-vitro* diffusion experiments, quantitative analysis, spreadability, pH, viscosity, and preliminary phytochemical analysis. Studies on the healing of wounds were conducted using the improved formulation (F10). The Soxhlet extraction method was used to get *Annona squamosa* extract, which was then added to the gel formulation. The gel's spreadability, viscosity, and *in-vitro* diffusion were all found to be within acceptable bounds by the results. When compared to a gel that is currently on the market, the improved formulation (F10) proved to be more effective. An in-vitro diffusion research conducted on formulation F-10 (0.5) revealed that the drug diffused from the optimized batch F-10 (0.5) *Annona squamosa* topical gel at a speed of 99.12%PH value for optimized formulation is 6.3±0.15, Spreadability is 23.24, viscosity 1.80, %drug content 99.12±0.18,In-vitro diffusion 93.74. **Conclusion:** A stable topical gel formulation of *Annona squamosa* was successfully developed, employing a combination of *Annona squamosa* extract and Carbopol. This formulation demonstrated enhance *in vitro*-diffusion, suggesting improved localized effects.

Keywords: *Annona squamosa*, Carbapol-940,Viscosity,Spreadability.

Abbreviations

FTIR : Fourier transform infrared
DSC : Differential scanning calorimetry
ICH : International council for Harmonisation
pH : Potential of Hydrogen

INTRODUCTION

Psoriasis presents as a recurrent, persistent autoimmune systemic condition marked by scaly lesions and inflammatory-driven joint and tendon issues, defining its chronic nature. In psoriasis skin lesions, symptoms like scaling, erythema, burning, and edema have been noted. [1]It happens when the immune system sends incorrect signals that encourage the development and division of skin cells, such as those caused by a pathogen cell of the skin that cause psoriasis.[2]Red, highly scaled skin lesions are a hallmark of clinical psoriasis. Patients frequently complain of excessive skin shedding and "itching," which is connected to their psoriasis.[3]In addition to the genetic predisposition and immunological conditions mentioned earlier, the progression of the illness is impacted by specific environmental factors, age, and gender, along with dysfunctions in immune system elements like T cells and cytokine release [4]. *Annona squamosa,* commonly referred to as "custard apple," is a notable medicinal plant belonging to the Annonaceae family [5]. It has a broad range of pharmacological effects and is utilized in conventional applications. The multipurpose tree *Annona squamosa* Linn (AS) has both medicinal and edible fruits. It is said to possess anti-tumour, antidiabetic, and antioxidant properties [6]. Chemical constituents are stigma sterol, taxaxerol, lofenol, phenyl propanoids and squalence [7].From the past history, ofthere is no evidence to prove *Annona squamosa* have an ability to treat the anti – psoriatic effect. The present study investigated the efficacy of seed extract from *Annona squamosa* in a gel formulation for its potential as an anti-psoriatic agent. To the best of our understanding, this study aims to showcase the anti-psoriatic properties of *Annona squamosa* seed oil (ASO).

Stigmasterolis a main chemical constituent showanti- inflammatory properties that help to treat psoriasis [8]. Additionally, after topical application, the safety of ASO has been demonstrated. Topical preparations are mixtures that are smeared, rubbed, sprayed, or infused directly into an exterior body surface. Topical administration has been utilized either to induce systemic medication effects or to target localized treatment for various skin disorders. Transparent gels have become more widely used with two important types of semi solid preparations are used in cosmetic and medicinal applications. In comparison to creams and ointments, gels often provide a faster release of active drug ingredients, irrespective of their water solubility. Due to their excellent biocompatibility and reduced risk of irritation or adverse reactions, they are user-friendly and do not necessitate removal [9]. Thixotropic, non-greasy, easily spreadable, swiftly removable, emollient, non-staining, compatible with various excipients, and either water-soluble or miscible are among the many advantageous characteristics of gels for dermatological use.**-**

MATERIALS AND METHODS

Annona squamosa (drug)seeds crushed and that can be used to make oil.Carbopol-940,methyl paraben, propyl paraben, triethanolamine, EDTA was supplied by Merck Mumbai. Methyl paraben are substances that are frequently added to products as preservatives to extend their shelf lives. Propyl and methyl paraben together are frequently used to improve antimicrobial efficaciousness. The function of methyl paraben in gel is to stop the growth of along with other dangerous germs, Mold.

Method of preparation

Collection of plant materials: The seeds of the *Annona* tree were collected and dried.

Gathering and Preparing the Seed Extract

The seeds were pulverized into a coarse powder using mechanical grinders. Then, 50.1 grams of the material was extracted using Soxhlet apparatus and methanol. Following extraction, the product was separated using steam distillation equipment. The resulting extract was dried and condensed under vacuum to yield an oily extract utilized in the study. This extract was subsequently prepared at various concentrations. A Soxhlet extraction is only necessary in situations where the contaminant is insoluble in the solvent and the target molecule has limited solubility in it. If the desired compound exhibits substantial solubility in the solvent, a simple filtration method can be employed to isolate it from the insoluble material. Typically, a thimble made of dense filter paper is placed inside the main chamber of the Soxhlet extractor, containing a solid substance that contains the desired chemicals. The extraction solvent-filled flask is positioned atop the Soxhlet extractor. Next, a condenser is added to the Soxhlet. Reflux is reached by heating the solvent. The solvent vapor rises through a distillation arm and enters the chamber containing the solid thimble [10].

Preformulation studies

Preformulation testing was discovered to be the first stage of developing an efficient and stable dosage form. Physical and chemical characteristics of the excipient and active medicinal ingredient were assessed for safe formulation. Preformulation research aims to ensure the development of a safe and efficient formulation.

Excipient -drug compatibility studies

Fourier transform infrared (FTIR) spectroscopy (Bruker alpha, Germany) was conducted to identify the constituents of the drug, polymers, and the physical mixture of drug and polymer. The drug and polymer blend were separately combined in an IR grade KBr ratio of (100:1). Comparable discs were fashioned utilizing an FTIR spectrophotometer and a hydraulic press pressure of 5.5 metric tons.

DSC (Differential scanning calorimetry)

DSC investigations were conducted on the drug, polymers, and physical blends of drug-polymer in a 1:1 ratio. Samples weighing three to four milligrams were placed on an aluminium pan and subjected to heating in a differential scanning calorimeter. The temperature was increased to 200°C at a rate of 10°C per minute**.**

Composition of developed formulation

One gram of Carbopol 940 was mixed with fifty millilitres of distilled water while being constantly stirred Following that, five millilitres of distilled water were utilized to dissolve the required quantities of methyl and propyl paraben, employing a water bath. After the solution cooled down, propylene glycol 400 was introduced. Furthermore, the appropriate quantity of EDTA was also included. Lastly, the fully mixed ingredients were thoroughly stirred into the Carbopol 940 gel, while being continuously stirred. Triethanolamine was gradually added to the formulation to regulate the skin pH (6.8–7) and achieve the desired gel consistency, followed by the gradual addition of *Annona squamosa* oil [11].

Evaluation Parameters

Visual examination was used to check each manufactured gel formulation for clarity, colour, syneresis, and occlusiveness, presence after the gels were stored in the containers [12].

Physical Evaluation

This refers to the examinations conducted based on sensory characteristics of the substance, such as its look, taste, smell, and habit.

pH:(1% w/v solution in water).A precise weight of 100 mg of the medication was dissolved through sonication in 100 ml of water and subsequently refined. The acidity level of the filtrate was measured using a standard electrode [13].

Spreadability

These evaluate crucial variables for every Gel composition. These experiments utilized a setup consisting of two glass slides, each equipped with a pan fixed on a pulley, alongside a wooden block featuring a scale for result evaluation. Two slides were coated with these formulas, and for five minutes, a 100g weight was set on the upper glass slide. To get a consistent thickness formulation, add 100g of weight to the pan. Following this procedure, timed in seconds, the slide was divided, and the Spread ability test was conducted [14].

S = M.L / T

M represents the weight attached to the upper slide.

L denotes the length of the glass slides.

T indicates the time required to separate the slides.

Viscosity

Viscosity was measured using a Brookfield viscometer. The viscosity tests were conducted at room temperature (25–27°C) with a Brookfield viscosity tester.[15].

Homogeneity

Every gel that produced were examined visually to ensure with uniformity after their placement in the container. They were examined to determine whether any aggregates were present [16].

Consistency:

To assess the consistency of the gels, a cone attached to a holding rod was released from a fixed distance of 10 cm into the center of a glass cup filled with the prepared gels. The penetration of the cone was measured from the outer surface of the gel to its tip within the gel. After ten seconds, the distance penetrated by the cone was recorded [17].

Extrudability

The gel compositions were filled into standard aluminium tubes with collapsible caps, which were then sealed tightly by crimping the ends. The masses of the tubes were recorded using tape. Subsequently, the tubes were clamped between two glass slides. Following the application of 500 g pressure on the slides, the cap was removed, and the amount of extruded gel collected was weighed. The extrudability of the gel was assessed as follows: Extrudability exceeding 90% was considered excellent, exceeding 80% was rated good, and exceeding 70% was deemed fair [18].

Drug content:

One gram of the produced gel was collected and dissolved in one hundred millilitres of pH 7.4 phosphate buffer. The gel solution in the volumetric flask was shaken on a mechanical shaker for two hours to obtain the drug's full solubility. Using phosphate buffer (pH 7.4) as a blank, the solution was filtered through a 0.45 μm membrane filter and measured spectrophotometrically at 293 nm [19]

.

***In-vitro* release**

5 with a 20receptor compartment capacity was used for *in-vitro* drug release experiments. The artificial is the diffusion cell's donor and receptor compartments were separated by a cellophane membrane. The drug release membrane was covered by the prepared gels, which weighed up to 1 g. Phosphate buffer with a pH of 7.4 was added to the diffusion cell's receptor compartment. The solution in the receiver chamber was continuously and steadily mixed with the entire assembly placed on a magnetic stirrer. maintained at 37 ± 0.50 °C with magnetic beads being used to continually agitate the mixture at 50 RPM. One millilitre sample were taken out at intervals of 15, 30, 60, 90, 120, 150, 180, 210, 240, 270, and 300 minutes. The samples were subsequently measured spectrophotometrically at 293 nm against a blank to determine the concentration of the medication. Each time a sample was removed, the phase of receptor was refilled with a same amount of phosphate buffer. Plotting the total medication quantities dispersed from gels against time [20].

Accelerated stability

According to ICH guidelines, all of the chosen formulations underwent a three-month stability test at 40°C ± 2°C.Employing the method described earlier, all selected formulations underwent assessment for alterations in appearance, pH, or drug content [21].

In- vivo anti psoriatic activity

The committee for the purpose of controlling and supervising animal experiments (CPSCEA) issued criteria for animal studies, which were followed. Six Sprague Dawley rats each were divided into two groups. In a chamber with regulated temperatures (22+2ºC) and daylight (12 hours of darkness and 12 hours of light), both genders were kept. Two groups participated in pharmacokinetic research. Imiquimod (IMQ gel 5%) was applied topically to the skin for seven days in order to produce psoriasis in rats (n=6). The reference formulation, *Annona squamosa,* and the test formulation, F10, were administered. applying IMQ to a person's back on a regular basis scaly, inflammatory lesions resembling plaque-type psoriasis appeared in response to the rat. These alterations were accompanied by erythema, altered blood vessels, and enhanced epidermal proliferation. From day 8 to day 13, treatments were administered. The Psoriasis Area and Severity Index (PASI) began to decrease in these animal groups on day 14, and by day 28, the inflammation had completely subsided. In order to be considered clinically successful, an ant psoriatic drug must decrease the PASI by a minimum of 75%.

Skin irritation test

A skin irritation test was used to assess the CSN's level of irritation safety. Fifteen male rats in good condition, weighing between 180 and 220 grams, had their backs thoroughly shaved and watched for symptoms of skin injury for a whole day. Following this Thereafter, we separated the regions that had been shaved into two groups: those that showed symptoms of skin injury and those that showed undamaged skin. We used a knife to cut incisions in the skin to represent injuries. The rats were then split up into three equal groups at random: one group was given saline, another was given a placebo semi solid, and the third group was given CSN. Next, we utilized these preparations to a two-by-two-centimetre space on each side. Every rat was kept in a separate enclosure with ample space for mobility, maintained at a consistent temperature of 25℃ and a relative humidity of 55%. All rats were examined again after 1, 24, 48, and 72 hours to check for any signs of erythema and oedema and to record how severe they were.

Statistical evaluation

The data is shown as mean ± SD (n = 6). Using two-way ANOVA post-hoc Bonferroni, the findings were substantially different from the control group at $p<0.05$ and test of many comparisons. For statistical analysis, Graph Pad Prism 5.0 from the USA was utilized.

RESULTS

10 milligrams of the medication, precisely weighed, were added to 10 millilitres of volumetric flask and dissolved in a 7.4 pH buffer solution. The created solution had a concentration of 1000 mg/ml. A single millilitre was withdrawn from the original solution and transferred into another volumetric flask with a capacity of 10 millilitres. The volume was subsequently adjusted by adding 7.4 pH buffer solutions resulting in the appropriate dilution range of 5–25 µg/ml concentration. Absorbance range at 351nm.

Compatibility between drugs and excipients by FT-IR

Fourier Transform Infrared (FTIR) Spectroscopy

Anona squamosa's spectrum and the physical combination's comparison show that there is no interaction and the medication is present in its unaltered form.

Differential scanning calorimetry(DSC)

The oil spectra of *Annona squamosa* revealed an endothermic peak at 262º03 C, which may have resulted from oxidation or recrystallization. With the DSc curve, the physical combination's melting peak is located at 255.65ºC, which is comparable to the melting point of anna squamosa oil. The physical combination and the melting peaks of the Anona squamosa oil DSC curve compare to show that there are no interactions and the drug present in its original form.

Experimental design

The prepared topical gel was subjected for fundamental evaluation tests, including spread ability, viscosity and the drug release studies conducted *In-vitro.* These evaluations were conducted using Design expert @11. Software.

Response 1(spread ability)

Spread ability =+5.89+0.7667A+0.6667B

After conducting an analysis of variance (ANOVA), it was evident that the developed linear model displayed high significance, as indicated by a probability of less than 0.05.The R-squared value was found to be 0.9817. The plot depicting observed spreadability versus predicted spreadability demonstrates a linear relationship. Hence, it can be inferred that the equation exhibits a robust predictive capability. Analysis of the 3D plot and regression coefficient values suggests that increasing the quantities of Carbopol and propylene glycol correlates with an increase in spreadability.

Response 2(viscosity)

Viscosity =+126.56+8.00A+7.00B

Following the analysis of variance (ANOVA), the outcome indicated that the developed linear model possessed high significance, as evidenced by a probability value of less than 0.05. The R-squared value was determined to be 0.9307. The plot depicting observed viscosity versus predicted viscosity exhibits a linear trend. Consequently, it can be inferred.

The equation demonstrates predictive capability. Analysis of the 3D plot and regression coefficient values of factors led to the conclusion that increasing the quantities of Carbopol and propylene glycol resulted in an increase in viscosity. The result also indicated that Carbopol was given with increased impact on the spreadability

Response 3(*In vitro* diffusion)

In- vitro diffusion =+76.82+4.76A+7.17B

After conducting the analysis of variance (ANOVA), the results indicated that the developed linear model was highly significant, as evidenced by a probability value less than 0.05The R-squared value was determined to be 0.9982. The plot illustrating observed ID versus predicted ID demonstrates a linear relationship.Hence, it can be inferred that the equation exhibits a robust predictive capability. Based on the 3D plot and the regression coefficient values of factors, it was concluded that an increase in the amounts of spreadability and viscosity corresponded to an increase in ID over time.

Design space

The contour plot for spreadability, viscosity, and within *in vitro* research on medication release depicted the design space for the investigated concentrations of Carbopol and propylene glycol. The central area of the contour plot, highlighted in yellow, delineated the limits of the design space.

Confirmatory trial

For validation purposes, the subsequent confirmatory check point batches were produced within the acquired design space. The composition of the formulation for the confirmatory batches is depicted

Formula optimization

The outcomes of the confirmatory trial aligned with the projected values obtained with in the design space. Parameters such as spread ability (seconds), viscosity (seconds)and within in vitro research on medication release (minutes)adhered to the established acceptance criteria. It is noteworthy that the optimized formula trails demonstrated minimal variations in these parameters. Consequently, the optimization studies conducted at the lab-

scale batch size facilitated the identification of viable concentration ranges for crucial formulation variables, notably Carbopol and propylene glycol. The formulation composition proposed for manufacturing *Annona squamosa* oil of topical gel was discovered to] be satisfactory.

Evaluation of *Annona squamosa* of topical gel

Physical evaluation:Physical trails conducted based on sensory characteristics of the substance, such as its colour, odour, PH and viscosity, and conductivity.

pH Studies indicate that the normal physiological pH range of the skin falls between 5.4 to 6.4. The gel's pH was initially measured on paper, yielding a reading of 6.1, which falls within an acceptable pH range. However, when tested with a pH electrode, it was found to be 6.3

Spread ability

The capacity of a substance such a gel, to be equally applied to a surface in this case, the skin is referred to as spread ability. With a spread ability score of 9.23, the topical gel for healing is considered to have a strong spread ability.

Viscosity

The test findings show that the gel has a moderate viscosity of 3454 centipoises (cps). This suggests that the gel is neither very thick nor overly transparent, placing it in a spectrum that allows for a really smooth and controlled application.

Extrudability

The ability of a substance to be pushed or forced out of a tube or bottle is known as extrudability. The gel is easily extruded with a moderate amount of pressure.

Wash ability

The gel was totally oil-free and left no trace on the skin after a full cleansing.

Stability studies for optimized formulation F10

The data indicate that the pH spreadability, extrudability, viscosity, and percentage medication release have changed very little or not at all.

***In vivo* anti psoriatic effect**

Rats with psoriasis were induced to develop the condition using the imiquimod-inducible psoriasis mouse model within seven days. A five-point rating system was used to assess each rat following treatment with the test and control groups, everyday Rats treated with IMQ had a significantly ($p<0.05$) reduced psoriasis score after using ASN gel than test animals. Two-way ANOVA was used to find the significant ($p<0.05$) interaction between test treatment and STD. Using a post hoc Bonferroni multiple comparison test on day 13 of treatment for post-psoriasis revealed a significant improvement in adjuvant psoriasis.

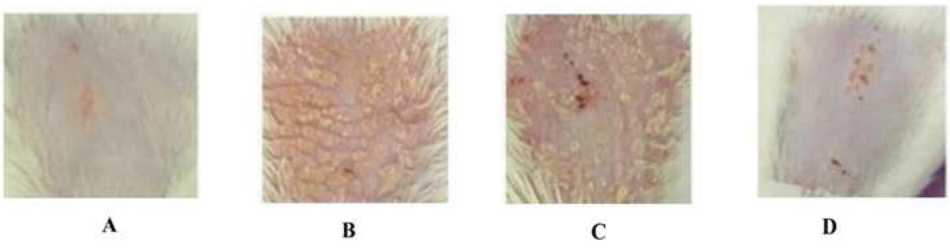
Skin irritation test

Although several techniques exist for treating skin disorders, topical therapy is thought to be the most practical and efficient strategy. Due to their poor efficacy and appearance, traditional topical treatments like gels and creams are losing Favor. Undesirable adverse effects of systemic methods such as phototherapy or other light therapies might be quite severe. Lipid-based drug delivery systems are one example of an inventive approach that has been developed to improve the oral bioavailability of medications with limited solubility. Better solubilization, longer medicine shelf-life, and increased bioavailability for both hydrophilic and hydrophobic drugs. This study analyseda salicylic acid and *Annona squamosa* semi solid, which showed promise for topical skin applications in terms of safety and efficacy. Before recommending the drug carrier as a workable topical drug delivery option, it is important to evaluate the test compounds' potential for causing skin irritation. Using a non-invasive technique on healthy rats, the effects of a

pharmaceutical solution containing salicylic acid and *Annona squamosa* gel on skin irritation were investigated. There were seen to be notable differences in the combined semi solid. When ASN (*Annona squamosa* oil &salicylic acid)was applied to hairless rat skin, erythema and scaling scores—measures of irritant potential—did not reveal any evidence of erythema, while significant skin erythema was seen with ASS(*Annona squamosa*& salicylic acid drug solution). In contrast to the blank gel, which had an average erythema score of 2.16, With a 0.66 score, CSN was placed. Studies on skin irritation revealed that the inclusion of semi-solid carrying medicines in a gel formulation did not result in appreciable edema or redness at the application site. Therefore, rat skin is not irritated by the produced semi-solid formulation. irritated by the produced semi-solid formulation.

Animal no	Control	ASS Gel	AUN Gel
1	0	3	0
2	0	2	1
3	0	3	1
4	0	2	1
5	0	1	0
Mean of erythema score	0	2.2±0.68	0.6±0.47

Represented as mean ±SD (N=5) ASS =*Annona squamosa* oil salicylic acid



Effect of AS on topical application of psoriatic animals

A - Control group, B - Psoriasis group, C - Standard group, D - Annona squamosalgel

DISCUSSION

Anona squamosa is recognized and advocated for the treatment of photo damaged skin and psoriasis. Physical observations conducted during preformulation studies revealed the efficacy of phosphate buffer at pH 7.4It readily dissolves in ethanol and methanol. The observed melting point was recorded at 0.84, with a mean pH value of 6.9. Additionally, a maximum absorbed wavelength of 351nm was identified. Obtained via a UV-visible spectrum photometer, a calibration curve was constructed, yielding an R-squared value of 0.997. The physical mixture's FT-IR measurements revealed that the functional groups of the *Annona squamosa* stay constant with their peak intensities there is no interactions for the physical mixture and the drug. It was acknowledged that the medicine and the excipients did not interact, and that this allowed the preparation process to continue topical lotion. According to preformulation research, the right procedures can be used to make an *Annona squamosa* topical herbal gel. The Soxhlet technique was used to create the total of nine topical gel formulations (F1 – F9)are taken to be obtain DoE. Optimized assessment parameters carriers were determined to be adequate in terms of colour, odour, drug entrapment effectiveness, and in-vitro diffusion research. However, formulation F-10 was refined based on and added to 0.5%, 1.0%, and 2.0% Carbopol gel. The pH, spreadability, viscosity, and medication content of each topical gel formulation incorporating *Annona squamosa* (F10) (0.5) were assessed, and the formulation was refined. An in-*vitro* diffusion research conducted on formulation F-10(0.5) revealed that the drug diffused from the optimized batch F-10(0.5) *Annona squamosa* topical gel at a speed of 99.12%. The data from the diffusion investigation was displayed as first- and zero-order kinetics, peppas, and Higuchi, with respective R2 values of 0.9859, 0.9421, 0.9841, and 0.9774. Stability tests were conducted on optimized preparations for 30 days at 25º±2ºC/60±5%RH and 40º±2ºC/75±5%RH.

