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RESEARCH ARTICLE

One Pot Green Synthesis of Biginelli Reaction Catalyzed by Novel Chitosan Immobilized Ionic liquid

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ABSTRACT

Chitosan–immobilized ionic liquid [DSIM][$AlCl_3$]$_x$-@CS(CSIL) has been synthesized at ambient temperature and used as a catalyst for synthesis of 3,4-dihydropyrimidine-2-(1H)-ones (DHPMs) via one-pot three component Biginelli reaction. The satisfactory results were obtained with good yields, shorter reaction time and simplicity in the experimental procedure. The catalysts could be recycled and reused six times without decrease in the catalytic activity.

Keywords: One-pot synthesis,3,4-dihydropyrimidine-2-(1H)-ones (DHPMs), Biginelli reaction, Chitosan – ImmobilizedIonic liquid

INTRODUCTION

Over the last decades, the interest in the synthesis of 3,4-dihydropyrimidine-2-(1H)-ones (DHPMs) and their derivatives are predominately increasing due to their therapeutic action, pharmaceutical properties. It also exhibits a wide range of biological activities such as antiviral, antibacterial and antihypertensive agents [1-3]. Moreover, these compounds, have emerged as the integral backbones of several calcium channel blockers [4]. Some marine alkaloids containing the dihydropyridine core unit show interesting biological properties, batzelladine alkaloids are potent HIV gp-120-CD4 inhibitors [5,6]. The most simple and straightforward procedure for the synthesis of DHPMs was first reported by the Italian chemist Pietro Biginelli in 1893, it involves a three-component one-pot condensation of benzaldehyde, ethyl acetoacetate and urea under strongly acidic conditions [7]. However, this reaction usually requires harsh conditions, long reaction times and low yields. To modify such a traditional reaction significant research has been carried out in the last decades. It involves modification in reaction procedure like as microwave irradiation [8,9] ultrasound irradiation [10,11], complex reaction [12] and varieties of catalysts such as nanoparticles [13,14], lathanide triflate [15], H_3BO_3 [16], VCl_3 [17], $Sr(OTf)_2$ [18], PPh_3 [19], Indium(III) halides [20], $Ca(NO_3)_2.4H_2O$

[21], L-proline[22] and Ascorbic acid[23] were proclaimed. However, despite their potential utility, many of these reported one-pot protocols suffer from drawbacks such as the use of expensive reagents, volatile strong acidic conditions and long reaction times. Therefore, to avoid these limitations, the introduction of a milder and more efficient approach accompanied with higher yields is needed. Over the last decades, the popularity of ionic liquids (ILs) has significantly increased because of their unique properties such as non-flammability, non-volatility, low vapor pressure, high chemical, and thermal stability, environmental compatibility, high selectivity, potential recoverability and so forth. Because of these qualities, ILs have been extensively employed in organic synthesis as green solvents and reagents [24] catalysis [25] electrochemistry [26] and liquid−liquid extractions [27]. Among the ILs, sulfonic acid-functionalized imidazolium salts have been used as homogeneous catalysts in various organic transformations such as protection of hydroxyl groups [28], nitration of phenols [29] synthesis of N-sulfonyl imines [30], bis(indolyl)methanes [31] benzimidazoles [32] and so forth. Using homogeneous catalysts, it has some drawbacks like producing a large amount of waste materials. It is unacceptable from an environmental point of view. To avoid such drawback, various ILs have been immobilized on a solid support to combine the advantages of ILs and heterogeneous materials. In the present era chitosan [33], zeolite[34], silica[35] have been used as solid support for ILs and used as heterogeneous catalysts. Due to the presence of hydroxyl and amino groups in chitosan [36-38], It shows unique properties such as three-dimensional structure, biodegradable nature, chelating nature, mechanical strength, and chemical reactivity. Solid- supported ILs based catalyst has been widely used in different organic reactions such as Knoevenagel-Michael cyclization [39], Aldol condensation [40], Mizoroki-Heck and Sonogashira reactions [41], Suzuki-Miyaura and Heck cross-coupling reactions [42]. Herein, In this present article, we have reported chitosan-supported Ionic liquid (CSIL) [43] catalyzed one-pot three-component Biginelli reaction, at ambient temperature.

MATERIALS AND METHODS

Materials

All chemicals were of research grade and were used as obtained. Melting points were measured in open capillaries and are uncorrected. TLC was performed on Silica Gel 60 F_{254} pre-coated plates (Merck). IR spectra were recorded on a FT IR Perkin Elmer Spectrum 100 spectrometer, mass spectra on a Shimadzu LCMS 2010 spectrometer, and elemental analysis on Perkin Elmer PE 2400 elemental analyzer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 400 MHz instrument with TMS as an internal standard. The IL [DSIM]Cl^- was prepared according to the procedure reported in literature [43].

General procedure

The mixture of benzaldehyde (1 mmol), ethyl acetoacetate (1.3 mmol), urea (2 mmol) and CSIL (50 mg)were charged into a 50 mL RBF with magnetic stirring bar. The reaction mixture was heated at 90 °C for the time reported in Table 3. The progress of reaction was monitored by TLC using hexane: ethylacetate (50:50). After completion of reaction, the reaction mass was extracted with ethylacetate. The catalyst was recovered and wash with ethanol to remove trace amount of reactants and dried in an oven for reuse. The ethyl acetate layer was distilled and pure product (4a-4p) was isolated and recrystallized with alcohol to afford pure 3,4-dihydropyrimidin-2-(1H)-ones 4.The products were identified by IR, ^{1}H NMR, and physical data (mp) by comparison with those reported in the literatures.

Spectral data for selected DHPMs

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (**4a**)

IR (KBr) νmax/cm-1: 3235, 2956, 1735, 1692, 1208, 700; ^{1}H NMR: d 9.22 (s, 1H), 7.76 (s,1H), 7.26 (m, 5H), 5.12 (s, 1H), 4.00 (q, J 7.1 Hz, 2H), 2.28 (s, 3H), 1.12 (t,J 7.1 Hz, 3H); ^{13}C NMR: d 13.8, 18.0, 53.6, 59.8, 98.2, 123.1, 126.1, 128.7, 144.8, 148.8, 152.5, 165.7. Calc. For$C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.61;H, 6.18; N, 10.74. MS: 261 (M+1).

RESULT AND DISCUSSIONS

At the beginning of this study, we examined the effect of the catalyst under different conditions. we carried out the reaction of benzaldehyde, ethyl acetoacetate and urea as a model reaction (Scheme 1).

Catalyst loading

The model reaction was screened by a different amount of catalyst loading. The results are presented in Table 1. In the absence of CSIL, no targeted product could be obtained, which indicated that the catalyst should be necessary for the Biginelli reaction (Table 1, entry 1). We also check the feasibility of the reaction in the presence of chitosan, we got only 70 % yield (Table 1, entry 2).

Our next object to examine the effect of the amount of CSIL on the model reaction (Table 1, entry 3-7). 30 mg of CSIL afforded the best results (entry 5). The higher amount of the catalyst did not improve the yield. Then, the influence of the reaction time on the yield was monitored (entries 8-11). It was found that higher yield was obtained when the reaction time was 30 min (Table 1, entry 10). The influence of the reaction temperature on the yield was investigated subsequently (entries 12-13). It was found that 90 °C was still the best reaction temperature (Table 1, entry 10). The present CSILs catalyst is extremely attractive for producing DHPMs of biological and pharmacological interest. Also, yields obtained for CSILs towards Biginelli reaction is better than or comparable with the literature reports (Table 2). We also perform a comparison study with different supported catalysts (Table 2, entry 1-6). And we summarize that CSIL performs adequately with high yield with low catalyst loading.

A series of DHPMs were synthesized with optimized conditions. The results are tabulated in Table 3. In all cases studied, the three-component reaction proceeded smoothly to give the corresponding DHPMs in excellent yields. Most importantly, aromatic aldehydes carrying either electron-donating or electron-withdrawing substituents reacted very well to give the corresponding DHPMs with high purity in good yields. Notably, this procedure is compatible with a wide range of functional groups such as methoxy, halides, nitro, and hydroxyl. When optimizing the reaction conditions, the recycling performance of CSIL was investigated in the model reaction. After the separation of the products, the filtrate containing the catalyst was reused in the next run without urification. A model reaction was run under the same conditions. The data listed in Table 4 showed that the CSIL could be reused six times without lowering the catalytic activity. Compared with the traditional solvents and catalysts, the easy recycling performance is an attractive property of the CSIL for the environmental protection and economic reasons.

CONCLUSIONS

We have demonstrated the utility of Chitosan – immobilized ionic liquid [DSIM][$AlCl_3$]x-@CS(CSIL)in Biginelli reaction. This IL obviates the need for an additional catalyst and has allowed the preparation of a range of 3,4-ihydropyrimidin-2-(1H)-ones/thionsin good to excellent yields (82–96%). This procedure permits recycling of the IL with almost retention in activity. On the basis of these current efforts, it is likely that a number of organic reactions could be performed equally well or perhaps even more effectively using this ionic liquid. Studies to determine the applicability to other catalytic reactions are currently underway in our laboratory.

REFERENCES

1. Kappe,C.O., “Recent Advances in the Biginelli Dihydropyrimidine Synthesis. New tricks from an old dog”. Account of chemical research, 2000, 33(12), 879-888.
2. Kappe, C.O., “Biologically active dihydropyrimidones of the Biginelli-type- a literature survey”. European Journal of Medicinal Chemistry, 2000, 35(12), 1043-1052.

3. Canto,R.F.S., Bernardi,A., Battastini,A.M.O., Russowsky, D., Eifler-Lim,V.L., "Synthesis of dihydropyrimidin-2-one/thione library and cytotoxic activity against the human U138-MG and Rat C6 glioma cell lines". Journal of the Brazilian Chemical Society, 2011, 22(7), 1379-1388.
4. Atwal,K.S., Rovnyak,G.C., Kimball,S.D., Floyd,D.M., Moreland, S., Swanson,B.N., Gougoutas,J.Z., Schwartz,J., Smillie, K.M., Malley, M.F., "Dihydropyrimidine calcium channel blockers. II. 3-Substituted-4-aryl-1,4-dihydro-6-methyl-5-pyrimidinecarboxylic acid esters as potent mimics of dihydropyridines", Journal of Medicinal Chemistry, 1990, 33(9), 2629-2635.
5. Patil,A.D., Kumar,N.V., Kokke,W.C., Bean,M.F., Freyer,A.J., Brosse,C.D., Mai,S., Truneh,A., Faulkner, D.J., Carte,B., "Novel Alkaloids from the Sponge Batzella sp.: Inhibitors of HIV gp120-Human CD4 Binding", The Journal of Organic Chemistry, 1995, 60(5), 1182-1188.
6. Snider,B.B., Chen,J., Patil, A.D., Freyer,A.J., "Synthesis of the tricyclic portions of batzelladines A, B and D. Revision of the stereochemistry of batzelladines A and D", Tetrahedron Letters, 1996, 37(39), 6977-6980.
7. Biginelli, P.,Gazz,P.,"Synthesis of 3,4-Dihydropyrimidin-2(1H)-Ones",Chem. Ital, 1893, 23,360-372.
8. Banik,B.K., Reddy,A.T., Datta, A., Mukhopadhyay,C., "Microwave-induced bismuth nitrate-catalyzed synthesis of dihydropyrimidones via Biginelli condensation under solventlessconditions",Tetrahedron Letters, 2007, 48(41), 7392-7394.
9. Safari, J., Gandomi-Ravandi,S., "Titanium dioxide supported on MWCNTs as an eco-friendly catalyst in the synthesis of 3,4-dihydropyrimidin-2-(1H)-ones accelerated under microwave irradiation",New Journal of Chemistry, 2014, 38, 3514-3521.
10. Li,J.T., Han,J.F., Yang, J.H., Li,T.S., "An efficient synthesis of 3,4-dihydropyrimidin-2-ones catalyzed by NH_2SO_3H under ultrasound irradiation". Ultrasonics Sonochemistry", 2003, 10(3), 119-122.
11. Wang, Q., Pei,W., "Synthesis of 3,4-dihydropyrimidin-2(1H)-ones catalyzed by nafion-H under ultrasound irradiation and solvent-free conditions",Journal of the Iranian Chemical Society, 2010, 7, 318-321.
12. Karthikeyan,P., Aswar,S.A., Muskawar,P.N., Bhagat, P.R., Kumar,S.S., "Development and efficient 1-glycyl-3-methyl imidazolium chloride–copper(II) complex catalyzed highly enantioselective synthesis of 3, 4-dihydropyrimidin-2(1H)-ones", Journal of Organometallic Chemistry, 2013, 723, 154-162.
13. Zamani, F., Izadi,E., "Synthesis and characterization of sulfonated-phenylacetic acid coated Fe3O4 nanoparticles as a novel acid magnetic catalyst for Biginelli reaction", "Catalysis Communications", 2013, 42, 104-108.
14. Keivanloo,A., Mirzaee,M., Bakherad, M., Soozani,A., "Boehmite nanoparticle catalyst for the one-pot multicomponent synthesis of 3,4-dihydropyrimidin-2-(1H)-ones and thiones under solvent-free conditions", "Chinese Journal of Catalysis", 2014, 35(3), 362-367.
15. Ma,Y., Qian,C., Wang, L., Yang,M., "Lanthanide Triflate Catalyzed Biginelli Reaction. One-Pot Synthesis of Dihydropyrimidinones under Solvent-Free Conditions", The Journal of Organic Chemistry, 2000, 65(12), 3864-3868.
16. Tu,S., Fang,F., Miao,C., Jiang,H., Feng,Y., Shi, D., Wang,X., "One-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones using boric acid as catalyst", Tetrahedron Letters, 2003, 44(32), 6153-6155.
17. Sabitha,G., Reddy,G.S. K.K., Reddy, K.B., Yadav,J.S., "Vanadium(III) chloride catalyzed Biginelli condensation: solution phase library generation of dihydropyrimidin-(2H)-ones", Tetrahedron Letters, 2003, 44(34), 6497-6499.
18. Su,W., Li,J., Zheng, Z., Shen,Y., "One-pot synthesis of dihydropyrimidiones catalyzed by strontium(II) triflate under solvent-free conditions", Tetrahedron Letters, 2005, 46(36), 6037-6040.
19. Debache,A., Amimour,M., Belfaitah,A., Rhouati, S., Carboni,B., "A one-pot Biginelli synthesis of 3,4-dihydropyrimidin-2-(1H)-ones/thiones catalyzed by triphenylphosphine as Lewis base", Tetrahedron Letters, 2008, 49(42), 6119-6121.
20. Fu,N.Y., Yuan,Y.F., Pang,M.L., Wang, J.T., Peppe,C., "Indium(III) halides-catalyzed preparation of ferrocene-dihydropyrimidinones", Journal of Organometallic Chemistry, 2003, 672(1-2), 52-57.
21. Debache,A., Boulcina,R., Tafer,R., Belfaitah,A., Rhouati, S., Carboni,B., " $Ca(NO3)2{\cdot}4H2O$-catalysed Biginelli Reaction: One-pot Synthesis of 1,2,3,4-Tetrahydropyrimidin-2-ones/pyrimidine-2-thiones under Solvent-free Conditions", Chinese Journal of Chemistry, 2008, 26(11), 2112-2116.

22. Yadav, J. S., PraveenKumar, S., Kondaji,G., Radmisettiand, S., Nagaiah, K., "A Novel L-Proline CatalyzedBiginelli Reaction: One-Pot Synthesis of 3,4-Dihydropyrimidin-2(1H)-ones under Solvent-Free Conditions", Chemistry Letters, 2004, 33(9), 1168-1169.
23. Sehout,I., Boulcina,R., Boumoud,B., Berree,F., Carboni, B., Debache,A., "Ascorbic acid-Catalyzed One-Pot Three-Component Biginelli Reaction: A Practical and Green Approach towards Synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones", Letters in Organic Chemistry, 2013, 10(7), 463-467.
24. Antonietti,M., Kuang,D., Smarsly, B., Zhou,Y., "Ionic Liquids for the Convenient Synthesis of Functional Nanoparticles and Other Inorganic Nanostructures", Angewandte International Edition Chemie, 2004, 43(38), 4988-4992.
25. Zhao,D., Wu,M., Kouand, Y., Min,E., "Room-Temperature Ionic Liquids. Solvents for Synthesis and Catalysis", Chemical Reviews, 1999, 99(8), 2071-2084.
26. Buzzeo,M. C., Evans, R. G., Compton,R. G., "Non-Haloaluminate Room-Temperature Ionic Liquids in Electrochemistry—A Review", ChemPhysChem, 2004, 5(8), 1106-1120.
27. Fadeev, A. G., Meagher,M. M., "Opportunities for ionic liquids in recovery of biofuels", Chemical Communications, 2001, 3, 295-296.
28. Khaligh,N. G., "Preparation, characterization and use of 3-methyl-1-sulfonic acid imidazolium hydrogen sulfate as an eco-benign, efficient and reusable ionic liquid catalyst for the chemoselective trimethylsilyl protection of hydroxyl groups", Journal of Molecular catalysis A: Chemical, 2011, 349(1-2), 63-70.
29. Zolfigol, M.A., Khazaei, A., Moosavi-Zare, A.R., Zare, A., Kruger, H.G., Asgari, Z., Khakyzadeh, V., Kazem-Rostami, M., "Design of Ionic Liquid 3-Methyl-1-sulfonic Acid Imidazolium Nitrate as Reagent for the Nitration of Aromatic Compounds by in Situ Generation of NO2 in Acidic Media", The Journal of Organic Chemistry, 2012, 77(7), 3640-3645.
30. Zolfigol,M. A., Khazaei,A., Moosavi-Zareand, A. R., Zare,A., "3-Methyl-1-Sulfonic acid imidazolium chloride as a new, efficient and recyclable catalyst and solvent for the preparation of N-sulfonyl imines at room temperature", Journal of the Iranian Chemical Society" 2010, 7, 646-651.
31. Zolfigol,M. A., Khazaei,A., Moosavi-Zareand, A. R., Zare,A., " Ionic Liquid 3-Methyl-1-sulfonic Acid Imidazolium Chloride as a Novel and Highly Efficient Catalyst for the Very Rapid Synthesis of bis(Indolyl)methanes under Solvent-free Conditions", Organic Preparations and Procedures International, 2010, 42(1), 95-102.
32. Khazaei,A., Zolfigol,M. A., Moosavi-Zareand, A. R., Zare,A., Ghaemi,E., Khakyzadeh**,**V., Asgari,Z., Hasaninejad,A., "Sulfonic acid functionalized imidazolium salts/ FeCl3 as novel and highly efficient catalytic systems for the synthesis of benzimidazoles at room temperature" Scientia Iranica, 2011, 18(6), 1365-1371.
33. Khalafi-Nezhad, A., Mohammadi,S., "Chitosan supported ionic liquid: a recyclable wet and dry catalyst for the direct conversion of aldehydes into nitriles and amides under mild conditions", RSC Advances, 2014, 4, 13782-13787.
34. Arya,K., Rawat, D. S., Sasai,H., "Zeolite supported Brønsted-acid ionic liquids: an ecoapproach for synthesis of spiro[indole-pyrido[3,2-e]thiazine] in water under ultrasonication", Journal of Green Chemistry, 2012, 14, 1956-1963.
35. Feher,C., Krivan,E., Hancsok, J., Skoda-Foldes,R., "Oligomerisation of Isobutene with Silica Supported Ionic Liquid Catalysts", Journal of Green Chemistry, 2012, 14, 403-410.
36. Xiao,L.-F., Li, F.-W., Xia,C.-G., "An easily recoverable and efficient natural biopolymer-supported zinc chloride catalyst system for the chemical fixation of carbon dioxide to cyclic carbonate", Journal of Applied Catalysis A: General, 2005, 279(1-2), 125-129.
37. Guibal,E., "Heterogeneous catalysis on chitosan-based materials: a review", Journal of Progress in Polymer Science, 2005, 30(1), 71-109.
38. Hardy,J. J. E., Hubert,S., Macquarrie, D. J., Wilson,A., "Chitosan-based heterogeneous catalysts for Suzuki and Heck reactions", Journal of Green Chemistry, 2004, 6, 53-56.
39. Rostamnia,S., Hassankhan,A., Hossieni,H. G., Gholipour, B., Xin,H., "Brønsted acidic hydrogensulfate ionic liquid immobilized SBA-15: [MPIm][HSO4]@SBA-15 as an environmentally friendly, metal- and halogen-free

recyclable catalyst for Knoevenagel–Michael-cyclization processes", Journal of Molecular Catalysis A: Chemical, 2014, 395, 463-469.

40. Cota,I., Medina,F., Gonzalez-Olmos,R., Iglesias,M., "Alanine-supported protic ionic liquids as efficient catalysts for aldol condensation reactions", Comptes Rendus Chimie, 2014, 17(1), 18-22.
41. Singh,V., Ratti,R., Kaur,S., "Synthesis and characterization of recyclable and recoverable MMT-clay exchanged ammonium tagged carbapalladacycle catalyst for Mizoroki–Heck and Sonogashira reactions in ionic liquid media", Journal of Molecular Catalysis A: Chemical, 2011, 334(1-2), 13-19.
42. Makhubela,B. C. E., Jardine,A., Smith,G. S., "Pd nanosized particles supported on chitosan and 6-deoxy-6-amino chitosan as recyclable catalysts for Suzuki–Miyauraand Heck cross-coupling reactions" Journal of Applied Catalysis A: General, 2010, 393(1-2), 231-241.
43. Khan,M. U., Siddiqui, S., Siddiqui,Z. N., "Novel Ionic Liquid-Functionalized Chitosan [DSIM][AlCl3]x–@CS: Synthesis, Characterization, and Catalytic Application for Preparation of Substituted Pyrazine Derivatives", ACS Omega, 2019, 4(4), 7586-7595.
44. Quan,Z. J., Da,Y. X., Zhang, Z., Wang, X. C., "PS–PEG–SO3H as an efficient catalyst for 3,4-dihydropyrimidones via Biginelli reaction", Journal of Catalysis Communications, 2009, 10(8), 1146-1148.
45. Lei,M., Wu,D., Wei, H., Wang,Y., "Polymer-Supported 4-Aminoformoyldiphenylammonium Triflate (PS-AFDPAT): An Effective and Recyclable Catalyst for the Biginelli Reaction", Journal of Synthetic Communications, 2009, 39, 475-483.
46. Shi,X. L., Yang,H., Tao, M., Zhang,W., "Sulfonic acid-functionalized polypropylene fiber: highly efficient and recyclable heterogeneous Brønsted acid catalyst"Journal of RSC Advances, 2013, 3, 3939-3945.
47. Mahdavinia, G. H., Sepehrian,H., "MCM-41 anchored sulfonic acid (MCM-41-R-SO3H): A mild, reusable and highly efficient heterogeneous catalyst for the Biginelli reaction", Journal of Chinese Chemical Letters, 2008, 19(12), 1435-1439.
48. Khiratkara,A. G., Muskawarb, P. N., Bhagat,P. R., "Polymer-supported benzimidazolium based ionic liquid: an efficient and reusable Brønsted acid catalyst for Biginelli reaction", Journal of RSC Advances, 2016, 6, 105087-105093.

Table 1. Effect of catalyst CSIL under different reaction conditions for condensation of benzaldehyde, ethyl acetoacetate and urea.

Entry	Catalyst (mg)	Time (min.)	Temp.(ºC)	Isolated Yield (%)
1	No catalyst	40	90	0
2	Chitosan	40	90	70
3	CSIL (10)	40	90	75
4	CSIL (20)	40	90	86
5	**CSIL (30)**	**40**	**90**	**96**
6	CSIL (40)	40	90	94
7	CSIL (50)	40	90	94
8	CSIL(30)	10	90	86
9	CSIL (30)	20	90	92
10	**CSIL(30)**	**30**	**90**	**96**
11	CSIL (30)	40	90	94
12	CSIL (30)	30	80	92
13	CSIL (30)	30	100	89

Table 2: Comparison study

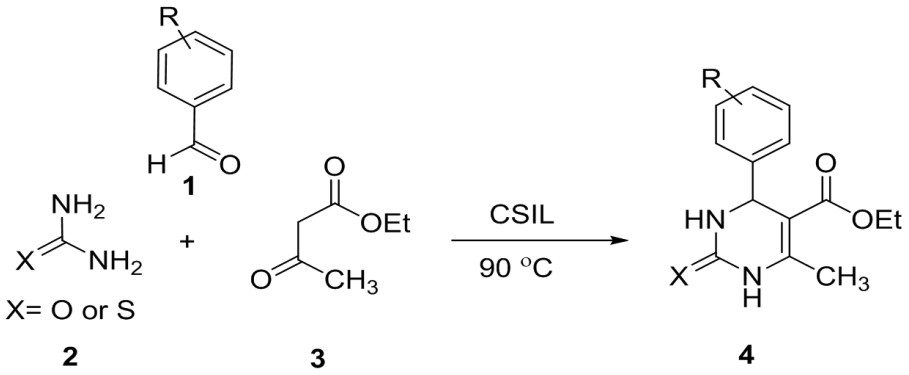
Entry	Heterogenous Catalyst	Amount of Catalyst (mg)	% Yield	Ref.
1	PS-PEG-OSO_3H	300	79	44
2	PS-AFDPAT	650	94	45
3	PPF-SO_3H	250	89	46
4	(MCM-41-R-SO_3H)	100	94	47
5	PSBIL	50	92	48
6	CSIL	50	96	Present Work

Table 3 CSIL catalysed one-pot synthesis of 3,4-dihydropyrimidin-2(1H)ones/thiones

Entry	Compound	R_1	X	Time	% Yield	MP(°C)
1	4a	C_6H_5	O	40	96	233-235
2	4b	C_6H_5	S	40	94	189-191
3	4c	2-OH	O	35	88	238-240
4	4d	2-OH	S	40	90	242-244
5	4e	3-OH	O	45	90	234-236
6	4f	3-OH	S	45	92	210-212
7	4g	4-OH	O	35	85	230-232
8	4h	4-OH	S	40	86	219-221
9	4i	2-NO_2	O	35	96	228-230
10	4j	2-NO_2	S	35	95	245-247
11	4k	4-OCH_3	O	55	82	165-167
12	4l	4-OCH_3	S	55	84	170-172
13	4m	4-Cl	O	35	88	223-225
14	4n	4-Cl	S	30	86	189-191
15	4o	4-OH-3-OCH_3	O	45	88	245-247
16	4p	4-OH-3-OCH_3	S	40	88	224-226

Table 4 Catalytic reusability of the ionic liquids of CSIL.

Entry	Yield (%)
1	96
2	94
3	93
4	92
5	91
6	91



Scheme 1 CSIL Catalysed Biginelli reaction

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RESEARCH ARTICLE

Synthesis, Characterization and Spectroscopic Analysis of Chromium (III) Chelates Derived from Schiff Bases of 4-Benzoyl-3-methyl-1-(4-methylphenyl)-2-pyrazolin-5-One

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ABSTRACT

4-benzoyl-3-methyl-1-(4-methylphenyl)-2-pyrazolin-5-one (BMMP) and its schiff bases with aniline (A), o-chloroaniline (OCA), m-chloroaniline (MCA), p-chloroaniline (PCA), o-toluidine (OT), m-toluidine (MT), p-toluidine (PT) has been prepared and characterized. These schiff bases are used for the synthesis of seven Chromium(III)chelates. All the synthesized chelates were well characterized by IR, NMR, elemental analysis, magnetic properties and TGA.

Keywords: 4-benzoyl pyrazolones, Chromium(III)chelates.

INTRODUCTION

The 1-phenyl-2-pyrazolin-5-one derivatives react with acid chlorides to give substitution at 4th position of the pyrazolone, giving the 4-benzoyl pyrazolones. Number of schiff bases of 4-benzoyl pyrazolones has been studied for their metal complexation study [1-3]. 4-benzoyl pyrazolones have proven as versatile ligands in coordination chemistry as an –ON bidentate ligand [1–8]. Several reports in the literature on metal complexes of 4-benzoyl pyrazolones for d-block metals are available which display good anticancer, antimalarial, antifungal, antibacterial and catalytic activities [4-6]. To the best of our knowledge, the complexation of schiff bases of 4-benzoyl pyrazolones with chromium metal is not been reported yet. Herein, we report the first synthesis and spectroscopic characterization of Chromium (III) chelates of schiff bases of 4-benzoyl pyrazolones.

EXPERIMENTAL

Materials

All the chemicals used in the present study were of the best quality. Dioxane was obtained from E.Merck (india) Ltd., Bombay and used after purificatio [7]. Absolute alcohol obtained from Baroda Chem. Industry Ltd., Dabhoi, was used after distillation. All the amines were obtained from Sisco-Chem. Pvt. Ltd., Mumbai and used after purification. Calcium hydroxide and acetyl chloride were obtained from Samir Tech. Chem. Pvt. Ltd., Vadodara. Sodium acetate was obtained from Sarabhai. M. Chemicals Pvt. Ltd., Baroda. DMF was obtained from Spectrochem Pvt. Ltd., Bombay. All other chemicals used were of reagent grade. In the preparation of the metal chelates of the Cr(III), 1-(4-methylphenyl)-3-methyl-2-pyrazolin-5-one (MMP) was obtained, as a free gift sample from Shree Sidhdhanath Industries, Sachin, Surat.

Synthesis of Ligands

The ligands used in the present study were prepared in two steps:
Synthesis of 4-benzoyl-3-methyl-1-(4-methylphenyl)-2-pyrazolin-5-one (BMMP){8}.
Synthesis of Schiff bases of BMMP [9].

Synthesis of 4-benzoyl-3-methyl-1-(4-methylphenyl)-2-pyrazolin-5-one (BMMP)

The 3-methyl-1-(4-methylphenyl)-2-pyrazolin-5-one (MMP) (0.1 mole, 20.1 g) was placed in a flask equipped with a stirrer, seperating funnel and reflux condensor. It was then dissolved in dioxane (80 ml.) by application of heat. To the reaction mixture, calcium hydroxide (0.2 mole, 14.81 g) was added, followed by the dropwise addition of the benzoyl chloride (0.1 mole, 18.01 g). At this stage the mixture became a thick paste and its temperature also increased, as this being a exothermic reaction. The reaction mixture was then refluxed for half an hour. The resulting calcium complex was then decomposed by pouring it into the dilute hydrochloric acid (200 ml, 2M). The resultant coloured crystals were then collected on a Buchner-funnel and recrystalized from an acidified methanol-water mixture (Fig. 1).

Synthesis of Schiff bases of BMMP

An identical procedure has been followed in the preparation of all the Schiff bases used in the present study. They were prepared by refluxing the equimolar quantities of 4-benzoyl-3-methyl-1-(4-methylpheny)-2-pyrazolin-5-one (BMMP) with aniline (A), o-chloroaniline (OCA), m-chloroaniline (MCA), p-chloroaniline (PCA), o-toluidine (OT), m-toluidine (MT), p-toluidine (PT) in absolute alcohol for 2 hours. The products thus obtained were filtered and recrystalized from ethanol (Fig. 1). The physical properties of ligands are listed in Table 1.

Synthesis of the Chromium(III)chelates

Chromium (III) nitrate salt was dissolved in a minimum amount of hot ethanol. The hot ligand solution (in DMF) in slight excess over the required metal: ligand ratio, was added dropwise with constant stirring. To the resulting mixture 2 grams of sodium acetate was added and then the mixture was refluxed for 2 hours. The resulting mixture thus obtained was then concentrated to half of its original volume. The product was filtered and washed several times with hot water and finally with hot ethanol. The product was dried at 45ºC (Fig. 2). The yields of the chelates were almost quantitative.

RESULT AND DISCUSSION

All the synthesized Cr(III) Chelates were analyzed by their colour, composition, conductivity and magnetic properties.IR spectra and electronic spectra has been also measured for the synthesized chelates. The conductivity data of the chelates are listed in Tables 2. All the chelates have some solubility in DMF, in which the molar

conductance have been measured. The molar conductivities of the chelates are found to be lower than the reported range for the 1:1 electrolytes, indicating that they are non-electrolyte in nature.

Magnetic Properties

The room temperature magnetic moments of the chelates are given in Table 2. The magnetic moments of all the Cr(III) chelates are in the required range for high spin octahedral structure [10-15].

Infrared Spectra

The ligands used in the present study, can take any of the following forms (Fig. 1). [16-21]. The infrared spectra of all the ligands show medium broad band with some structures in the region 3600-3000 cm^{-1}, indicating the presence of strongly hydrogen bonded OH [22-24]. The ligands as well as chelates show absorption in the region 3000-2800 cm^{-1} which may be due to the ν_{C-H} [24-26]. The free ν_{OH} is generally found between 3650-3500 cm^{-1}, similar to that of alcoholic ν_{OH}. [27-28] The ν_{OH} of all the ligands show bands in the region 3500-3000 cm^{-1}. This indicates the involvement of a 5-OH group in the intramolecular or intermolecular hydrogen bonding with the π-electrons of the azomethine group and may also correlated with the lone pair of nitrogen[29, 30]. This also suggests that the ligands exist in the enol form (II) in the solid state [31-36]. All the ligands show fairly strong absorption band in the region 1280-1290 cm^{-1}, which may be due to the O-H deformation vibration in hydrogen bonded ring. On coordination this band disappears or its intensity decreases. This may be due to the deprotonation of the 5-OH group of the ligands[37-41].All the chelates show a characteristic band of intermediate intensity at ~ 1095 cm^{-1} which may be assigned to ν_{CO}[42-44]. On cordination this band is shifted towards higher frequency indicating that oxygen of the 5-OH group of the ligands has taken part in the coordination[45-46] .All the ligands show sharp and strong band due to the $\nu_{C=N}$ of the azomethine group at ~ 1620 cm^{-1}. The observed low energy shift of this band in the chelates suggests nitrogen coordination[47-48] .All the ligands as well as the chelates show band at ~1595 cm^{-1} due to $\nu_{C=N}$(cyclic). The $\nu_{C=N}$(cyclic) is observed at the same energy in all the chelates, indicating the non-participation of the cyclic nitrogen in the coordination[49-50].

Electronic Spectra

Six coordinated octahedral chelates of the chromium(III) show two spin-allowed d-d bands in the visible region.[51] The spectral data of all the chelates show (Table 3) two bands corresponding to the $^4A_{2g}$ (F) → $^4T_{2g}$ (F) (ν_1; ~ 17000 cm^{-1}) and $^4A_{2g}$ (F) → $^4T_{1g}$ (F) (ν_2; ~ 23000 cm^{-1}) transitions. The $^4A_{2g}$ (F) → $^4T_{1g}$ (P) (ν_3) transition is expected to appear above 30000 cm^{-1}[52-53]. It was possible to calculate the ν_3, B_{35} and β_{35} for each chelate using and observed ν_1 and ν_2 bands following the ligand-field theory of spin-allowed transitions[54]. The low values of β_{35} indicate the presence of π - as well as σ type delocalizations [55].An attempt has also been made to calculate the spin-orbit coupling constants using the following empirical expression[55-56].$\lambda = 0.0110 (B_{35} + 1.080)^3 + 0.0062$ γ values have also been obtained using the relation $\lambda/90$. The calculated values of λ and γ are given in Table 3. γ is a covalency parameter [57]. analogous to the nephelauxetic parameter β. The ligands used in the present study gives the following order for γ :BMMP-A ≅ BMMP-MT > BMMP-PT > BMMP-PCA > BMMP-OCA ≅ BMMP-MCA > BMMP-OT. The low values of λ, compared to the free ion value of 90 cm^{-1}, indicates fair amount of covalent character of the metal-ligand bond[58].

Thermo gravimetric analysis (TGA)

The TGA data provide an important experimental evidence in determining the number of water molecules present in the chelates. Number of water molecules present in the chelates were determined from the percentage weight loss of the chelate from the thermograms. A representative thermograms of some chelates are shown in Fig. 4. This group of the metal chelates is found to be stable up to 200°C without any weight loss. Then they undergo sudden decomposition, which might be due to the loss of the ligands. On the basis of TGA and analytical data of these chelates correspond to the general formula ML_3 group. All the thermograms of the Cr(III) chelates are of this nature.

CONCLUSION

A novel series of Chromium (III) chelates of schiff bases of 4-benzoyl pyrazolones has been synthesized and characterized. The protocol is found to be simple and highly efficient for the preparation of Chromium (III) chelates using simple synthetic methodology.

REFERENCES

1. J. Bailar; D. Busch. "The Chemistry of coordination Compounds", Reinhold Publishing Corporation, New York, (1956) 41.
2. G. Bamford; D. Lind. Proc.Roy.Soc.Ser.A., (1959) 02.
3. B. Jansen. Acta Chem.Scand, 13(1959) 1668.
4. F. Marchetti, J. Palmucci, C. Pettinari, R. Pettinari, S. Scuri, I. Grappasonni, M. Cocchioni, M. Amati, F. Lelj, A. Crispini, Inorg. Chem. 55 (2016) 5453.
5. Marchetti, C. Pettinari, R. Pettinari, Coord. Chem. Rev. 249 (2005) 2909.
6. J. Quirante, D. Ruiz, A. Gonzalez, C. Lopez, M. Cascante, R. Cortes, R. Messeguer, C. Calvis, L. Baldoma, A. Pascual, Y. Guerardel, B. Pradines, M. Font-Bardia, T. Calvet, C. Biot, J. Inorg. Biochem. 105 (2011) 1720.
7. A. I. Vogel, "Practical Organic Chemistry", London, (1961) 177.
8. B. S. Jenson, Acta Chem. Scand., 13 (1959) 1668.
9. A. I. Vogel, "Practical Organic Chemistry", London, (1961) 653.
10. H. B. Suthar, U. G. Deshpande, and J. R. Shah, Bull. Soc. Chim. Fr., 1 (1986) 55.
11. P. R. Mandlik, S. R. Aswale and A. S. Aswar, J. Indian Chem. Soc., 79(2002) 689.
12. M.Saidul Islam and M. M. Uddin,J. Indian Chem. Soc., 72(1995) 541.
13. P. M. Parikh and J. R. Shah, Synth. React. Inorg. Met.-Org. Chem., 15(6) (1985) 769.
14. E. Konning, E. Linder, I. P. Lorenz and G. Ritter, J. Inorg. Nucl. Chem., 33(1971) 3305.
15. S. Chandra, P. Pipil and S. D. Sharma, Synth. React. Inorg. Met.-Org. Chem., 31(5)(2001) 779.
16. A. K. Rana and J. R. Shah, Indian J. Chem., 21A (1982) 929.
17. J. F. Young, R. D. Gillard and G. Wilkinson, J. Chem. Soc., (1964) 5176.
18. P. M. Parikh and J. R. Shah, Bull. Soc. Chim. Fr., 4 (1985) 617.
19. A.K.Rana and J.R.Shah, J. Indian Chem. Soc., 58(1981) 1100.
20. P. M. Parikh and J. R. Shah, Synth. React. Inorg. Met. - Org. Chem., 15(1985) 975.
21. H. K. Soni and J. R. Shah, Bull. Soc. Chim. Fr., 2(1985) 147.
22. S. Satpathy and B. Sahoo, J. Inorg. Nucl. Chem., 33(1971) 1313.
23. S. K. Jogani, S. K. Menon and Y. K. Agrawal, Synth. React. Inorg. Met.-Org. Chem., 30(2000) 1317.
24. P. M. Parikh and J. R. Shah,Synth. React. Inorg. Met.-Org. Chem., 15(1985) 1073.
25. Y. M. Issq and W. H. Hegazy, Synth. React. Inorg. Met.-Org. Chem., 30(2000) 1731.
26. S. A. Sadeek, S. M. Teleb and A. M. Al-Kority, J. Indian Chem. Soc., 70(1993) 61.
27. S. Califano and W. Luttke, Z. Physik. Chem., 5(1955) 240; C.A. : 50(1956).
28. L. Birdadeanu, "IR Spectra of Organic Compounds" Wiley, Interscience, New York, (1972) 333.
29. M. S. Patil and J. R. Shah, Chemical Era., XIX (4), (1983) 88.
30. H. Koksal, M. Tumer and S. Serin, Synth. React. Inorg. Met.-Org. Chem., 26(9) (1996) 1577.
31. N. S. Biradar and V. H. Kulkarni, Z. Inorg. Allg. Chem., 381(1971) 312.
32. N. S. Biradar and V. H. Kulkarni, J. Inorg. Nucl. Chem., 33(1971) 3781.
33. S. C. Marvel, S. A. Aspey and E. H. Dudley, J. Am. Chem. Soc. , 78(1956) 4905.
34. K. Ueno and A. E. Martell, J. Phys. Chem., 60(1956) 1270.
35. V. P. Sokolov, V. A. Kogan, O. A. Osipov and L. G. Kolomin, Zh. Neorg. Khim., 14(1969) 2401.
36. J. C. Bailar and B. D. Sharma, J. Am. Chem. Soc., 77 (1955) 5476.

37. M. M. Abd-Elzaher Synth. React. Inorg. Met-Org. Chem., 30(2000) 1805.
38. S. M. E. Khalil and H. F. O. El-Shafiy, Synth. React. Inorg. Met-Org. Chem., 30(2000) 1817.
39. K. Y. El-Baradie, R. M. Issa and Maber, Indian J. Chem., 43A (2004) 1126.
40. Jiang-Ming Ouyang, Wei-Han Lin, Zhi-Ming Zhang and Chao-Yang Jiang, Synth. React. Inorg. Met.-Org., Chem., 30(2000) 1.
41. H. B. Suthar and J. R. Shah J. Indian Chem. Soc., 65(1988) 444.
42. M. M. Mostafa, E. A. H. Gomua, M. A. Mostafa and F. J. El-Dossouki, Synth. React. Inorg. Met-Org. Chem., 30(2000) 157.
43. Laijin Tian, Zhengyu Zhou, Bin Zhao, Haitao Sun, Wentao Yu and Ping Yang, Synth. React. Inorg. Met. -Org. Chem., 30(2000) 307.
44. Ahmet Karaday and Veysel T. Yilmaz, Synth. React. Inorg. Met-Org. Chem., 30(2000) 359.
45. R. C. Maurya, D. D. Mishra, N. S. Rao and N. N. Rao, Polyhedron, 22 (1992) 2837.
46. S. G. Teoh, G. Y. Yeap, C. C. Loh, L. W. Foong, S. B. Toe and H. Fun, Polyhedron, 16(1997) 2213.
47. B. T. Thaker and C. K. Modi, Indian J. Chem. 41A (2002) 2544.
48. R. C. Maurya, B. Shukla and A. Pandey, Indian J. Chem. 41A (2002) 554.
49. P. M. Dhadke and B. C. Haider, J. Indian Chem. Soc., 55(1978) 18.
50. K. Nakamoto, "Infrared and Raman Spectra of Inorganic and Coordination Compounds", Wiley-interscience, New York, (1978).
51. A. B. P. Lever, "Inorganic Electronic Spectroscopy", Elsevier, Amsterdam (1984) 417, 448, 452.
52. M. H. Sonar and A.S.R.Murty, J. Inorg. Nucl. Chem., 39(1977) 2155.
53. M.Saidul Islam and M. M. Uddin, J. Indian Chem. Soc., 72(1995) 541.
54. B. N. Figgis, "Introduction to Ligand Fields" Interscience, New York (1967).
55. D. K. Rastogi and P. C. Jain, Indian J. Chem., 10(1972) 100.
56. N. R. Shah and J. R. Shah, Indian J. Chem., 21A (1982) 312.
57. E. R. Prece and J. R. Wasson, J. Inorg. Nucl. Chem., 36(1974) 67.
58. Y. M. Patel and J. R. Shah, Synth. React. Inorg. Met.-Org. Chem., 16(1) (1986) 1.
59. A. V. Nikolaev, V. A. Logvinenko and L. I. Myacina, Thermal Analysis, Volo.2, Academic, New York, (1969) 779.