The topical gel's mean particle size, percentage medication content, and physical appearance did not vary. A 3^2 factorial was used for the optimization, and we determined the ideal formulation, f10, by running a DoE on the nine formulations that were previously indicated. Evaluation tests, such as those for homogeneity, medication content, stability studies, viscosity, pH, and spreadability, have been conducted, it was concluded that when the amount of Carbopol and propylene glycol were increased, viscosity also increased, more spreadability and less viscosity. In comparison to the cream samples, the gel samples were more spreadability and had a lower viscosity.

Chelation of metal ions

EDTA binds to metal ions (like calcium, magnesium, or iron) that may be present in the formulation or can enter through contamination. Metal ions can catalyse degradation processes, reducing the stability and shelf life of the product.

CONCLUSION

Due to their perceived safety and fewer adverse effects compared to synthetic medicines, natural remedies are increasingly embraced. Consequently, there is a growing demand for herbal formulations in the global market. The effort to create the herbal gel using extract from Anno*ns squamosa* seeds. When applied daily for seven days in rats, all of the herbal formulations were non-irritating and did not exhibit any skin toxicity, according to the research. However, the created single herbal formulation with *Annona squamosa* extract performed comparably better than the subsequent formulations. The formulation of *Annona squamosa* gel has demonstrated significant potential in topical skin applications, particularly due to its beneficial properties such as antioxidant, antimicrobial, and anti-inflammatory effects. The inclusion of *Annona squamosa* extract, when combined with a suitable base, may enhance skin health, reduce irritation, and support wound healing. For future applications, the gel formulation could be explored further in clinical studies to determine its efficacy for specific skin conditions such as acne, eczema, and minor cuts or abrasions. Additionally, optimizing the concentration of active ingredients and testing its compatibility with other skincare products will be critical to ensuring safety, efficacy, and stability over time.

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Table.1: Formulation table

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Annona squamosa	10 ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml
Carbopol -940	0.4	0.5	0.6	0.4	0.5	0.6	0.4	0.5	0.6
Propylene glycol	3ml	3ml	3ml	5ml	5ml	5ml	7ml	7ml	7ml
EDTA	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Triethanolamine	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Methyl paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Propyl paraben	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Distilled water	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S

Table.2: Solubility of *Annona squamosa* in various solvents

Solvent	**Inference**
Distilled water	Soluble
Methanol	Slightly soluble
Ethanol	Soluble

Table.3: Rd Absorbance values of *Annona squamosa*

S. No	Absorbance	Concentration(µg/ml)
1	0	0
2	0.1	5
3	0.2	10
4	0.3	15
5	0.4	20
6	0.5	25
7	0.6	30
8	0.7	35
9	0.8	40

Table.4:Reported and observed peaks of drug and physical mixture

Bond	Characteristic bond(cm-1)	Observed bands of the pure drug(cm-1)	Observed bands of f5(cm-1)
Aromatic C=C bending	1700-1500	1511	1543.10
Carboxylic acid 0-H Stretch	3000-2500	2621	2922.36

Table.5: DoE generated 3^2 factorial designs

Run	Factor 1 Carbopol -940	Factor 2 Propylene glycol	Response 1 Spread ability	Response 2 viscosity	Response3 In-vitro diffusion
1	0.4	3	4.5	115	69.74
2	0.5	3	5.2	120	67.78
3	0.6	3	6.1	129	74.67
4	0.4	5	5.1	116	67.25
5	0.5	5	5.9	122	72.66
6	0.6	5	6.4	131	84.07
7	0.4	7	5.8	125	85.99
8	0.5	7	6.5	137	76.47
9	0.6	7	7.5	144	92.77

Table.6: Optimized formulation for DoE

S. No	Name of pharmaceutical ingredient	F10
1	*Annona squamosa* (ml)	10
2	Carbapol-940(gm)	0.6
3	Propylene glycol(ml)	7
4	EDTA (gm)	0.05
5	Methyl paraben (gm)	0.02
6	Propyl paraben (gm)	0.01
7	Triethanolamine (gm)	0.6

Table.7: pH, Spreadability, viscosity, *in vitro* diffusion studies of optimized formulation (f10)

S. No	Parameters	Results
1	pH	6.3±0.15
2	Spreadability	23.24

3	Viscosity	1.80
4	% Drug content	99.12±0.18
5	*In- vitro* diffusion	93.74
6	Extrudability	18.22±0.41

Table.8*: In-vitro* release of drug

Time	%CDR
0	0
2	12.24
4	16.71
6	24.62
8	32.67
10	44.25
12	54.63
14	66.27
16	72.08
18	79.97
20	83.78
22	88.64
24	93.74

Table.9: Regression analysis of formulation10

Formulation code	Zero order R^2	First order R^2	Higuchi Matrix R^2	Korsmeyers peppas		Hixson-Crowell R^2	Best Fit model
				R^2	n		
F10	0.9859	0.9421	0.9774	0.9814	0.89967	0.9681	Peppas

Table.10: Stability studies of *Annona squamosa* gel formulation (f10)

Formulation	Days	Temperature and relative Humidity	Appearance	pH	%Drug content	*IN- vitro* diffusion studies
F10	0	25º±2ºC/60±5%RH	Clear	6.25	100.2	98.66
F10	15	25º±2ºC/60±5%RH	Clear	6.28	101.1	98.61
F10	30	25º±2ºC/60±5%RH	Clear	6.20	99.7	98.54
F10	60	40º±2ºC/75±5%RH	Clear	6.17	99.6	98.32
F10	90	40º±2ºC/75±5%RH	Clear	6.15	99.3	98.21

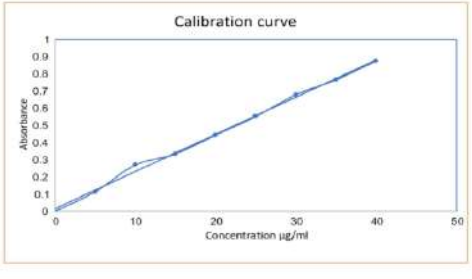

Fig 1: Calibration curve for Annona squamosa gel

Figure.1: Calibration curve for *Annona squamosa* gel

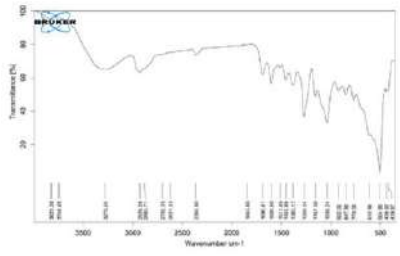

Fig 2: FT-IR Spectrum of Annona squamosa excipients

Figure.2:FT-IR Spectrum of *Annona squamosa* excipients

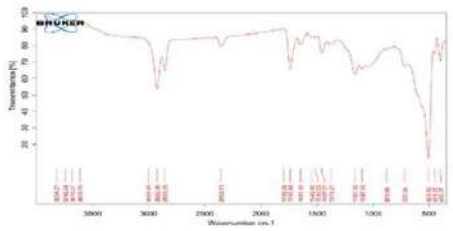

Fig 3: FT-IR Spectrum of Annona squamosa drug

Figure.3: FT-IR Spectrum of *Annona squamosa* drug

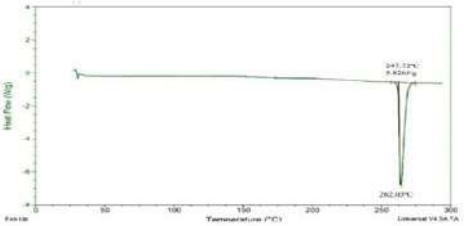

Fig 4: Thermogram of Anona squamosa

Figure.4: Thermogram of *Annona squamosa*

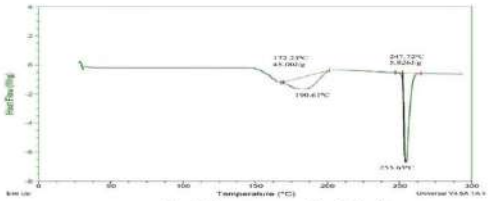

Fig :5: Thermogram of physical mixture

Figure.5: Thermogram of Physical mixture

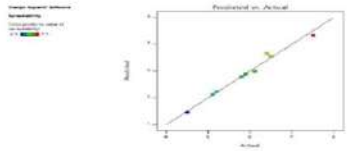

Fig 6: Predicted vs Actual plot for response 1

Figure.6: Predicted vs Actual Plot For Response 1

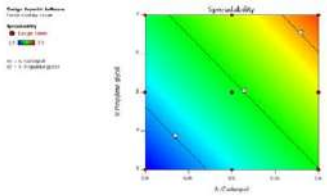

Fig 7: Contour plot for response1

Figure.7: Contour plot for response 1

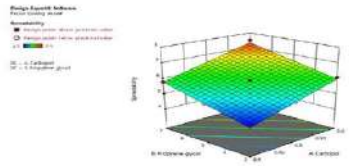

Fig 8: 3D response surface graph for response 1

Figure.8: 3D response surface graph for response 1

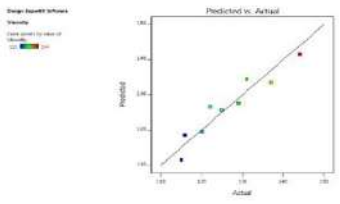

Fig 9: Predicted vs Actual plot for response

Figure.9: Predicted vs Actual Plot for response

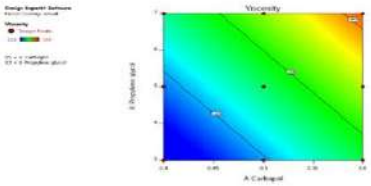

Fig 10:Countour plot for response2

Figure.10: Countour plot for response 2

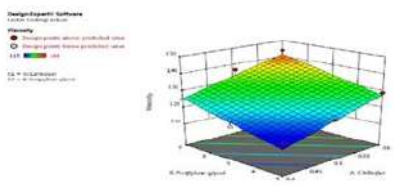

Fig 11: 3D Response surface plot for response 2

Figure.11: 3D Response surface plot for response 2

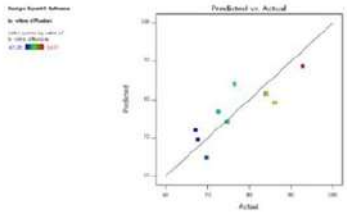

Fig 12: predicted vs Actual for plot

Figure.12: Predicted vs Actual For Plot

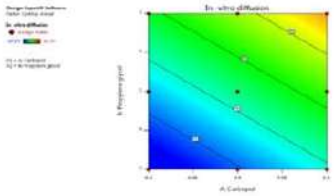

Fig 13: Contour plot for response3

Figure.13: Contour plot for response 3

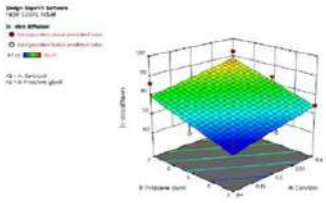

Fig 14: Response surface plot for response3

Figure.14: Response surface plot for response3

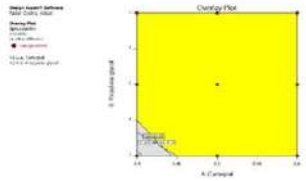

Fig 15: overlay plot

Figure.15: Overaly plot

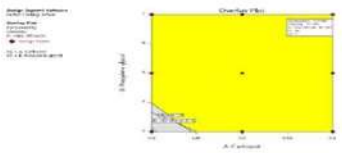

Fig 16: Confirmatory plot

Figure.16: Confirmatory plot

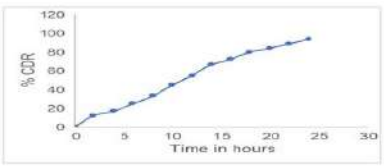

Fig 17: *In – vitro* diffusion optimized formulation graph

Figure.17: *In-vitro* diffusion optimized formulation graph

Fig 18: Zero order

Figure.18: Zero order

Fig: 19: first order

Figure.19: First order

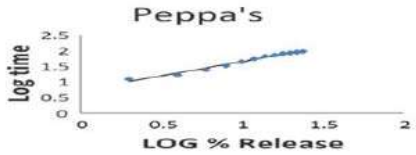

Fig 20: peppas model

Figure.20: peppas model

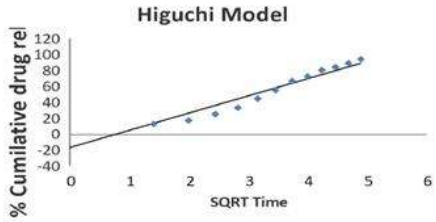

Fig 21: Higuchi model

Figure.21: Higuchi model

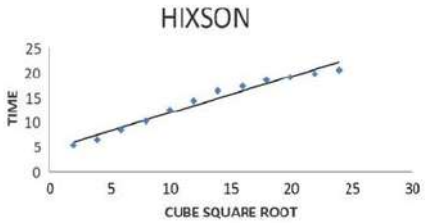

Fig 22: Hixson graph

Figure.22: Hixson graph

Figure.23: Dense filter

RESEARCH ARTICLE

Transformative Ayurvedic Treatments for Ocular Foreign Bodies: Insights from Clinical Cases

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ABSTRACT

Ocular foreign bodies are a prevalent cause of ocular trauma, often resulting from activities such as grinding, drilling, and welding, or even incidental exposure like driving. Despite being superficially lodged, these foreign bodies can cause significant discomfort and potential complications. Prompt and systematic evaluation is crucial to prevent deeper embedment and infection. Three cases of ocular foreign bodies were examined at the Eye OPD of Parul Ayurved Hospital. Each patient presented with symptoms of pain, discomfort, and redness, with the foreign body embedded during different activities. Standard removal procedures were followed, and *Ayurvedic* treatments including *Shatavari GhritaAschyotana, Amalaki Pindi*, and *GandhakaRasayana Vati* were administered. The combination of these medicines provides a comprehensive approach to managing ocular foreign bodies, highlighting the potential of *Ayurveda*. Preventive measures, including protective eyewear are essential in reducing the incidence of such injuries.

Keywords: *Aschyotana, Ayurveda, Ocular foreign body, Pindi, Shatavari Ghrita*

INTRODUCTION

Ocular foreign bodies account for the second most common form of ocular trauma, with corneal abrasions being the most. Most common site for the foreign body to be lodged into eyes is cul-de-sac and cornea.[1]Although many foreign bodies are superficial, they can still cause discomfort. Most commonly, its causes are a combination of a lack of protective eye-wear and high-risk activities. This includes grinding, hammering, drilling, and welding. Along with these common causes, unexpected elements like debris from walking or driving can also be observed. All suspected ocular foreign bodies or ocular trauma should be assessed systematically, thoroughly, and with great care. Establishing a standard routine eye examination is advisable to prevent the common error of focusing only on the most apparent findings and overlooking more subtle issues. Foreign body removal should begin as soon as possible, ideally within 24 hours, to avoid the foreign body becoming embedded in the corneal stroma, which complicates removal and raises the risk of infection. If the foreign body is suspected to involve full stromal thickness or presents physical exam findings indicative of this, it should be removed urgently by an ophthalmologist. A step-wise approach is generally preferred for foreign body removal.[2] After ruling out globe perforation, initial techniques include simple irrigation and the use of a moist cotton swab, which are often effective for recent and superficial foreign bodies. If these methods fail, the bevel of a needle can be employed under slit lamp guidance for further removal. Upon successful removal of the corneal foreign body, treatment consists of pain control, follow-up, and consideration given to prophylactic management. In *Ayurveda*, the treatment of an ocular foreign body involves addressing both alleviating immediate symptoms and correcting *Dosha*im balances to promote healing and sustain overall eye health. Medicines with anti-inflammatory, antimicrobial, healing properties and soothing effects can be beneficial in treating symptoms caused by ocular foreign body. Integrating *Ayurveda* with modern equipment offers a comprehensive approach to treatment.

AIM and OBJECTIVES

Aim : To evaluate the efficacy of *Ayurveda* treatment protocol in the management of ocular foreign bodies.

Objectives:

- Study of ocular foreign bodies in detail.
- *Ayurveda* management in ocular foreign bodies.
- Probable mode of action of *Ayurveda* treatment of ocular foreign bodies.

MATERIAL AND METHODOLOGY

Case reports:

Case:1

A 32 years old male patient visited Eye OPD of Parul Ayurved Hospital. He has complaints of pain, discomfort, photophobia, redness and watering from left eye. History of – H/O foreign body embedded 1 day ago while drilling. Patient rubbed the eye which led to more discomfort and painful eye. O/E: (Table 1) and (Figure 1,2,3)

Case: 2

A 35 years old male patient visited Eye OPD of Parul Ayurved Hospital. He has complaints of pain, discomfort, blurring of vision, redness and watering from right eye. H/o foreign body embedded 1 day ago while welding work in his workshop. The Patient attempted to wash his eye, but he did not get relief and discomfort and pain persisted. O/E: (Table 2) and (Figure 4,5)

Case: 3

A 52 years old female patient visited Eye OPD of Parul Ayurved Hospital. She had complaints of Foreign body sensation, discomfort, redness and watering from right eye. H/o foreign body embedded before half hour while driving. Attempts to wash out the object did not relived the symptoms but watering from the eyes and foreign body sensation increased. O/E: (Table 3) and (Figure 6,7)

Management
In all the cases, same treatment protocol was followed.

Emergency management
- Foreign body was removed with cotton bud under topical anaesthesia.

DISCUSSION

Post-removal of an ocular foreign body, patients may still experience residual symptoms such as burning, swelling, pain and watering from the eyes. *Ayurveda* treatments play a vital role for managing these symptoms effectively. Eyes are considered as an important sense organ in our body utmost care should be taken in managing any injuries. Appropriate therapeutic approaches can prevent secondary infection and support overall eye health. In present study, the foreign body was removed under aseptic measures followed by *Shatavari Ghrita Aschyotana* and *Amalaki Pindi*and *Gandhakarasayanavati*. The probable mode of action of these drugs is discussed below

Shatavari GhritaAschyotana
*Aschyotana*is indicated in *Purva Rupavastha*of *NetraRoga*where *Toda, Kandu, Gharsha, Daha, Raga, Paka*and *Sopha* are present.[3]In these cases, patients had severe pain, redness, foreign body sensation along with watery discharge from the eye. So, *ShatavariGhritaAschyotana* was done after removing the foreign body. *Shatavari Ghrita*is known for its adaptogenic and immune-boosting properties due to saponins, antioxidant and anti-inflammatory due to flavonoids and rejuvenating and nourishing qualities due to presence of steroidal saponins. It enhance vitality and acts as best *Vranaropaka* caused by *Shastraghata*[4]*Ghrita*is said to be *Yogavahi*, acts as a carrier for medicinal herbs and provides lubrication and nourishment. It is known for its ability to enhance the absorption of nutrients and medicinal properties. *Ghrita* having lipophilic property easily facilitates transportation of active principles of medicine to a target cells as cell membrane also contains lipid.[5]It also contains Vitamin A, Vitamin E and β carotene which are anti- oxidants and are helpful in reducing ketone bodies and prevents the oxidative injury to the body. Mainly Vitamin A keeps the epithelial tissue of the body intact, keeps the outer layer of the eyeball moist.[6]

***Pindi* with *Amalaki*[7,8,9,10]**
The presence of a foreign body in the eye can trigger a localized inflammatory response characterized by redness, swelling, and increased sensitivity, symptoms typically associated with *Pitta dosha* imbalance due to its heat and inflammatory qualities. *Pindi*, often composed of anti-inflammatory and cooling substances, helps mitigate these symptoms. By reducing inflammation and cooling the affected area, *Pindi* effectively alleviates discomfort and pain related to *Pitta Dosha* disturbances. *Amalaki*is the primary ingredient, known for its high vitamin C content and antioxidant properties due to presence of polyphenols like gallic acid and other flavonoids which contribute to its antioxidant and anti-inflammatory properties. *Amalaki* has been shown to reduce inflammation, which can be helpful for soothing the eyes if they are irritated by foreign bodies. The high vitamin C content and tannins in *Amalaki*, helping to neutralize free radicals and may aid intissue repair. Antioxidants and other nutrients in *Amalaki* support the repair of damaged tissues and can contribute to faster recovery. *Amalaki* may help boost local immune responses, which is beneficial for preventing infections and aiding in the overall health of the eye. Applying *AmalakiPindi* might provide relief from discomfort and irritation caused by foreign body. It can be used to potentially prevent complications.

GandhakaRasayana Vati
In *GandhakRasayana*, certain *Bhavanadravyas* (triturated medicines) act as bactericidal agents. The herbs employed in this trituration include *Guduchi* (Tinospora cordifolia), *Bhringaraj* (Eclipta alba), *Dalchini* (Cinnamomum verum), *Tamalpatra* (Cinnamomum tamala), *Nagkeshar* (Mesua ferrea), *Haritaki* (Terminalia chebula), *Shunthi* (Zingiber officinale), and *Bibhitaki* (Terminalia belerica). These herbs are characterized by *KatukashayRasa* (pungent and

astringent taste) and *Ushna Virya* (hot potency). This combination imparts several pharmacological effects to *GandhakRasayana*, including *Deepana* (enhancement of digestive function and metabolism), *Pachana* (appetizer effect), *Kaphaghna* (reduction of *Kapha dosha*), and *Kledaghna* (reduction of excess moisture). The synergistic action of these herbs contributes to the overall therapeutic efficacy of the formulation. While *GandhakRasayana* is more beneficial in treating the ailments associated with *Kapha*, it also has effects on *Pitta Dosha*. Microorganisms are increasingly developing resistance to existing antibiotics. Therefore, instead of employing a localized modern treatment, oral administration of *GandhakRasayana vati* was opted. In ancient Ayurvedic scriptures, *Gandhaka* is referred to as *Krimighna* (anthelminthic). Sulphur has been linked to the antibacterial agent sulphonamides. These medications have been shown to work by preventing the growth of sensitive bacteria by inhibiting their folic acid metabolism.[11] As a result, Sulphur in *GandhakaRasayana* could have the same antibacterial mechanism. Since penta-thionic acid, a compound derived from sulphur, was thought to help break down skin layers, sulphur ointment was commonly used topically as both a scabicide and pediculocide.

CONCLUSION

Ocular foreign bodies constitute the majority of eye casualties. A proper preoperative history, examination and investigations will help in deciding the management. Foreign body lodged in cul-de-sac can be removed with cotton bud by eversion of lower eyelid or double eversion of upper eyelid. Superficial epithelial foreign bodies can be removed with the help of a hypodermic needle or cotton bud. *Shatavari GhritaAschyotana* may help relive irritation and discomfort by its soothing effects and promoting healing and recovering from minor injuries or irritation. Lubricating effect of *Ghrita* can help reduce inflammation and swelling associated with ocular irritation. *AmalakiPindi* can offer supportive benefits for eye health due to its anti-inflammatory, anti-oxidant and immune-boosting properties. *GandhakRasayan Vati* can potentially help in reducing discomfort, inflammation and the risk of infection associated with ocular foreign bodies. Counselling on the use of protective eyewear or shields in the workplace, avoiding hazardous sports activities, and providing health education at various levels can help reduce the occurrence of such accidents.