Table 1. Physical Properties of Ligands

Ligands	Melting Point °C	Found (Calculated) Percentage			Yield %
		Carbon	Hydrogen	Nitrogen	
BMMP-A	154	78.89 (78.44)	5.63 (5.76)	11.01 (11.44)	67
BMMP-OCA	144	81.02 (80.10)	5.45 (5.60)	11.51 (11.68)	65
BMMP-MCA	153	79.66 (80.10)	5.31 (5.60)	11.44 (11.68)	64
BMMP-PCA	161	80.03 (80.10)	5.87 (5.60)	11.74 (11.68)	65
BMMP-OT	165	77.99 (78.70)	6.01 (6.07)	11.10 (11.02)	69
BMMP-MT	173	77.93 (78.70)	6.87 (6.07)	11.35 (11.02)	68
BMMP-PT	184	78.61 (78.70)	6.38 (6.07)	11.37 (11.02)	68

Table 2. Colour, Composition, Conductivity and Magnetic Data of Cr(III) Chelates

Chelate	Colour	Found (calculated) percentage				Λ^{a}_{M}	$\mu_{eff.}$ B.M.
		Metal	Carbon	Hydrogen	Nitrogen		
$[Cr(BMMP\text{-}A)_3]$	Blackish brown	4.47 (4.49)	74.68 (74.71)	5.70 (5.75)	10.85 (10.89)	3.50	3.83
$[Cr(BMMP\text{-}OCA)_3]$	Light brown	4.27 (4.30)	71.48 (71.54)	5.20 (5.25)	10.40 (10.43)	3.95	3.70
$[Cr(BMMP\text{-}MCA)_3]$	Light brown	4.32 (4.30)	71.50 (71.54)	5.19 (5.25)	10.41 (10.43)	5.19	3.72
$[Cr(BMMP\text{-}PCA)_3]$	Light brown	4.26 (4.30)	71.49 (71.54)	5.18 (5.25)	10.39 (10.43)	6.09	3.71
$[Cr(BMMP\text{-}OT)_3]$	Brown	4.29 (4.33)	75.07 (75.09)	6.00 (6.05)	10.48 (10.51)	4.15	3.75
$[Cr(BMMP\text{-}MT)_3]$	Brown	4.31 (4.33)	75.04 (75.09)	6.02 (6.05)	10.52 (10.51)	5.22	3.79
$[Cr(BMMP\text{-}PT)_3]$	Brown	4.29 (4.33)	75.01 (75.09)	6.07 (6.05)	10.49 (10.51)	5.91	3.76

a = $Ohm^{-1}.cm^{2}.mole^{-1}$ in DMF

Table 3. Electronic Spectral Data of Cr(III) Chelates (cm-1)

Chelate	Observed transition energies $^4A_{2g}(F) \rightarrow$			B_{35}	β_{35}	λ	γ
	$^4T_{2g}$ (F)	$^4T_{1g}$ (F)	$^4T_{1g}$ (P)[a]				
$[Cr(BMMP\text{-}A)_2(H_2O)_2]$	18455	25380	40170	679	0.73	34.59	0.38
$[Cr(BMMP\text{-}OCA)_2(H_2O)_2]$	17543	23584	37737	579	0.63	21.47	0.23
$[Cr(BMMP\text{-}MCA)_2(H_2O)_2]$	17240	23255	37146	578	0.63	21.36	0.23
$[Cr(BMMP\text{-}PCA)_2(H_2O)_2]$	17391	23640	37618	605	0.65	24.48	0.27
$[Cr(BMMP\text{-}OT)_2(H_2O)_2]$	17761	23474	37910	540	0.58	17.42	0.19
$[Cr(BMMP\text{-}MT)_2(H_2O)_2]$	16863	23640	37130	678	0.73	34.44	0.38
$[Cr(BMMP\text{-}PT)_2(H_2O)_2]$	17250	23809	37625	645	0.70	29.66	0.32

a : calculated band energy

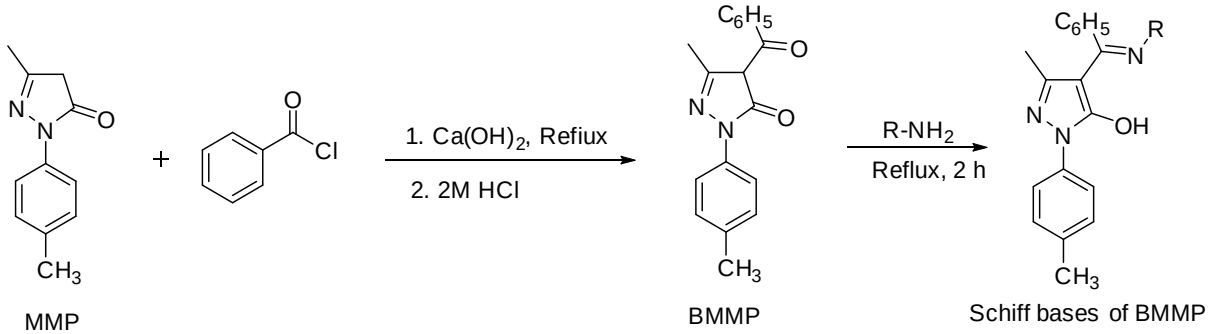

Fig 1. Synthesis of Chromium(III)chelates

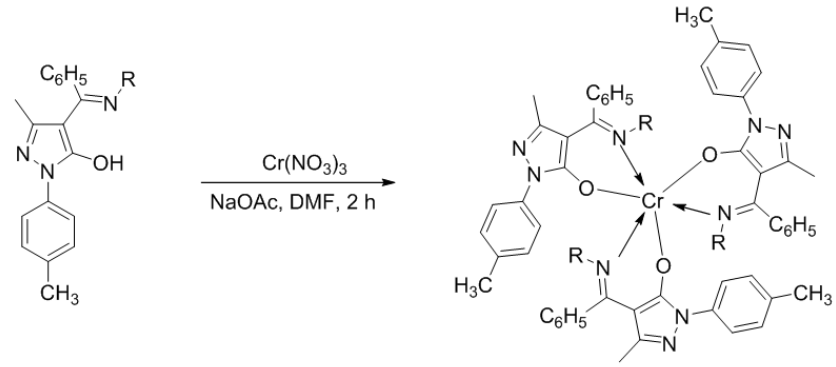

Fig 2. Synthesis of the Chromium (III) chelates

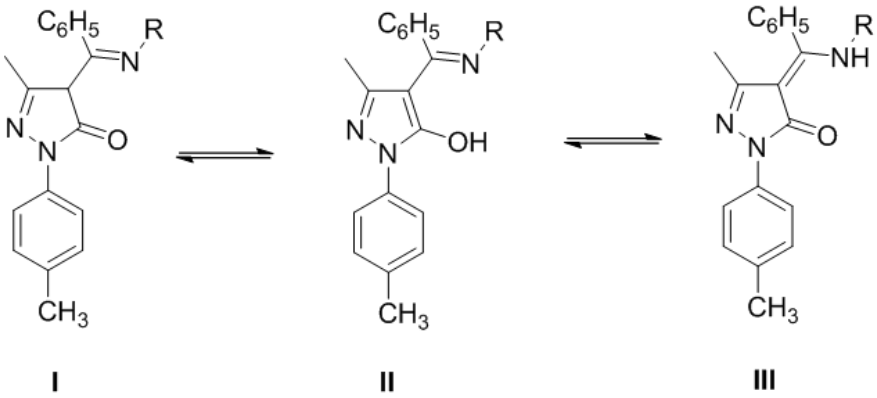

Fig. 3. various conformers of ligands

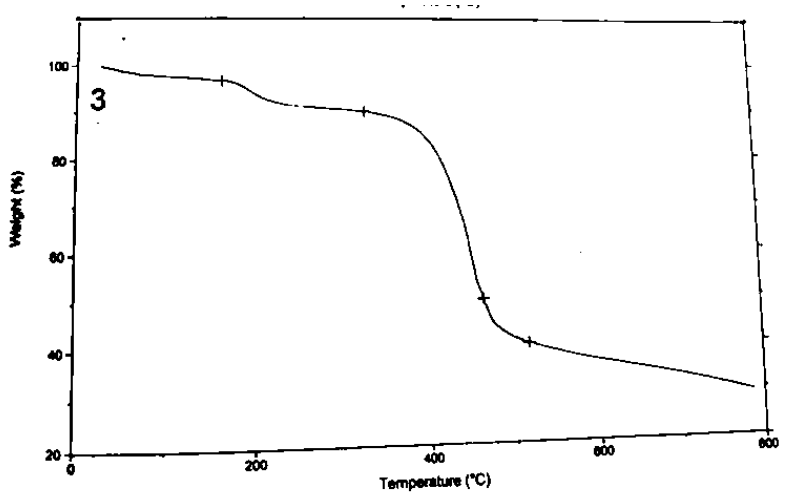

Fig. 4. TGA of Cr (BMMP-OT)$_3$

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RESEARCH ARTICLE

Synthesis, Characterization and Antifungal Activity of C-Mannich Bases of Ethyl 7 – Methyl – 3 – oxo – 5 – Bhenyl - 2, 3 –Dihydro - 5H - Thiazolo [3,2-a] Pyrimidine - 6 - Carboxylate Derivatives

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ABSTRACT

Two new series of C-Mannich bases of ethyl 5-(2-chlorophenyl) – 7 - methyl-3-oxo-2,3-dihydro-5H-thiazolo [3,2-a] pyrimidine-6-carboxylate 6a and ethyl 5- (4-bromophenyl) - 7- methyl -3-oxo-2,3-dihydro-5H-thiazolo [3,2-a] pyrimidine-6-carboxylate 6b have been synthesized by a three - component Mannich reaction (MCR) involving formaldehyde 7 and seven different heterocyclic 2^0amines 8a-g. The newly synthesized compounds were well characterized by elemental analysis, IR, ^{1}H NMR and mass spectral studies. They were also screened for their antibacterial and antifungal activities against a variety of microorganisms and the results of such studies have been discussed in this article.

Keywords: C-Mannich bases, Thiazolo[3,2-a]pyrimidine, Pyrimidine, Antifungal activity, Antibacterial activity

INTRODUCTION

Multicomponent reactions (MCR), defined as synthetic protocols that join together three or more substrates in a highly regio- and stereo-selective manner to deliver structurally complex organic molecules, have seen a dramatic rise in applications in all fields of organic synthesis [1].To synthesize new heterocyclic compounds in a single step, this is one of the best ways [2]. It is a very powerful tool in drug discovery and combinational chemistry [3]. Mannich reaction is a multicomponent and enormously useful reaction for the construction of nitrogenous molecules and the formation of C-C and C-N bonds [4]. In the Mannich reaction, the amino alkylation of compounds which have at least one active hydrogen atom, is performed through the condensation with formaldehyde (or another aldehyde) and ammonia (or ammonia derivatives). Additionally, double Mannich reaction can occur, if the starting compound contains two adjacent active hydrogen atoms [5-8].Beta-amino carbonyl compounds, the products of the Mannich reaction, are recognized to present different biological activities such as antibacterial, antifungal, antiviral, anti-

inflammatory, anticancer, antioxidant, antibiotic, larvicidaletc [9-14]. Electron-rich nitrogen heterocycles and sulfur compounds play an important role in diverse biological activities. These heterocyclic systems are the key chemical building blocks for numerous compounds that play important roles in the functioning of biologically active molecules. Pyrimidines have received much attention in medicinal chemistry due to their biological activities and therapeutic applications. One possible reason for their biological activities is the presence of pyrimidine base as nucleobases (Uracil, thymine and cytosine), which are essential building blocks of nucleic acids, DNA and RNA. Pyrimidine derivatives have also played an important role in the medicinal chemistry [15-17]. Pyrimidines have a long and distinguished history extending from the days of their discovery as important constituents of nucleic acids to their current use in the chemotherapy of AIDS [18]. Thiazolo [3,2-a] pyrimidine nucleus has been consistently regarded as structural analogues of biogenic purine bases and can be considered as potential purine antagonists [19,20].As one type of those heterocyclic rings, 5H-thiazolo[3,2-a]pyrimidin-5-ones are considered a promising class of bioactive heterocyclic compounds encompassing a diverse range of biological activities such as anti-inflammatory [21,22], antihypertensive [23], antifungal [24], antibiofilm, antibacterial [25],antiviral [26], antioxidant [27], antitumor [28,29], anti-HIV [30], calcium channel blocking [31], antitubercular [32],glutamate receptor antagonistic, group II metabotropic glutamate receptor antagonist activities [33] and 5-HT2a receptor antagonistic [34].Those compounds have also been reported as inhibitors of CDC25B phosphatase, Bcl-2 family proteins [35] and acetylcholinesterase enzymes [36]. Encouraged by the MCR, enormous pharmacological importance of thiazolo [3,2-a]pyrimidin and the various heterocyclic 2^0-amines, we wish to report a new, simple and efficient method for the synthesis of C-Mannich bases of substituted thiazolo [3,2-a] pyrimidin derivatives from substituted thiazolo [3,2-a] pyrimidin, formaldehyde and different biologically active heterocyclic 2^0-amines. These compounds were subsequently evaluated for their antimicrobial activity.

MATERIAL AND METHODS

o-chlorobenzaldehyde and p-bromobenzaldehyde (1a & 1b) reacts with ethylacetoacetate (2) and thiourea(3) via Biginelli reaction to give3,4-dihydropyrimidine-2(*1H*)-thione(4a & 4b) (Scheme I) followed by the cyclization reaction with chloroacetic acid (5) gives Ethyl 5,7-dimethyl-3-oxo-2,3-dihydro-5H-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (6a & 6b)(Scheme II)which upon mannichreaction with formaldehyde 7and different heterocyclic 2^0-amines(8a-g) gives two series of C-Mannich bases namely, Ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylatederivatives (9a-g) and Ethyl 5-(4-bromophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylatederivatives(10a-g). Scheme III and IV show the synthetic protocol of the final compounds (9a-g&10a-g). Procedure for the synthesis of ethyl 4-(2-chlorobenzaldehyde)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4a) A mixture of o-chlorobenzaldehyde (1a) (0.05 mol), ethylacetoacetate(2) (0.05 mol), and thiourea(3) (0.05 mol) and a few drops of 37% HCl as catalyst was refluxed in ethanol for about 3-4 hrs. The progress of the reaction was monitored continuously by TLC. After completion of reaction, the resulting mixture was cooled and poured into crushed ice. The solid separated was filtered off and washed several times with water to remove unreacted thiourea. The product was further washed with ether, and purified by recrystallization from methanol. In a similar way,4-(3-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b).

Ethyl4-(2-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate(4a) White solid, mp214-215^{0}C, Yield 81%, Anal. cacld for $C_{14}H_{15}ClN_2O_2S$M.W.:310.5 Calc. C, 54.10; H, 4.86; N, 9.01; found: C, 54.47; H, 4.60; N, 9.10.IR (υ cm^{-1}): 3100(Aromatic C-H str), 1228 (-$COOCH_2CH_3$), 1259 and 1156 (C-O-C), 1707 (C=O),1290 (NH-C=S-NH), 1087 (C=S), 3310 (N-H), 760 (-C-Cl). ^{1}H NMR:δ 1.2 (3H,t,-OCH_2CH_3), 1.7 (3H,s,CH_3), 3.3(2H,q,-CH_2CH_3), 4.5 (1H,s,H), 6.8-7.2 (4H,m, aromatic rings), 8.8 (1H,s,NH), 9.1 (1H,s,NH);^{13}C NMR: 14.5, 17.6, 55.5, 60.0, 101.4, 114.3, 122.2, 128.1, 136.2, 142.4, 145.2, 159.2, 165.6, 174.5 Ethyl 4-(4-bromophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b) Cream white solid, map 188-190^{0}C, Yield 73%, Anal. cacld for $C_{14}H_{15}BrN_2O_2S$. M.W.:354 Calc. C, 47.33; H, 4.26; N, 7.89; found: C, 47.76; H, 4.20; N, 7.37.IR (υ cm^{-1}): 3100 (Aromatic

C-H str), 1710(-COOCH$_2$CH$_3$), 1320 and 1160(C-O-C str), 1743 (C=O); 1090 (C=S), 3375 (N-H str), 629 (C-Br). ^{1}H NMR:δ 1.1 (3H,t,CH$_3$ of -OCH$_2$CH$_3$), 2.2 (3H,s,CH$_3$ of pyrimidine ring), 4.0 (2H,q,CH$_2$ of -OCH$_2$CH$_3$), 5.1 (1H,s,H on pyrimidine ring), 6.9-7.1 (4H,m,one aromatic rings), 7.6 (1H,s,NH of pyrimidinering), 9.2 (1H,s,NH of pyrimidine ring);^{13}C NMR: 14.4, 17.6, 56.1, 60.1, 101.4, 114.3, 124.4, 128.0, 130.1, 132.2, 136.1, 145.2, 164.6, 165.6, 174.5. Procedure for the synthesis of ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate(6a) Cyclization of dihydropyrimidine thiones (DT$_{1-9}$) into fused thiazolo [3,2-a] pyrimidines has been carried out by using chloroacetic acid in dimethylformamide (DMF) [36]. A mixture of Ethyl 4-(2-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate 4a(2.14 g, 0.01 mol) and chloroacetic acid(1.04 g, 0.011 mol) in DMF (10 ml) was refluxed for 4hrs. The resulting solution was allowed to stand at room temperature for an hour and cooled to 0°C. The solid separated was filtered off, washed with chilled water and recrystallized from ethanol to yield 6a. In a similar manner other ethyl 5-(4-bromophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a] pyrimidine-6-carboxylate 6bwere prepared by using Ethyl 4-(4-bromophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate 4b. Ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate(6a) White solid, mp 212-214^{0}C, Yield 67%, Anal. cacld for $C_{16}H_{15}ClN_2O_3S$ M.W.: 350.5 Calc. C, 54.78; H, 4.31; N, 7.99; found: C, 54.67; H, 4.53; N, 8.23.IR (υ cm^{-1}): benzene ring: 3100 (Aromatic C-H str), 1230 and 1145 (C-O-C str), 1718 (-COOCH$_2$CH$_3$), 1743 (C=O), 1229, 1209 (C-N str), 691 (C-Cl).^{1}H NMR: δ 1.2 (3H,t,-OCH$_2$CH$_3$), 1.9 (3H,s,CH$_3$), 3.3 (2H,q, CH$_2$thiazole ring), 4.1 (2H,q,-OCH$_2$CH$_3$), 4.5 (1H,s,H), 6.8-7.2 (4H,m,aromatic rings). ^{13}C NMR: 14.4, 17.6, 35.2, 55.5, 60.0, 101.4, 114.3, 122.2, 128.1, 136.2, 142.4, 145.2, 152.3, 159.2, 165.3, 174.5. Ethyl 5-(4-bromophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate(6b) White solid, mp 254-256^{0}C, Yield 69%, Anal. cacld for $C_{16}H_{15}BrN_2O_3S$M.W.: 395Calc. C, 48.62; H, 3.82; N, 7.09; found: C, 48.89; H, 3.67; N, 7.17. IR (υ cm^{-1}): benzene ring: 3115 (Aromatic C-H str), 1242 and 1130 (C-O-C str), 1715 (-COOCH$_2$CH$_3$), 1740 (C=O), 1232, 1210 (C-N str), 645 (C-Br). ^{1}H NMR: δ 1.2 (3H,t,-OCH$_2$CH$_3$), 1.8 (3H,s,CH$_3$), 3.3 (2H,q, CH$_2$thiazole ring), 4.2 (2H,q,-OCH$_2$CH$_3$), 4.9 (1H,s,H), 6.8-7.2 (4H,m,aromatic rings). ^{13}C NMR: 14.4, 17.6, 35.2, 55.5, 60.0, 101.4, 114.3, 122.2, 128.1, 136.2, 142.4, 145.2, 152.3, 159.2, 165.3, 174.5.

Synthesis of C-Mannich bases; Ethyl 2-((1H-benzo[d]imidazol-1-yl)methyl)-5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo [3,2-a]pyrimidine-6-carboxylate 9a In a three necked flask equipped with a stirrer and dropping funnel, ethanolic solution of benzimidazole 8a(0.05 mol) and 37%formaldehyde (0.05 mol) were added under stirring. The reaction mixture was stirred at room temperature for half an hour to complete the reaction of formaldehyde to form methylol derivative.To the resulting mixture, a solution of ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate6a(0.05 mol) in ethanol containing catalytic amount of conc. HCl was added drop wise with stirring and refluxed for 6-7 hrs. The reaction was monitored continuously by TLC. After completion of reaction, the resulting mixture was cooled to room temperature and poured into crushed ice with continuous stirring. The solid obtained was filtered off, washed thoroughly with hot water, air-dried and recrystallized from appropriate solvent to yield the C-Mannich base9a. Mannich reaction of ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate6awas further carried out respectively with 2-methyl benzimidazole8b, 2-benzyl benzimidazole8c, benzotriazole8d, morpholine8e, phthalimide8f, tetrahydrocarbazole8g secondary amines using the same procedure to yield other six C-Mannich bases (9b-g) forming a series of C-Mannich bases of ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate 6a. IUPAC name of all the synthesized compounds (9a-g & 10 a-g) are represented in

Ethyl2-((1H-benzo[d]imidazol-1-yl)methyl)-5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidine-6-carboxylate (9a) White solid, mp 244-246^{0}C, Yield 73%, Anal. cacld for $C_{24}H_{21}ClN_4O_3S$M.W.: 480 Calc. C, 59.93; H, 4.40; Cl, 7.37; N, 11.65; found: C, 60.21; H, 4.17; Cl, 7.57; N, 11.97. IR (υ cm^{-1}): benzene ring: 3098 (Aromatic C-H str), 1303 and 1175 (C-O-C str), 1730 (-COOCH$_2$CH$_3$),1676 (C=O), 1247 (C-N str), 698 (C-Cl).^{1}H NMR: δ 1.2 (3H,t,-OCH$_2$CH$_3$), 1.8 (3H,s,CH$_3$), 3.9 (2H,q,-OCH$_2$CH$_3$), 5.2 (1H,t,-H of thiazole), 5.4-5.8 (2H,q,aminomethylene bridge), 6.1 (1H,s,pyrimidine), 7.1-7.7 (8H,m,aromatic rings), 8.1 (1H,s,benzimidazole). ^{13}C NMR: 14.1, 18.6, 49.2, 55.7, 57.4, 58.7, 63.5, 113.1, 118.2, 128.3, 128.5, 128.9, 130.8, 130.9, 131.5, 131.6, 134.3, 136.7, 145.7, 146.2, 146.8, 155.0, 159.9, 171.2, 178.8.

Ethyl5-(2-chlorophenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazol-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo [3,2-a] pyrimidine-6-carboxylate (9b) Brown solid, mp146-148^{0}C, Yield 61%, Anal. cacld for $C_{25}H_{23}ClN_4O_3S$M.W.: 494 Calc. C, 60.66; H, 4.68; Cl, 7.16; N, 11.32;found: C, 60.32; H, 4.97; Cl, 6.89; N, 11.07. IR (υ cm^{-1}): benzene ring: 2900 (Aromatic C-H str), 1248 and 1145 (C-O-C str), 1723 (-COOCH$_2$CH$_3$),1617 (C=O), 1217 (C-N str), 694 (C-Cl).^{1}H NMR: δ 2.2 (3H,t,-OCH$_2$CH$_3$), 2.7 (3H,s,-CH$_3$, 2-methylbenzimidazole), 2.8 (3H,s,CH$_3$), 3.9 (2H,q,-OCH$_2$CH$_3$), 4.8 (1H,t,-H of thiazole), 5.4-5.6 (2H,q,aminomethylene bridge), 6.1 (1H,s,pyrimidine), 6.8-7.8 (8H,m,aromatic rings).^{13}C NMR: 16.3, 19.5, 22.4, 48.5, 60.0, 65.4, 113.4, 121.8, 124.6, 124.9, 125.0, 128.0, 129.5, 129.6, 129.8, 133.0, 143.3, 143.6, 143.7, 151.6, 157.6, 159.9, 167.7, 171.2.

Ethyl 2-((2-benzyl-1H-benzo[d]imidazol-1-yl)methyl)-5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-hiazolo[3,2-a]pyrimidine-6-carboxylate (9c) Pale yellow solid, mp187-189^{0}C, Yield 57%, Anal. cacld for $C_{31}H_{27}ClN_4O_3S$M.W.: 570 Calc. C, 65.20; H, 4.77; Cl, 6.21; N, 9.81;found: C, 65.38; H, 4.95; Cl, 5.98; N, 9.62. IR (υ cm^{-1}): benzene ring: 3079 (Aromatic C-H str), 1271 and 1142 (C-O-C str), 1701 (-COOCH$_2$CH$_3$),1610 (C=O), 1197 (C-N str), 691 (C-Cl).^{1}H NMR: δ 2.1 (3H,t,-OCH$_2$CH$_3$), 2.3(3H,s,CH$_3$), 3.5 (2H,q,-OCH$_2$CH$_3$), 4.2 (2H, s, 2-benzylbenzimidazole), 4.7 (1H,t,-H of thiazole), 5.3 (2H,q,aminomethylene bridge), 6.2 (1H,s,pyrimidine), 6.8-7.9 (13H,m,aromatic rings).^{13}C NMR: 15.2, 19.6, 33.2, 52.8, 55.5, 59.9, 62.6, 108.7, 120.4, 122.0, 122.1, 122.2, 125.4, 126.3, 126.7, 128.5, 128.6, 128.7, 128.8, 132.9, 133.0, 134.4, 134.7, 138.1, 145.9, 146.0, 146.4, 150.0, 156.1, 158.3, 163.5, 173.4.

Ethyl5-(2-chlorophenyl)-7-methyl-2-(morpholinomethyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate (9e) Cream white solid, mp234-236^{0}C, Yield 84%, Anal. cacld for $C_{21}H_{24}ClN_3O_4S$M.W.: 449 Calc. C, 56.06; H, 5.38; Cl, 7.88; N, 9.34;found: C, 55.89; H, 5.51; Cl, 7.69; N, 9.22. IR (υ cm^{-1}): benzene ring: 2954 (Aromatic C-H str), 1300 and 1120 (C-O-C str), 1700 (-COOCH$_2$CH$_3$),1609 (C=O), 1182 (C-N str), 700 (C-Cl).^{1}H NMR: δ 2.1 (3H,t,-OCH$_2$CH$_3$), 2.4(3H,s,CH$_3$), 2.4-2.6 (4H,m, morpholine), 2.9 (2H,q,-OCH$_2$CH$_3$), 3.5-3.9 (4H,m, morpholine), 4.1 (1H,t,-H of thiazole), 4.7(2H,q,aminomethylene bridge), 5.8 (1H,s,pyrimidine), 7.1-7.7 (13H,m,aromatic rings).^{13}C NMR:11.4, 17.9, 47.0, 60.0, 60.1, 62.7, 63.4, 69.9, 70.0, 120.0, 126.4, 130.0, 130.6, 130.7, 134.5, 144.2, 159.1, 159.9, 169.8, 175.4.

Ethyl5-(2-chlorophenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidine-6-carboxylate (9f) Brown solid,mp250-252^{0}C, Yield 59%,Anal. cacld for $C_{25}H_{20}ClN_3O_5S$M.W.: 509 Calc. C, 58.88; H, 3.95; Cl, 6.95; N, 8.24; found: C, 59.02; H, 4.14; Cl, 6.72; N, 8.03.IR (υ cm^{-1}): benzene ring: 2929 (Aromatic C-H str), 1248 and 1142 (C-O-C str), 1700 (-COOCH$_2$CH$_3$),1610 (C=O), 1171 (C-N str), 677 (C-Cl).^{1}H NMR: δ 2.1 (3H,t,-OCH$_2$CH$_3$), 2.4 (3H,s,CH$_3$), 3.8 (2H,q,-OCH$_2$CH$_3$), 4.4 (1H,t,-H of thiazole), 4.5-4.9(2H,q,aminomethylene bridge), 6.0(1H,s,pyrimidine), 7.0-7.9 (8H,m,aromatic rings).^{13}C NMR:14.2, 17.1, 46.9, 47.1, 56.5, 60.1, ,118.7, 123.6, 123.7, 127.6, 128.7, 128.8, 130.0, 130.1, 130.4, 130.7, 137.5, 153.0, 158.2, 167.9, 168.0, 168.2, 174.1.

Ethyl 5-(2-chlorophenyl)-2-((3,4-dihydro-1H-carbazol-9(2H)-yl)methyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidine-6-carboxylate (9g) Brick red solid,mp145-147^{0}C, Yield 65%,Anal. cacld for $C_{29}H_{28}ClN_3O_3S$M.W.: 533Calc. C, 65.22; H, 5.28; Cl, 6.64; N, 7.87; found: C, 65.17; H, 5.43; Cl, 6.46; N, 8.03. IR (υ cm^{-1}): benzene ring: 2824 (Aromatic C-H str), 1278 and 1183 (C-O-C str), 1705 (-COOCH$_2$CH$_3$),1652 (C=O), 1101 (C-N str), 700 (C-Cl).^{1}H NMR: δ 1.6 (3H,t,-OCH$_2$CH$_3$), 1.8-2.0 (4H,m, tetrahydrocarbazole),2.4-2.8 (4H,m, tetrahydrocarbazole), 3.1 (3H,s,CH$_3$), 3.8 (2H,q,-OCH$_2$CH$_3$), 4.3 (1H,t,-H of thiazole), 5.2-5.3(2H,q,aminomethylene bridge), 5.8(1H,s,pyrimidine), 7.1-7.6 (8H,m,aromatic rings).^{13}C NMR:13.3, 24.7, 25.0, 29.1, 29.5, 30.0, 49.1, 55.2, 60.8, 63.0, 92.7, 107.7, 111.0, 118.2, 119.0, 122.0, 124.6, 127.3, 129.5, 130.7, 130.9, 131.0, 134.3, 134.6, 144.6, 151.7, 152.6, 168.4, 174.7.

RESULTS AND DISCUSSION

Chemistry

Compounds9a-g and 10a-gwere synthesized by Mannich base method, reaction sequences of synthesis outline in Schemes I, II, III and IV. We explored the effects of different solvents on the model Mannich reaction (Table II). The

reaction medium played an important role in this reaction. In our initial endeavour, we have investigated a three component reaction of ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate6a, formaldehyde 7 and benzimidazole 8ain different solvent systems like benzene,1,4-dioxane, CH_2Cl_2, MeCN, H_2O, EtOH, benzene, THF, DMF and cyclohexane(Table II)and in presence of hydrochloric acid under reflex condition to afford ethyl 2-((1H-benzo[d]imidazol-1-yl)methyl)-5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate9a(Scheme III). Generally, no clear correlation was observed between solvent polarity and the reaction yield. The best results were obtained by refluxing the reaction mixture in ethanol. Under optimized conditions with HCl catalysis, two different thiazolo [3,2-a]pyrimidine derivatives (4a & 4b), seven different 2^0-heterocyclic amines (8a-g) and formaldehyde 7 to provide two series of C-Mannich bases of thiazolopyrimidine derivatives (9a-g & 10a-g) in good yields (56–84 %, Schemes 4, 5).Based on the above results, a plausible mechanism is proposed (Scheme V). [a]Reaction conditions: a mixture of benzimidazole (0.05 mol), formaldehyde (0.05 mmol), ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (5 mmol), solvent (20 mL) and HCl (1 mL) was refluxed for 6-8 hrs.

Spectral study: Dihydropyrimidone

The IR spectra of the reaction products 4a (Fig.I), showed characteristic absorption band at 3310-3240, 1710-1650 and 1200-1050 cm^{-1}attributed to NH, C=O and C=S, respectively. The characteristic sharp intensity band at 760 cm^{-1} attributed to C-Cl functional group. The ^{1}H NMR spectrum of 4a, showed two singlets at δ 1.2 and 1.7 ppm integrating for three protons of C_{10} and C_7 respectively and quartet at δ 4.2 ppm integrating for two protons at C_9. The C_4-proton of pyrimidine appeared as singlet at δ 4.5 ppm integrating for one proton. The $N_1$and N_3-proton appeared as a singlet at δ 8.8 and 9.1 ppm respectively. The aromatic protons were observed as multiplate in the region δ 6.8 to 7.2 ppm. The ^{13}C-NMR spectra of the isolated products showed the signals for carbons C-7,C-9 and C-10 at δ 17.6, 60.0 and 14.5 ppm respectively, pyrimidine ring carbons C-4, C-5 and C-6 at δ 55.5, 101.4 and 159.2 ppm, C-12 bonded with Chlorine showed the signal at δ 136.2 ppm, aromatic carbons C-11 showed a signal at 145.2 δ ppm, C-13 to C-16 at δ 114.3, 122.2, 128.1 and 142.4 ppm, carbonyl carbon C_8 at 165.6 δ ppm, thiocarbonyl carbons C-2 at δ 174.5 ppm and this may be explained on the basis of effect caused by the S atom in the thiones. In conclusion, the spectral analytical data of DHPMs are in accordance with proposed chemical structure and literature. Thiazolo [3,2-a] pyrimidine The spectral characterization of ethyl 5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate6a (Fig.II) has been carried out with the help of its general structure shown below. IR spectra of parent compound 6a showed all the characteristic absorption bands except that, the disappearance of an absorption band at 3310-3240 cm^{-1} due to secondary –NH of 4aas both of these two groups have participated in cyclization to form thiazolopyrimidine fused ring. Besides this, the characteristic absorption bands of thiazole ring systems are observed at 1383-1333 cm^{-1}attributed to the ring stretching, 924-753 cm^{-1}indicates the C-H out of plane bending, several bands, 691 cm^{-1} attributed to the C-Cl streching, 1743 cm^{-1} attributed to the C=O stretching of thiazole ring, 1718 cm^{-1} indicates the C=O stretching of an ester group. Comparison of ^{1}H NMR spectra of 6a with that of 4areveals presence of a singlet at δ 3.3 ppm integrating for 2H of C_{18} and disappearance of two singlets at δ 8.8 and 9.1 ppm due to 1H of N_1 and N_3. This has been further confirmed by two chemical shifts at δ 35.5 and 174.5 ppm for C-18 (-CH_2) and C-17 (C=O) respectively in ^{13}C NMR spectrum of 6a. C-Mannich Bases On the basis of experimental results, a reasonable reaction mechanism of the formed compounds (9a-g & 10a-g) is postulated in (Scheme V). With the first Biginelli reaction between aromatic aldehyde 1a-b, urea 2 and ehtylacetoacetate3 to furnish DHPMs 4a-b which undergoes cyclization reaction using chloroacetic acid 5to give compound 6a-b followed by Mannich reaction, the condensed imines which formsfrom the reaction of formaldehyde 7 with heterocyclic 2^0-amines 8a-g, undergoes nucleophilic addition to the active CH group of compound 6a-b to produce the two series of C-Mannich bases(Fig. III). *9a-g Series:*

9a-g Series of C-Mannich bases consist of parent 6a linked with amino methylene bridge to heterocyclic secondary amino component. Therefore, the IR spectra of Mannich bases (9a-g Series) showed the characteristic absorption bands of parent 6aand amino methylene linkage as well as those of corresponding heterocyclic secondary amino moieties (8a-g)present in each of seven C-Mannich bases. Further evidences in support of the proposed structure on

the basis of ^{1}H NMR,^{13}C NMR and mass spectral data for above mentioned series of C-Mannich bases are discussed in the detail. The characteristic ^{1}H NMR signals of heterocyclic secondary aminomoieties in C-Mannich bases were observed at (8.1 δ, 1H, singlet) for benzimidazole,(2.8 δ, 3H, singlet) for 2-methylbenzimidazole, (3.5 δ 2H, singlet) for2-benzylbenzimidazole, (2.5-2.7 δ, 4H, multiplet and 3.6-3.9 δ, 4H, multiplet) for morpholine, (1.7-2.1 δ, 4H, multiplet and 2.4-2.8 δ, 4H, multiplet) for tetrahydrocarbazole in 9a, 9b, 9c, 9e and 9g respectively. In addition to this, the ^{13}C NMR signals of heterocyclic secondary amines are at δ 19.5ppm (-CH_3 of 2-methylbenzimidazole), δ 33.3 ppm (-CH_2 of 2-benzylimidazole), δ 60.1 and 70.0 ppm (-CH_2 of morpholine ring), δ 168.2 and 168.3 ppm (C=O of phthalimide ring), δ 25.0, 29.1, 29.5 and 30.0 ppm (-CH_2 of 1,2,3,4-tetrahydrocarbazole ring) in9b, 9c, 9e, 9f and 9g respectively. Evidences for the formation C-Mannich bases Analytical data of C, H, N content of these compounds are in agreement with the calculated values based on the proposed structure given in Scheme 3 & 4.

Comparison of ^{1}H NMR spectra of the C-Mannich bases (9a-g) with its parent 6a have shown the absence of singlet at δ 3.3 ppm (2H, -CH_2 of thiazole ring) suggested that the 1H of carbon atom (C_{18}, Fig-2) of thiazolopyrimidine reacted with formaldehyde and heterocyclic secondary amine to yield the corresponding C-Mannich base. Besides this, the presence of triplet and doublet at δ 4.1-5.3 and 4.7-5.7 ppm due to 1H of C_{18} and 2H of C_{19} of thiazole ring and methylene bridge (Fig.:3) respectively support the formation of C-Mannich bases. This is further confirmed by the appearance of new signals at δ 46.9-63.0 ppm for the C-19 ^{13}C NMR spectrum of 9a-g.

Antibacterial activity

Antibacterial activity of compounds 9a-g&10a-g were evaluated for their antibacterial activity in vitro against five bacterial microorganism(*Escherichia coli*, *Bacillus subtilis*, *Bacillus megaterium*, *Staphylococcus aureus* and *Vibrio cholera*) and two fungal microorganism (*A.niger*, *C.albican*) using disc diffusion method.Inhibition zones were measured at mm. Antimicrobial activity of each of the C-Mannich bases of thiazolopyrimidine (9a-g & 10a-g) against both bacterial and fungal species was enhanced as compared to the corresponding parent thiazolopyrimidines(6a-b) and heterocyclic secondary amines(8a-g) individually. The compounds 9a and 9d are highly active against *Escherichia coli* and *Bacillus subtilis* compared with standard respectively. Compound 10f highly active against *Staphylococcus aureus*and compound 9e as well as 10e highly active against *Vibrio cholera* compared with standard ciprofloxacin. None of the synthesized compounds do not show promisable activity against *Bacillus megaterium*. The bacterial zones of inhibition values are given in (Table III). Antifungal activity of the compounds 9a-g and 10a-gwere evaluated for their antifungal activity against in vitro *Aspergillus niger* and *Candida albicans* using disc diffusion method. The compound 9e and 10a are highly active against *A.niger* compared with standard clotrimazole.

Compound 10d and 10e highly active against both *A.niger* and *C.albicans* compared with standard. The values are summarized in (TableIV). Structural activity relationship was investigated by synthesized compounds 9a-g and 10a-g, among the compounds 9a,9d,9e, 10a, 10d, 10e and 10fare highly active compared with other compounds. Benzimidazole, benzotriazole, morpholine as a heterocyclic 2^0-amine and halogenated phenyl ring act as a biological importance of this domain, in particularly the compound 10e containing p-bromo substituted phenyl ring and morpholine as a heterocyclic 2^0-amine shows that highly active against *Vibrio cholera* compared with ciprofloxacin and also highly active against both *A.niger* and *C.albicans* in antifungal screening. From these antimicrobial activity study of 9a-g and 10 a-g, we do not find any major antimicrobial activity difference between chloro- as well as bromo-substitution on phenyl ring in both the series (9a-g and 10 a-g).