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TABLE.1: OCULAR EXAMINATION: CASE 1

	Right eye	**Left eye**
Eyelashes	NAD	NAD
Eyelids	NAD	Mild Swelling on upper eyelid
Bulbar Conjunctiva	NAD	Mild congestion+
Palpebral Conjunctiva	NAD	Congestion++
Cornea	Clear	Embedded superficial foreign body at 3 o'clock position and 5 o'clock position
Sclera	NAD	NAD
Pupil	RRR	RRR
Lens	Transparent	Transparent

TABLE. 2:OCULAR EXAMINATION: CASE 2

	Right eye	Left eye
Eyelashes	NAD	NAD
Eyelids	NAD	NAD
Bulbar Conjunctiva	Mild Congestion+	NAD
Palpebral Conjunctiva	Congestion++	NAD
Cornea	Embedded superficial foreign body at 3 o'clock position near limbus	Clear
Sclera	NAD	NAD
Pupil	RRR	RRR
Lens	Transparent	Transparent

TABLE.3: OCULAR EXAMINATION: CASE 3

	Right eye	Left eye
Eyelashes	NAD	NAD
Eyelids	NAD	NAD
Bulbar Conjunctiva	Congestion++ • Embedded foreign body at 2 o'clock position 2mm away from limbus on bulbar conjunctiva	NAD
Palpebral Conjunctiva	Mild Congestion+	NAD
Cornea	Clear	Clear
Sclera	NAD	NAD
Pupil	RRR	RRR
Lens	Transparent	Transparent

TABLE.4: TREATMENT PROTOCOL

Treatment protocol:					
Sr No.	Procedure/ medicine	Name of Drug	Dosage	Route of administration	Duration
1	*Aschyotana* (Procedure)	*Shatavari Ghrita*	8-10 drops approx	Topical	Once in a morning , daily for 7 days
2	*Pindi* (Procedure)	*Amalaki*	3-5 gm	Local application on closed eyelid	Once in evening, daily for 7 days
3	Medicine	*GandhakaRasayana Vati*	2 tablets twice a day after meal	Oral	7 days

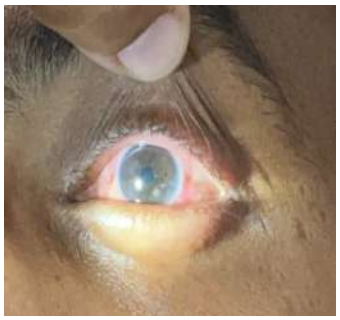

Figure 1: Embedded FB at 3 o'clock and 5 o'clock position in left eye (case 1)

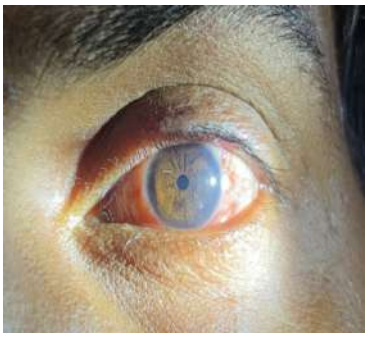

Figure 2: Day 5 (case 1)

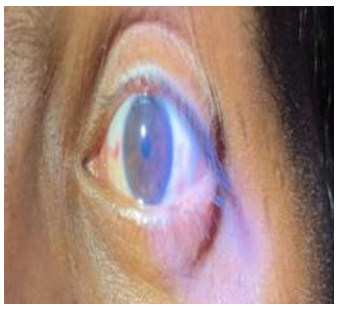

Figure3: After treatment (case 1)

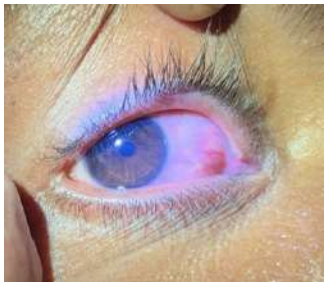

Figure 4: Embedded FB at 3 o'clock position in right eye (case 2)

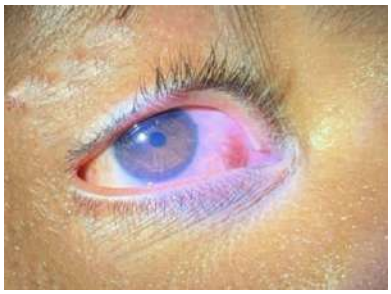

Figure 5: After treatment (case 2)

Figure 6: Embedded FB at 2 o'clock position on bulbar conjunctiva in right eye (case 3)

Figure 7: After treatment (case3)

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RESEARCH ARTICLE

A Prospective Study on the Risk Determinants and Economic Burden of Adverse Drug Reactions in Tertiary Care Hospital

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ABSTRACT

Adverse drug reactions (ADRs) represent crucial factors affecting patient safety, health care outcomes, and economic resources. The objective of this study was to determine the incidence, risk factors, patterns and economic burden of ADRs in the medicine wards of Government Doon Medical College and Hospital, Dehradun. A one-year prospective observational study included 1,490 patients, among whom 110 experienced 116 ADRs, resulting in an 8% incidence rate. Risk factors such as age, polypharmacy, prolonged hospital stays, and multiple diagnoses were statistically significant contributors to ADR occurrence ($p < 0.05$). ADRs were predominantly associated with anti-infectives (25%), cardiovascular drugs (24.13%), and alimentary tract medications (19.82%). Gastrointestinal disorders were the most affected organ system (36.20%), with constipation being the most frequent ADR (20.68%). Most ADRs were classified as Type A (90%), mild in severity (55%), and non-preventable (93%). Using Naranjo's causality assessment, 53% of ADRs were probable, 46% possible, and 1% highly probable. The economic burden of ADR management averaged ₹111.29 per patient, with a total cost of ₹9,905 for 90 patients. Mild ADRs incurred the highest cumulative costs, while severe ADRs were rare but costly. This study underscores the need for enhanced ADR monitoring, preventive strategies, and targeted interventions to reduce their incidence and economic impact. These findings provide valuable insights for improving patient safety and optimizing healthcare resource utilization in tertiary care settings.

Keywords: Adverse drug reactions, incidence, risk factors, economic impact, polypharmacy, tertiary care hospital.

INTRODUCTION

Drugs are an essential medicine to restore the quality of life and the life expectancy of people; however, their diverse and multifaceted use such as prescribing, dispensing, and administering of drugs, can increase the risk of experiencing ADRs. ADRs represent 5–7% of all hospitalizations, and 10–20% of inpatient experiences them. Fatalities or serious outcomes occur in 3–6% of cases, resulting in approximately 140,000 deaths annually in the USA

and over $30 billion in hospital costs per year (5% of hospital costs) [1-2]. In India, ADR incidence is 5.9% to 22.3% and attributed in 1.8% of the deaths. Hospital admissions due to ADR contribute to 0.7% of total admissions and average cost per patient was INR 690. Age, sex, polypharmacy, co-morbidities, inappropriate medication use, and disease severity are major risk factors for adverse drug reactions (ADRs). According to the literature, factors associated with the patient, disease, therapy, healthcare and genetics, have been identified as the five major categories of risk factors that influence ADR occurrence; polypharmacy and inappropriate medication use are the major contributors [3,4,5]. Exploring these factors in current research is important for enhancing patient safety, achieving effective treatment result and cost reduction in health care system. Few studies have evaluated financial burden and risk factors of ADRs in public teaching hospitals in Uttarakhand. The aim of this study was to evaluate the prevalence, risk factors and pattern of ADRs as primary objective and to assess the economic burden of ADRs in tertiary care public hospital as secondary objective.

MATERIALS AND METHODS

A one-year prospective observational study was carried out in three medicine wards of a Government Doon Medical College and Hospital (GDMCH), Dehradun, Uttarakhand. The time period of the study was from February 2023 to January 2024. The study protocol was approved by the Research Review Board (RRB) and Institutional Ethics Committee (IEC) of GDMCH. The study included patients with ADRs that occurred while they were receiving treatment in the medicine wards and ADRs that were identified from patient records on the basis of the reporting of health care professionals. ADRs occurring out of the medicine wards and incomplete laboratory results were not included. Unfinished prescriptions and incomplete daily notes were not considered, as well as cases of drug misuse or poisoning (accidental or intentional). Patients admitted to the wards were reviewed every day, and their prescription regimens, medical history, and nursing notes were reviewed. The data from eligible patients were recorded on a specially designed form called the "data collection form" (DCF) which contained fields for the patients' allergy status, previous use of the particular drug, symptoms of the ADR, co-morbidities, mode of drug administration, accuracy of dosage and date of onset of ADR. Monitoring was continued until discharge or transfer to the intensive care unit. The hospital medicine department head confirmed suspected ADRs. Risk factors were analysed according to age (adults aged 18–60 years and geriatrics aged >60 years), gender (male and female), days in hospital (1–5 days, 6–10 days, 11–15 days, 16–20 days, 21–25 days, and >26 days), number of diagnoses (1–3, 4–6, and 7–9), and number of medications administered (1–5, 6–10, 11–15, 16–20, 21–25, and 26–30) [5,6,7].

Drugs were categorized by the Anatomical Therapeutic and Chemical (ATC) classification system and ADRs according to the Medical Dictionary for Regulatory Activities (MedDRA) terminology [8]. ADRs were categorized under the Rawlins and Thompson classification scheme as Type A (dose-dependent and predictable) or Type B (idiosyncratic and unpredictable) [9, 10]. The causality was evaluated using Naranjo's Probability Scale of ADR, and ADRs were categorized as definite (≥9), probable (5–8), possible (1–4) or doubtful (≤0) disorders [11,12]. Modified Hartwig et al. criteria into mild (1–2), moderate (3–4) or severe (5–7b) [13,14]. ADRs were classified based on the modified Schumock and Thornton criteria as definitely preventable, possibly preventable or not preventable [15,16]. Costs of ADR management were estimated from the onset of ADR until the termination of treatment [4]. All the results were presented as mean (±SEM) and percentages. Categorical variables were analysed by chi-square test and were considered.

RESULT

In total 1,570 patients were monitored under close observation in the medicine wards of the hospital. Of these, a total of 80 patient were excluded from analysis because of incomplete data or MLC (medical legal case) so a total of 1490 patients were analyzed. Out of these, 110 patients had a total of 116 adverse drug reactions (ADRs). Estimated incidence of the overall ADRs was 8%. A total of 11,954 medications were prescribed for 1490 patients and the mean number of medications was 8.02±0.038. The average number of diagnoses was 2.18±0.032 and average length of stay

was 4.45±0.071 days. The Explanatory variables used to analysis the ADR were gender, age, length of stay,polypharmacy, no of diagnosis. No significant difference was found with regard to incidence of ADRs in males (62/787) and females (54/593) ($\chi2 = 3.693$, $p = 0.158$). However, the distribution of ADRs in different age groups was significantly different ($\chi2 = 23.845$, $p = 0.000$). Other significant factors we found in this study that could indicate an ADR included a higher number of diagnoses ($p < 0.05$; $\chi2 = 66.88$, $p = 000$; $\chi2 = 106.83$, $p = 0.000$; $\chi2 = 57.83$, $p = 0.000$) and length of stay and polypharmacy. Anti-infectives were the most associated drug, with 25% of ADRs, in the study, such as isoniazid (hepatotoxicity) and ciprofloxacin (body pain). Adverse Drug Reactions (ADRs) implicated of Cardiovascular drugs (24.13%) as neuropathic pain (atorvastatin) and hypokalaemia (furosemide) are shown in Table No. 1. Out of 1,490 patients, 110 patients complained of ADRs (104 patients had one ADR and 6 patients had two ADRs). Gastrointestinal disorders system were the most common (42, 36.20%), predominantly constipation (24, 20.68%). There were endocrine system disorders (n = 13, 11.20%), which were subdivided into hypoglycemia (n = 8, 6.89%) and hyperglycemia (n = 5, 4.31%). Skin disorders (12 cases, 10.34%) were all mentioned as rashes. Respiratory complications (n=7, 6.03%) were also related to cough. Various types of neurological disorders (9, 7.75%) included headache (4; 3.44%). Other reported adverse drug reactions were hepatotoxicity (4, 3.44%), hypokalaemia (6, 5.17%), hypotension (3, 2.58%), while rare reactions included anaemia, dizziness and lumbar pain.

Drugs most associated with the ADRs were furosemide (14), ceftriaxone (8), pantoprazole (8), amlodipine (7), metronidazole (7), hydrocortisone (6), tramadol (6), and insulin (6). ADRs were categorized using the Rawlins and Thompson classification method as described previously. The classification also based on the occurrence of ADR in research is showing that 90% was type A reaction and 10% was type B reactions. According to Naranjo's algorithm, 53% (n=62) was probable, 46% (n = 53) possible and 1% (n = 1) highly probable. Mild ADRs accounted for 55% (n=64) while 44% (n=51) occurred in the moderate level category (categories 3, 4a, and 4b Ads) with one case (1%, n=1) categorized as severe level (level 5 and 7) ADRs. 8 (7%) of the 116 ADRs were classified as "probably preventable" while 108 (93%) of the ADRs were classified as "non-preventable. One hundred sixteen ADRs were identified, of which 96 ADRs [83%] occurred in 90 patients and required management. The average cost for each ADR per patient was ₹111.29 (₹9905/90) and the total cost accrued by these 90 patients seemed to be ₹9905 for the financial burden caused by these ADRs (Table No.2).

DISCUSSION

ADR during treatment are significant public health problems that result in a marked decrease in patients' quality of life and constitute a significant economic cost for the health system. These costs encompass increased medical expenses, additional hospital time and the loss of productivity. The adoption of appropriate mitigation strategies is critical to reduce the frequency, severity, and economic burden of ADRs. This demands more awareness of ADR patterns, adequate monitoring and report systems, and proactive measures to be taken [17].The present study showed an ADR of 8%, which is consistent with earlier prospective studies. For example, Ganesan S et al., (2020) reported 8.8% incidence ADR rate among hospitalized patients whereas Peter J. V. et al., study carried out in tertiary care hospital and the prevalence rate was stated as 10.42% [4,18]. ADRs occurred comparably in male (7%) and female (8%) participants. Somestudies showed the gender to be a significant factor, but in our study ithad no statistical significance because of relatively small female patients number[19,20,21]. ADRs were more frequent in elderly (14%) compared to adults (6%).Marengoni A et al. indicating that 36.4% of geriatric inpatients sustained at leastone ADR, while Saha et al., reported that 42% of elderpatients had ADRs [22, 23].The prevalence of ADRs increased withe age which may beassociated with aging changes in pharmacodynamics and pharmtakinetics[24,25,26]. Finally, the diagnosis number was listed among the independent riskfactors for ADRs. Patients with 4–6 co-existing diseases contributed 12% to theADRs, whereas 7–9 diseases did so with 9% of the ADRs. These findings are inagreement with the findings of Jose et al. (2006) and Hardmeier et al. (2004)confirmed the association that number of diagnoses is a predisposing risk factor in2004 [27, 28]. Higher risks of ADRs associated serious illnesses, co-morbidities andpolypharmacy were also associated with longer durations ofin-hospital stay.

Length of stay as a risk factor for ADRs has only been demonstrated in a few studies[27,29]. Polypharmacy also became another significant risk factor. Patients with ADRs had increased significantly more than those without ADRs Davies et al[29]. Several studies have confirmed the positive association between polypharmacy and ADRs [30, 31]. The ATC classification showed that the gastrointestinal antibiotics for system icuse (25%) were the most common ADR, followed by cardiovascular agents(24.13%), and drugs affecting the alimentary tract and metabolism (19.82%).Furosemide had the highest drug-specific rate of ADRs (12.07%), followed by ceftriaxone and pantoprazole (both 6.90%). These results were consistent with Zaman SU et al. (2021), which showed that the most common drug group that triggers ADRs is anti-infective (36.73%) [32]. Similarly, Haile BD et al. More than a quarter (26.6%) of the ADRs involved cardiovascular medicines [5]. Our findings confirm those published previously by Davies EC et al. that drugs most commonly used in ADRs were loop diuretics, that was furosemide [29]. Chronic organ system involvement included gastrointestinal disorders (36%),endocrine disorders (11%), and skin/subcutaneous tissue disorders (10%).Almost similar findings reported in United States, which classified gastro in test in a land dermatological systems to be primarily affected by ADRs [33]. Similar trends were also seen in studies from South India with nervous, gastrointestinal, and dermatological being the commonly involved systems [34,35]. The commonest ADRs were constipation (21%), skin rash (11%), hypoglycemia (7%), and cough(6%). Yadesa et al. reported that 40% of ADRs affected the gastrointestinal tract; studies of Arulmani R. et al., and Jose J. et al. found that dermatological reactions were reported to be the most frequent ADRs [27,36,37].

For the purpose of this study, we assumed around 90% of ADRs to be Type A(predictable and dose-dependent) and 10% Type B (unpredictable and not dose dependent).As observed and reported by Kumar A et al. that in their study, 87%Type of ADR were Type A and 13% Type B, and Benkirane R et al. who reported80.3% type A reactions and 19.7% type B reactions [3,38]. 46% of the ADRs were rated "possible" and 53% "probable"; 1% was rated "highly probable" or "definite," according to Naranjo's causality-assessment tool. Khan A et al. and M.Venkatasubbaiah et al. Reported that 55% and 48.2% of ADRs classified as probable [39,40]. According to the severity grading of Modified Hartwig's severityscoring, severity analysis documented that 55% of the adverse drug reactions(ADRs) were mild, 44% were moderate and 1% were severe. The prevalence of mild ADRs is also comparable with Kumar A, et al., having 52.4% of mild ADRs,[27]and Jose, et al. also reported mild and moderate ADR of 50.5% and 44%,respectively[41]. According to the Modified Schumock and Thornton criteria, we identified 93% of ADRs as non-preventable and the remaining 7% as preventable. These imply that the implementation of efficient monitoring systems, likely to decrease avoidable ADRs, are in the offing. Sneha et al. Presented that 87% of ADRs were not preventable, and 6% were probably preventable [42]. Total cost of medication due to ADRs was ₹111.29/patient, total loss due to 90patients with 96 ADRs was ₹9,905. The results have been quite in line with an economic evaluation done in a private hospital which found direct costs borne by patients to be ₹412.79 (US$ 9.30) per ADR, and as seen, the cost variation can be accounted to the differences in the different types of hospitals and research settings[43].

CONCLUSION

In the small sample of relatively well patients with a low proportion of ADRs (8%, most commonly constipation, skin rash, cough). The main drug associated with ADRs was furosemide. The majority of ADRs were type A, predictable, and dose dependent, 53% probable and 55% mild. Notably, 93% were categorized as non-preventable. The expense of managing ADRs was₹111.29/patient. The results demonstrate the importance of a tighter pharmacovigilance, electronic prescribing, and activity control of ADRs, not just to lower the costs to the health system, but also to provide more security to patients.

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Table 1: Anatomical and Therapeutic class of Medication implicated in ADRs

Anatomical Class [Code] (Number of ADRs, %)	Drug Name Code	ADR Name
J Antiinfectives For Systemic Use (29 , 25)	J04AC01 Isoniazid	Hepatotoxicity (4)
	J01MA02 Ciprofloxacin	Body Pain (1)
	J01CR05 Piperacillin and Beta-Lactamase Inhibitor	Restlessness (1)
	J01GB06 Amikacin	Acute Kidney Injury (1)
	J01CR02 Amoxicillin and Beta-Lactamase Inhibitor	Diarrohoea (1), Allergy (2), Sore Throate (1)
	J01XD01 Metronidazole	Anorexia (1), Sore throat (2), Restlessness (1), Diarrohoea (1) , Skin Rash (1), Loss of Appetite(1)
	J01DD04 Ceftriaxone	Constipation (3), Allergy (4), Pain Abdomen (1)
	J01DH51 Imipenem	Skin Rash (1)
	J01CA13 Ticarcillin	Increase Liver Enzymes (2)
C Cardiovascular System (28 , 24.13)	(C10AA05) Atorvastatin	Nuropathic Pain (1)
	C10AA07 Rosuvastatin	Bakache (1)
	C03CA04 Torasemide	Hypokalemia (3), Hyponatremia (1)
	C03CA01 Furosemide	Constipation (6), Headache (1), blood in Urine (1), Hypotension (3), Hypokalemia (3)
	C01CA03 Norepinephrine	Tachycardia (1)
	(C08CA01)Amlodipine	Constipation (3), Allergy (1), Sore Throate(2), Padal Edema (1)
A Alimentary Tract And Metabolism (23, 19.82)	A02BC02 Pantoprazole	Cough (6), Headache (1), Diarrohoea (1)
	A02BC04 Rabeprazole	Constipation (1)
	A10AE01 Insulin (Human)	Hypoglycemia (5)
	A04AA01 Ondansetron	Constipation (4)
	A10BA02 Metformin	Hypoglycemia (1)
	A03AA07 Dicycloverine	Constipation (1)
	A01AB22 Doxycycline	Heartburn (1)

	(A10BD02) Glimepiride (2mg) + Metformin (500mg)- metformin and sulfonylureas	Hypoglycemia (2)
N Nervous System (14 , 12.06)	(N03AB02) Phenytoin	Cough (1), Megaloblastic Anemia (1)
	(N02AX02) Tramadol	Constipation (3), Bradycardia (2)
	(N02AA01) Morphine	Constipation (1)
	(N05BA12) Alprazolam	Maigrain Pain (1)
	(N07CA01) Betahistine	Pain Abdomen (2)
	(N05AA01) chlorpromazine	Palpitation (1)
	(N02BE01) Paracetamol	Stool for occult blood (1), Constipation (1)
B Blood And Blood Forming Organs (8, 6.89)	(B05BC01) Mannitol	Palpitation (2)
	(B01AC06) Acetylsalicylic Acid	Dyspepsia (1), Bleeding (2)
	(B05AX01) Erythrocytes	Skin Rash (3)
H Systemic Hormonal Preparations, Excl. Sex Hormones And Insulins (8, 6.89)	(H02AB09) hydrocortisone	Insomnia (3) , Hyperglycemia (3)
	(H02AB04) Methylprednisolone	Hyperglycemia (2)
M Musculo-Skeletal System (2, 1.72)	(M01AX17)Nimesulide	Constipation (1)
	M02AA15 Diclofenac	Constipation (1)
R Respiratory System (3, 2.58)	(R03BA02) Budesonide	Mouth Ulcer (1), Dyspepsia (1), Headache (1)
V Various (1, 0.86)	(V03AZ01) Ethanol	Pancreatitis (1)

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RESEARCH ARTICLE

Ayurvedic Management of Polycystic Ovarian Disease (PCOD): Diet, Herbs and Lifestyle

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ABSTRACT

Polycystic Ovarian Disease (PCOD) is a prevalent endocrine illness that affects women of reproductive age, with a prevalence rate ranging from 6- 10%. It is distinguished by the presence of hyperandrogenism, either clinical or biochemical, chronic anovulation, and polycystic ovaries. According to Rotterdam criteria, it is usually related with insulin resistance and obesity. It is the most well-known and investigated cause of ovulatory infertility in reproductive-age women.In the current period of globalization, there has been a temporary shift in lifestyle to a more sedentary exercise over time, as well as a lack of physical activity, stress, high-calorie foods, and indiscriminate eating habits. We can associate it with several disorders described in Ayurveda in regard to Aartava, such as Nashtartava, Aartavadushti, ArtavaKshya, Strotasdushti, Anartava, VandhyaYonivyapad, Bijkosh granthi, and PuspaghniJataharini. PuspaghniJataharini, as described in Kashyap Samhita and Revati Kalpadhyaya, can be associated with hyperandrogenism. However, no description reveals indications of metabolic dysfunction or polycystic ovarian morphology. As previously stated, PCOD is a metabolic illness, hence treatment should focus on calming the vitiated kapha, making the vataanulomana, and enhancing the patient's agni by administering agneyadravya. Ayurvedic chikitsa paddhati, such as Shodhan (Virachana, Basti, Vamana), as well as various medication formulations, should be the most effective treatment for PCOD. Dietary and physical activity adjustments are the primary means of treatment.