CONCLUSIONS

In summary, a series of 7-(substituted phenylamino)-5H-thiazolo [3,2-a]pyrimidin-5-ones and sulfonated cyclized products were designed, synthesized and evaluated for antibacterial and antitubercular activities in this study. An efficient synthetic method led to 5H-thiazolo[3,2-a] pyrimidin- 5-ones or the corresponding sulfonic acid derivatives at different temperatures in high yield and purity. During our extensive literature survey it was found that N3 of

substituted pyrimidines was the cyclization site when S-alkylated derivatives was utilized to give 5H-thiazolo[3,2-a]pyrimidin-5-ones. Our results reveal that compounds having nitro substituents displayed significant antibacterial inhibitory activity, while compounds containing the amino group, show better activity against *M.smegmatis.* Further structural modification could be performed to improve the bioactivity. We believe that these compounds can be developed into potential class of antimicrobial and antitubercular agents

REFERENCES

1. Helena C.Malinakova, "Multicomponent Reaction Sequences Using Palladacyclic Complexes",*Palladacycles Catalysis and Beyond*, 2019,Chapter 6, 263-295.
2. GudalaSatish, "Synthesis of Different Heterocyclic Compounds by Using DHA, Dehydroacetic"*Acid and its Derivatives-Useful Synthons in Organic Synthesis*, 2017,Chpater 3,37-60.
3. Alvim HGO, da Silva Júnior EN, Neto BAD, "What do we know about multicomponent reactions? Mechanisms and trends for the Biginelli, Hantzsch, Mannich, Passerini and Ugi MCRs"*RSC Advances*, 2014, 97, 54282-54299.
4. M. Arend, B. Westermann and N. Risch, "Modern variants of the Mannich reaction" *AngewandteChemie*,1998,110, 1096-1122.
5. Z. Wang, T. You and H. Shi, "Synthesis of 3,6-Disubstituted Tetrahydro-S-triazolo[3,4-b][1,3,5]thiadiazines" *Molecules*,1996, 1, 89-92.
6. H. A. H. El-Sherief, Z. A. Hozien, A. F. M. EL-Mahdy and A. A. O. Sarhan, "Intramolecular cyclization of Mannich reaction for synthesis of pyrimido[2,1-b]-1,3,5-tiadiazines"*Journal of Heterocyclic Chemistry*, 2010,47(6),1294-1302.
7. (a) Z. A. Hozien, A. A. O. Sarhan, H. A. H. El-Sherief and A. M. Mahmoud, Z. "A convenient one-pot synthesis of pyrazolo [3, 4-d] pyrimidines and s-triazolo [3, 4-b][1, 3, 5] thiadiazines"*ZeitschriftfürNaturforschung B*, 1997,52b,1401-1412; (b) A. M. Mahmoud, H. A. H. El-Sherief, O. M. A. Habib and A. A. O. Sarhan, "An efficient and rapid intramolecular cyclization of a quadruple Mannich reaction for one-pot synthesis of pentaazaphenalenes and their antimicrobial activities" *RSC Advances*, 2016, 6, 92134-92143.
8. A. A. O. Sarhan, S. H. Abdel-Hafez, H. A. H. El -Sherief and T. Aboel-Fadl, "Utility and Synthetic Uses of Mannich Reaction: An Efficient Route for Synthesis of Thiadiazino-[1, 3, 5][3, 2-a] benzimidazoles"*Synthetic Communications*, 2006,36, 987–996.
9. S. Bala, N. Sharma, A. Kajal, S. Kamboj, V. Saini, "Mannich bases: an important pharmacophore in present scenario"*International Journal of Medicinal Chemistry*,2014, ID 191072.
10. HasniyeYaşa, BelmaHasdemir&Özge Erken, "β-Amino Carbonyl Compounds from Iodine-Catalyzed Three Component Mannich Reactions and Evaluation of Their Antioxidant Activity"*Organic Preparations and Procedures International*, 2019, 51(6), 537-546.
11. T.E. Chiwunze, R. Azumah, M. Ramtahal, A.M. Somboro, P.I. Arvidsson, 72 H.G. Kruger, T. Govender and T. Naicker, "Organocatalyzed Mannich reactions on minocycline: towards novel tetracycline antibiotics"*South African Journal of Chemistry*, 2016, 69, 72–78.
12. A.Alaklab,S. K. Radhakrishnan, A. Ahamed, I. A. Arif, A.Manilal, A.Idhayadhulla, "Synthesis of novel three compound imidazole derivatives via Cu (II) catalysis and their larvicidal and antimicrobial activities"*MonatsheftefürChemie*,2017,148, 275–290.
13. T. B. Shah, A. Gupte, M. R. Patel, V. S. Chaidhari, V. C. Patel, "Synthesis and in vitro study of biological activity of heterocyclic N-Mannich bases" *Indian Journal of Chemistry-Sec. B*, 2009,48B(1), 88-96.
14. T. B. Shah, A. Gupte, M. R. Patel, V. S. Chaidhari, V. C. Patel, "Synthesis and in vitro study of biological activity of heterocyclic N-Mannich bases of 3,4-dihydropyrimidine-2(1H)-thiones" *Indian Journal of Chemistry-Sec. B*, 2010,49B(5), 578-586.
15. V. D. Joshi, M. D. Kshirsagar, S. Singhal, "Synthesis and Pharmacological Study of Some Novel Pyrimidines", *Der Pharmacia Sinica*,2012, 3 (3), 343.

16. S. P. Prajapati, D. P. Patel and P. S. Patel., "Synthesis, spectral and microbial studies of 4-(substitutedphenyl)-1-(2,4- dinitrophenyl)-3-methyl-4,5-dihydro-pyrazolo[3,4-d]pyrimidin-6-ol"*Der Chemica Sinica*, 2012, 3(4), 830.
17. H. Al-Sharifi, H. S. Patel., "Synthesis, spectral investigation and biological evaluation of novel hydrazones derivative of substituted 1,2-dihydropyrimidine ring" *Der Pharmacia Sinica*, 2012,3 (3), 305.
18. K. S. Jain, T. S. Chitre, P. B. Miniyar, M. K. Kathiravan, V. S. Bendre, "Biological and medicinal significance of pyrimidines"*Current Science*, 2006, 90, 6, 793.
19. El-Bayouki, K.A.; Basyouni, W.M., "Thiazolopyrimidines without bridge-head nitrogen: thiazolo [4,5-d] pyrimidines"*Journal of Sulfur Chemistry*,2010,31, 551–590.
20. Nagarajaiah, H.; Khazi, I.; Begum, N.S., "Synthesis, characterization and biological evaluation of thiazolopyrimidinederivatives"*Journnal of Chemical Science*,2012,124, 847–855.
21. Tozkoparan, B.; Ertan, M.; Krebs, B.; Läge, M.; Kelicen, P.; Demirdamar, R., "Condensed Heterocyclic Compounds: Synthesis and Antiinflammatory Activity of Novel Thiazolo[3,2-a]pyrimidines"*Arch Pharm,* 1998, 331, 201–206.
22. Tozkoparan, B.; Ertan, M.; Kelicen, P.; Demirdamar, R., "Synthesis and anti-inflammatory activities of some thiazolo [3, 2-a] pyrimidine derivatives"*IIFarmaco*, 1999, 54, 588–593.
23. Jeanneau-Nicolle, E.; Benoit-Guyod, M.; Namil, A.; Leclerc, G., "New thiazolo [3, 2-a] pyrimidine derivatives, synthesis and structure-activity relationships" *European Journal of Medicinal Chemistry,* 1992, 27, 115-120.
24. Pan, B.; Huang, R.; Zheng, L.; Chen, C.; Han, S.; Qu, D.; Zhu, M.; Wei, P., "Thiazolidione derivatives as novel antibiofilm agents: Design, synthesis, biological evaluation, and structure–activity relationships"*European Journal of Medicinal Chemistry*, 2011,46, 819–824.
25. Ghorab, M.; Abdel-Gawad, S.; El-Gaby, M., "Synthesis and evaluation of some new fluorinated hydroquinazoline derivatives as antifungal agents"*Farmaco*,2000,55, 249–255.
26. Mohamed, S.F.; Flefel, E.M.; Amr, A.E.G.E.; El-Shafy, "Anti-HSV-1 activity and mechanism of action of some new synthesized substituted pyrimidine, thiopyrimidine and thiazolopyrimidine derivatives" *European Journal of Medicinal Chemistry*, 2010,45, 1494–1501.
27. Maddila, S.; Damu, G.; Oseghe, E.; Abafe, O.; Rao, C.V.; Lavanya, P., "Synthesis and biological studies of novel biphenyl-3, 5-dihydro-2H-thiazolopyrimidines derivatives" *Journal of Korean Chemical Society*,2012,56, 334–340.
28. Flefel, E.; Salama, M.; El-Shahat, M.; El-Hashash, M.; El-Farargy, A., "A novel synthesis of some new pyrimidine and thiazolopyrimidine derivatives for anticancer evaluation"*Phosphorus Sulfur Silicon Related Elements*, 2007, 182, 1739–1756.
29. Al-Omary, F.A.; Hassan, G.S.; El-Messery, S.M.; El-Subbagh, H.I., "Substituted thiazoles V. Synthesis and antitumor activity of novel thiazolo [2, 3-b] quinazoline and pyrido [4, 3-d] thiazolo [3, 2-a] pyrimidine analogues"*European Journal of Medicinal Chemistry*, 2012,47, 65–72.
30. Danel, K.; Pedersen, E.B.; Nielsen, C., "Synthesis and Anti-HIV-1 Activity of Novel 2,3-Dihydro-7H-thiazolo[3,2-a]pyrimidin-7-ones"*Journal of Medicinal Chemistry*,1998,41, 191–198.
31. Balkan, A.; Uma, S.; Ertan, M.; Wiegrebe, W., "Thiazolo [3, 2-α]-pyrimidine derivatives as calcium antagonists" *Pharmazie*, 1992, 47, 687–688.
32. Geist, J.G.; Lauw, S.; Illarionova, V.; Illarionov, B.; Fischer, M.; Gräwert, T.; Rohdich, F.; Eisenreich, W.; Kaiser, J.; Groll, M., "Thiazolopyrimidine Inhibitors of 2-Methylerythritol 2,4-Cyclodiphosphate Synthase (IspF) from Mycobacterium tuberculosis and Plasmodium falciparum"*ChemMedChem*,2010, 5, 1092–1101.
33. Wichmann, J.; Adam, G.; Kolczewski, S.; Mutel, V.; Woltering, T., "Structure-activity relationships of substituted 5H-thiazolo [3, 2-a] pyrimidines as group 2 metabotropic glutamate receptor antagonists"*Bioorganic and Medicinal Chemistry Letters*,1999, 9, 1573–1576.
34. Awadallah, F.M., "Synthesis, pharmacophore modeling, and biological evaluation of novel 5H-thiazolo [3, 2-a] pyrimidin-5-one derivatives as 5-HT2A receptor antagonists" *ScientiaPharmaceutica*,2008, 76, 415–438.
35. Kolb, S.; Mondésert, O.; Goddard, M.L.; Jullien, D.; Villoutreix, B.O.; Ducommun, B.; Garbay, C.; Braud, E., "Development of novel thiazolopyrimidines as CDC25B phosphatase inhibitors" *ChemMedChem*, 2009, 4, 633–648.

36. Liu, S.; Shang, R.; Shi, L.; Wan, D.C. C.; Lin, H., "Synthesis and biological evaluation of 7H-thiazolo [3, 2-b]-1, 2, 4-triazin-7-one derivatives as dual binding site acetylcholinesterase inhibitors "*European Journal of Medicinal Chemistry*, 2014,81, 237–244.

Table I: IUPAC name of C-Mannich Bases (9a-g & 10 a-g)

Entry	Heterocyclic 2⁰-amines (8a-g)	IUPAC Name	Mole. formula	m.p⁰C	Yield %
9a	Benzimidazole	ethyl 2-((1H-benzo[d]imidazol-1-yl)methyl)-5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{24}H_{21}ClN_4O_3S$	245	73
9b	2-Methyl benzimidazole	ethyl 5-(2-chlorophenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazol-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{23}ClN_4O_3S$	147	61
9c	2-Benzyl benzimidazole	ethyl 2-((2-benzyl-1H-benzo[d]imidazol-1-yl)methyl)-5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{31}H_{27}ClN_4O_3S$	188	57
9d	Benzotriazole	ethyl 2-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-5-(2-chlorophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{23}H_{20}ClN_5O_3S$	241	62
9e	Morpholine	ethyl 5-(2-chlorophenyl)-7-methyl-2-(morpholinomethyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{21}H_{24}ClN_3O_4S$	235	84
9f	Phthalimide	ethyl 5-(2-chlorophenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{20}ClN_3O_5S$	251	56
9g	Terahydro carbazole	ethyl 5-(2-chlorophenyl)-2-((3,4-dihydro-1H-carbazol-9(2H)-yl)methyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{29}H_{28}ClN_3O_3S$	146	65
10a	Benzimidazole	ethyl 2-((1H-benzo[d]imidazol-1-yl)methyl)-5-(4-bromophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{24}H_{21}BrN_4O_3S$	168	79
10b	2-Methyl benzimidazole	ethyl5-(4-bromophenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazol-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{23}BrN_4O_3S$	210	64
10c	2-Benzyl benzimidazole	ethyl 2-((2-benzyl-1H-benzo[d]imidazol-1-yl)methyl)-5-(4-bromophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{31}H_{27}BrN_4O_3S$	151	77

10d	Benzotriazole	ethyl2-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-5-(4-bromophenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{23}H_{20}BrN_5O_3S$	231	60
10e	Morpholine	ethyl5-(4-bromophenyl)-7-methyl-2-(morpholinomethyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{21}H_{24}BrN_3O_4S$	148	81
10f	Phthalimide	ethyl5-(4-bromophenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{20}BrN_3O_5S$	171	79
10g	Terahydro carbazole	ethyl5-(4-bromophenyl)-2-((3,4-dihydro-1H-carbazol-9(2H)-yl)methyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{29}H_{28}BrN_3O_3S$	224	64

Table II. Influence of solvent on Mannich reaction[a]. (typically for compound 9a)

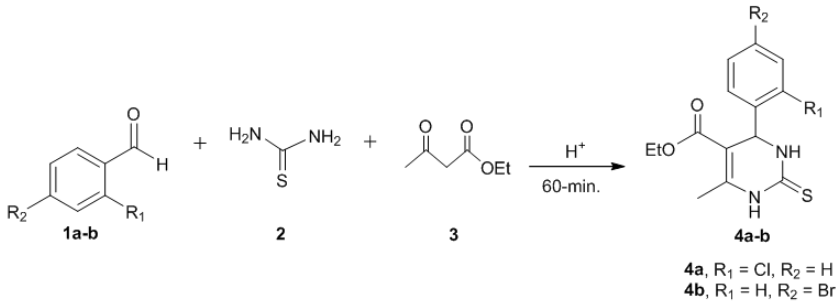
Entry	Solvent	Yield %
1	1,4-dioxane	No reaction
2	CH_2Cl_2	46
3	MeCN	74
4	H_2O	35
5	EtOH	96
6	Benzene	No reaction
7	THF	38
8	DMF	39
9	Cyclohexane	56

Table III: Antibacterial activity of compounds 9a-g and 10a-g, zone of inhibition/mm

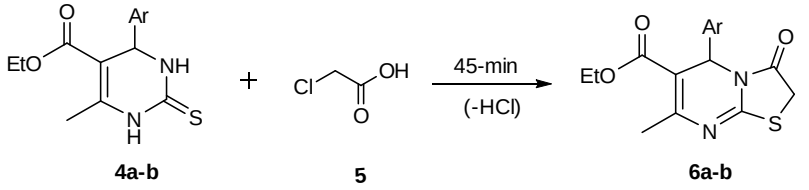
Compound	*Escherichia coli*	*Bacillus subtilis*	*Bacillus megaterium*	*Staphylococcus aureus*	*Vibrio cholera*
9a	29	24	14	19	24
9b	19	17	11	14	--
9c	--	--	10	--	14
9d	26	24	15	21	23
9e	26	21	16	23	30
9f	21	17	13	22	18
9g	19	18	12	14	17
10a	26	21	16	21	24
10b	20	16	15	18	20
10c	10	13	10	--	--
10d	24	20	15	21	23
10e	27	22	16	23	31
10f	20	17	13	26	21
10g	18	16	13	16	21
Cipro floxacin	27	23	18	24	28

Table IV: Antifungal activity of compounds 9a-g and 10a-g, zone of inhibition/mm

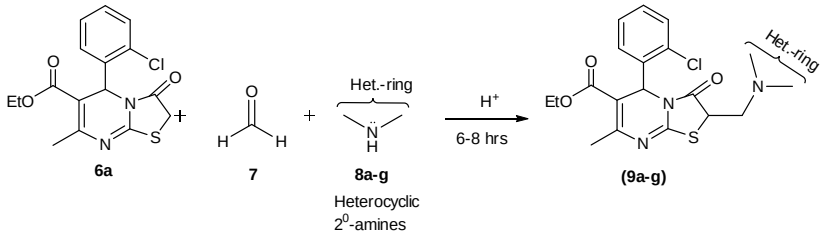
Compound	*Aspergillus niger*	*Candida albicans*
9a	20	21
9b	17	16
9c	11	12
9d	--	--
9e	24	20
9f	13	15
9g	12	15
10a	23	21
10b	16	18
10c	13	13
10d	24	25
10e	24	26
10f	15	17
10g	13	16
Clotrimazole	22	24



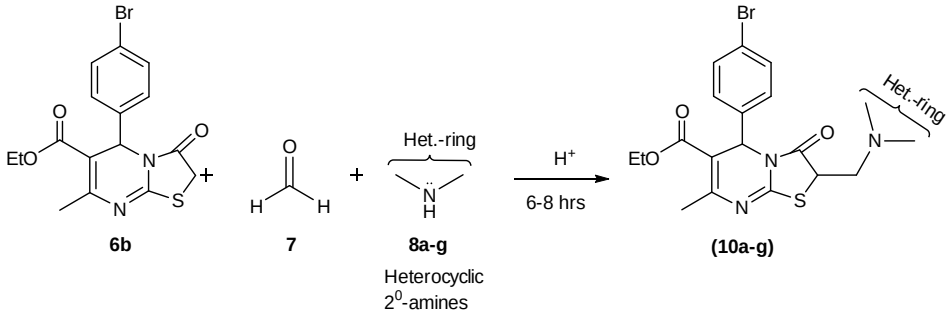
Scheme I: Biginelli Reaction



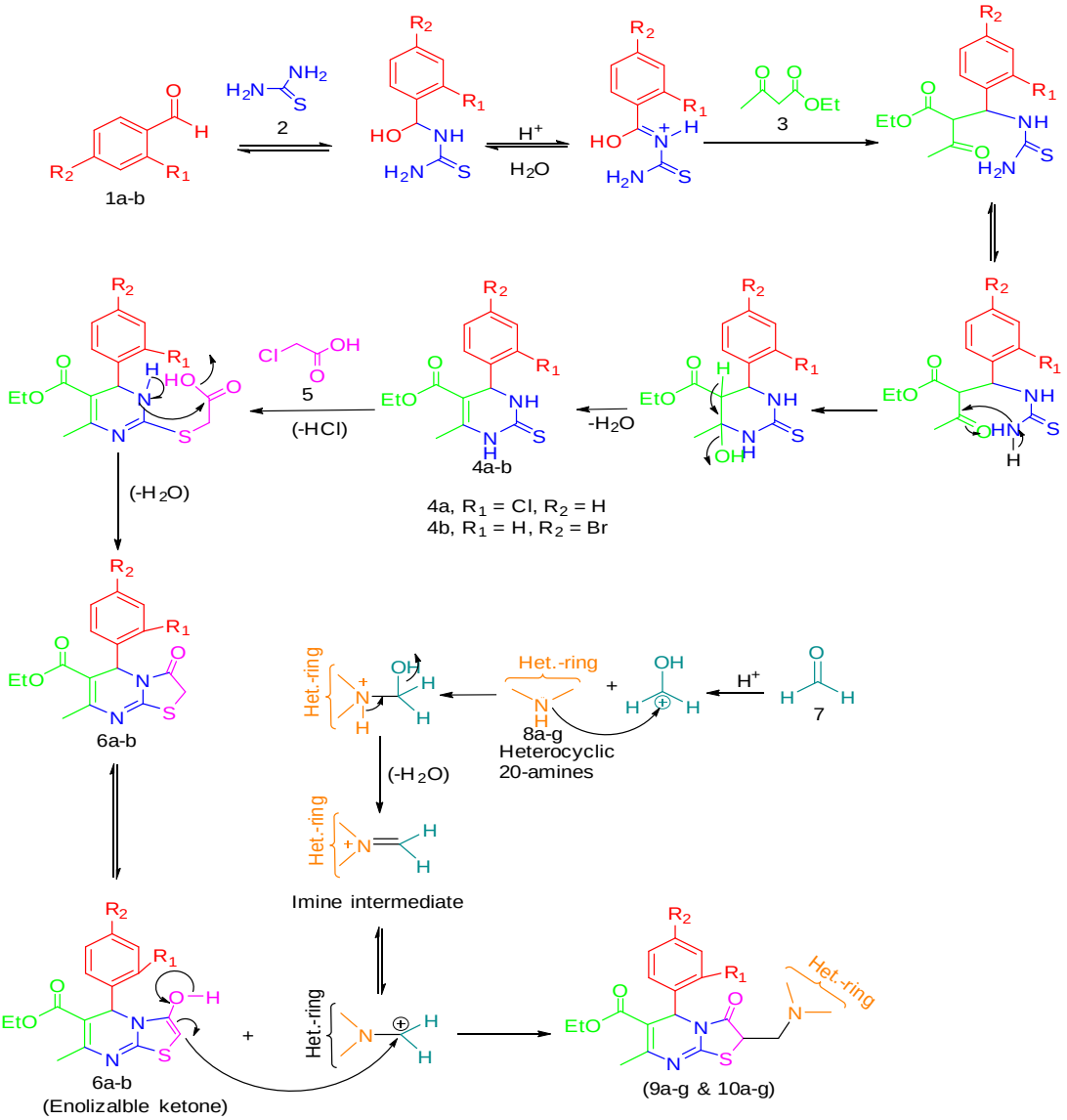
Scheme II: Cyclization reaction of Dihydropyrimidine