Keywords: PCOD, *Ayurveda, Aartavadushti, Shodhana karma, Pathya-Apathya, Yoga.*

INTRODUCTION

The complex and diverse illness known as polycystic ovarian disease has no recognized cause. One out of ten women are affected. In 1935, Stein and Leventhal first identified polycystic ovarian syndrome (PCOS) as a condition characterized by obesity, hirsutism, and amenorrhea linked to enlarged polycystic ovaries.[1]The primary characteristic of this heterogeneous illness is the ovaries' excessive synthesis of androgen. PCOS is a polygenic and complex disorder. Because to sedentary lifestyles, pollution, and excessive junk food consumption, the prevalence of this disease is rising these days. Ovarian enlargement is a symptom of polycystic ovarian syndrome. The ovary's volume has grown by more than 10 cm3. The stroma is increased. The capsule is pearly white and thicker. Around the cortex, there are numerous (> 12) follicular cysts that range in diameter from 2 to 9 mm. Infertile women are more likely to experience this incidence, which ranges from 0.5% to 4%. It is common in the 20–30% of young reproductive age group. 20% of healthy women may have polycystic ovaries.

Diagnosis is based upon the presence of any two of the following three criteria ASRM/ESHRE, Rotterdam(2003).
1.Anovulation and/or Oligomenorrhea
2.Hyperandrogenism (clinical and/or biochemical).
3.Polycystic ovaries.

Clinical Features of Pcod

- Infertility and irregular menstruation, such as oligomenorrhea, amenorrhea, or DUB.
- Increasing obesity (abdominal)
- Presence of hirsutism and acne are the important features
- Virilism is rare.
- Insulin resistance causes specific skin abnormalities that are indicative of Acanthosis Nigricans. The skin is pigmented (grey brown) and thickened. The groin, inner thighs, axilla, and nape of the neck often get affected.

Investigations

Sonography

Transvaginal sonography is specially useful in obese patient. Ovaries are enlarged in volume (>10 cm3). Increased number (> 12) of peripherally arranged cysts (2–9 mm) are seen.

Serum values

- The ratio of LH to FSH is greater than 2:1, meaning the LH level is excessive.
- Increased levels of estrone and estradiol
- The level of SHBG is lower.
- Hyperandrogenism, mostly from the ovaries and to a lesser extent from the adrenal glands.
- The and rostenedione is elevated.
- DHEA-S may be slightly high, along with elevated serum testosterone (> 150 ng/dl).
- Resistance to Insulin (IR): IR (50%), as indicated by elevated fasting insulin levels > 25 μIU/ml and a fasting glucose/insulin ratio < 4.5.
- Serum insulin response levels greater than 300 μIU/ml at two hours after a 75 gm glucose load indicate significant insulin resistance.

Laparoscopy: Bilateral polycystic ovaries are characteristic of PCOS.

Thyroid function test: Mostly in an obese women.

Ayurvedic Perspective Of Pcos

According to Ayurveda, PCOS involves the *Dosha, Dhatu,* and*Upadhatu* equally. The condition is not associated with a specific disease , However, the symptoms are similar to those of terms like *Anartava* (amenorrhea), *Yonivyapad* (anatomical and physiological disorder of the reproductive system), *Arjaska* (oligomenorrhea due to vitiation of *Vatadosha*), *Lohitakshaya* (oligomenorrhea due to vitiation of *Vata-Pitta Dosha*), *Vandhya* (infertility), *Pushpaghni*, *Revati* (idiosyncratic anovulatory menstruation), *Abeejata* (anovulation), *Rajodushti* and *AshtartavaDushti* (vitiation of *Dosha*), and *ShandhiYonivyapad* (vitiation of Vata).Reduced digestive fire and the generation of *Ama* are caused by the *Vata* and *KaphaDoshas*, as well as *VishamaAhara* and *Vihara*. Inappropriate enzymatic responses brought on by this Ama synthesis result in incomplete metabolism and hormone instability. Hyperinsulinemia and hyperandrogenism brought on by this hormonal imbalance eventually result in anovulation, amenorrhea/oligomenorrhea, and ovarian abnormalities such as polycystic ovaries. If *Aartava* is considered as ovarian hormones, then the basic pathology of PCOS in the context of *Avarana* by Dosha can be understood. This *avarana* disrupts the homeostasis of the HPO axis, causing hormonal imbalance that leads to PCOS.

NIDANA (ETIO-PATHOGENESIS OF PCOD)

Samanya Nidana

- Nidana of 20Yonivyapad are also Nidana for ArtavaDushti.
- Uttar Dhatu's Vriddhi and Kshaya are dependent upon Purva Dhatu's Vriddhi and Kshaya. Since Rasa Dhatu's Upadhatu is Artava, Rasa Kshaya will produce Artava Kshaya.[2]
- Samanya Kshaya Hetu like Vyayama, Anashana , Chinta, Rooksha, Alpa Pramitashana, exposure to Vata (external polluted wind), Atapa , Bhaya , Shoka Rooksha Pana, Prajagarana, excessive expulsion of Kapha, Shonita, and Mala, Kala and Bhutopaghata (Agantuja) are also causes for ArtavaKshaya".

Vishishtanidana

Mithyachara

It denotes abnormal *aahar* and *vihar*. India has turned into a fast-food nation when compared to western nations. Our nutritious Indian cuisine is gradually being replaced by unhealthy fast food (such as *Tridoshvardhakaahar*), abnormal lifestyle choices like *ratrijagaran, Diwaswapna* and unnecessary stress, anger, and anxiety, as well as addictions like smoking and alcohol consumption. These factors all contribute to the development of lifestyle disorders like diabetes, obesity, PCOD, infertility, and more.

Pradushtaartava

*Artava*is *Agneya,* has characteristics of *Rakta* and *leads* to formation of *Garbha.* The *Tejas* is the predominant *Mahabhuta.* The *Artava* may be ovum as well as the menstrual blood; When *Beeja Dushti* causes *Abeejatwa* (loss of reproductive function), it can also manifest as *PutraghaniYonivyapad, Asrija*, and other symptoms, including recurrent pregnancy loss, which is also seen in PCOS.

Beeja Dosha

Incorrect nutrition and behavioural issues may be thought of as PCOS triggers if the *Sahaja Hetu* of *Beejadushti*is seen as *Utpadaka Hetu*. The *Beeja*, a part of *Beeja* and subtle part of *Beeja* which develops into reproductive organ when gets affected by *Dosha Dushti*, results in the disease or dysfunction in the respective reproductive organ, a part of it i.e, somatic component; and psychosomatic component of *Beeja* then leads to psycho-sexual aberration of the individual in due course of growth and development.

Daiva

Unknown or idiopathic cause The presence of Daiva as a causal factor for Yonivya pad shows that tracing the etiological variables for the condition was more challenging than for other disorders.

Purvarupa

Purvarupa are warning lights that alert the patient and doctor to the pathophysiology occurring in the body and direct them towards an accurate diagnosis of the ailment. However, prodromal aspects of PCOD are not described in the books.

Rupa

- *Artavadushti* (oligomenorrhea, Amenorrhea)
- *Sthaulya* (obesity)
- *Yauvanapidaka* (acne)
- *Atiloma* (excessive hair growth)
- *Nilika* (discolouration of skin)
- *Anapatyata*(Primary infertility)

SAMPRAPTI GHATAKA

- ***Dosha****-Vata,kapha*
- ***Dushya****-Rasa,rakta,Mamsa,Meda, Asthi*
- ***Agni****-Dhatvagnimandya*
- ***Srotas****-Rasavaha, Raktavaha, Mamsavaha, Medavaha, Ashthivaha*
- ***Srotodusht****i-Sanga, Siragranthi*
- ***Udbhavasthana****- Amashaya*
- ***Rogamarga****-Abhyantara*
- ***Sadhya-Asadhyata****-Yapya,Kashtasadhya*

Ayurvedic Management of PCOD

Nidana Parivarjana

it denotes the total elimination of the causative factor. In *Ayurveda*, it is the first course of treatment. Dietary avoidance or elimination of *agnimandya* and *Medovridhi* practices should be prioritized over food consumption.

Shamana Aushadhi

Singal herbal drugs:

Citraka, Sunthi ,Pippali, Maricha ,Shatavari ,Paribhadra, Nimba ,Katuka , Haridra, Shigru Lashuna, Shatapushpa, Yastimadhu Nagakesara, Haritaki,Guduchi, Kumari, Guggulu, Shilajatu,Paniyakshara.

Classical formulations

Vati kalpana*- Chandraprabha Vati[3],Chitrakadi Vati[4],Rajapravartini Vati[5],Shatavari Gulam [6],Pradarantaka Lauha, Punarnava Mandura.*
Kalka kalpana*- Lashuna Kalka[7]*
Churnakalpana*-Pathadi Churna[8], Sudarshana Churna*
Ghritakalpana-*ShatavaryadiGhrita, ChitrakadyaGhrita*
Taila kalpana*- Bala Taila, Shatapaka Taila, Shatapushpa Taila[9], Tila Taila*
Guggulukalpana*-KanchanaraGuggulu, TriphalaGuggulu,YogarajaGuggulu,Sthiradigutika.*
Kwathakalpana*-PunarnavashtakaKwatha,Varunadi Kashaya,Dashamula Kashaya*
Asava/ arishta*- Ashokarishta[10], Kumaryasava[11],Drakshasava, Dashamularishta[12]*
SAMSODHANA CHIKITSA*[13]*

Vamana

*Vamana*is done to clear toxins before to taking the drug for menstruation regularity and ovulation induction. It helps to balance hormones and improves fertility. *Vamana* in *Sthoulya* and *RasapradoshajaVikara,* in comparison to modern science, all of the etiological elements of PCOD are the same as those responsible for vitiation of *Kapha Dosha* and

Medo Dhatu, such as sedentary lifestyle, excessive consumption of fast foods, day sleep, etc. Hence, *VamanaKarma* can be highly effective in the treatment of PCOD.

Virechana

*Virechana*is effective in controlling obesity, irregular or heavy periods, hormonal imbalances, skin discoloration and many other symptoms triggered by PCOD.. Since *Samshodhana* is the primary treatment in *Bahudoshavastha*, *Virechana* is planned for *Beeja Karmukta*. *Agnimandyavastha* is linked to the *Kapha Vata Pradhana* condition. The essence of *Virechana* is biocleansing. It cleanses the body of accumulated toxins, metabolic waste, and vitiated Dosha. Additionally, it aids in restoring the body's imbalanced hormone levels. Thus *Virechana* helps in normalizing *Pitta* (metabolic quotient), *Vatanuloma*, *Dhatuposhana,* and *Agni-deepana.*

Basti

Basti Karma control*Vata* and relieves *Rasa Dhatu dushti* thus helps in PCOD. *Uttarabasti* is most effective because it clears *aartavavahastrotas*, calms *Apana vayu*, promotes follicular maturation, and controls circulatory function.

Udvartana

Dry powder is used to massage the entire body in this non-invasive treatment. Several dry herbs are combined to make the powder. In addition to cleansing and detoxifying the skin, this massage helps strengthen the body's lymph nodes and circulatory system. One of the most bothersome signs of PCOD is excessive acne. Additionally, it increases metabolism, which aids in weight control and, in the majority of cases, weight loss.

Nasya

Nasya's effect on the pituitary gland makes it even more beneficial for women with PCOD by regulating the HPO axis.

Life Style Modifications

It consists of a diverse strategy of food, exercise, and behavioral therapies that try to educate an individual to have the best reproductive ovulatory outcome.

Foods to Include (*Pathya Ahara)*

- *Shookdhanya Varga* recommends eating whole grains, low glycemic index foods (*Ruksha anna*), and low-calorie, high-satiety foods (*Guru, Aptarapan Ahar*) such as barley, barnyard millet, Job's tear Kodo millet, and *Godhum*.[14,15]
- Consuming a protein-rich diet, including green gram, lentils, split pigeon peas, brown chickpeas, horse gram, and black gram.[16]
- Seeds such as sesame, flax, sunflower, and pumpkin are abundant in mono-unsaturated fatty acids, oleic acid, and essential vitamins and minerals. These serve as antioxidants, lowering blood cholesterol levels. Flax seeds assist maintain the hormonal profile in PCOS by lowering the body's androgen levels.[17]
- According to *Acharya Bhav Prakash*, citrus fruits and green leafy vegetables might help treat hypomenorrhea .[18]Citrus fruits have a low glycemic index, are high in dietary fiber, and contain vitamin C, resulting in a steady, constant, and regulated rise in blood sugar and insulin levels. To avoid a spike in insulin levels, take whole fruit rather than juice. Fruits include pomegranate, Phalgu, lemon, jackle jujube, gooseberry , apple, orange, peaches, plum, raspberry, strawberry, cranberry, blackberry, kiwi, pear, watermelon, and papaya. Green leaves include Patha, Green Pea (Sateen), Chenopodium album ,*Changeri*, Garlic, Broclli, Carrot, Cauliflower, Cucumber, Green Beans, Spinach, Tomato, and *Musli*.
- Use *Pippali, Hingu, Saindhav,* Cumin seeds and*Yavani* as spices in food preparations to cure the *Ayurvedic* pathogenesis of PCOS, known as *Agney Vatakaphahar*. This alleviates *vata* and kapha dosha and maintains *doshik* balance in the body.
- Consuming honey (*Madhu*), aged alcoholic beverages (*Sura*), and vinegar (Sukta) will help reduce *Vata Kapha*, a known cause of PCOS.

- Use alternative cooking methods including baking, grilling, boiling, and steaming instead of deep frying.

Foods to Avoid (Apathya Ahara)

- *Acharya Charak* has advised to avoid Milk and Dairy products[19] in over saturation diseases (*SantarponathVyadhi)* as these increases androgen level e.g. various milk products, Cheese, yogurt, butter.
- Avoid high-fat, sugary foods like fried bread (Poori) and fritters (Pakoda) as they contain dangerous trans fats.
- Avoid jaggery [20] as these are sweets with high glycemic index leading to spiky rise of glucose.
- Avoid carbonated drinks, fried snacks/chips.
- Avoid canned juices especially sugarcane juice.
- Avoid processed food like bread, pasta, white rice, muffins, cakes, cookies, candies etc.
- Cut down caffeine intake.

Modifications in Eating Pattern

- Eat only after full digestion of previously taken meal[21]
- Eat non – antagonistic food.
- Always eat easily digestible food in the evening.
- Eat at regular intervals: Taking high calorie heavy food in morning and low calorie small meals in evening helps in improving hormonal level, decreases insulin resistance and improves fertility outcome.

YOGA

Acharya *Charak* stated the necessity of physical exercise (*Vyayam*) in oversaturation sickness (*SantarpanothVyadhi*) and advocated for regular exercise.[22] yoga poses (*asanas*) specifically for PCOS serve to open up the pelvic area and promote relaxation.

- *Suryanamshkar* (Sun salutation),
- *Suptbandhkonasan* (Reclining Butterfly Pose),
- *Halasana* (Plough pose) ,*Dhanurasan* (Bow pose) ,
- *Bhujangasana* (Cobra pose) ,
- *Chakkichalanasan* (Moving wheel pose),
- *Padmasan* (Lotus pose)

Probable mode of action of yoga asanas

Yoga therapy focuses on the body's energy system, which includes multiple chakras. Yoga poses such as forward and backward bending improve the energy flow of the second chakra, often known as the seat of creation, which contains reproductive functions. Yoga movements stretch the abdomen region, increasing blood flow to the reproductive organs and relieving stress around them. Yoga positions promote ovulation by decreasing stress.[23]Yogic techniques benefit physical and mental health by regulating the hypothalamus pituitary adrenal axis, sympathetic nervous system, and neuroendocrine axis. Schmidt *et al.* discovered that after yoga therapy, there is a drop in urinary excretion of adrenaline, noradrenaline, aldosterone, serum testosterone, and LH levels.[24]

Pranayam

Pranayama is the control of one's breath. *Prana* represents vital energy, and *Ayam* denotes control. *Pranayama* techniques help to extend life and maintain health by managing the breathing process.

Anulomvilom, Bhramari, Kapalabhati

Controlled breathing techniques strengthen the nervous system, promote emotional stability, reduce anxiety, boost self-esteem, and raise insulin sensitivity.[25]

CONCLUSION

The most prevalent health issue affecting women of reproductive age is polycystic ovarian disease, which is brought on by a hormonal imbalance brought on by bad habits and a busy, stressful lifestyle. Although PCOD is a lifestyle illness, Ayurveda can help prevent it. Drugs, lifestyle, and *shodhanakarma* all play a significant part in both preventing and treating it. Therefore, it is imperative that we include Ayurveda into our lives in order to eradicate lifestyle conditions such as PCOD. Certain dietary and daily routines must be altered, and including yoga and meditation into daily routines can help with PCOD.

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RESEARCH ARTICLE

Development, Validation and Psychometric Properties of a KAP Questionnaire on Biosafety and its Application in Daily Life among Senior Secondary Students

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ABSTRACT

Day-to-day life biosafety extends biosafety principles beyond laboratories to daily activities, aiming to prevent disease transmission and improve human, animal, and environmental health. It emphasizes cultivating health-conscious habits through training and practice. This research work focuses to develop, validate and analyse psychometric properties of a questionnaire to measure the knowledge, attitude and practice of the senior secondary students regarding day to day life biosafety to be used by educational and public health authorities, policy makers and researchers. Using a mixed-methods approach, the study followed a standardized KAP survey validation process. Initial steps included a literature review and expert evaluation by 25 professionals, with content validity assessed through CVI, CVR, S-CVI, and S-CVR. A one-time survey of 290 senior secondary students was conducted to test reliability and construct validity. Exploratory factor analysis established construct validity, while KR-20 and Cronbach's α determined internal consistency, ensuring the questionnaire's robustness for educational and public health applications. The content validity, construct validity and internal consistency were projected with S-CVR = 0.79 and S-CVI = 0.96, KR-20=0.6062 for knowledge, Cronbach'salpha = 0.7426 for attitude and Cronbach's alpha = 0.8060 for practice. Exploratory factor analysis converged into 4 factors. Questionnaire on Biosafety and its Application in Daily Life (BADL) is a qualitatively and quantitatively validated questionnaire with a good level of reliability. It finally includes 58 items (23, 13, 22 items in knowledge, attitude and practice respectively).

Keywords: Biosafety, KAP Questionnaire, Validity, Reliability, Factor Analysis

INTRODUCTION

Biosafety encompasses practices and principles to prevent unintentional exposure to harmful biological agents, traditionally focused on laboratories but increasingly relevant to public health. It includes hygiene, disease prevention, vaccination, and promoting actions that enhance public health security, especially among children. The COVID-19 pandemic underscored its importance, pressuring global health systems to prioritize diagnosis, treatment, zoonotic risk mitigation, and infectious disease prevention [1], [2]. The pandemic disrupted trade, tourism, and daily activities, posing severe economic risks [3]. Experts introduced biosafety protocols adapted for home and public use, emphasizing measures like social distancing, mask-wearing, surface disinfection, and decontamination zones to minimize transmission risks, ensuring safer navigation of spaces during the crisis [4]. Proper hygiene, including hand washing and respiratory etiquette, significantly reduces infection transmission in schools [5], [6]. Integrating hygiene education into curricula equips students with lifelong disease prevention skills [7]. Challenges such as inadequate sanitation facilities [8] and resource limitations for waste disposal [9] hinder effective hygiene practices. The COVID-19 pandemic heightened awareness of personal hygiene, curbing the spread of diseases and fostering cultural shifts toward sustained hygiene habits [10], [11]. Holistic well-being, as emphasized by Myers et al. (2020) [12], aligns with increased attention to physical, mental, and social health [13]. Improved hygiene practices in schools also reduced absenteeism due to illnesses [14]. Studies indicate that biosafety practices effectively reduce disease transmission and promote health awareness, yet their emphasis among school students in India remains limited. Educating children on biosafety is essential to counter biological threats through risk perception, mitigation, and practice the etiquettes to prevent disease transmission. This questionnaire is prepared to measure the Knowledge, Attitude and Practices (KAP) of the senior secondary students on Biosafety and its Application in Daily Life (BADL). This KAP survey questionnaire to assess the biosafety protocols presently followed by the students after their learning from their syllabus and from the protocols learned during COVID-19. Biosafety, viewed here as preventive measures against biological hazards, fosters a culture of awareness and responsibility, preparing students as future societal stakeholders [15], [16]. A KAP survey questionnaire assesses individuals' knowledge, beliefs, and behaviors on specific topics. Its development involves ensuring content validity [17], aligning design with objectives [18], and refining questions for clarity and relevance [19], [20]. Validation techniques, such as statistical methods [21], [22], and cultural adaptation [23] are crucial for reliability. Examples like Simbar et al. (2020) [24] highlight the importance of iterative testing to ensure sensitivity and usability, adhering to methodological rigor [25], [26].