Scheme III: Mannich Reaction



Scheme IV: Mannich Reaction



Scheme V: plausible mechanism is proposed

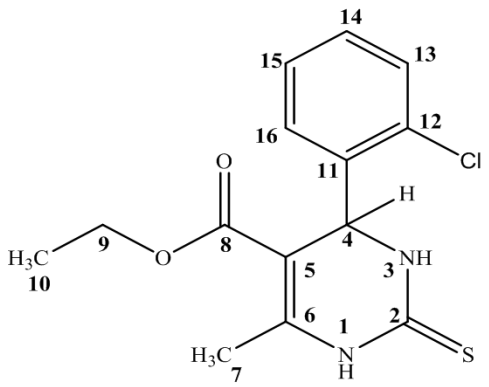


Fig. I: General structure of Dihydropyrimidone

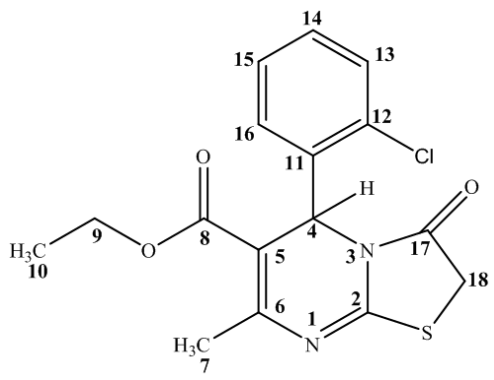


Fig. II: General structure of thiazolo [3,2-a]pyrimidine-6-carboxylate

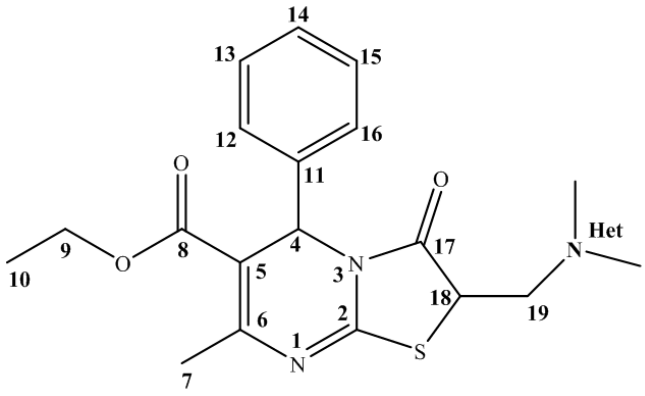


Fig. III: General structure of series of C-Mannich bases (9a-g&10a-g)

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RESEARCH ARTICLE

Study on Heavy Metals and Physicochemical Properties of Water of Abandoned Open Cast Coal Mine Pit: Special Reference to Damalia OCP, Raniganj, West Bengal

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ABSTRACT

The present study was undertaken to determine the amount of different heavy metals and physicochemical properties of water of surface water of abandoned open cast pit (OCP) in coal mine of Damalia. The concentrations of eight heavy metals (Cu □0.013 mg/l, Zn □0.013 mg/l, Cr 0.133 □mg/l, Pb □0.058 mg/l, Se □0.013 mg/l, □As 0.018 mg/l, F 0.015 □mg/l and Mn 0.01 mg/l) were comparatively higher than their mean background values of the surface water of that area. The spatio-temporal variation was recorded in physical, chemical and biological characteristics of water collected from three different locations of Raniganj coalfield area. Heavy metal contaminations in the Damalia abandoned OCPs was comparatively higher during the monsoon and lower in post-monsoon. Seasonal variation in physicochemical properties of water was also recorded. The present study on the surface water of coal mine pits around open cast mines of coal field area indicates that mining activity has a severe negative impact on water and soil characteristics. Analysis of biodiversity Index (WQI) of this mining area showed a correlation with the hazardous impact of heavy metals on aquatic ecosystem. The outcome of present water parameter analyses may be a sustainable basis for the preparation of management plans and utilitarian perspective. This study can be used as a baseline data on the determination of environmental degradation and its effective management in similar mining field in world.

Keywords: Abandoned OCP, Coal mine pits, Heavy metals, toxicity, Spatio-temporal variation, Physicochemical properties, Water Quality Index (WQI)

INTRODUCTION

During open cast mining activity degradation of ecological environment of the OCP occurred due to removal of top soil layers, land erosion, loss of soil profile and runoff from surrounding surface area reducing the fertility status of top soil (Kundu and Ghose, 1994). The chemical composition including heavy metals of the water in OCP are mainly dependent on the nutrients present in the top soil that come to the water bodies through rain water during monsoon (Ghose, 2001; Dutta and Agrawal, 2002; Ghose, 2004; Mercuri et al., 2005; Maiti, 2007; Sheoran et al., 2010). Different heavy metals found in the rocky bottom sediments are the major contaminants of the OCP water bodies. (Stoertz et al., 2002; Johnson, 2003; Pagnanelli et al., 2004; Razo et al., 2004; Marín-Guirao et al., 2005; Maiti, 2007; Bhuiyan et al., 2010; Das and Chakrapani, 2011). The mine-water discharge containing high concentration of different heavy metals (Fe, Cu, Zn, Co, Cr, Mn, Pb, Cd etc.) leads to metal pollution to the coal pit aquatic ecosystem in the Raniganj Coalfield (De and Mitra, 2002; Singh et al., 2009; Singh et al., 2010; Das and Chakrapani, 2011). In the open cast area, groundwater table is basically dependent on post mining reclamation. The final physical and chemical composition of OCP water purely depends on the composition of the receiving flooded water. The several other factors that have great influence on the OCP water quality are geological structure, wall rock texture and physical and chemical strata of the surrounding area along with sediment generated through biogeochemical processes (Castendyk et al 2015). The objective of the present study was to determine the nature and magnitude of concentration of different heavy metals and physicochemical properties of surface water of abandoned open cast pit (OCP) in coal mine of Damalia, Raniganj, West Bengal during pre-monsoon, monsoon and post-monsoon.

Physiography of the area

Raniganj Coalfield is geographically spread mainly in stretch of the Damodar river bank in the Asansol and Durgapur Subdivision of West Bengal and few portion of Jharkhand. The coal field is encircled with Archean rock system in West, South & North side, but in east side the coal field surrounded by Gondwana Shield. There is an alluvium stratum beneath the coal field area. Our present study site is Damalia OCP which is an abandoned open cast coal opening. It is located in Satgram area under ECL near South of Harabanga Village. The geographical location of this OCP is 23^{0}36' 32'' N Lat and 87^0 04' 00'' E Long (Figure 1). The altitude of this site is 88.45m from MSL. The length of this reverse "L" shaped OCP is 650m where the width of this OCP is 710m. The average depth of this OCP is 220m.

MATERIALS AND METHODS

Our present study is based on direct sample collection from the study site Damalia. Data were collected from surface water of Damalia abandoned OCP during pre-monsoon, monsoon and post-monsoon periods (Figure 2). Locational and geological data were collected from ECL office of Satgram area. The study was done in different climatic conditions like pre-monsoon, monsoon and post-monsoon. Water sample was collected on February, June and October 2019 from the study site, i.e. Damalia abandoned OCP to analyse the nature and proportion of heavy metal (HM) and its variability during three seasons. We have been selected February month for pre-monsoon, June for the monsoon season and October for post-monsoon season for water sample collection and for better understanding about the season wise dispersion of heavy metal in this OCP. Standard protocols and methodologies were maintained during sampling and analyses of the mine water (BIS 1987, APHA, 1989). Different heavy metals were taken into consideration to analyse the nature and magnitude of their concentrations during different seasons. Community response and their experiences were also recorded during site visit. Background and history of this study area were taken from earlier literatures (Karim et al, 2014). The whole study was based on primary data and was analysed in NABL accredited laboratory. Different statistical methods were used to compute the data. Methodologies like Arithmetic mean, ANOVA, frequency distribution (bar or comparative bar) were used for the study of significance and correlation of the data. The statistical method ANOVA was used to determine the views and dependency of variables between the groups and within the group. This statistical method is good tool for

analysing the relationship between several parameters and components. We have putted the data in SPSS software to represent the cartograms. Correlation statistics was performed by using SPSS statistical software version 16.0 for analysing the data set and get better result. Arithmetic Mean (AM) was calculated on the basis of data sets regarding three different climatic conditions. This methods are used to compare the inter monsoon relationship in respect of concentration of heavy metals. It is a vital technique to determine the mode of deviation of each parameter.

RESULTS AND DISCUSSION

As we know that the OCP is fall under Raniganj coalfield area of ECL, India and the mining activity is extensively observed here throughout the year. Mode of mining operation is done in two ways, i.e. deep mining and open cast mining. The said OCP was under open mining operation, which is now abandoned in nature. The last mining has been done in the year. In respect to analyse the water quality MOEF (Ministry of Environment and Forest) has given a standard protocol in scheduled VI. As per the analysis of collected sample, heavy metals data are computed in tabular set up and as a seasonal basis (Table 1). As (Arsenic) concentration is the highest in rainy season, but in other three seasons the concentration of As remains under permissible limit. Pb (Lead) may vary in different season like post-monsoon<pre-monsoon<monsoon. Se (Selenium) concentration is the highest as per permissible limit in comparison to other heavy metal (HM). The concentration of other heavy metal, like Zn (Zinc), Cu (Copper), F (Fluoride), Mn (Manganese) is low as per the standard level. But in every case, it is observed that the seasonal concentrations of heavy metals remain in following order: Monsoon> post-monsoon> pre-monsoon except Pb (Lead) and F (Fluoride) concentration. In case of these two heavy metals, their concentrations remain in the order of Monsoon>pre-monsoon>post-monsoon. Season wise concentration of Mn (Manganese) is same. It is mainly occur, due to heavy water discharge from surrounding mining area in monsoon season and the loose material existence in the upper surface portion, which easily pile up with water. HM are well mixed with rain water and flow towards Damalia abandoned OCP continuously as surface discharge.

From ANOVA (Two Way Analysis), the relation between different rows, i.e. within properties and between different columns, i.e. within the season, has been discussed easily. When we calculate and observed the F value and F critical value in respect of different properties. There was significant difference is observed. That means F critical value is less than F value. It signifies that there is no effect or relationship in between different heavy metals. But when we see at the season wise ANOVA, it is showed that Critical value is higher than F observed value. That means there is no such significant difference within the three monsoon season. So, it may be argued that the parameters may change and the rate of concentration in the said water bodies may also be change. Season wise mean value of each HMs were also calculated and represented in relative bar diagram. In each case it has been seen that monsoon is the dominant season. As per mean value, the season wise HMs concentration of Hexavalent chromium , Cr, Zn, Se are as follows- PRM=POM<MON Where PRM denotes pre-monsoon, POM denotes post-monsoon and MON denotes Monsoon season. From comparative study, it was observed that Se, Cr, As, Zn, Cu concentration was half in pre-monsoon in comparison to monsoon season. Other case of HMs, i.e. F, Pb, Mn, the rate of concentration is almost same in respect to monsoon season. pre-monsoon and post-monsoon value of each heavy metals was almost same every season. It may be stated that there is no significant variance in pre and post-monsoon data base.

CONCLUSION

Since the 18th century, due to excessive and long time coal mining in the area has created massive geo-environmental (Vartanyan 1989; Aswathanarayana 1995) depletion. In the various geo-environmental impacts of coal mining, degradation of abandoned water bodies (OCP) are the most significant issues in present days. In the study area, coal mining activity was carried out mainly through the open-cast method, which resulting in the dumping of large amounts of removal material around the O.C.P (De, S. and Mitra, A.K., 2002). In Raniganj Coal field the abandoned OCPs are great important on hydrologic sphere. The fluvial water bodies came into the coal mine areas

and stored in the mine-cave. It is partially used during mining activities and the excess amount is released into the upper surface system through pumping removal system. In the coal mining project area, it imposes significant effects on water quality and its supply. In this aspect it is argued that the mine surface and underground water supplies will remain suitable for different human purposes and the quality of upper surface water of the OCPs will favourable for zooplanktons and phytoplankton's and wildlife (Russell, 1999; Groudev et al., 2008; Chernaik, 2010). Good water quality is the most important as well as necessary condition for human life and the better and structured economy (Absalon and Matysik, 2007). In several countries, scientific monitoring of OCP water is now not only an utmost responsibility but also ethical as well as moral duty (Kallis and Butler, 2001). Our present findings revealed that the abandoned Damalia OCP water is polluted due to of contamination of heavy metals (HM) through surface water discharge. In this study, the heavy metals concentration in the pit water is within permissible limit as per MoEF Schedule-VI Standard. Normally it is found that the quality of pit water is deteriorated badly due to accumulating of toxic HMs and sediment drainage from adjacent area. In this aspect to improve the quality of pit water is needed of continuous observation and monitoring on pollution level and simultaneously promote limnology.

REFERENCES

1. Absalon, D. & Matysik, M. 2007. Changes in water quality and runoff in the Upper Oder River Basin. Geomorphology, 92(3-4): 106—118.
2. Akburak, S., Kul, A.A., Makineci, E., Ozdemir, E., Aktaş, N.K., Gürbey, A.P., Yurtseven, H., Köse, M. and Akgün, T., 2020. Chemical water parameters of end pit lakes in abandoned coal mines. Arabian Journal of Geosciences, 13(13), pp.1-12.
3. APHA, 1989. Standard Methods for the Examination of Water and Wastewater. American Public health Association, Washington, DC.
4. Aswathanarayana U (1995) Geoenvironment – an introduction. Balkema, Rotterdam
5. Avantika Chandra, M.K.J. and Kumar, V. 2014 Quality index of surface water near overburden dumping site in coal mining area.
6. Bhuiyan M.A.H., Parvez L., Islam M.A., Dampare S.B., Suzuki S., (2010), Heavy metal pollution of coal mine-affected agricultural soils in the northern part of Bangladesh, Journal of Hazardous Materials, 173(1-3), pp 384-392.
7. Carter, J. & Howe, J. 2006. The Water Framework Directive and the Strategic Environmental Assessment Directive: Exploring the linkages. Environmental Impact Assessment Review, 26(3): 287-300.
8. Carter, J. & Howe, J. 2006. The Water Framework Directive and the Strategic Environmental Assessment Directive: Exploring the linkages. Environmental Impact Assessment Review, 26(3): 287-300.
9. Castendyk DN, Eary LE, Balistrieri LS (2015) Modelling and management of pit lake water chemistry:Theory.AppliedGeochemistry57: 267-288, doi: 10.1016/j.apgeochem.2014.09.004.
10. Cheng, W., Lei, S., Bian, Z., Zhao, Y., Li, Y. and Gan, Y., 2020. Geographic distribution of heavy metals and identification of their sources in soils near large, open-pit coal mines using positive matrix factorization. Journal of hazardous materials, 387, p.121666.
11. Chernaik, M. 2010. Guidebook for evaluating mining project EIAs. 1st edn. Environmental Law Alliance Worldwide. 8.
12. Das S.K., and Chakrapani G.J., (2011), Assessment of trace metal toxicity in soils of Raniganj Coalfield, India, Environ Monitoring and Assessment, 177, pp 63-71.
13. De S., and Mitra A.K., (2002), Reclamation of mining-generated wastelands at Alkusha–Gopalpur abandoned open cast project, Raniganj coalfield, eastern India, Environmental Geology, 43, pp 39-47.
14. De, S. and Mitra, A.K., 2002. Reclamation of mining-generated wastelands at Alkusha–Gopalpur abandoned open cast project, Raniganj Coalfield, eastern India. Environmental Geology, 43(1-2), pp.39-47.
15. Dutta R.K., and Agrawal M., (2002), Effect of tree plantations on the soil characteristics and microbial activity of coal mine spoil land, Journal of tropical ecology, 43(2), pp 315-324.

16. European Commission (2000). Directive 2000/60/EC of the Community action in the field of water policy. Official Journal of the European Union, 1-77.
17. Ghose M.K., (2001), Management of topsoil for geo-environmental reclamation of coal mining areas, Environment geology, 40(11-12), pp 1405-1410.
18. Ghose M.K., (2004), Effect of opencast mining on soil fertility, Journal of scientific and industrial research, 63, pp 1006-1009.
19. Groudev, S. N., Georgiev, P., Spasova, I. & Nicolova, M. 2008. Prevention of acid drainage from mining wastes from a uranium deposit. Hydrometallurgy. 94: 93-99.
20. Johnson D.B., (2003), Chemical and microbiological characteristics of mineral spoils and drainage waters at abandoned coal and metal mines, Water air soil pollution, 3, pp 47-66.
21. Kundu N.K., and Ghose M.K., (1994), Studies on the topsoil of an underground coalmining project, Environment conservation, 21(2), pp 126-132.
22. Maiti S.K., (2007), Bioreclamation of coalmine overburden dumps—with special empasis on micronutrients and heavy metals accumulation in tree species, Environmental Monitoring and Assessment,125, pp 111-122.
23. Maiti S.K., (2007), Bioreclamation of coalmine overburden dumps—with special empasis on micronutrients and heavy metals accumulation in tree species, Environmental Monitoring and Assessment,125, pp 111-122.
24. Marín-Guirao L., Cesar A., Marín A., Lloret J., and Vita R., (2005), Establishing the ecological quality status of soft-bottom mining-impacted coastal water bodies in the scope of the Water Framework Directive, Marine pollution bulletin, 50, pp 374-387.
25. Mercuri A.M., Duggin J.A., and Grant C.D., (2005), The use of saline mine water and municipal wastes to establish plantations on rehabilitated open-cut coal mines, Upper Hunter Valley NSW, Australia, For ecological management. 204(2-3), pp 195-207.
26. Pagnanelli F., Moscardini E., Giuliano V., and Toro L., (2004), Sequential extraction of heavy metals in river sediments of an abandoned pyrite mining area: pollution detection and affinity series, Environment pollution, 132(2), pp 189-201.
27. Pal, S., Mukherjee, A.K., Senapati, T., Samanta, P., Mondal, S. and Ghosh, A.R., 2014. Study on littoral zone sediment quality and aquatic Macrophyte diversity of opencast coal pit-lakes in Raniganj coal field, West Bengal, India. International Journal of Environmental Sciences, 4(4), p.575.
28. Pandey, B., Mukherjee, A., Agrawal, M. and Singh, S., 2019. Assessment of seasonal and site-specific variations in soil physical, chemical and biological properties around opencast coal mines. Pedosphere, 29(5), pp.642-655.
29. Prathap, A. and Chakraborty, S., 2020. Assessment of surface water quality around opencast coal mines for sustainable utilization potentials: a case study in Jharkhand, India. Environment, Development and Sustainability, 22(4), pp.3179-3205.
30. Razo I., Carrizales L., Castro J., Díaz-Barriga F., and Monroy M., (2004), Arsenic and heavymetal pollution of soil,water and sediments in a semi-arid climate mining area in Mexico, Water Air Soil Pollution, 152, pp 129-152.
31. Sheoran V., Sheoran A.S., and Poonia P., (2010), Soil reclamation of abandoned mine land by revegetation: a review, International journal of soil sediment water, 3(2), pp 1940-3259.
32. Russell, H. P. (Jr). 1999. Characterization of mine leachates and the development of a ground water monitoring strategy for mine sites. Environmental Protection Development Agency Washington, D.C. United States Office of Research and EPA/600/SR-99/007.
33. Singh A.K., Mahato M.K., Neogi B., and Singh K.K., (2010), Quality Assessment of Mine Water in the Raniganj coalfield Area, India, Mine water environment, 29(4), pp 248-262.
34. Singh A.K., Mondal G.C., Tewary B.K., and Sinha A., (2009), "Major ion chemistry, solute acquisition processes and quality assessment of mine water in Damodar Valley Coalfields, India", International mine water conference 19th – 23rd October 2009, Pretoria, South Africa, Document transformation technologies, 267-276.
35. Stoertz M., Bourne H., Knotts C., and White M., (2002), the effects of isolation and acid mine drainage on fish and macroinvertebrate communities of Monday Creek, Ohio, USA, Mine water environment, 21(2), pp 60-72.
36. Vartanyan GS (1989) Mining and the geoenvironment. In: Kozlovsky EA (ed) Geology and the environment, vol 2. UNESCO, Paris, UNEP, Nairobi.

37. Karim, Z., Qureshi, B.A., Mumtaz, M. and Qureshi, S., 2014. Heavy metal content in urban soils as an indicator of anthropogenic and natural influences on landscape of Karachi—a multivariate spatio-temporal analysis. Ecological indicators, 42, pp.20-31.

Table 1. Season (Pre-monsoon=Prm; Monsoon=Mon; Post-monsoon=pom) wise heavy metals concentration (mg/l) in Damalia abandoned OCP

Name of chemical	Quantity (mg/l)			Mean value (mg/l)	Comparision	Permissible limit (as per MoEF schedule-VI standard) (mg/l)
	Pre-monsoon	Monsoon	Post-monsoon			
Arsenic	0.015	0.03	0.01	0.0183	pom<prm<mon	0.2
Lead	0.055	0.07	0.05	0.0583	pom<prm<mon	0.1
Hexavalent chromium	0.001	0.002	0.001	0.0013	prm=pom<mon	0.1
Total chromium	0.1	0.2	0.1	0.1333	prm=pom<mon	2
Copper	0.01	0.02	0.01	0.0133	prm=pom<mon	3
Zinc	0.01	0.02	0.01	0.0133	prm=pom<mon	5
Selenium	0.01	0.02	0.01	0.0133	prm=pom<mon	0.05
Fluoride	0.015	0.02	0.01	0.0150	pom<prm<mon	2
Manganese	0.01	0.01	0.01	0.0100	prm=pom=mon	2

Table 2. ANOVA (Two Way) on season wise concentrations (Pre-monsoon, Monsoon, Post-monsoon) of heavy metals (mg/l) in Damalia abandoned OCP and their variability

Source of Variation	SS	df	MS	F	P-value	F crit
Rows	0.034394	7	0.004913	9.09787227	0.004662	3.787044
Columns	0.00162	1	0.00162	2.999768545	0.126883	5.591448
Error	0.00378	7	0.00054			
Total	0.039794	15				

Notes: SS = Sum of Squares, df = Degree of Freedom, MS = Mean Sum of Squares, F_{obs} = Observed F, P- value = Probality, F_{crit} = Critical F.

Figure -1(A)

Figure -1(B)

Figure 1. Topographical (A) and satellite (B) views of Damalia abandoned OCP

Figure 2(A)

Figure 2(B)

Figure 2. Photographic views of Damalia abandoned OCP

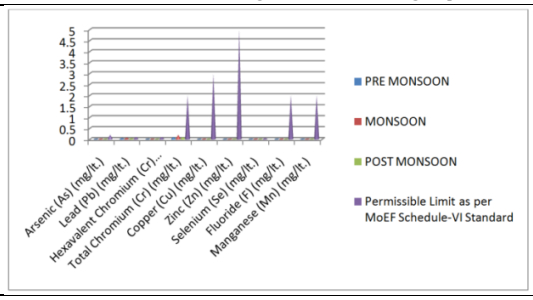

Figure 3. Comparative Bar for showing seasonal variability of Heavy Metals

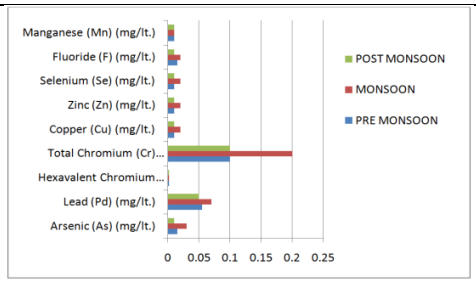

Figure 4. Relative concentrations of heavy metals during Pre-monsoon, Monsoon, Post-monsoon

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REVIEW ARTICLE

Applications of Solid Lipid Nanoparticle

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ABSTRACT

Solid lipid nanoparticles are the excellent tools of nanotechnology widely used in medicine for drug delivery and research. The SLNs have widen their applications from medicine to food science, cosmetics and dermaceuticals. This review presents a broad application of solid lipid nanoparticles in the various fields of medicines in the drug therapy. The explore of SLNs for delivery of Phyto actives also reviewed. The current use and future potential of SLNs in medicine phytopharmaceuticals and cosmetics are to be explored.

Keywords: Solid lipid nanoparticles (SLN), Application of SLNs

INTRODUCTION

Solid lipid nanoparticles are one of the novel potential colloidal transporter system. Solid lipid nanoparticles (SLNs) are considered to be the most effective lipid based colloidal carriers introduced in early nineties. SLNs are in the range of submicron size (50-1000 nm) and are composed of physiologically tolerated lipid components which are in solid state at room temperature. SLNs offer various advantages as compared to other nano carriers .This promising drug carrier system is at the interface in the preexisting lipid systems (emulsions and liposomes) and polymeric nanoparticle systems. Lipid nanoparticles, known as SLNs [1]. The SLNs open the door in nano medicine for various applications .

SLNs for cosmetics

SLNs used in the most modern moisturizing and antiaging preparations, conditioners, or sunscreens [2].SLNs have been used in the delivery of sunscreen agents and to improve cosmetics efficacy. Suter et al developed SLNS loaded with heptapeptide to improve peptide delivery in to the skin and allowing to perform protective functions and cosmetic anti aging applications and they finally enabled to deliver heptapeptides [3]. The *In vivo* study concluded that skin hydration improvement of 31% after 4 weeks with the creams having 4% SLNs. the molecular sunscreens amount is decreased to 50% with the formulation with SLNs.[4]

SLNs in dermaceuticals

The solid lipid nano particle explored new way to deliver the epidermis and dermis with its special properties of occlusion, adhesiveness, improved chemical stability and sustained release properties. Delivery of antimicrobials like econazole, miconazole, fluconazole, Amphotericin B is possible through SLNs. and other diseases like psoriasis, contact dermatitis, acne, melanoma, skin cancer has been shown effective results with SLNs [5]. Long term oral administration limited drug piroxicam an anti-inflammatory, antipyretic, analgesic drug is formulated as nono lipidic SLNs gel for enhancing skin permeation and found a better permeation rate as compared to marketed piroxicam gel [6]. Moazeni et al formulated fluconazole loaded SLNs and evaluated the efficacy on the fluconazole resistant species of *Candida* species and the study reported the effectiveness of the novel formulation [7]. Tupal et.al formulated Doxorubicin SLNs for topical delivery to skin cancer. The *In vitro* and *In vivo* cytotoxicity effect shows superior as compared to Doxorubicin solution and it shows the possibility of topical delivery to skin cancer through SLNs [8].

SLNs in vaccine delivery

The sub unit vaccine efficiency can be improved by adjuvants, which improves the immune response during vaccination. The degradable O/W emulsion systems of SLNs are employed to use as adjuvant [09].Li et.al studied the potential of cationic solid lipid nanoparticles (cSLN) as efficient adjuvants for inactivated foot and mouth disease virus (iFMDV) vaccine. They formulated the SLNs and loaded with the Ifmdv and found it with enhanced stability. Animal trials showed that enhanced memory immune response including effector-memory T cells and central-memory T cells compared to free iFMDV antigen and antigen adjuvanted with ISA 206.so it can be a better adjuvant for vaccine delivery[10].Cancer immunotherapy uses mRNA vaccines which elict immune response including antibodies and cytotoxic T cells and it also used as prophylactic vaccines. Lipid nanoparticles are used for efficient delivery of mRNA vaccines the targeted approach to any cell and stability of mRNA are added advantage with lipid nanoparticles[11].

SLNs for proteins and peptides

Therapeutic peptides, proteins and antigens can be delivered as Solid lipid nanoparticles. The hydrophilic and hydrophobic proteins can be delivered through SLNs. The SLNs loaded with proteins and antigens with the advantage of protein stability, sustained drug release and protection from proteolytic degradation are administred by various routes like oral, nasal routes. peptides like insulin, calcitonin somatostatin are incorporated into SLNs for efficient drug delivery [12]. Su et al studied the effect of SLNs on the stability profile of Oat globulin derived peptides in simulated gastrointestinal fluids. The two fractions of Oat globulin derived peptide are loaded into SLNs and found that both the fraction having different release rate however both the fractions have high bioactivity and secondary hydrolysis is prevented. The stability also well established from the IR spectroscopy and X ray diffraction study all the study shows the improved functionality of peptides with SLNs [13].

SLNs for anti-tubercular drugs

Tuberculosis an infectious disease worldwide killing millions. The treatment of T.B associated with long term therapy and frequent dosing frequency which leads to non adherence to the treatment ultimately results into MDR T.B. SLNs can attribute to improve the efficacy of the Anti-T.B drugs for effective treatment of Tuberculosis. Choksi et.al developed SLNs with rifampicin, a first line drug for tuberculosis with low bioavailability by using high pressure homogenization technique and the Rifampicin loaded SLNs shows antilipolytic effect and high invitro G.I stability and accelerated stability studies shows a long term stability of SLNs [14]. Nemati et al formulated dry powder inhaler of SLNs loaded with Ethambutol for pulmonary administration and found that the SLNs are biocompatible and nontoxic and the aerodynamic properties also suitable for inhalation. These inhalable EMB-SLNs are a suitable formulation for avoiding the cellular toxicity and side effect of oral administration. [15]

SLNs for ocular drug delivery

The ocular drug delivery with conventional system unable to achieve the desired ocular bioavailability so SLNs can improve the corneal absorption of various ocular drugs to improve the bioavailanility the of autoclave sterilization of SLNs fulfills the requirement of ocular formulations.[16] Sharma et.al developed SLNs loaded with celecoxib to overcome the low bioavailability of the conventional drug delivery system for treatment of Ophthalmic flammations. The final results shows that the prolonged retention of the drugs in the ocular surface the corneal permeation also far better than the aqueous suspensions [17]. Wadetwar et al investigated the novel Bimatoprost solid lipid nanoparticles in-situ gel for the treatment of glaucoma. They found the drug release for a prolonged period of time and histopathological studies also revealed that no tissue damage. So SLN formulation can be a better treatment management for glaucoma.[18]

SLNs for Neuro diseases

The various obstacles to deliver drugs into CNS is crossing BBB and other problems encountered are poor water solubility, poor absorption, drug stability against chemical and enzymatic degradation. The SLNs can be a best solution to deliver the drugs in to the target site for treatment of Alzheimers and parkinsons disease [19].b-elemene is a essential oil with antitumor activity having limited bioavailability and poor water solubility. The SLNs delivery of b-elemene crosses Blood brain barrier and shows the same efficacy like commercial elemene with increased brain drug accumulation with less toxicity [20]. The SLNs offer to cross the BBB due to its lipophilic nature and targeted drug action also can be seen with Lactoferin conjugation of SLNs for neurotherapeutics like docetaxel loaded SLNs for brain drug delivery. The conjugation of SLNs can improve the targeting potency to the brain than simple SLNs [21].

SLNs for Phyto bioactive delivery

Phyto bioactive compounds shows various pharmacological effects to treat chronic diseases like diabetes, cancer, neurodegenerative diseases. oral delivery through SLNs is possible due to small size, high stability, and lymphatic uptake with increased bioavailability about 5 -10 times more than their original form. however the bust release makes the SLNs less adequate to use in oral drug delivery. Surface Modified SLNs can be prepared to overcome this limitation and Sustained release of phytoactives can also be achived. The various phyto bioactives like curcumin, Resveratrol, caffeic acid, ferulic acid can be delivered to various diseases through SLNs or MSLNs [22]. The plant actives and extracts which are used for many purposes can be delivered through nano vehicles like phytosomes, nanoparticles, hydrogels, microspheres, transferosomes and ethosomes, self nano emulsifying drug delivery systems (SNEDDS), self micro emulsifying drug delivery systems (SMEDDS).The use of nanotechnology approach enhances the bioavailability of the poorly water soluble herbal extracts[23]. SLNS can be used for delivery of food functional ingredient having antioxidant activity and phenolic compound rich extracts. Different phenloic compounds from sage and savoury extracts loaded in witespol SLNs and carnauba SLNs. The witespol SLNs showed most stable vehicle for delivery of the sage and savoury extracts [24].

SLNs for Food bioactive components

Potential application of SLNs as carrier of Bioactive components in food material can be explored with various applications. The poorly soluble bioactives can loaded in SLNs for food applications. Nanostructured lipid carriers and SLNs for encapsulation of β-carotene, [26] ergocalciferol (D2) [27], γ-tocotrienol, coenzyme Q10, curcumin [28] are studied with enhanced bioavailability and encapsulation for food industry [24].

SLNs for Delivery of anticancer Drugs

A no. Of drugs for anticancer treatment are in clinical practice have limited capacity in terms of bioavailabity and poor aqueous solubility, tissue toxicity due to non specific biodistribution ,drug resistance and cellular uptake .these limitation leads to lesser cytotoxic activity of anticancer drugs and ultimate sub optimal therapeutic efficacy and patient cure. Lipid based Nano carriers like SLNS can improve the limitations of conventional anticancer treatment

by highly capable anticancer drugs in terms of therapeutic activity and functionality. SLN for the encapsulation and delivery of cytotoxic anticancer compounds. Normal tissue toxicity, poor specificity and stability and a high incidence of drug- resistant tumor cells, are at least partially overcome by delivering them using SLN. Newer forms of SLN such as polymer– lipid hybrid nanoparticles, nanostructured lipid carriers and long-circulating SLN may further expand the role of this versatile drug carrier in cancer treatment [29]. Paclitaxel SLNs can be developed to improve its anticancer efficacy and to improve the uptake by MDR breast cancer cells. the increase uptake of the SLNs to MDR breast cancer cells by evading efflux pumps is found [30]. Mahmoudian et al selected the lipid carrier to improve the intestinal permeability of Bortezomib and the formulated SLNs loaded bortezomib shows improved intestinal permeability in intestinal perfusion studies [31].

CONCLUSION

The Solid lipid nanoparticles excelling itself in various field of drug therapy, cosmetics and food science. It has improved the limitations of various bioactives and drugs for better therapy and applications. The future will see the SLNs with their expanded possibilities

REFERENCES

1. Campos, J. R., Severino, P., Santini, A., Silva, A. M., Shegokar, R., Souto, S. B., & Souto, E. B. (2020). Solid lipid nanoparticles (SLN). In *Nanopharmaceuticals*. Elsevier. https://doi.org/10.1016/b978-0-12-817778-5.00001-4
2. Suter, F., Schmid, D., Wandrey, F., & Zülli, F. (2016). Heptapeptide-loaded solid lipid nanoparticles for cosmetic anti-aging applications. *European Journal of Pharmaceutics and Biopharmaceutics*, *108*, 304–309. https://.org/10.1016/j.ejpb.2016.06.014
3. Wissing, S. A., & Müller, R. H. (2003). Cosmetic applications for solid lipid nanoparticles (SLN). *International Journal of Pharmaceutics*, *254*(1), 65–68. https://doi.org/10.1016/S0378-5173(02)00684-1
4. Zielinska, A., & Nowak, I. (2016). Solid lipid nanoparticles and nanostructured lipid carriers as novel carriers for cosmetic ingredients. *Nanobiomaterials in Galenic Formulations and Cosmetics: Applications of Nanobiomaterials*, 231–255. https://doi.org/10.1016/B978-0-323-42868-2.00010-3
5. Kaur, I. P., Sharma, G., Singh, M., & Ramzan, M. (2020). Solid lipid nanoparticles in dermaceuticals. In *Nanomaterials for Clinical Applications*. INC. https://doi.org/10.1016/B978-0-12-816705-2.00001-1
6. Mohammadi-Samani, S., Zojaji, S., & Entezar-Almahdi, E. (2018). Piroxicam loaded solid lipid nanoparticles for topical delivery: Preparation, characterization and in vitro permeation assessment. *Journal of Drug Delivery Science and Technology*, *47*, 427–433. https://doi.org/10.1016/j.jddst.2018.07.015
7. Moazeni, M., Kelidari, H. R., Saeedi, M., Morteza-Semnani, K., Nabili, M., Gohar, A. A., Akbari, J., Lotfali, E., & Nokhodchi, A. (2016). Time to overcome fluconazole resistant Candida isolates: Solid lipid nanoparticles as a novel antifungal drug delivery system. *Colloids and Surfaces B: Biointerfaces*, *142*, 400–407. https://doi.org/10.1016/j.colsurfb.2016.03.013
8. Tupal, A., Sabzichi, M., Ramezani, F., Kouhsoltani, M., & Hamishehkar, H. (2016). Dermal delivery of doxorubicin-loaded solid lipid nanoparticles for the treatment of skin cancer. *Journal of Microencapsulation*, *33*(4), 372–380. https://doi.org/10.1080/02652048.2016.1200150
9. Sarangi MK, Padhi S. Solid lipid nanoparticles-a review. J Critical Rev 2016;3:5-12.
10. Li, S., Yang, Y., Lin, X., Li, Z., Ma, G., Su, Z., & Zhang, S. (2020). Biocompatible cationic solid lipid nanoparticles as adjuvants effectively improve humoral and T cell immune response of foot and mouth disease vaccines. *Vaccine*, *38*(11), 2478–2486. https://doi.org/10.1016/j.vaccine.2020.02.004
11. Reichmuth, A. M., Oberli, M. A., Jeklenec, A., Langer, R., & Blankschtein, D. (2016). mRNA vaccine delivery using lipid nanoparticles. *Therapeutic Delivery*, *7*(5), 319–334. https://doi.org/10.4155/tde-2016-0006
12. Almeida, A. J., & Souto, E. (2007). Solid lipid nanoparticles as a drug delivery system for peptides and proteins. *Advanced Drug Delivery Reviews*, *59*(6), 478–490. https://doi.org/10.1016/j.addr.2007.04.007

13. Su, L., Zhou, F., Yu, M., Ge, R., He, J., Zhang, B., Zhang, Y., & Fan, J. (2020). Solid lipid nanoparticles enhance the resistance of oat-derived peptides that inhibit dipeptidyl peptidase IV in simulated gastrointestinal fluids. *Journal of Functional Foods*, *65*(December 2019), 103773. https://doi.org/10.1016/j.jff.2019.103773
14. Chokshi, N. V., Khatri, H. N., & Patel, M. M. (2018). Formulation, optimization, and characterization of rifampicin-loaded solid lipid nanoparticles for the treatment of tuberculosis. *Drug Development and Industrial Pharmacy*, *44*(12), 1975–1989. https://doi.org/10.1080/03639045.2018.1506472
15. Nemati, E., Mokhtarzadeh, A., Panahi-Azar, V., Mohammadi, A., Hamishehkar, H., Mesgari-Abbasi, M., Ezzati Nazhad Dolatabadi, J., & de la Guardia, M. (2019). Ethambutol-Loaded Solid Lipid Nanoparticles as Dry Powder Inhalable Formulation for Tuberculosis Therapy. *AAPS PharmSciTech*, *20*(3). https://doi.org/10.1208/s12249-019-1334-y
16. Seyfoddin, A., Shaw, J., & Al-Kassas, R. (2010). Solid lipid nanoparticles for ocular drug delivery. *Drug Delivery*, *17*(7), 467–489. https://doi.org/10.3109/10717544.2010.483257
17. Sharma, A. K., Sahoo, P. K., Majumdar, D. K., Sharma, N., Sharma, R. K., & Kumar, A. (2016). Fabrication and evaluation of lipid nanoparticulates for ocular delivery of a COX-2 inhibitor. *Drug Delivery*, *23*(9), 3364–3373. https://doi.org/10.1080/10717544.2016.1183720
18. Wadetwar, R. N., Agrawal, A. R., & Kanojiya, P. S. (2020). In situ gel containing Bimatoprost solid lipid nanoparticles for ocular delivery: In-vitro and ex-vivo evaluation. *Journal of Drug Delivery Science and Technology*, *56*, 101575. https://doi.org/10.1016/j.jddst.2020.101575
19. Cacciatore, I., Ciulla, M., Fornasari, E., Marinelli, L., & Di Stefano, A. (2016). Solid lipid nanoparticles as a drug delivery system for the treatment of neurodegenerative diseases. *Expert Opinion on Drug Delivery*, *13*(8), 1121–1131. https://doi.org/10.1080/17425247.2016.1178237
20. He, H., Yao, J., Zhang, Y., Chen, Y., Wang, K., Lee, R. J., Yu, B., & Zhang, X. (2019). Solid lipid nanoparticles as a drug delivery system to across the blood-brain barrier. *Biochemical and Biophysical Research Communications*, *519*(2), 385–390. https://doi.org/10.1016/j.bbrc.2019.09.017
21. Singh, I., Swami, R., Pooja, D., Jeengar, M. K., Khan, W., & Sistla, R. (2016). Lactoferrin bioconjugated solid lipid nanoparticles: A new drug delivery system for potential brain targeting. *Journal of Drug Targeting*, *24*(3), 212–223. https://doi.org/10.3109/1061186X.2015.1068320
22. Press, D. (2018). *Recent developments in solid lipid nanoparticle and surface-modified solid lipid nanoparticle delivery systems for oral delivery of phyto- bioactive compounds in various chronic diseases*. 1569–1583.
23. Alexander, A., Patel, R. J., Saraf, S., & Saraf, S. (2016). CR. *Journal of Controlled Release*. https://doi.org/10.1016/j.jconrel.2016.09.017
24. Campos, D. A., Raquel, A., Sarmento, B., Maria, A., & Manuela, M. (2015). Stability of bioactive solid lipid nanoparticles loaded with herbal extracts when exposed to simulated gastrointestinal tract conditions ☆. *FRIN*, *78*, 131–140. https://doi.org/10.1016/j.foodres.2015.10.025
25. Clark, J. P., & Doona, C. J. (2015). Nanotechnology and Functional Foods. In *Nanotechnology and Functional Foods*. https://doi.org/10.1002/9781118462157
26. Hentschel, A., Gramdorf, S., Müller, R. H., & Kurz, T. (2008). β-Carotene-loaded nanostructured lipid carriers. *Journal of Food Science*, *73*(2), 1–6. https://doi.org/10.1111/j.1750-3841.2007.00641.x
27. Patel, M.R. and San Martin-Gonzalez, M.F. (2012) Characterization of ergocalciferol loaded solid lipid nanoparticles. Journal of Food Science, 77(1), N8–N13.
28. Ban, C., Jo, M., Park, Y. H., Kim, J. H., Han, J. Y., Lee, K. W., Kweon, D. H., & Choi, Y. J. (2020). Enhancing the oral bioavailability of curcumin using solid lipid nanoparticles. *Food Chemistry*, *302*(March 2019), 125328. https://doi.org/10.1016/j.foodchem.2019.125328
29. Wong, H. L., Bendayan, R., Rauth, A. M., Li, Y., & Wu, X. Y. (2007). Chemotherapy with anticancer drugs encapsulated in solid lipid nanoparticles. *Advanced Drug Delivery Reviews*, *59*(6), 491–504. https://doi.org/10.1016/j.addr.2007.04.008

30. Xu, W., Bae, E. J., & Lee, M. K. (2018). Enhanced anticancer activity and intracellular uptake of paclitaxel-containing solid lipid nanoparticles in multidrug-resistant breast cancer cells. *International Journal of Nanomedicine*, *13*, 7549–7563. https://doi.org/10.2147/IJN.S182621
31. Mahmoudian et al selected the lipid carrier to improve the intestinal permeability of Bortezomib and the formulated SLNs loaded bortezomib shows improved intestinal permeability in intestinal perfusion studies.