MATERIALS AND METHODS

The study employed both qualitative and quantitative measures to develop a valid and reliable KAP questionnaire on biosafety and its practical application in daily life [24]. It used qualitative approach to develop the construct of the questionnaire and used quantitative psychometric properties to test the face validation, content validation, construct validation and reliability of the developed questionnaire. The questionnaire was developed and validated through a number of standardized methods used in KAP survey questionnaire validation process. The initial steps comprised of literature review, evaluation and suggestions by 25 experts. Later, pilot study and psychometric analysis were conducted to ensure and establish the validity and reliability in a quantitative way [27] (Table: 1).

Development of Construct and Item Generation

Existing questionnaires on biosafety predominantly focus on laboratory safety aligned with biosafety levels, with limited tools addressing its application in daily life, particularly for students post-COVID-19. The lack of instruments highlights the need for developing a new questionnaire. Firstly, literature review was rigorously executed to explain the concept and dimensions of Biosafety and its application in day to day life from the perspectives of the students. Initially, the concept of biosafety was categorised into 12 domains- Biosafety Protocols, Transmission of Diseases, Hygiene, Food Safety, Water Safety, Waste Management, Chemical Safety, GMO, Zoonoses, Environmental Safety, Sanitation, and Prevention of Diseases. Then, comprehensive literature from the sources like ABSA, WHO, CDC, LANCET, Science direct, Google Scholar, Ministry of Science & Technology of India, UNICEF, NCERT books of class

XI & XII, Sanitation and Hygiene, and Health and Physical Education for class IX & X were used to generate items for a questionnaire intended for KAP survey. Some used keywords are "KAP survey validation", "Biosafety", "Biosafety measures during COVID-19", "Biosafety measures in schools", "Biosafety measures used out of the Lab", "Hygiene", "Food safety", "Water safety", "Biosafety awareness", etc. Finally, 112 items were developed relevant to the construct. Following a literature review, the questionnaire was critically reviewed by 25 experts from diverse fields, including education, microbiology, agriculture, biotechnology, and healthcare, resulting in the removal of 16 items and consolidation of 8 biosafety domains into four parameters: Practices, Awareness, Risk Perception, and Mitigation. Eleven additional overlapping items were removed to align with expert feedback and the questionnaire's objectives. The final construct, structured as a KAP survey questionnaire, comprised 85 items distributed across three categories: 37 for knowledge, 15 for attitude, and 33 for practice, reflecting the refined four parameters.

Types of Questions Involved

The questionnaire includes multiple-choice, yes/no, and Likert-scale items, with sections for knowledge (MCQs and yes/no), attitude (5-point Likert scale for agreement), and practice (5-point Likert scale for behavior frequency). Designed to be simple and concise, it balances comprehensiveness with respondent fatigue [23, 28]. Initially comprising 112 items, it was refined to 58 through systematic development for pilot testing.

Validating the Questionnaire

Face Validity Assessment

Face validity judges if a questionnaire appears appropriate and understandable to respondents, effectively measuring the intended domain [29]. In this study, face validity was evaluated using expert feedback quantified on a 4-point Likert scale (where 4= very clear and 1 = not clear at all) to ensure items were accurate, grammatically correct, and free from confusing language [30]. Clarity was measured with the clarity index= (The number of experts selecting scores 3 and 4 / Total number of experts). Items with a value of 0.79were considered to have a good level of clarity.

Content Validity Assessment

A body of 11 experts familiar with the questionnaire's construct evaluated its content validity. A group of 11 faculties were selected as experts from the departments of education, health sciences, physiology, anesthesiology, Engineering and Technology, agriculture, and Techno-Laboratory from different parts of the country and abroad. All the experts have more than 2 years of working experience in their concerned field of study. For quantitative analysis, CVR and CVI were figured out. The experts rated 85 items on a 3-point Likert scale (essential = 3and not essential = 1). The formula set to determine CVR is$CVR=(ne-N/2)/(N/2)$, where nerepresents total experts selecting "essential" and $N$is the total number of experts. According to Lawshe's table [17], a CVR greater than 0.636 for 11 raters indicates statistical significance at (P=0.05). CVI was assessed by the same experts, who rated each item for "relevance" on a 4-point Likert scale (4 = highly relevant and 1 = not relevant).CVI was computed using the same experts, who rated each item for "relevance" on a 4-point Likert scale (4 = highly relevant, 3 = relevant but needs minor revision, 2 = needs revision, 1 = not relevant). Based on Waltz & Bausell's guidelines [24],CVI was estimated by the formula: CVI = (Number of raters choosing points 3 and 4/Total number of raters).Items with a CVI above 0.79 were deemed suitable. The scale's overall content validity ratio (S-CVR) and overall content validity index (S-CVI) were calculated by averaging the CVR and CVI of all items.

Final Questionnaire for Pilot Study

After going through face validity and content validity process the 27 items were removed from the 85 items. The remaining 58 items were selected for pilot testing out of which 23, 13 and 22 items were related to knowledge, attitude and practice respectively.

Construct Validity Assessment

Design of the Study

Construct validity of BADL was gauged through pilot testing and internal consistency and exploratory factor analysis (EFA).The researcher conducted a pilot study to evaluate the feasibility of a questionnaire designed to collect relevant information as intended [31]. This quantitative study involved analyzing feedback from 290 senior secondary students, determined by a sample size ratio of 5:1—five respondents for each of the 58 questionnaire items, resulting in a total of 58×5=290 participants. The pilot study focused to ensure that the questionnaire effectively captured the intended data, which is a critical phase in research methodology [32]. The population of this research work comprised of the senior secondary students. A total of 290 senior secondary students were randomly selected from 8 schools situated in the different parts of Dehradun district, Uttarakhand. BADLwas used as the tool for data collection. The 23 MCQ items in the knowledge section were scored using binary scale of 1 and 0 for each right answer and wrong answer. The 13 items of the attitude section and 22 items of the practice section were scored on a 5-point Likert scale from 5 to 1.

Data analysis

Construct validity was examined through exploratory factor analysis (EFA) to evaluate the domain structure and its substructure. To ensure the sample size was adequate for EFA, the Kaiser-Meyer-Olkin (KMO) measure and Bartlett's Sphericity Test were applied. A KMO index greater than 0.5 and a Bartlett's Sphericity Test p-value less than 0.001 were considered indicative of sufficient sample adequacy for the analysis [24].

Reliability Assessment

BADL's reliability was determined through Kuder-Richardson Formula 20(KR-20) calculation for binary scale items of the knowledge section and Cronbach's alpha calculation for the Likert scale scores of the attitude and practice section. In most cases the value of both KR-20 and Cronbach's alpha is considered good with 0.70 or higher although a value ranging between 0.60 to 0.70 is acceptable.

RESULTS

Face and Content Validity

Out of 85 items selected for face and content validity by 11 experts, 58 items were above the threshold value according to Lawshe's table of critical value. The clarity index scores were .91 and above for face validity for those 58 items. The CVI values of those items for content validity assessment were 0.91 and above. The 58 items also cleared the threshold value of 0.636 for CVR. The S-CVI and S-CVR scores of those 58 items were 0.96 and 0.79 respectively which fell in good range.

Factor Analysis

EFA applying varimax rotation was conducted to get the desired result of factor analysis. The KMO values for the 58 items of the BADL met the minimum threshold value of 0.50 both for the binary and Likert scales (Table 2). All those items were significant in the Bartlett's Test of Sphericity ($p<0.001$). The values of Chi-Sqare test for both the binary and Likert scales were 471.308 and 1171.795 (Table 3).

Using the scree plot, four factors were identified as optimal (Fig:1). The factors aligned conceptually with the questionnaire's structure: 1) Practices: Actions taken to mitigate risks; 2)Awareness: Knowledge and understanding of biosafety principles; 3)Risk Perception:Assessment of potential hazards; 4)Mitigation: Proactive measures to address biosafety risks.

Reliability: Internal Consistency

Separate scores for KR-20 and Cronbach's Alpha have been calculated for binary and Likert scales. For the knowledge section which follows a binary scale the KR-20 value is 0.6062. The Cronbach's Alphafor the attitude scale was 0.7426 while the Cronbach's Alpha for practice scale was 0.8060 (Table 4).

DISCUSSION

BADL is the first valid and reliable tool to measure the knowledge, attitude and practices of senior secondary students on Biosafety and its application in daily life. Face and content validity of BADL was substantiated qualitatively and quantitatively through standardized process. The S-CVI and S-CVR score of the scale proves it to be a valid KAP questionnaire. The results show that all scales exhibit satisfactory internal consistency, with Cronbach's alpha values above 0.7 for Likert scales and a KR-20 value above 0.6 for binary scales. This ensures that the items within each construct measure the intended latent variables consistently. The KMO values, while at the threshold, justify proceeding with factor analysis. This is particularly relevant given the mixed data types and the exploratory nature of this study. The significance of Bartlett's test indicates that the correlation matrices are not identity matrices, further supporting the appropriateness of factor analysis. The EFA revealed four factors that aligned with the dimensions identified in the qualitative analysis. The factor Practices showed high loadings for actions like sanitizing hands and covering wounds reflect the emphasis on behavioral change. The factor Awareness indicated Items relating to understanding biohazards and preventive measures highlight cognitive engagement.

The factor Risk Perception validates questions like recognizing risks in specific scenarios (e.g., raw meat contamination) align with this construct. The last factor Mitigation focused on proactive steps, such as carrying sanitizers or using masks, underscore efforts to address biosafety challenges actively. The combination of binary and Likert items allowed for a comprehensive evaluation of biosafety knowledge and behaviors. While Likert items provided depth in attitude measurement, binary items offered clarity in factual understanding. This study demonstrates the reliability and validity of the questionnaire in capturing biosafety-related constructs. The results align well with the intended dimensions, providing actionable insights into practices, awareness, risk perception, and mitigation strategies. The factor structure, as visualized and supported by statistical evidence, provides a robust foundation for assessing biosafety-related attitudes and behaviors. BADL will be very much helpful for educational and public health authorities, policy makers and researchers in future to work closely with school students and in paving the way for future pandemic preparedness. The developed BADL will also be effective in achieving better insight of the students' KAP about Biosafety.

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Table 1: Steps of Methodology

Steps	Activities	Methods	Number of Domains	Domain Names	Number of Items	Response Type	Addition or Subtraction of Items
1	Development of Construct	Review of Related Literature	12	Biosafety Protocols, Transmission of Diseases, Hygiene, Food Safety, Water Safety, Waste Management, Chemical Safety, GMO, Zoonoses, Environmental Safety, Sanitation, Prevention of Diseases	112	MCQ Options, 5-point Likert Scale	Nil
2	Development of Construct	Discussion with Experts and Suggestions	8	Hygiene, Food Safety, Water Safety, Transmission and Prevention of Diseases, Waste Management, Zoonoses, Environmental Safety, Sanitation	96	MCQ Options, 5-point Likert Scale	Subtraction of 16 Items
3	Development of Construct	Combining Literature Review and Expert Suggestions	8	Hygiene, Food Safety, Water Safety, Transmission and Prevention of Diseases, Waste Management, Zoonoses, Environmental Safety, Sanitation	85	MCQ Options, 5-point Likert Scale	Subtraction of 11 Items
4	Final Item Generation	Development of Items into Major Domains	3	Knowledge, Attitude, Practice (KAP)	Knowledge= 37 Items, Attitude= 15 Items, Practice= 33 Items, 85 Items in total	MCQ Options for Knowledge, 5-point Likert Scale for Attitude and Practice	Nil
5	Establishment of Face Validity and Content Validity	Expert Validation and Psychometry	3	KAP	58	4-point separate Likert Scales for Relevance and Clarity and 3-point Likert Scale for Essentiality	Removal of 27 Items
6	Pilot Testing	Randomly Selecting 290 Samples from the Whole Population, 5:1 Ratio, 58 Items x 5= 290 Items	3	KAP	Knowledge= 23 Items, Attitude= 13 Items, Practice= 22 Items, 58 Items in total	MCQ Options for Knowledge, 5-point Likert Scale for Attitude and Practice	Nil
7	Establishment of Construct Validity	Psychometry- Item Analysis and Factor Analysis	3	KAP	58	1 for Right and 0 for Wrong for Each MCQ for Knowledge, 5-point Likert Scale for Attitude and Practice	Nil
8	Establishment of Reliability	Psychometry- Cronbach's Alpha, Cohens Kappa	3	KAP	58	2 for Right and 0 for Wrong for Each MCQ for Knowledge, 5-point Likert Scale for Attitude and Practice	Nil

Table:2 Kaiser-Meyer-Olkin (KMO) Measure

Data Type	KMO Value	Interpretation
Binary	0.50	Minimum threshold for factor analysis met.
Likert	0.50	Minimum threshold for factor analysis met.

Table 3: Bartlett's Test of Sphericity

Data Type	Chi-Square ((\chi^2))	p-value
Binary	471.308	<0.001
Likert	1171.795	<0.001

Table 4: Cronbach's Alpha and KR-20

Scale	Measure	Value	Interpretation
Attitude (Likert)	Cronbach's Alpha	0.7426	Indicates good internal consistency.
Practice (Likert)	Cronbach's Alpha	0.8060	Reflects high reliability for practice-related items.
Concept (Binary)	KR-20	0.6062	Acceptable reliability for binary items.

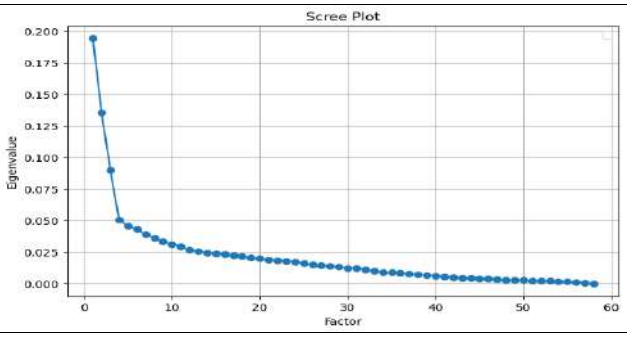

Figure 1: Scree Plot

RESEARCH ARTICLE

A Case Series on Effectiveness of C*alendula officinalis* as an External Application in Treatment of Wounds, Boils and Acne

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ABSTRACT

This article highlights the importance of use of *Calendula officinalis* as an external application in the treatment of boils and abscess. As per the homoeopathic literature *Calendula officinalis* has antiseptic, anti-inflammatory as well as wound healing properties. This article tries to justify the claim of *Calendula officinalis* have the antiseptic as well as anti-inflammatory properties

Keywords: Boils, Abscess, wounds, *Calendula Officinalis*, Case Series.

INTRODUCTION

Boil and Acne both are very commonly encountered clinical conditions in a day to day practice. Both of them are caused due to infections of skin or its appendages. Most common cause of boil and acne is bacterial infection and obstruction of the sebaceous glands, the commonly encountered bacteria responsible for causing them is staphylococcus aureus. Boil is a superficial skin infection whereas acne is caused due to the obstruction to the sebaceous glands. Acne is of two different types'; acne vulgaris and acne rosacea. Acne rosacea is the severe form of acne. On the basis of severity of symptoms acne can be classified into 4 grades grade 1 acne, grade 2 acne, grade 3 acne and grade 4 acne[1]. Boil and acne both are characterized by the circumscribed areas of inflammation, redness and areas of accumulation of pus.

Both boils and acne are characterized by area of inflammation, pain, tenderness, swelling, redness, discharge of pus, and fever[2]. Certain conditions favor boils and acne such as lack of hygiene, small wounds that are left untreated, elevated blood sugar levels etc. if left untreated, boil can result into formation of abscess which later on can form multiple pus pockets beneath the skin and discharging sinuses; in severe cases it can result in formation of fistula as well[3]. Internal abscess have its own wide range of complications. Boils and acne can be treated by medicinal therapy as well as surgical interventions can also be done [3]. Some house hold remedies are also available for the treatment of boils and acne ex. hot fomentation of the affected part is one of the most popular home remedy for treatment. In this case series I have used *Calendula officinalis* mother tincture externally to see for its effectiveness in the healing process. I came to know that it hastens the process of healing by reducing the intensity of pain and redness of affected parts. It reduces the swelling as well as tenderness on affected parts son in a way it acts as an anti-inflammatory agent[4]. At the same time it also reduces the process of suppuration and thus prevents the further complications of boils like formation of abscess which later on can end up into formation of draining sinus or even fistula. Thus it has anti septic action as well, hence it is performing dual actions at the same time. Anti-inflammatory, anti-edematous and anti-septic as well[5]. It can be safely administered in the wide range of population. *Calendula officinalis* ointment is cost effective as compared to other available anti septic lotions and ointments. As it is made up with ethanol it has high stability and it don't requires any special storage conditions as well.

MATERIALS AND METHODS

Type of study:
It was a Prospective clinical study conducted at the hospital of Parul Institute of Homoeopathy and Research.

Type of participants:
The patients fulfilling the diagnostic criteria for boils were included in the study

Diagnostic criteria of boils:
Presence of red or purple colored bumps on skin
The bumps are painful or tender to touch
There is accumulation or discharge of pus from bumps
The bumps tend to grow in size
Fever may or not be present

Type of intervention:
Calendula officinalis ointment was applied externally in all the patients once in a day.

Inclusion criteria: All the patients fulfilling the diagnostic criteria for boils were included in the study.

Exclusion criteria: Small children below the age of 10 years and elderly above the age of 55 years were excluded from this study.

RESULTS AND DISCUSSION

Table 2: Distribution of patients according to gender. Table3: Distribution of patients according to diagnosis. Table 4: Distribution of patients according to gender and diagnosis. Table 5: Distribution of patients according to the symptoms. Table 6: Distribution of patients according to the number of follow ups required. Table 7: Distribution of patients on the basis of improvements of symptoms in first follow up. Table 8: Distribution of patients on the basis of improvements of symptoms in second follow up. Table 9: Distribution of patients on the basis of improvements of symptoms in third follow up. Table 10: Distribution of patients on the basis of improvements of symptoms in fourth follow up. Table 11: Distribution of patients on the basis of improvements of symptoms in fifth follow up.

DISCUSSION

In this case series total 10 patients were enrolled to see the effectiveness of *Calendula officinalis* ointment as an effective wound healing agent. Out of the 10 patients 7 patients were male and 3 were female. Out of the 10 patients 8 patients were suffering from boils whereas 1 patient each were suffering from acne and wounds. In all the patients dressing with *Calendula officinalis* ointment were done on alternate day till the recovery ensues. The duration of follow up maintained was minimum 3 days. It has been noticed that none of the patients were improved in first follow up. 4 patients got improvement in terms of pain, oozing and tenderness in 2nd follow up, whereas 3 patients improved in 3rd follow up, 2 patients were improved on 4th follow up and only 1 patient suffering from boils on gluteal region needed 5 follow ups. 2 out of the 10 patients required incision and drainage of the pus before application of dressings. In rest of the patients the boils ruptured spontaneously and after cleaning of the site, *Calendula officinalis* dressings were applied under all aseptic conditions.

CONCLUSION

From the above case series we can conclude that *Calendula officinalis* have an excellent wound healing property even if it is applied as an external application alone. It has been noticed that it is equally effective in both male and female sex and in different age groups. It did not caused any irritation or inflammation of skin when applied externally. So it indicates that it is safe for administration as an external application. No patient compliant of any adverse reaction with ointment, it was safe and effective in one patient having the past history of type 2 diabetes mellitus. All these things establishes the safety and efficacy of *Calendula officinalis* ointment in treatment of wounds, acne and boils.

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Table 1:Patient Information

Patient no.	1	2	3	4	5	6	7	8	9	10
Age of pt.	23	18	23	24	40	43	31	39	42	34
Sex of pt.	M	F	M	M	M	F	M	M	M	F
C/c	Multiple boils	Multiple boils	Swelling,	Painful Pimple	Single indura	Swelling,	Swelling, Pain,	Red, Painful	Lacerations on	One single

	on both thighs	on Rt. leg	induration, redness and discharge of pus from Rt. hand	s on face with discharge of pus	ted large boil on nape of neck	tenderness, inflammation and discharge of pus from Rt. Hand	Inflammation and discharge of pus from the nail of index finger of Lt. Hand, Boils in Lt. axilla	bump present on back of neck with discharge of pus	Rt. Leg and Rt. hand	large boil is present on Lt. gluteal region
Duration of complains	5 days	5 days	3 days	1 month	10 days	6-7 days	4-5 days	6 days	15 minutes	15 days
Past medical history	Nil	Nil	Nil	Nil	H/o Fall resulting into fracture of wrist joint, H/o DM Type 2	NIl	H/o injury to nail Past h/o Type 2 DM	Nil	H/o fall from bike	H/o severe itching on affected art
Past surgical history	Nil	Nil	Nil	Nil	Closed reduction of fracture done	NIl	Nil	Nil	Nil	Nil
Investigations advised	Not advised	Not advised	Not advised	Not advised	CBC RBS	CBC RBS	CBC RBS	Not advised	Not advised	Not advised
Findings on investigation	Nil	Nil	Nil	Nil	Hb – 12 RBC – WNL WBC – WNL Plt – WNL RBS – 138 mg/dl	CBC – all parameters - WNL RBS – 140 mg/dl	CBC – Mild anemia and Leucocytosis RBS – 188 mg/dl	Nil	Nil	Nil
Diagnosis	Boils	Boils	Boils	Acne simplex	Boil	Boils	Boils in axilla Paronychia	Boils on neck	Laceration injury	Boil on Lt. Gluteal region
Manage	Dressi	Dressi	Dressi	Dressi	I & D	I & D of	Dressings	Dressi	Dressin	I/D

ment	ngs were done with Cal. off. Ointment under all aseptic conditions	ngs were done with Cal. off. Ointment under all aseptic conditions	ngs were done with Cal. off. Ointment under all aseptic conditions	ngs were done with Cal. off. Ointment under all aseptic conditions	of boil was done and Dressing was done with Cal. off. ointment under all aseptic conditions	boil was done and Dressing Was done was done with Cal. off. ointment under all aseptic conditions	were done was done with Cal. off. ointment under all aseptic conditions	ngs were done was done with Cal. off. ointment under all aseptic conditions	gs were done with Cal. Off. ointment under all aseptic conditions	was done, 15 ml pus drained Dressings were done with Cal. Off. Ointment with undue all aseptic conditions
No. of follow up	3	3	2	4	4	2	4	2	2	5
outcome	Boils healed completely	Boils healed completely	Boils healed completely	Pimples healed completely	Boils healed completely	Boils healed completely	Boils and paronychia healed completely	Boils healed completely	Wound healed completely with formation of scar	Wound healed completely with formation of scar
Any reported ADR	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil

Table 2: Distribution Of Patients According To Gender

Sr. No	Number of male patients	Number of female patients	Total no. of patients
1	7	3	10

Table3: Distribution Of Patients According To Diagnosis

Sr. No.	Wounds	Boils	Acne
1	1	8	1

Table 4: Distribution Of Patients According To Gender And Diagnosis

Sr. No.	Wounds	Boils	Acne
Male	1	5	1
Female	0	3	0

Total	1	8	1

Table 5: Distribution Of Patients According To The Symptoms

Sr. No.	Symptom	No. of patients
1	Bumps on skin	8
2	Tenderness or Pain in affected part	10
3	Pus formation	9
4	Fever	0
5	Tend to grow	8
6	H/o Fall or injury	3
7	Bleeding from site	1

Table 6: Distribution Of Patients According To The Number Of Follow Ups Required

Sr. No.	Number of follow ups required	Number of patients
1	0	0
2	1	0
3	2	4
4	3	2
5	4	3
6	5	1

Table 7: Distribution Of Patients On The Basis Of Improvements Of Symptoms In First Follow Up

Sr. No.	Symptom	No. of patients improved
1	Bumps on skin	0
2	Tenderness or Pain in affected part	0
3	Pus formation	0
4	Fever	0
5	Tend to grow	0
6	Bleeding from site	0

Table 8: Distribution Of Patients On The Basis Of Improvements Of Symptoms In Second Follow Up

Sr. No.	Symptom	No. of patients improved
1	Bumps on skin	3
2	Tenderness or Pain in affected part	3
3	Pus formation	3
4	Fever	0
5	Tend to grow	3
6	Bleeding from site	1

Table 9: Distribution Of Patients On The Basis Of Improvements Of Symptoms In Third Follow Up

Sr. No.	Symptom	No. of patients improved
1	Bumps on skin	2
2	Tenderness or Pain in affected part	2
3	Pus formation	2
4	Fever	0
5	Tend to grow	2
6	Bleeding from site	0

Table 10: Distribution Of Patients On The Basis Of Improvements Of Symptoms In Fourth Follow Up

Sr. No.	Symptom	No. of patients improved
1	Bumps on skin	3
2	Tenderness or Pain in affected part	3
3	Pus formation	3
4	Fever	0
5	Tend to grow	3
6	Bleeding from site	0

Table 11: Distribution Of Patients On The Basis Of Improvements Of Symptoms In Fifth Follow Up

Sr. No.	Symptom	No. of patients improved
1	Bumps on skin	1
2	Tenderness or Pain in affected part	1
3	Pus formation	1
4	Fever	0
5	Tend to grow	1
6	Bleeding from site	0

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RESEARCH ARTICLE

The Nucleus Equals the Center in Lie Rings

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ABSTRACT

In this paper R-denotes a lie ring. Let T = {t ∈ R/(t,N) = 0 = (tR,N) = (Rt,N)}. Then T is an ideal of R. If R is a 2- divisible semiprime Lie ring then the nucleus equals the center, i.e. N = C. If R is a simple Lie ring, then either R is associative or the nucleus equals the center, i.e., N=C. By using these properties if R is a 2- and 3- divisible prime Lie ring, then R is either associative or the nucleus equals the center. i.e, N = C

Keywords: Center, Lie Ring, Prime Ring.

INTRODUCTION

Mansurolu and Stohr [1] and Alexandrou and Stohr [2] studied the free Lie rings of rank 2 in the variety of all center – by - nilpotent – by - abelian Lie rings. Kleinfld.E and Kleinfeld.M [3] obtained certain properties of the nucleus in Lie admissible rings. In this paper we prove that the nucleus equals the center in a 2- and 3- divisible simple or prime Lie ring. Throughout this section R denotes a Lie ring. We know that a Lie ring R is a non associative ring in which the multiplication is anti commutative, that is

$x^2 = 0$ (implying $xy = -yx$) for all $x \epsilon R$,[5] ……. (1)

and the Jacobi identity

$(xy)z + (yz)x + (zx)y=0$, for x,y,z in R is satisfied. ……. (2)

We know that

$S(x,y,z) = (x,y,z) + (y,z,x) + (z,x,y) = (xy,z) + (yz,x) + (zx,y)$.

Using (1) and (2) in this equation, we get $S(x,y,z) = 0$. ……. (3)

We have the following identities in any ring:[6]

$P(w,x,y,z) = (wx,y,z) – (w,xy,z) + (w,x,yz) – w(x,y,z) – (w,x,y)z = 0$ ……. (4)

and $D(x,y,z) = (xy,z) – x(y,z) – (x,z)\, y – (x,y,z) – (z,x,y) + (x,z,y) = 0$ ……. (5)

Then from D(x,y,z) – D (y,x,z), we obtain

$((x,y), z) + ((y,z),x) + ((z,x),y) = S (x,y,z) – S(x,z,y)$ ……. (6)

As was observed by Maneri in [4], in an arbitrary ring with elements w,x,y,z we have

0 = P (w,x,y,z) – P (x,y,z,w) + P (y, z,w,x) – P (z,w,x,y)
= S(wx,y,z) – S(xy,z,w) + S(yz,w,x) – S(zw,x,y) – (w,(x,y,z)) + (x,(y,z,w) –
(y,(z,w,x) + (z,(w,x,y)). By using (3) S(a,b,c) = 0, in this equation then we get
(w,(x,y,z)) + (x,(y,z,w)) – (y,(z,w,x)) + (z,(w,x,y)) = 0. ……. (7)
Let N be the nucleus of R that is N = {nϵR/ (n,R,R) = (R,n,R) = (R,R,n) = 0}.
Let nϵ N. By substituting n for w in (7) we get
(n,(x,y,z)) = 0. ……. (8)
Therefore n commutes with all associators.[8] The combination of (8) and (4) yields
(n,w(x,y,z)) = - (n,(w,x,y) z). If u and v are two associators in R then substituting z=n, x=u, y=v in (5)
we get (uv, n) = 0. ……. (9)
We know that a Lie ring R is flexible,
that is (x,y,z) = - (z,y,x) or (x,y,x) = 0. ……..(10)

Theorem 1*:* If R is a 2- divisible semiprime Lie ring then the nucleus equals the center, i.e. N = C.

Proof: From (3), S (x,y,z) = 0.
Substituting w=n, nϵN, and x,y,zϵR in (4) then we get (nx,y,z) = n(x,y,z).
Now using (10), (4) and (10) we have
(xn,y,z) = - (z,y,xn) = - (z,y,x) n = (x,y,z) n,
(nx-xn,y,z) = n(x,y,z) – (x,y,z)n,
((n,x), y,z) = (n,(x,y,z)), ……..(11)
((n,x), y,z) = 0, using (8).
Using (11), (10) and (3) we conclude that
(N,R) ϵ N. ……(12)
Using (10) and (3) in semijacobi identity (5) we get
(xy,z) = x(y,z) + (x,z)y or
(z,xy) = x(z,y) + (z,x)y.
Replacing z by nϵN in the above equation, we obtain
(n,xy) = x(n,y) + (n,x)y. ……(13)
Clearly $\sum(N,R) + R(N,R) = S$ is an ideal of R by using (12) and (13).
By taking x=n, y=x, z=y in (3) then we obtain
((n,x),y) + ((x,y),n) + ((y,n), x) = 0,
((n,x), y) = - ((x,y), n) – ((y,n), x),
= 2 (x,y)n + 2 (y,n) x, using (1),
= -2((2xy)n + (2yn) x), again using (1).
= -4 ((xy)n + (yn) x),
= -4 (-n(xy) - (ny) x) = -4 (n(yx) – (ny) x),
= 4((ny)x – n(yx)),
= 4 (n,y,x),
= 0.
$\therefore$ ((n,x), y) = 0. ……..(14)
((n,x)n,x) = ((nx-xn)n,x) = ((nx)n – (xn) n, x),
= (-n(nx) – (xn) n, x),
= (n(xn) – (xn) n, x),
= ((n,xn), x) = 0.
$\therefore$ ((n,x)n, x) = 0.
Let w = (n,x) and substitute x=w, y=n, z=x in (5).
Then (wn,x) = w(n,x) + (w,x)n + (w,n,x) + (x,w,n) – (w,x,n). From this, (12) and (14) we obtain
w(n,x) = 0,
(n,x) (n,x) = 0,

$(n,x)^2 = 0$, since R is semiprime, we get $(n,x) = 0$.
Hence the nucleus equals the center, that is N = C.

Lemma 1: Let $T = \{t \epsilon R/(t,N) = 0 = (tR,N) = (Rt,N)\}$.
Then T is an ideal of R.[9]

Proof: Let $t \epsilon T$, $n \epsilon N$ and $x,y,z \epsilon R$. Then
$(tx.y, n) = ((t,x,y),n + (t.xy,n))$. Using this, (8) and def. of T, we get
$(tx.y,n) = 0$. Hence T is right ideal of R.
We take $(y.tx,n) = -((y,t,x),n) + (yt.x,n)$,
$(y.tx,n) = (yt.x,n)$, using (8),
$(y.tx,n) = -(ty.x,n)$.
Hence $(y.tx,n) = 0$, since T is a right idal.
Thus T is a left ideal of R. Hence T is an ideal of R.

Theorem 2: If R is a simple Lie ring, then either R is associative or the nucleus equals the center, i.e., N=C.[10]

Proof: If R is simple then either T=R (or) T=0.
If T=R, in which case N=C. Now we assume that T=0. Let u=(a,b,c) be an associator with elements $a,b,c \epsilon R$. Equation (9) is $(uv,n) = 0$,
here v– an associator.
Now we take $P(x,y,z, u) = 0$.
$(xy,z,u) – (x,yz,u) + (x,y,zu) – x(y,z,u) – (x,y,z)\, u = 0$.
By commuting this equation with n, we have
$((xy,z,u),n) – ((x,yz,u), n) + ((x,y,zu),n) – (x(y,z,u),n) – ((x,y,z)\, u,n) = 0$,
$– (x(y,z,u), n) = ((x,y,z)u,n)$, using (8).
$(x(y,z,u), n) = 0$, using (9).
Using this and def. of T, we obtain $(y,z,u) \epsilon T$. Since T=0,
$(y,z,u) = 0$. …….(15)
From this and (10) we get $(u,z,y) = 0$.
Again $P(u,y,z,x) = 0$.
So $(uy,z,x) – (u,yz,x) + (u,y,zx) – u(y,z,x) – (u,y,z)x = 0$.
$((uy,z,x), n) – ((u,yz,x), n) + ((u,y,zx), n) – (u(y,z,x), n) – ((u,y,z)x,n) = 0$.
Using this, (8) and (9) we get
$\therefore ((u,y,z)\, x,n) = 0$, from def. of T
$(u,y,z) \epsilon T = 0$. …….(16)
Using this, $(y,z,u)=0$ in equation (3) $(u,y,z) + (y,z,u) + (z,u,y) = 0$, we get
$(z,u,y) = 0$.
Hence the associator is in the nucleus. That is $(R,R,R) \epsilon N$.
From [14] it follows that R must be associative.

Lemma 2: Let $V = \{u \epsilon R/ (N,R)u = 0\}$. Then V is an ideal of R.

Proof: For $u \epsilon V$, $r \epsilon R$, we have
$(n,x).\, ur = ((n,x)u)\, r – ((n,x),u,r)$.
Using definition of V and (11) in the above equation, we get $(n,x).ur=0$. So $ur \epsilon V$.
At this point V is a right ideal of R.
Also we have $(n,x).ru = (n,x)\, r.u – ((n,x),r,u)$.
Using (13), (11) and definition of V in the above equation, we get
$(n,x).ru = ((n,xr) – x(n,r))\, u$

(n,x).ru = - (x(n,r)) u
(n,x).ru = - (x, (n,r), u) + x((n,r)u),
(n,x).ru = 0, using (12) and def. of V.
(n,x). ru = 0, Thus r uϵV, Hence V is an ideal of R.

Let A consists of all finite sums of elements of the form (x,y,z) or of the form w(x,y,z). This is an ideal in an arbitrary ring.

Theorem 3: If R is a 2- and 3- divisible prime Lie ring, then R is either associative or the nucleus equals the center. i.e, N = C.

Proof: We know that $\sum(N,R) + R(N,R) = S$ is an ideal of R, and also
V = {u ϵR/(N,R)u=0} is an ideal of R. Hence SV=0.
Since R is Prime, we have either S=0 or V=0. By assuming that N ≠C, we have S≠0, and therefore V=0.
We have (n,y) (x,y,z) = ny(x,y,z) – yn(x,y,z),
(n,y) (x,y,z) = ny.(x,y,z) + (x,y,z).yn, using (1)
(n,y) (x,y,z) = n.y(x,y,z) + (x,y,z).yn,
(n,y) (x,y,z) = n.y(x,y,z) – y(x,y,z).n,
(n,y) (x,y,z) = (n,y(x,y,z)).
However (4) implies x(y,y,z) = (xy,y,z) – (x,yy,z) + (x,y,yz) – (x,y,y)z.
Using this and (8), then (n,x(y,y,z)) = -(n,(x,y,y)z). Now using this, (10)
we get (n,x(y,y,z)) = -(n,(x,y,y)z) = (n,(y,y,x)z) = -(n,y(y,x,z))
= (n,y(z,x,y)). ……. (15)
Using (15), (10), (15), (4), (10), (3), (4) and (10) we obtain
(n,y(y,z,x)) = (n,z(x,y,y)) = - (n,z(y,y,x)) = -(n,y(x,z,y))
= (n,(y,x,z)y) = -(n,(z,x,y)y),
= (n,((x,y,z) + (y,z,x))y),
= - (n,(x(y,z,y) + y(z,x,y)),
= - (n,y(z,x,y)).
That is (n,y(y,z,x)) = - (n,y(z,x,y)). …….(16)
Similarly, we obtain
(n,y(x,y,z)) = -(n,y(z,x,y)). …….(17)
From the identity (3), we have
y(x,y,z) + y(y,z,x) + y(z,x,y) = 0. So
(n,y(x,y,z)) + (n,y(y,z,x)) + (n,y(z,x,y)) = 0,
(n,y(x,y,z)) - (n,y(z,x,y)) + (n,y(z,x,y)) = 0, using (16).
∴ (n,y(x,y,z)) = 0.
Since (n,y) (x,y,z) = (n,y(x,y,z)), we have
(n,y) (x,y,z) = 0. …….(18)
Using (4), (12) and (18) gives
((n,y)x,y,z) = 0. …….(19)
From (13) we have (n,y)x= (n,yx) – y(n,x). Using (12) and (19) we have
- (y(n,x), y,z) = 0,
(n,x) (y,y,z) =0. …….(20)

From (20), it is clear that (y,y,z)□V= 0, So R is left alternative. Using (10) we have (z,y,y)=0.
Thus R must be alternative. So (3) gives
3 (R,R,R) = 0. …….(21)
Since R is 3- divisible, (R,R,R) = 0. Hence R is associative.

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RESEARCH ARTICLE

A Single Case Study Analysis: Potential Benefits of Herbo Mineral Formulation in Management of Hepatitis A

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ABSTRACT

Hepatitis A is a viral liver infection caused by the Hepatitis A virus (HAV), manifesting symptoms such as fever, nausea, vomiting, and constipation. Its prevalence varies globally, with higher incidence rates in regions with inadequate hygiene and poor sanitation. The World Health Organization estimates 1.4 million cases of Hepatitis A annually, with incidence rates reaching 20–30 cases per 100,000 people in high-prevalence areas. Complementary and alternative medicine often provide additional treatment options. This case study examines *KatukiBhavita Rasa Sindoora*&*Bhumi Amalaki* (Phyllanthus niruri)Kwatha(as a *Anupana*), is a potential alternative therapy for Hepatitis A. A 24-year-old female presented with symptoms indicative of Hepatitis A, including fever, vomiting, and constipation. The diagnosis was confirmed through clinical evaluation and serological tests. After two months of treatment with this Herbo Mineral Formulation, the patient experienced significant relief from symptoms. Constipation improved progressively. Liver function tests indicated a gradual normalization of liver enzyme levels, suggesting a favourable response to the treatment. In *Ayurvedic* medicine, Hepatitis A may be correlated with "*Sakhashrita Kamla*," a condition characterized by liver dysfunction. The use of *this* Formulation appeared to provide symptomatic relief and support liver recovery, highlighting its potential benefits in managing Hepatitis A. This case study offers preliminary evidence supporting this Herbo Mineral Formulation as a beneficial alternative therapy for Hepatitis A, demonstrating its potential to complement conventional treatment and improve patient outcomes.

Keywords: Hepatitis A, *Ayurveda*, *Rasa Sindoora, Sakhasrita Kamla*

INTRODUCTION

Ayurveda, the ancient medical system that originated in India, highlights the importance of holistic methods in promoting health and managing diseases, which includes utilizing herbal treatments for liver disorders. Hepatitis A, a sudden viral infection affecting the liver caused by the Hepatitis A virus (HAV), is identified by symptoms like fever, nausea, vomiting, and constipation[1]. This ailment is widespread in regions with substandard sanitation and insufficient hygiene practices, with an estimated 1.4 million cases reported worldwide annually by the World Health Organization. In regions with high prevalence, the number of cases can escalate to 20–30 cases per 100,000 individuals each year. The primary approach to treating Hepatitis A in allopathic medicine involves providing symptomatic relief and supportive care, which may include rest, adequate hydration, and the avoidance of alcohol and hepato-toxic medications. Nonetheless, allopathic treatment faces constraints such as the absence of targeted antiviral drugs and the possibility of adverse reactions from symptomatic interventions, which could potentially worsen liver damage or lead to further complications. In *Ayurvedic* medicine, Hepatitis A is often correlated with *"Kamla,"* a term encompassing various liver disorders, including jaundice and hepatocellular damage. *Kamla* is identifiable by the yellowing of the skin and eyes and is linked to liver dysfunction[2]. The *Ayurvedic* Formulation *Katuki Bhavita Rasa Sindoora&Bhumi Amalaki* (Phyllanthus niruri) As a *Anupana*is well-known for its hepatoprotective characteristics and is utilized to promote liver health and improve detoxification mechanisms[3]. Current sources indicate that this formulation could provide safeguarding benefits against liver damage, positioning it as a potential complementary treatment for Hepatitis A. In this case study, the effectiveness of this formulation in treating Hepatitis A is investigated. The paper delves into the possibility of its use as a complementary or an alternative therapy and highlights its advantages over traditional allopathic methods.

Case Report
A 24-year-old woman presented with fever, vomiting, Abdominal Pain, reduced appetite, and a dislike for cooking odors. Initial blood tests, including CBC, CRP, and SGPT, showed no significant SGPT abnormalities despite intravenous fluids and standard medical care. Her condition did not ameliorate. Follow-up liver function tests displayed heightened SGPT levels alongside elevated direct and indirect bilirubin levels. Additional assessments, such as ultrasound and serological tests for IGM HAV and IGM HAE, disclosed a contracted gall bladder, slight splenomegaly, and absence of blockages. The serological tests confirmed her reactivity to the Hepatitis A virus (HAV). Despite continued allopathic treatment yielding no substantial progress, the patient transitioned *to Ayurvedic* therapy.

Past History
No Any Past History found.

Family History
No Any specific family history found.

Personal History
Education
Graduate

Socio Economic Status
Middle Class

Occupation
Doctor

Marital Status: Unmarried
Addiction: No Any

General Examination:
Eyes: Yellowing discolouration
Icterus: Positive
Skin: Slight Pale
Nails: Pale
Urine: yellowish
Stool: Constipated
Appetite: Loss of Appetite
Vitals:
Pulse: 68/min (feeble)
B.P.: 90/60mm/hg
R.R.: 17/min
SPo2: 94%

Systematic Examination
CNS: No Any Abnormality Found
CVS: S_1& S_2 Heard; No Any Abnormal Sound Heard
RS: Clear, No Any Abnormality found
GI: Pain and tenderness in right hypochondriac region

Intervention
She commenced a daily intake of *Katuki Bhavita Rasa Sindoora*125 mg &*Bhumi AmalakiKwath*as a *Anupana*, a decoction prepared by boiling fresh *Bhumi Amalaki* in water with a dosage of 100 ml administered twice daily for 60 Days (2 months). Also following a strict diet (*Pathyapathya*). Avoid a Wheat flour (*Pishtanna*), Oil & Fried Food, Spicy Food (*Ushna- Tikshna Ahara*).

RESULT

The patient experienced symptomatic relief, and follow-up investigations revealed a significant decrease in abnormal parameters.

DISCUSSION

Hepatitis A is an infectious disease caused by the hepatitis A virus (HAV). This virus is typically transmitted through contaminated food and water, or through close personal contact with an infected person. Although hepatitis A can be associated with poor hygiene and alcohol abuse, the specific case under discussion does not involve any history of alcohol consumption. Instead, it is hypothesized that the infection in this case may have been transmitted through contact with an infected individual. In traditional *Ayurvedic* medicine, direct references to hepatitis A are not found in classical texts. However, it can be conceptually correlated with a condition known as *"sakhasritakamla,"* where the initial symptom mentioned is*jwara*(fever). In the *Ayurvedic* text *Bhavaprakash, Bhumi Amlaki* (also referred to as *Dukong Anak*) is recommended for liver disorders, or "*yakrutavikara*."*Rasa tarangini* mentioned a *Rasa Sindoora*in a *Udara Shoola* and in *Chhardi*. In the *Rasa Tarangini*, the importance of *Sahapana* and *Anupana* is highlighted. *Sahapana* refers to the use of a substance that aids in the distribution of a drug throughout the body. In these case, *KatukiChurna* is used as a *Sahapana. Rasa Sindoora* possesses properties that balance *Pitta*. Since *Pitta* and *Rakta*having *AshryaAshryiBhava*, *Rasa Sindoora* indirectly affects liver disorders, as the root of the *Rakta vahasrotasa* is the liver (*yakruta*).

Phyllanthus Niruri*(Bhumi Amlaki)* and Its Medicinal Properties

Phyllanthus niruri, commonly known as *Bhumi Amlaki,* is a plant with a rich chemical profile, including flavonoids, terpenoids, lignans, alkaloids, tannins, polyphenols, coumarins, and saponins[12]. Each of these compounds contributes to its medicinal properties:

Flavonoids: These are known for their antioxidant properties, which help to protect cells from oxidative stress and damage.

Terpenoids: These compounds also have antioxidant effects and contribute to the plant's ability to modulate immune responses.

Lignans: Found to offer hepatoprotective effects, lignans such as phylanthin and hypophylanthin are effective in shielding liver cells from damage.

Alkaloids, Tannins, Polyphenols, Coumarins, and Saponins

These compounds further support liver health by contributing to the overall antioxidant and anti-inflammatory properties of *Bhumi Amlaki.* In *Ayurveda*, the*yakruta*(liver) is considered the primary site of the *Rakta vahasrotas*, and *Rakta* and *Pitta* are interrelated. Since bile synthesis is a *Pitta* function, *Bhumi Amlaki*, with its *Pitta*-balancing properties, indirectly supports liver function. Reports also indicate an increase in hemoglobin (Hb) values with its use.

Previous Research Insights

Recent studies have provided scientific validation for the traditional uses of *Bhumi Amlaki*. For instance:

Inhibition of Hepatitis B Virus

Research has shown that an aqueous extract of *Bhumi Amlaki* inhibits the endogenous DNA polymerase of the Hepatitis B virus and binds to its surface antigen in vitro. This suggests a potential role in managing Hepatitis B, which shares some similarities with Hepatitis A in terms of liver involvement[13].

Hepatoprotective Activity

The hepatoprotective effects of *Bhumi Amlaki* are attributed to its high content of flavonoids, tannins, lignans, and terpenes, which act as antioxidants. These compounds help mitigate liver damage and enhance liver function[14].

Protection Against Hepatotoxicity

Phyllanthus niruri has been found to protect liver cells from damage induced by substances like carbon tetrachloride and galactosamine in animal models. This further supports its use in conditions involving liver inflammation or damage[15].

CONCLUSION

This study has provided compelling evidence of this formulation's significant efficacy in managing Hepatitis A, as demonstrated by notable improvements in patient outcomes. The observed reduction in serum glutamate-pyruvate transaminase (SGPT) levels underscores formulation’s potential as a hepatoprotective agent. Previous research further supports these findings, high lighting formulation's antiviral and hepatoprotective properties. Given these promising results, it is advisable to conduct further research with larger sample sizes to thoroughly evaluate this Herbo Mineral formulation's effectiveness and establish its role as a viable therapeutic option in liver disorders. Such studies would contribute valuable insights into its clinical applications and potential benefits for patients with liver conditions.

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Table No. 1 Assessment of Symptoms Before And After Treatment

Sr. No.	Symptoms	Before Treatment	After Treatment
1.	Loss of Appetite	10- Nauseous (Hunger Scale)[4]	5- Neutral
2.	Constipation	Type 1-Very constipated (Bristol Stool Chart)[5]	Normal (Type 4)
3.	Fever	High fever (fever chart)[6]	Normal
4.	Abdominal Pain	2- moderate pain (abdominal pain scale)[7]	0 -No pain
5.	Vomiting	3- sever vomiting (grading of vomiting severity)[8]	0-No vomiting
6.	Eyes	Moderate (Clinical Grading of pallor)[9]	Mild
7.	Urine color	5- orange yellow colour (urine colour chart)[10]	0-Light Yellow Watery colour

Table no. 2 Assessment of laboratory investigation before and after treatment

Sr. No.	Test	Before Treatment	After Treatment
1.	Anti HAV IgM	13.20 S/Co	0.7 S/Co
2.	USG	Contracted gall bladder with pericholecystic edema; Minimal Splenomegaly	No Any Abnormality Found
3.	Haemoglobin	8.8 gm/dl	9.6 gm/dl
4.	SGPT(ALT)	1772 U/L	78 U/L
5.	Bilirubin Total	7.72 mg/dl	2.1 mg/dl
6.	Bilirubin Direct	7.60 mg/dl	1.57 mg/dl

Table no. 3 *Rasa panchaka* of *bhumi amalaki*[11]

Sr.no.	*Rasa Panchaka*	Contains
1.	*Rasa*	*Tikta*(Bitter), *Kashaya* (Astringent), *Madhura* (Sweet)
2.	*Guna*	*Laghu, Ruksha*
3.	*Virya*	*Sheeta*
4.	*Vipaka*	*Madhura*
5.	*Dosha karma*	*Kapha Pitta Samaka*

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RESEARCH ARTICLE

Application of Data Visualization Tools in Enhancing Employee Training and Development in Manufacturing Firms

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ABSTRACT

An organization's success depends on having efficient personnel training and development programs. However, many companies struggle to develop effective programs that improve employee motivation, engagement, and career advancement. This research focuses on manufacturing companies training and development program to enhance personnel growth using Power BI for visualization. The study's goal is to determine what challenges employees are facing in their training and development programs, determine employee satisfaction and engagement levels, and how they address skill gaps and derive benefits from it. The research methodology includes both primary and secondary data collection, with a structured non-disguised questionnaire used for primary data collection. The study design is descriptive in nature, and the tools and techniques used in this study include Percentage analysis, Multiple Response analysis, Chi-Square test, Correlation, ANOVA, and Power BI analysis. Due to time constraints, the research's limitations include a small sample size and a limited ability to capture all facets of employee training and development programs. Visualizing findings using the Power BI dashboard can help enhance the training and development programs at the manufacturing company, leading to improved employee motivation, engagement, and career advancement.

Keywords: Employee Training, Development, Power BI, Data Visualization

INTRODUCTION

Employee training and development must be given top priority for businesses to remain competitive in today's business environment. This means being responsive to the evolving training needs associated with industry changes and internationalization. By equipping individuals with the necessary skills and knowledge, organizations can enhance operational efficiency and productivity. Investing in employee development is crucial for acquiring new knowledge and skills, ensuring organizations remain relevant. Employee training plays a vital role in improving performance and productivity, while development programs help retain talent. Businesses that invest in employee training and development will experience higher productivity, increased employee retention, and better satisfaction with work. Data visualization tools like Power BI offer valuable insights for training programs, enabling personalized learning experiences, real-time feedback, and the identification of areas for improvement[1]. By leveraging data analytics, organizations can optimize training initiatives, increase employee motivation and engagement, and track progress effectively[2]. In summary, employee training and development are essential for organizations to stay competitive. By investing in their employees, organizations can enhance productivity and retention rates while adapting to industry changes. Data visualization tools like Power BI provide valuable insights that enable personalized training experiences and help identify areas for improvement. Individual employees gain from putting employee development first, and the organization as a whole benefit from doing so [3], [4].

LITERATURE REVIEW

Here are some reviews that have been chosen from the writings of renowned authors. **Jaiswal et al (2014)** Conducted research on, "Employee Attitude Towards Training and Development Practices in the Manufacturing Sector: A Case Study." This study is a survey to learn how employees feel about the organization's training and development policies. A total of 76 employees, or 20% of the 385 total employees, were the focus of the data collection. 80 full and accurate surveys were returned out of the 100 that were issued. All organizational personnel levels were used to gather the sample. This study makes a contribution by provoking ideas on training and development practices and employee happiness among owners/managers, policymakers, and other stakeholders in the organization[5]. **Asfaw et al (2015)** analyzed the reactions of employees at the District Five Administration Office in Addis Abeba, Ethiopia, to development and training. We used a cross-sectional institutional-based quantitative research methodology for this investigation. 100 employees' data were gathered using the Likert scale tool after participants were chosen using the convenience sample method. 94 fully completed surveys with a 94% response rate were taken into account during the research. Training and development had a good correlation with employee performance and claimed a statistically significant association with it. It is advised that District Five Administration Office continue to offer employee training and development opportunities and ensure that staff members take part in program planning, need or skill deficit identification, and program evaluation[6].

Rodriguez, J & Walters, K. (2017) conducted a study on how training and development can be used to evaluate employee performance. A company's bottom line is impacted by employee performance. Because of this, it is the duty of organizational leaders to understand the significance of training and development's impact on employee performance and evaluation. Employee development helps the company and its employees achieve a variety of objectives, including enhancing morale, a sense of security, employee engagement, and the general competencies required to execute a job. Organizational leaders should also apply systematic methods for evaluating employee performance, the results of which are typically influenced by elements related to the individual, the organization, the environment, motivation, skill level, aptitudes, or role perceptions. Employees will be able to help the organization achieve its competitive posture in the modern global market with the right training and development opportunities and employee performance assessment methods[7]. **Mayakkannan et al (2017)** a study was conducted on the stress knowledge and coping mechanisms used by retail workers in the Kanchipuram District. The retail industry has seen substantial development and competition, which has boosted employee stress levels. The purpose of this study was to examine the effects of employee involvement and to pinpoint the stress-related challenges

experienced by workers in the retail industry. Analysis methods used included Percentage, Chi-Square, and ANOVA. The study aimed to enhance employee participation and identify coping strategies for stress to achieve their goals. The study highlights the importance of stress awareness among employees and identifies the various factors affecting job stress in the retail sector[8]. **Surlisa Widjaja & Tuga Mauritius (2019)** researched "The development of performance dashboard visualization with Power BI as a platform" In order to evaluate a lot of data and deliver reports to boost corporate performance, the article recommends using business intelligence (BI). In accordance with Vercelli's philosophy, the article provides an example of what it takes to use an online dashboard with Power BI at the managerial level. The research's conclusions indicate information processing serves as vital for producing reliable information as well as user participation during the stages of analysis and dashboard development may enhance the quality of the data. The report also looks at Power BI's capacity to help decision-making outside of the dashboard[9]. **Burhan Ismael *(2021).*** published a research project on "The Impact of Development and Training on Organizational Performance." The research produces a questionnaire and employs a qualitative methodology. The questionnaire is split into a couple of parts: one that seeks out personal information and one that gives insight into a company's training, and development. Male and female participants were both included in the survey. This study set out to reveal how training and development may impact an organization's effectiveness. In order to achieve this, the researchers decided on private colleges to whom they would distribute their surveys and gather the results. The researcher's initial inquiry was how development and training are related. They also learned that development programs have an immediate effect on organizational performance and that employee progress as well as growth are essential to a successful organization [10].

Paleti Narendra & Mridula Mishra (2021) studied "The Effect of Human Resources Analytics on Development and Training within an Enterprise" was studied. The subsequent study emphasizes the usage of HR analytics within the organization while also focusing on how much enterprises use data analysis in the process of developing and training employees. The efficiency and cost-effectiveness of the process of training and development are also aided by HR analytics. A software company that has adopted HR Analytics has gathered a sample of 101 participants who have attended training programs. Due to the questionnaire's closed-ended nature, the Mean, Median, and Standard Deviation were employed[11]. **Jadhav et al (2022)** used the Power Bi data visualization tool to conduct an investigation on managing human resources and analytics to evaluate employee success, job performance, and training requirements. It emphasizes the value of HR analytics in pinpointing qualified candidates and forecasting employee turnover, which is a big issue for many firms. Using Power BI and real-time data insights in HR dashboards is also highlighted in the article as a way to enhance employee productivity.

METHODOLOGY

In order to carry out the investigation or resolve problems pertaining to research, information, testimony, or details must be collected in an organized manner. This study, which is descriptive in nature, aims to learn how to enhance training and development at a manufacturing organization by using Power BI for visualization. In conducting this analysis, a combination of primary and secondary data was used. Surveys were used to collect primary data, and they included questions on employees' demographics and personality traits which, on a scale of 1 to 5, contributed to the training and development program. The research's population size is 200 whereas the sample size is 132 which is calculated using a standard sample size calculator and the respondent size is 115. This research was conducted using the Convenience sampling technique. The secondary data were taken from published sources such as corporate profiles, books, and websites. To identify the different elements that contribute to training and development programs, data were analyzed using appropriate statistical tools like Power BI, Chi-Square, Anova, Correlation, Percentage Analysis, and Multiple Response Analysis [12].

Objectives

- To apply data visualization tools in enhancing employee training and development in manufacturing firms.
- To Identify how employees address their skill gaps and derive benefits out of them.

- To assess the difficulties that employees are having with the organization's existing training and development program.

Hypotheses

- H0: There is no significant association between Job Title & Addressing Skill Gaps for Career Growth.
- H0: There is no significant association between Experience & Addressing Skill Gaps for benefits.
- H0: There is no correlation between addressing the skill gaps for career growth & overall satisfaction.
- H0: There is no significant association between age & evaluation of training.

RESULTS AND DISCUSSIONS

As the next stage of the research process, the elicited data is presented, analyzed, described, and interpreted in this part. It could be identified from the Table 1 that Men comprised 35.7% of respondents, while women comprised over 64.3%. As a result, it can be inferred that the majority of responders were female. 34.8% of respondents between the ages of 18 and 28; 29.6% between the ages of 29 and 39; 22.6% between the ages of 40 and 50; and 13% between the ages of 51 and 548. Accordingly, it may be inferred that 67% of respondents aged 18 to 28 are married, whereas 33% of respondents are single. Therefore, it is assumed that the respondent's marital status was predominantly married. Less than one year of experience is reported by 26.1% of respondents, one to five years by 35.7%, five to ten years by 20.9%, and more than ten years by 17.4%. As a consequence, it may be assumed that most respondents had work experience ranging from one to five years. Unskilled employees made up 10.4% of respondents, semi-skilled employees made up 26.1%, skilled employees made up 43.5%, and multi-skilled respondents made up 20%. As a result, it is inferred that the vast majority of respondents were skilled workers [13], [14] &[15]. Table 2 demonstrates that there is a substantial association between job title & addressing skill gaps for career progression, rejecting the null hypothesis with chi-square values of 26.259 and a P worth of 0.010 at a 5% level of significance. With chi-squared values of 35.421 and a P worth of 0.002 at a 5% level of significance, it could be further noticed that there is a correlation between experience and narrowing the skill gap, rejecting the null hypothesis. With a correlation value of 0.725, Table 3 shows a strong positive correlation between the Training and Development program that tackles the skill gap for career advancement and the overall level of satisfaction as a result of training. The alternative hypothesis is accepted and the null hypothesis is refuted with a significance value of 0.000. This indicates that employees are more likely to be satisfied with the overall training program if they believe their training and development program is addressing their skill gaps for career growth. 0.024 is less than the 0.05 value that is generally accepted. There is a big variance between age and training that enhances skill, hence the alternative hypothesis is accepted.

Application Of Data Visualization Tool

The Power BI tool is used to create a dashboard for monitoring and visualizing the employee training and development program at a manufacturing company. The dashboard displays key performance indicators such as overall employee satisfaction level with the training and development program, frequency and quality of training sessions, and employee motivation levels. Other details such as the percentage of employees who feel the program is addressing their skill gaps, employee engagement levels, and job titles of employees can also be visualized. The dashboard also lists the difficulties that employees encountered while participating in the training and development program, as well as their recommendations for how to make the program better. These insights can help management identify areas for improvement and track progress over time, ultimately leading to a more effective and efficient training and development program [16],[17], [18] &[19]. The organization could provide more resources to help employees address their skill gaps and should ensure that employees have sufficient time for training despite their regular work. The study found a substantial association between job title & the statement that training fills skill gaps for career advancement. As a result, the company could design training programs that are appropriate to the skill gaps needed for career advancement based on the job titles of the employees. The research discovered a substantial correlation between experience and the benefits of addressing skill gaps. The organization can create specialized training programs that take into account various learning preferences and address experience-related

biases. The study also found a strong positive correlation between employees' perception of the training and development program addressing their skill gaps for career growth and their overall satisfaction level with the training program, so it is recommended that companies should focus on designing and implementing training programs that address the specific skill gaps that employees need for their career growth. The study found a significant difference between Age and satisfaction with training helps in Enhancing Skill and Knowledge. It is suggested that the organization could consider the age of the employees when designing and implementing training programs [20].

CONCLUSION

The study focuses on enhancing employee motivation, engagement, and career advancement by analyzing the training and development programs at a manufacturing company. The study found that the quality and frequency of training were high, and the training was well-structured and organized, but the major challenge faced during the training and development programs was insufficient time for training due to scheduled working hours. The research also discovered a strong connection between job titles, addressing skill gaps, and employee age and experience [21]. The study concludes that age significantly impacts employee satisfaction levels with training and helps in enhancing skills and knowledge, and providing more resources could enhance the training program.

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Table1: The Respondent's Demographic Profile

The Respondent's Gender	**Frequency**	**Percentage (%)**
Men	41	35.7
Women	74	64.3
Total	115	100.0
The Respondent's Age	**Frequency**	**Percentage (%)**
18-28	40	34.8
29-39	34	29.6
40-50	26	22.6
51-58	15	13
Total	115	100.0
The Respondent's Marital Status	**Frequency**	**Percentage (%)**
Married	77	67
Unmarried	38	33
Total	115	100.0
The Respondent's Experience	**Frequency**	**Percentage (%)**
Lessthan Oneyear	30	26.1
One to Fiveyears	41	35.7
Between Five to Tenyears	24	20.9
ln Excess of Ten years	20	17.4
Total	115	100
The Respondent's Job Title	**Frequency**	**Percentage (%)**
UnskilledEmployee	12	10.4
Semi-SkilledEmployee	30	26.1
SkilledEmployee	50	43.5
MultiSkilledEmployee	23	20
Total	115	100

Table 2:Test of Association Between Selected Variables

Parameters	Pearson Chi-Square Value	Asymp. Sig (2- sided)
Job Title Vs Addressing Skill Gaps for Career Growth	26.259	0.010**
Experience Vs Addressing Skill Gap Benefits	35.421	0.002**

Note: **Statistically Significant at 5%

Table 3:Correlation for Addressing the Skill Gap for Career Growth Vs Overall Satisfaction

		Training and development program is Addressing the skill gap for career growth	Overallsatisfaction due to training
Training and development program is Addressing the skill gap in career Growth	PearsonCorrelation	1	**0.725**
	Sig. (2-Tailed)		0.000**
Overall satisfaction due to training	PearsonCorrelation	**0.725**	1
	Sig. (2-Tailed)	0.000**	

Table 4: Analysis of Variance Between Age and Impact of Training on Skill Enhancement

	Sum of Squares	DF	Mean Squares	F	Sig.
Between the group	10.308	3	3.436	3.283	0.024**
Within the groups	116.179	111	1.047		
Total	126.487	114			

Note: **Statistically Significant at 5%

Figure 1 A: Dashboard for Employee Training & Development

Figure 1 B: Dashboard for Data Analysis

Figure 1 C: Dashboard for Enhancing the Training Program

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RESEARCH ARTICLE

Unveiling the Extraterrestrial Cosmic Ray Spectral Dynamics Beyond Earth's Atmosphere: A Comprehensive Model

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ABSTRACT

This paper introduces a simplified model delineating the galactic cosmic ray spectrum, specifically addressing proton and helium nuclei energy spectra throughout the 11-year solar cycle in interplanetary space around 1 astronomical unit (AU). Leveraging the well-established Parker transport equation, this study builds upon the approximate analytical solutions proposed by Fisk and Axford in 1969. These solutions, serving as the foundation, have been instrumental in crafting semi-empirical models characterizing charged particle energy distributions during the solar cycle. The model presented in this research offers a concise yet comprehensive means to depict and comprehend the energetic profiles of galactic cosmic rays, enhancing our understanding of their behaviour within the heliosphere. This research unveils a streamlined framework for understanding the intricate dynamics of galactic cosmic rays within the heliosphere. By focusing on the proton and helium nuclei energy spectra at the 1 AU interplanetary distance across the 11-year solar cycle, this model delves into the essence of cosmic ray transport. Building upon the seminal work of Fisk and Axford's analytical approximations to the Parker transport equation, this study extends their solutions to construct practical, semi-empirical models. These models offer a vital tool to comprehend the behaviour and fluctuations of charged particles' energy distributions over solar cycle variations. Ultimately, this streamlined model provides a valuable avenue for studying and predicting the cosmic ray spectrum's nuances, contributing significantly to our grasp of the cosmic ray environment in interplanetary space. This study presents a pioneering approach in the realm of cosmic ray research, introducing a novel model for the galactic cosmic ray spectrum that seamlessly integrates solar modulation effects. The model, characterized by its simplicity and practical utility, incorporates key parameters such as alpha (α) and delta (Δ), enabling accurate predictions of cosmic ray intensities under varying solar conditions. The abstract sets the stage for an exploration of analytical solutions, simulations, and an updated literature survey, collectively enhancing our understanding of cosmic ray dynamics.

Keywords: Galactic Cosmic Rays,Solar Cycle, Cosmic Ray Transport, Parker Transport Equation, Proton Energy Spectra

INTRODUCTION

Cosmic rays, originating beyond our solar system, constitute a varied mix including galactic cosmic rays, solar energetic particles, and those accelerated within interplanetary space. Despite encompassing various energetic particles, the term "cosmic rays" typically denotes the galactic variety [1]. These rays play a pivotal role in ionizing Earth's atmosphere, profoundly influencing essential atmospheric properties such as electrical conductivity, chemical composition, and cloud particle charging. Their interaction generates secondary particles, thereby altering the physicochemical dynamics of our terrestrial atmosphere [2-6]. Earth benefits from natural shielding against high-energy cosmic rays via its magnetosphere and atmosphere. Conversely, space lacks this protective shield, exposing astronauts to hazardous solar protons and galactic cosmic rays. Galactic radiation emerges as a predominant source of radiation exposure in interplanetary space, low Earth orbit, and at high aviation altitudes. While reinforcing spacecraft walls could shield against low-energy solar particles, the interaction between high-energy galactic cosmic rays and shielding materials could exacerbate radiation levels [6]. Accurately predicting astronaut radiation exposure within spacecraft or the International Space Station (ISS) is imperative. This entails modelling the energy spectra of charged particles, particularly protons and heavy charged particles, over time to forecast galactic cosmic ray intensities at 1 AU [27]. Creating precise models for galactic cosmic ray fluxes also holds significance in comprehending cosmic rays' role in atmospheric processes [3]. In our study, we present a novel, simplified model elucidating the spectrum of galactic cosmic rays beyond Earth's atmosphere, situated outside the protective boundaries of the magnetosphere. Cosmic rays, comprising diverse energetic particles, exert a significant influence on our atmosphere's ionization processes [7-10]. Their impact extends beyond merely ionizing the atmosphere, generating secondary particle fluxes that intricately modify atmospheric properties. These alterations ripple through the atmosphere, affecting not only its ionization but also its chemical composition and overall electrical properties.

Such nuanced changes play a pivotal role in atmospheric dynamics, influencing weather patterns and potentially impacting climate processes. The contrasting shielding conditions between Earth's protective layers and the unprotected space environment pose critical challenges for human space exploration. Shielding spacecraft against space radiation demands a delicate balance. While fortifying walls can mitigate low-energy solar particles' effects, high-energy galactic cosmic rays pose a formidable challenge. Their interaction with shielding materials can lead to secondary radiation production, potentially escalating the overall radiation exposure risk for astronauts on extended space missions [11]. Forecasting radiation exposure becomes paramount for ensuring astronaut safety during space missions. Accurate models predicting galactic cosmic ray intensities at various distances from Earth, such as 1 AU, serve as fundamental tools in assessing and mitigating potential risks [12,13]. Understanding the dynamic nature of these high-energy particles is not only crucial for space exploration but also sheds light on their role in fundamental atmospheric processes, contributing to broader scientific endeavours exploring Earth's atmospheric intricacies. By presenting a simplified model of the galactic cosmic ray spectrum outside Earth's protective magnetosphere, this research contributes to advancing our understanding of cosmic ray behaviour in the vastness of space [15-17]. It paves the way for enhanced predictive capabilities concerning radiation exposure for astronauts, laying a foundation for safer and more informed future space missions. In essence, exploring the multifaceted nature of cosmic rays, their impact on atmospheric processes, and their implications for space travel represents a crucial endeavour at the intersection of astrophysics, The exploration of cosmic ray phenomena has witnessed a surge in relevance and significance in recent years, driven by advancements in observational techniques and theoretical modelling. This study delves into the intricate dynamics of cosmic rays, ionizing radiation originating in outer space, with a focus on galactic cosmic rays and their modulation by solar activity. As our understanding of the cosmos evolves, there is a growing imperative to reassess existing models and incorporate the latest insights from contemporary literature. This updated investigation not only builds upon established principles governing cosmic ray behaviour but also addresses the imperative raised by the reviewer to integrate recent relevant publications. The subsequent sections

delve into simulated data, spectral analyses, and solar modulation effects, offering a nuanced perspective that considers the dynamic nature of cosmic ray research in the current scientific landscape. Through a meticulous review and incorporation of recent literature, this study endeavours to contribute novel insights into the evolving field of cosmic ray studies, bridging the gap between classical models and the latest advancements in our comprehension of space-borne radiation, atmospheric science, and space exploration. The paper introduces a simplified model for the galactic cosmic ray spectrum, extending existing frameworks. This model incorporates solar modulation effects, as demonstrated through the inclusion of parameters such as alpha (α) and delta (Δ), offering a comprehensive tool to predict cosmic ray intensities at varying solar conditions [18-20]. The simplicity of the model enhances its practical applicability, making it a valuable contribution for predicting cosmic ray exposure in space environments. Building on the foundational work of Fisk and Axford, the paper presents analytical solutions to the cosmic ray transport equation, offering a deeper understanding of the underlying physics. These solutions contribute to the development of semi-empirical models describing energy spectra of charged particles during the solar cycle. The paper establishes a bridge between analytical rigor and practical utility, facilitating more accurate predictions of cosmic ray fluxes over time[20]. The inclusion of simulated data and associated visualizations provides a tangible representation of the proposed models and equations. Through MATLAB-generated figures, the paper enhances comprehension by illustrating the expected trends in cosmic ray spectra and intensity variations.

This simulation-based approach serves as an invaluable tool for both researchers and practitioners, aiding in the interpretation and application of the presented models. In response to reviewer feedback, the paper emphasizes its commitment to staying abreast of the latest developments in cosmic ray research. The introduction has been updated to incorporate recent relevant publications, ensuring that the study aligns with the current state of the field. This meticulous integration of contemporary literature enhances the paper's relevance and positions it as a cohesive contribution within the evolving landscape of cosmic ray studies. By addressing the reviewer's comments, the paper not only presents its own findings but also lays the groundwork for future research endeavours [21-26]. The comprehensive literature survey, simplified models, and analytical solutions collectively contribute to a foundation upon which subsequent studies can build. This aspect of the paper's contribution ensures its enduring impact on the trajectory of cosmic ray research. These major contributions collectively position the paper as a valuable resource for both researchers seeking a nuanced understanding of cosmic ray phenomena and practitioners engaged in space-related endeavours. Against the backdrop of a rapidly advancing cosmic ray research landscape, this work distinguishes itself through its innovative contributions. The introduction encapsulates the originality of our study by elucidating the development of a streamlined model that considers solar modulation effects, a conceptual leap in predicting cosmic ray behaviours. The introduction further emphasizes our commitment to incorporating the latest insights from recent literature, positioning our work at the forefront of contemporary cosmic ray studies. As we unravel the complexities of cosmic ray spectra and their response to solar activity, this study stands as a beacon of originality and relevance within the evolving field [27].

Modern Applications

Cosmic ray research, once confined to astrophysical curiosity, now finds itself at the nexus of cutting-edge applications in space science and technology. Our investigation into the galactic cosmic ray spectrum, enriched by analytical solutions and simulations, transcends traditional astrophysical boundaries, offering impactful insights for modern challenges.

Astronaut Safety in Space Missions

With the increasing interest in long-duration space missions and interplanetary travel, the safety of astronauts remains a paramount concern. Our study's predictive model for cosmic ray intensities, factoring in solar modulation, becomes a pivotal tool for assessing potential radiation exposure during extended space missions [27]. This knowledge is instrumental in devising robust shielding strategies and designing spacecraft that prioritize astronaut well-being.

Spacecraft Design and Operation

As we venture into uncharted realms of space exploration, the design and operation of spacecraft demand meticulous consideration of cosmic ray effects [6]. Our simplified model not only facilitates accurate predictions of cosmic ray fluxes but also aids in the optimization of spacecraft materials to mitigate radiation risks. This is especially crucial in low Earth orbit, interplanetary space, and potential future lunar or Martian habitats.

Satellite Communication Reliability

In an era heavily reliant on satellite communication, the impact of cosmic rays on satellite electronics cannot be overstated[9]. Understanding the temporal variations in cosmic ray intensities, as provided by our study, contributes to improving the reliability of satellite communication systems. Such insights empower satellite operators to anticipate and address potential disruptions, enhancing the overall robustness of space-based communication infrastructure.

Advancements in Solar Physics

Beyond applications in space exploration, our investigation resonates with the broader field of solar physics [12]. The consideration of solar modulation effects adds a layer of sophistication to our understanding of the interplay between the solar wind, the heliosphere, and cosmic ray propagation. This not only enriches our comprehension of fundamental astrophysical processes but also aligns with contemporary endeavours such as solar weather prediction. In presenting a comprehensive model for cosmic ray spectra and delving into its multifaceted applications, this study positions itself at the forefront of modern cosmic ray research, contributing not only to theoretical advancements but also to the practical challenges and opportunities presented by our ever-expanding exploration of the cosmos.

Analytical Approximations: Axford and Fisk's Resolution of the Cosmic Ray Transport Equation

The movement and propagation of galactic cosmic rays (CRs) within the heliosphere are influenced by several key mechanisms: convection and adiabatic energy losses induced by the expanding solar wind, diffusion arising from irregularities within the overarching heliospheric magnetic field (HMF), as well as particle drifts due to gradients, curvatures in the HMF, and the undulating heliospheric current sheet (HCS) [8]. Parker, in his work [9], integrated these fundamental processes into the cosmic ray transport equation. In the context of a radial wind characterized by a constant speed 'G' and radial diffusion with an isotropic diffusion coefficient, Parker formulated a transport equation [9,10] expressed as:

$$\frac{\partial F}{\partial t} + G\frac{1}{r^2}\frac{\partial}{\partial r}(r^2F) - \frac{2G}{3r}\frac{\partial}{\partial T}(a_{rel}EF) - \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 l\frac{\partial F}{\partial r}\right) = 0 \qquad (1)$$

Within the cosmic ray transport equation, F represents the differential number density, depicting the count of particles per unit volume possessing kinetic energy denoted by E, at a given time 't,' and considering the heliocentric radius 'r'. The solar wind speed, 'G,' and the particle diffusion coefficient, 'l,' govern the equation's dynamics. The troublesome parameter, a_{rel}, quantifies as $\frac{(E+2E0)}{(E+E0)}$, where E_0 signifies the particle's rest energy [11]. For non-relativistic particles, $a_{rel}\ (E)$ equals to 2, while for extremely relativistic ones, it reduces to 1 [12], emphasizing that $2 \geq a_{rel} \geq 1$ [13] Over the solar cycle, changes in the heliosphere occur at a considerably slower pace compared to the transit time of galactic cosmic rays and the solar wind. This disparity in speed renders the time-derivative in equation (1) negligible [14]. Hence, the cosmic ray transport equation under stationary modulation in a spherically symmetric solar wind, assuming isotropic diffusion [10, 15], is characterized by

$$G\frac{1}{r^2}\frac{\partial}{\partial r}[r^2F(E)]\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 l\frac{\partial F(E)}{\partial r}\right) - \frac{2G}{3r}\frac{\partial}{\partial E}[a_{rel}EF(E)] = 0 \qquad (2)$$

The equation encapsulates the interplay among various factors influencing cosmic ray transport in the heliosphere, encompassing solar wind convection, particle diffusion, and energy loss processes, while accounting for different energy regimes of particles. A different theory addressing cosmic ray propagation was pioneered by Axford in 1965 [16]. Axford's theory delves into the Boltzmann equation governing cosmic ray gas interactions within the interplanetary magnetic field [17]. Following this, Gleeson and Axford independently re-derived the transport equation for cosmic rays in 1967, commencing from a Boltzmann-type equation specifically tailored for radial

geometry The resultant cosmic ray transport equation formulated by Gleeson and Axford in 1967 [18] takes on the form:

$\frac{1}{r^2}\frac{\partial}{\partial r}[r^2\sigma(E)] = -\frac{1}{3G}\frac{\partial^2}{\partial r \partial E}[a_{rel}EF(E)]$ (3)

$\sigma(E) = \sigma(r, E)$denotes the radial differential current density or streaming

$S_E = GF(E) - l\frac{\partial F(E)}{\partial r} - \frac{G}{3}\frac{\partial}{\partial E}(a_{rel}EF(E))$ (4)

The cosmic ray transport equation for the differential number density $F(E)$ is obtained by eliminating the streaming term $\sigma(E)$ between equations (3) and (4). Equation (2), describing the cosmic ray transport, was derived by Parker in 1965 [9], utilizing the concept of adiabatic deceleration. Conversely, Gleeson and Axford in 1967 [18] formulated equations (3) and (4) based on the concept of radially moving magnetic "scatterers" [19].

Under the assumptions of constant values for G and a_{rel}, along with $l = l_0E^{\alpha}r^{\beta}$, where α and β are parameters and β> 1, and considering F(r, E) → $AE^{-\gamma}$ as r → ∞, Axford and Fisk in 1969 [1] demonstrated that when S(E) ≈ 0; equation (4) could be directly solved for the number density F(E).

$F(E) = AE^{-\gamma}(1 - \frac{\alpha a_{rel}.G.r}{3(1-\beta)l_0E^{\alpha}r^{\beta}})^{\frac{[1+\frac{a_{rel}(\gamma-1)}{3}]}{-\frac{\alpha a_{rel}}{3}}}$ (5)

$F(E) = AE^{-\gamma}\varphi(E)$ (5i)

Where $\varphi(E) = (1 - \frac{\alpha a_{rel}.G.r}{3(1-\beta)l_0E^{\alpha}r^{\beta}})^{\frac{[1+\frac{a_{rel}(\gamma-1)}{3}]}{-\frac{\alpha a_{rel}}{3}}}$ (6)

The functional representation $\varphi(E)$ within the aforementioned equation has found extensive application across multiple research endeavors [5, 7, 20, 21, 22]. Various research groups have employed this functional form in constructing semi-empirical models aimed at delineating the time-dependent energy spectra of galactic cosmic rays [23]. This functional form, shared among different studies, serves as a cornerstone for modeling the intricate energy spectra of galactic cosmic rays over time. Additionally, a similar function with analogous characteristics is integrated into the model presented below.

Empirical Modelling of Galactic Cosmic Ray Spectrum Across the Eleven-Year Solar Cycle

The relationship between the differential cosmic ray intensity *D*(*E*), unmodulated GCR spectrum $D_0(E)$, and the differential number density F_T as a function of particle energy E

The galactic cosmic ray's differential spectrum *D*(*E*), incorporating variations due to solar activity, is defined by the equation.

$D(E) = D_0(E)\ (1 + \frac{a}{E})^{-\omega}$ (7)

Where $D_0(E)$ represents the unmodulated GCR spectrum (LIS) concerning the particle's kinetic energy E, and the parameters a and ω depend on the level of solar activity.

The relationship between the differential cosmic ray intensity *D*(*E*) and the differential number density F(E) in terms of particle energy E is expressed as

$D(E) = \frac{vF(E)}{4\pi}$ (8)

Where, v represents the Cosmic Rays Speed. Then,

$\frac{D(E)}{D_0(E)} = \frac{F(E)}{F_0(E)}$; (9)

$F_0(E) = AE^{-\gamma}$ (10)

From equations (8), (9) and (10) by assuming that $\tau = \frac{v}{c}$, c is the velocity of light, to get

$D_0(E) = \frac{vAE^{-\gamma}}{4\pi} = \frac{\tau cAE^{-\gamma}}{4\pi}$ (11)

Put $M = \frac{cA}{4\pi}$ in equation (11) to get the equation for LIS

$D_0(E) = M\,\tau E^{-\gamma}$ (12)

This equation characterizes the unmodulated spectra (LIS) concerning particle energy E, indicating a power-law relationship with E raised to the power of $-\gamma$. Furthermore, considering parameters α =1 and *r*=1 AU in equation (5) and aligning it with equation (9) and (10), equation (6) adopts a similar format to equation (5). The model equation for calculating GCR proton and helium fluxes at 1 AU, considering solar modulation, adopts the form

$D_{(p,He)}(E) = D_{0(p,He)}(E)\left(1 + \frac{a_{(p,He)}}{E}\right)^{-\Delta_{(p,He)}}$ (13)

Here, $a_{(p,He)}$ and $\Delta_{(p,He)}$are parameters reliant on the particle type (protons, helium nuclei) and solar activity level. The LIS spectra of individual particle species *i* follow a similar power-law structure

$D_{0,i}(E) = M_i \tau_i E^{-\gamma_i}$; i = (p, He) (14)

This representation emphasizes the dependence of the GCR fluxes on particle type and solar activity, mirroring a power-law relationship with E raised to $-\gamma_i$.

The parameters$M_i$and $\gamma_i$uniquely characterize the charged particle type (protons, helium nuclei). The values of M_i and $\gamma_i$exclusively depend on the particle species and remain constant for each type throughout the analysis.

The formulation of $\tau_i$for each particle type, such as protons (mass of Helium =0.938 GeV) and helium nuclei (=0.939 GeV/nucleon), is expressed as

$\tau_i = \frac{\sqrt{E(E+2m_i)}}{E+m_i}$, $m_i$is the rest mass of the particle (15)

The proposed model equation (13) aptly characterizes the energy spectra of protons and helium nuclei within the energy range spanning approximately 100 MeV to 100 GeV over the entire solar cycle. This model comprehensively accounts for the fluctuation in solar activity, providing insights into the varying intensities of protons and helium nuclei across thisenergy spectrum during the solar cycle.

RESULTS AND DISCUSSIONS

In Figure 1, the energy spectra of protons (red) and helium nuclei (blue) are depicted, revealing a consistent trend of diminishing spectral intensity with increasing particle energy, aligning with anticipated cosmic ray behaviour. Figure 2 portrays the nuanced variation in cosmic ray intensity over an 11-year solar cycle, demonstrating periodic undulations synchronized with solar activity. Figures 3 to 5 utilize different visualization techniques to unravel patterns within data: a histogram (Figure 3) captures frequency distribution, a bar graph (Figure 4) compares numerical values across categories, and a pie chart (Figure 5) conveys proportional sizes of distinct slices. Figure 6 delves into simulated cosmic ray spectra. The unmodulated spectrum (D_0, blue line) exhibits decreasing intensity with rising particle energy. The modulated spectrum (D, red line) introduces solar modulation effects (α and Δ), showcasing intensity variations across energy levels. While based on simulated data, this underscores the need for empirical validations and comparisons with observed data for a profound understanding of cosmic ray dynamics. Adjustments and cross-referencing with real-world data remain paramount for meaningful insights.

CONCLUSION

The fluctuations observed in cosmic ray intensities are a direct outcome of the intricate interplay between galactic cosmic rays and the dynamic solar magnetic field, which continually deflects these cosmic particles. As the solar wind carries the altered cosmic rays away from the Sun, variations in the intensity of galactic cosmic rays reach Earth. These variations exhibit a periodic pattern correlated with solar activity, notably reflected by the sunspot number, typically recurring over an approximate 11-year cycle. Moreover, the amplitude of these variations tends to amplify as particle rigidity decreases. The transport dynamics of galactic cosmic rays within the heliosphere find a comprehensive explanation through the cosmic ray transport equation [9]. This paper delves into the discussion of an approximate solution proposed by Fisk and Axford in 1969 [1] concerning the cosmic ray transport equation. This solution serves as the foundation of a simplified model delineating the spectrum of galactic cosmic rays. Specifically, this model aims to describe the spectral compositions of protons and helium nuclei amidst the 11-year solar cycle within interplanetary space at a distance of approximately 1 AU. The forthcoming work will involve the rigorous fitting of the proposed model equation to empirical data and theoretical computations, which will significantly contribute to validating and refining the model's accuracy and predictive capabilities. The simulated cosmic ray spectra exhibit characteristic behaviour where the intensity of cosmic rays varies inversely with particle energy in the unmodulated spectrum (D_0). This aligns with anticipated patterns observed in cosmic ray spectra, showing a decrease in intensity with increasing particle energy. The modulated spectrum (D) exemplifies the impact of solar

modulation represented by the parameters alpha (α) and delta (Δ) in the equation. These parameters influence the intensity variations with respect to particle energy, signifying the role of solar activity in modulating cosmic ray spectra. Scatter plots or intensity variation graphs over the solar cycle (not explicitly shown in the simulated data) illustrate periodic fluctuations in cosmic ray intensity. This cyclic variation corresponds to the changes in solar activity, exemplifying the connection between the solar cycle and cosmic ray intensities. The discussions and conclusions drawn are based on simulated data and equations. They serve as illustrative examples to demonstrate expected behaviours and relationships in cosmic ray spectra. Real cosmic ray studies often involve empirical observations, precise measurements, and detailed analyses, which must be considered for more accurate interpretations. In essence, while the simulated data and discussions provide fundamental insights into cosmic ray behaviour, real-world observations and empirical data are crucial for comprehensive and precise conclusions about the complex nature of cosmic rays, their modulation by solar activity, and their implications on space environment and related phenomena.

Nomenclature

Conflicts of Interest

Authors declared that there is no Conflicts of interest

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Table:1 Nomenclature

S. No.	Symbol / Abbreviation	Definition / Representation
1	AU	Astronomical Unit
2	ISS	International Space Station
3	CR	Cosmic Rays
4	GCR	Galactic Cosmic Rays
5	HMF	Helio Magnetic Field
6	HCS	Helio-spheric Current Sheet
7	LIS	Local Interstellar Spectrum
8	GeV	Giga electron Volts
9	MeV	Mega electron Volts
10	α	Solar Modulation Parameter
11	Δ	Solar Modulation Parameter
12	F	Differential Number Density
13	E	Kinetic Energy
14	t	Time
15	r	Helio-Centric
16	G	Solar Wind Speed
17	l	Particle Diffusion Coefficient
18	E_0	Particle's Rest Energy
19	α and β	Constant Parameters
20	a_{rel}	Troublesome Parameter
21	$\sigma(E)$	Radial differential current density or Streaming
22	$D(E)$	Galactic Cosmic ray's differential spectrum
23	m_i	Rest mass of the particle

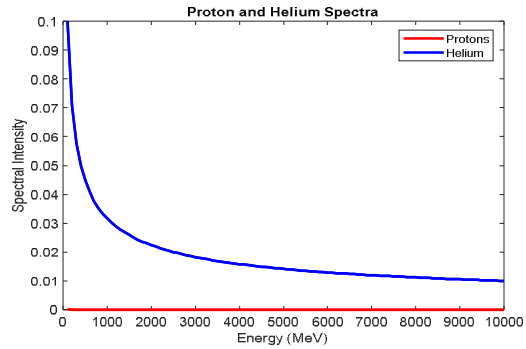

Figure 1: Proton and Helium Spectra

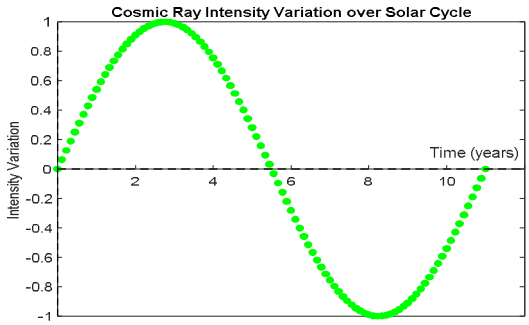

Figure 2: Cosmic Ray Intensity Variation over Solar Cycle

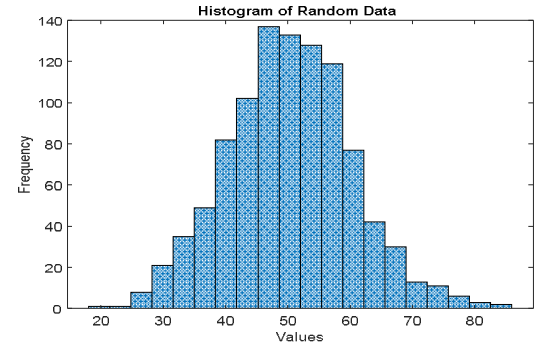

Figure 3: Histogram of Random Data

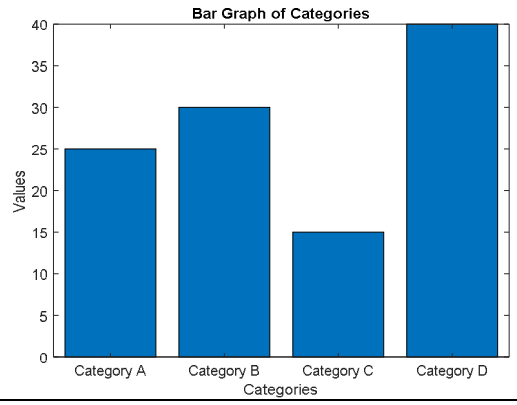

Figure 4: Bar Graph of Categories

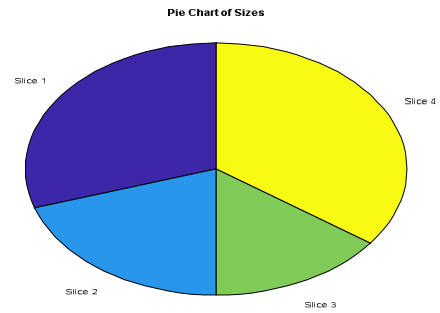

Figure 5: Pie Chart of Sizes

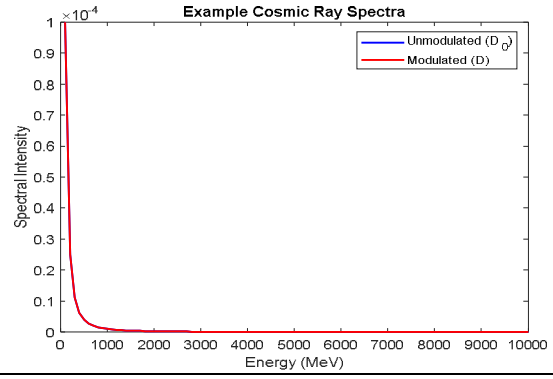

Figure 6: Example of Cosmic Ray Spectra