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RESEARCH ARTICLE

Faculty and Students' Survey Assessment on Ssct-Mainit VGMO

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ABSTRACT

In this study university's vision, mission, goals and objectives were given emphasis. Whereby a descriptive-survey research was employed determining the level of awareness and acceptability and understanding of faculty, staff and students as to specific objectives of the curricular programs. A survey-questionnaire was designed based from the existing VMGO of SSCT Mainit Campus. Study used random sampling to the selected respondents in a ratio of 60:60:60 in three different program BSAF, BSED and BAT. As per records, participants conformed that they were aware of the university's VMGO from radio broadcast, flyers and bulletin boards.Findings revealed that respondents could only state a few words about the VGMO but then, they have understood the concept. Based on weighted mean the level of acceptance, awareness and understanding among faculty, staff and students showed that most of them agreed that the VMGO is clearly stated, easy to memorize and easy to understand. They agreed also that the content of the VMGO will lead to the realization of the vision of the said institution and the statement shown the consistency and congruency to the aims of Philippines Education, Outcomes Based Education, CMOs Policies Standards and Guidelines of CHED. Therefore, it is concluded that there were a proper dissemination of the VMGO. The students, faculty, administrative staff and other stakeholders were informed of the VMGO of the SSCT with a moderate level of acceptance. However, with a minimal number of respondents in this initial survey, Area 1 team has a new on-going set of survey which is more expansive in scope and participants.

Key words: awareness, administrative, institution, Education, broadcast

INTRODUCTION

The study helped improved the understanding of educators and learners towards the vision, goals, mission and objectives of the schools linked the aims of the Philippines Education, the outcomes-based education and CHED

Memorandum Orders Policies Standards and Guidelines of CHED as it was explained that Implementation of out-based (OBE) is the main thrust of most Higher Education Institutions in the Philippines as of today and go along with the standards of foreign universities and colleges all over the world (Laguador & Dotong, 2014). It is also inculcated to the minds of the constituents on how educations in the Philippines protects and promote the rights of all citizens to quality education under Article 14, Sec. 1 of the Philippines Constitution. And it also desirable that students and teachers should adhere and be knowledgeable about CHED CMOs and its mandates as it was said by Salazar & Clemena (2006) that in the context of these changing conditions, higher education is faced with the task of reconceptualizing or reengineering its mission and roles, it is declared by the participants of the Asia and Pacific regional Conference on "National Strategies and Regional Co-operation for the 21st Century. To put more credence and emphases, below are the precise data of the mentioned SSCT VGMO, Philippines Education related issues, OBE and CHED CMOs policies standards and guidelines on education.

SSCT VMGO

- **The Vision of the University/College**
  An innovative and technologically – advanced State College in Caraga.

- **The Mission of the University/College**
  To provide relevant, high quality and sustainable instruction, research, production and extension programs and services within a culture of credible and responsive institutional governance.

- **The Goals of the University/College**
  To achieve its mission, the college aims to:

Foster application of the disciplines and provide its learners with industry-based training and education particularly in engineering, fisheries, and agriculture. conduct and utilize studies for the development of new products, process, systems and services relevant to Philippine life and of the global village; Promote transfer of technology spread useful technical skills, thus empowering its learners and their activities.

The Goals of the Academic Unit of the Education Program

The program commits to attain the following:
Empowered teaching – learning processes through a responsive academic culture of excellence;
Dutiful professionals with strong education foundation for service to humanity;
Unwavering commitment for personal and professional advancement;
Community – oriented graduates ready to meet international challenges;
Applied learning through intensive research and extension activities;
Theoretically – influenced knowledge, values and skills;
Institutionalized technology and sustainable passion for academic world;
Optimal harmonization of harnessing talents and potential for quality life; and
Nurturing a rewarding learning environment toward authentic and meaningful experiences.

The Objectives/ Outcomes of the Program

The program is expected to:
Discuss the latest developments in the specific field of practice;
Communicate effectively using both English and Filipino, orally and in writing;
Work effectively and independently in multi – disciplinary and multicultural teams;
Exemplify professional, social and ethical responsibility;
Preserve and promote "Filipino historical and cultural heritage".
Articulate the relationship of education to larger historical, social, cultural and political processes;
Facilitate learning using a wide range of teaching methodologies in various types of environment;

Develop alternative teaching approaches for diverse learners;
Apply skills in curriculum development, lesson planning, materials development, instructional delivery and educational assessment;
Demonstrate basic and higher levels of thinking skills in planning, assessing and reporting;
Practice professional and ethical teaching standards to respond to the demands of the community; and
Pursue lifelong learning for personal and professional growth.

BAT Program Educational Objectives

Provide students with practical and theoretical knowledge in animal and crop production, postharvest technology and agribusiness management. Prepare students for careers in farm management, agriculture and food technology, agri – entrepreneurship and business and teaching. Educate students in the scientific habit of thought, entrepreneurial skills and prepare them to become professionals with entry level competencies in technical agriculture. To gain fundamental understanding of agricultural process and the type of equipment and tools used to grow plants, breed animals and maintain outdoor environment.

Aims of Philippines Education

Educational mandates based on the Philippines Constitution of 1987, directly emphasized curriculum aims, goals and objectives that all associate shall aim to: inculcate patriotism and nationalism; foster love of humanity; promote respect for human rights; appreciate the role of national heroes in the historical development of the country; and teach the right and duties of citizenship by Jurado, et al. (2008). As it was also determined by Constantino, R. (1970)that Education is a vital weapon of a people striving for economic emancipation, political independence, and cultural renascence.

Outcome-based education

(OBE) is an educational theory that bases each part of an educational system around goals (outcomes). By the end of the educational experience, each student should have achieved the goal. There is no single specified style of teaching or assessment in OBE; instead, classes, opportunities, and assessments should all help students achieve the specified outcomes.[1] The role of the faculty adapts into instructor, trainer, facilitator, and/or mentor based on the outcomes targeted.(Wikipedia) Spady defines OBE as a comprehensive approach to organizing and operating an education system that is focused on operating an education system that is focused on and defined by the successful demonstrations of learning sought from each student. (Malan, S. P. T. (2000).

METHODOLOGY

A descriptive-survey research used and determined the level of awareness and acceptability and understanding among students, faculty, staff and other stakeholders on the vision, mission, goals and specific objectives of the curricular programs. A researcher designed his survey-questionnaire modeled from the existing VMGO of the SSCT and gathered data were summarized and analyzed through weighed mean as means of statistical tool.

RESULTS AND DISCUSSION

Table 1 shows the profile of the respondents.There were 180 student-participants in this initial survey, and 60 of them were from Bachelor in Secondary Education, 60 from Bachelor in Agricultural Technology and 60 from Bachelor in Agro – Forestry. As for the year level of the participants, out of 180 participants, 45 of them were 1st year, 45 were 2nd year, 45 were 3rd year and 45 were 4th year.

FINDINGS

Table 1. Profile of the Participants

Students

There were 180 student-participants in this survey, and 60 of them were from Bachelor in Secondary Education, 60 from Bachelor in Agricultural Technology and 60 from Bachelor in Agro – forestry.

Year Level

The participants were from different year levels. Out of 180 students, 45 of them were 1st year, 45 were 2nd year, 45 were 3rd year, and 45 were 4th year.

Faculty

There were 15 faculty-participants. Out of the number mentioned, 5 were from Bachelor in Agricultural Technology, 5 from Bachelor in Secondary Education, and 5 from Bachelor in Agro – Forestry.

Rank and Position

As to their rank and position, none was from the Professorial level but there were 2 Associate Professors, 3 Assistant Professors, 3 Instructors, and 7 Guest Lecturers.

Table 2 - Result of the Interview/Survey Questionnaire on the Students

Understanding and awareness of the VMGO

This area asked the participants on their understanding and awareness of the VMGO. The first one was on how aware they were of the college's VMGO. Their answers were varied. Out of a total of 180 participants, 121 responded in affirmative; 2 said he was not aware; 50 said they partly understood since they just heard it; and 0 answered he didn't mind at all the VMGO. But it is also noticeable that there were 7 respondents who did not answer the question. Question 2 was about reciting the VMGO. Only 102 out of 180 said they could; 6 said they couldn't because they were not aware of it; only 62 could state with few words; and 10 said they were not sure if they could.
In question 3 it asked the participants if they understood the VMGO. There were 114 who understood well the VMGO; only 2 answered that they did not have any idea about it; 46 answered sort of; and none answered he did not understand. However, there were 18 respondents who chose not to answer.

Acceptance of the VMGO

Under this area, students were asked what they could say about the VMGO. Specifically, the survey asked if the VMGO were stated clearly. Out of 180 student-respondents, 90 agreed strongly; 83 agreed; 7 agreed moderately; and nobody disagreed. The second statement pointed out if the VMGO was easy to memorize. There were 72 respondents who agreed strongly, 77 who agreed, 29 moderately agreed, and 2 who disagreed. No respondents decided not to answer the question. The next item under this part of the survey led to the respondents' perception if the VMGO was understandable. There were 91 who agreed strongly, 65 agreed, 11 agreed moderately, and only one disagreed. Again, the remaining 12 respondents decided not to answer the question. The fourth item asked the respondents' perception on the consistency of the goals and objectives of the academic unit to the college's vision and mission. There were 63 respondents who agreed strongly, 86 agreed, 26 agreed moderately, and 2 who disagreed. There were 3 respondents who did not answer the question. The last question of the survey asked the respondents' thoughts if the goals and objectives of the academic unit would lead to the realization of the vision and mission of the college. 89 of the respondents agreed strongly, 72 agreed, 16 agreed moderately, and 1 disagreed. There were 2 respondents who chose not to answer.

Result of the Interview/Survey Questionnaire on the Faculty Members:
Understanding and awareness of the VMGO

This area asked the participants, particularly the faculty members on their understanding and awareness of the VMGO. The first one was on how aware they are of the college's VMGO. The respondents gave various answers. Out of a total of 15 teacher-participants, all responded favorably. Question 2 would test the teachers' memory of the VMGO. Only 10 out of 15 answered they could; 1 said he could not because he was not aware of it; 4 said they could state with few words; and none said they were not sure if they could. In question 3 it asked the teacher-participants if they understood the VMGO. There were 13 who understood well the VMGO; none answered that he did not have any idea about it; 2 answered sort of; and none answered he did not understand.

Acceptance of the VMGO

Under this area, the teachers were asked what they could say about the VMGO. Specifically, the survey asked if the VMGO were stated clearly. Out of 18 teacher-respondents, 10 agreed strongly, 2 agreed, 2 moderately agreed and 1 opted not to answer. The second statement pointed out if the VMGO was easy to memorize. There were 8 respondents who agreed strongly, and 7 who agreed. The next item under this part of the survey led to the respondents' perceptions if the VMGO was understandable. There were 10 who agreed strongly, and 5 agreed. The fourth item asked the respondents' perceptions on the consistency of the goals and objectives of the academic unit to the college's vision and mission. There were 10 respondents who agreed strongly, 3 agreed, 1 agreed moderately and 1 opted not to answer.The last question of the survey asked the respondents of their thoughts if the goals and objectives of the academic unit would lead to the realization of the vision and mission of the college. 10 of the respondents agreed strongly, 5 agreed

CONCLUSION

In this study faculty, staff and students' awareness and understanding of the SSCT-MAINIT CAMPUS vision, mission, goals and objectives were given importance and this situation reflected on management strategies. Altıok, P. (2011). In consideration to the large number of students and faculty, this result is not definite since there were only 180 students out of the almost a thousand, and only 15 faculty members out of the long roster of teachers under the different programs. Noticed that from the responses of the respondents on their awareness of the VMGO it is evident that the administration and with the teaching personnel are hand-in-hand and made some initiatives to let the whole constituents accept and understand better the VMGO.

RECOMMENDATIONS

Out from the study, the following recommendations are presented:

- In the making and use of syllabus, 3 hours should be allotted for the dissemination and explanation of the vision, mission, and goals of the college, and the objectives of the academic unit. Teachers should discuss the VMGO and cascade it to content of their syllabus.
- Big posters of the original and translated VMGOs should be posted at the entrance and exit gates for the awareness of other stakeholders.
- For the realization of the vision, the administration and teaching personnel shouldset more meaningful activities for the learners.

REFERENCES

1. Altıok, P. (2011). Applicable vision, mission and the effects of strategic management on crisis resolve. *Procedia-Social and Behavioral Sciences*, *24*, 61-71;
2. Jurado, P., Gonzales, N., Jurado, R., & Pedrosa, F. (20018). The Philippines Government and The 1987 Philippine Constitution;
3. Constantino, R. (1970). The mis-education of the Filipino. *Journal of contemporary Asia*, *1*(1), 20-36;
4. Laguador, D. J. M., & Dotong, D. C. I. (2014). Knowledge versus Practice on the Outcomes-Based Education Implementation of the Engineering Faculty Members in LPU. *International Journal of Academic Research in Progressive Education and Development*, *3*(1). https://doi.org/10.6007/IJARPED/v3-i1/640;
5. Salazar-Clemena, R. M. (2006). Higher education research in the Philippines: Policies, practices, and problems. In *Higher Education, Research, and Knowledge in the Asia Pacific Region* (pp. 185-200). Palgrave Macmillan, New York.

Table 1. Profile of the Respondents

STUDENTS			
Department	**No. of Response**	**Year Level**	**No. of Response**
Bachelor in Secondary Education	60	1st Year	45
Bachelor in Agricultural Technology	60	2nd Year	45
Bachelor in Agro – Forestry	60	3rd Year	45
		4th Year	45
TOTAL	**180**	TOTAL	**180**
FACULTY			
Department	**No. of Response**	**Rank and Position**	**No. of Response**
Bachelor in Agricultural Technology	5	Professor	0
Bachelor in Secondary Education	5	Associate Professor	2
Bachelor in Agro – Forestry	5	Assistant Professor	3
		Instructor	3
		Lecturer	7
TOTAL	**15**	TOTAL	**15**

Table 2. Interview/Survey Questionnaire (Students)

Understanding & Awareness of VMGO	**Students**	**Faculty**	**Acceptance of VMGO**	**Students**	**Faculty**
Q1. Are you aware of the College's Vision, Mission, Goals, and Objectives?			Q.4 What can you say about our school's VMGO?		
-Yes, I read it.	121	15	4.1 The VMGO is clearly stated.		
-No, I am not aware of it.	2	0	-Strongly Agree	90	10
-Partly, I just heard it.	50	0	-Agree	83	2
-I don't mind it.	0	0	-Moderately Agree	7	2
No answer.	7	0	-Disagree	0	0

Total	180	15	No answer.	0	1
			Total	180	15
Q2. Can you recite the VMGO?					
-Yes, I can.	102	10	4.2 The VMGO is easy to memorize.		
-No, I can't because I'm not aware.	6	1	-Strongly Agree	72	8
-I can only state few words.	62	4	-Agree	77	7
-I'm not sure if I can.	10	0	-Moderately Agree	29	0
No answer.	0	0	-Disagree	2	0
Total	180	15	No answer.	0	0
			Total	180	15
Q3. Do you understand the VMGO?					
-Yes, I understand it well.	114	13	4.3 The VMGO is understandable.		
-I'm sorry because I don't have an idea about it.	2	0	-Strongly Agree	91	10
-Sort of.	46	2	-Agree	65	5
-No, I don't understand it.	0	0	-Moderately Agree	11	0
No answer.	18	0	-Disagree	1	0
Total	180	15	No answer.	12	0
			Total	180	15
			4.4 There's a consistency in the statements of the GO of the academic unit to the college's VM.		
			-Strongly Agree	63	10
			-Agree	86	3
			-Moderately Agree	26	1
			-Disagree	2	0
			No answer.	3	1
			Total	180	15
			4.5 The content of the academic unit's GO will lead to the realization of the college's VM.		
			-Strongly Agree	89	10
			-Agree	72	5
			-Moderately Agree	16	0
			-Disagree	1	0
			No answer.	2	0
			Total	180	15

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RESEARCH ARTICLE

Phytochemical Screening of Two Medicinal Plants, *Piper nigrum* Linn. and *Nigella sativa* Linn.

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ABSTRACT

The phytochemical analysis of medicinally important plants, namely, *Piper nigrum* Linn. and *Nigella sativa* Linn. seeds have been carried out in this research work. Extraction process was carried out by using a Soxhlet apparatus. The extraction was carried out using non- polar solvents such as petroleum ether and polar solvents such as methanol and water. In both the plants, the percentage yield of the extracts was obtained in the order of aqueous > methanol > petroleum ether. Using standard chemical tests, the preliminary phytochemical analysis of the extract was carried out. In *Piper nigrum* Linn. and *Nigella sativa* Linn., the results indicate the presence of phytochemicals such as alkaloids, sterols, carbohydrates, tannins, flavonoids, phenols, saponins, terpenes, amino acids and proteins. In both the plants, most of the phytochemicals were detected in the methanol as well as in aqueous extracts, as high solubility of the phytochemicals in this solvent as compared to petroleum ether. Due to the presence of various phytochemicals, both of the plants have a huge demand in the herbal drug preparation.

Keywords: *Piper nigrum* Linn., *Nigella sativa* Linn., phytochemical analysis, soxhlet extraction

INTRODUCTION

Plants are a rich source of various nutrients. Owing to this, the importance and the demand of the plant as an herbal medicine is increasing day by day. Herbal drugs are easily available, safe to use, so there are fewer side effects. Since ancient times, parts of plants have been used as herbal medicines to treat various diseases. It acts as an anticancer drug [1] and antimicrobial drugs [2], and shows many activities. In developed countries, about 80% of the population believe mainly on herbal medicine to cure various diseases [3]. Plant parts such as roots, bark, flowers, leaves, seeds and fruits are rich in phytochemicals or biologically active compounds or secondary metabolites [4]. These bioactive chemicals synthesized in plants by primary or secondary metabolism include alkaloids, saponins, tannins, carbohydrates, proteins, sterols, terpenes, flavonoids [5,6] and are widely used in scientific research, agriculture, animal therapy, human therapy [7], as inhibitory effects on microorganisms *in vitro* [8], and many more. *Piper nigrum* Linn., also called as “The King of Spices”, belongs to the family Piperaceae, is an annual flowering dicotyledonous

plant that grows mainly in Kerala, Karnataka, Konkan and Aasam [9,10]. The plant part such as fruit or peppercorn, is used in various herbal medicines and shows many activities such as biocontrol agent [11], anti-microbial [12], anti-oxidant [13-15], radical scavenging [16-17], anti-fungal [18], hepatoprotective[19], anti-thyroid[20], analgesic, anti-inflammatory [21], and anti-tumor activity [22]. The pungency of seeds is due to the presence of the alkaloid Piperine. A total of 592 compounds were isolated and studied from *Piper nigrum* Linn. fruit which contains various lignans, alkaloids and terpenes. Therefore, this plant has a great contribution to the manufacture of Ayurveda [21,23,24]. *Nigella sativa* Linn.is also called black cumin, and it belongs to the Ranunculaceae family. It is an annual flowering dicotyledonous plant that grows mainly in Punjab, Ganges Plain, Bihar, Maharashtra, Assam, and Bengal [25]. The fruit of the plant has numerous black colored seeds, which are aromatic and bitter [26]. The seeds are rich in various nutrients and show various pharmacological and medicinal activities, such as anti-cancer [27], immune modulatory [28], anti-diabetic, anti-hypertensive, diuretic, and anti-microbial [29].This miraculous herb is the richest source of thymoquinone, various sterols, and alkaloids, so it can treat almost all diseases except death. This work focuses on the qualitative detection of various phytochemicals in *Piper nigrum* Linn and *Nigella sativa* Linn. seed. Various standard chemical methods were used for preliminary phytochemical analysis.

MATERIALS AND METHODS

Plant Materials

Seed of *Piper nigrum* Linn. and *Nigella sativa* Linn. were collected by Krishi Kendra, Nagpur, Maharashtra, India, and identified, and authenticated by The Department of Botany, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur (Authentication no. for *Nigella sativa* Linn.- 9990 and for *Piper nigrum* Linn.-9991).

Chemicals

Methanol, sodium hydroxide, chloroform, hydrochloric acid, ferric chloride, glacial acetic acid, Wagner's reagent, ninhydrin solution, acetic anhydride, ethanol, magnesium metal, Dragendorff's reagent, Molisch's reagent.

Preparation of plant extracts

Seed of *Piper nigrum* Linn. and *Nigella sativa* Linn. were rinsed with water to remove any dirt or dust. Further, these seed were dried at room temperature for 10 to 12 days. Seed ground in fine powder in a grinder and stored in an airtight glass bottle for further analysis.

Soxhlet extraction of sample

For *Piper nigrum* Linn. about 50 g of dry seed powder was extracted separately with 100 ml of petroleum ether, methanol and water for 15 hours. After extraction, the extra solvent was distilled off from the extract. These extracts were air dried, stored in glass bottles and used for phytochemical analysis. Similarly, for *Nigella sativa* Linn. About 50 g of seed powder was extracted separately with 100 ml of petroleum ether, methanol and water for about 15 hours. Further, these extracts were distilled off to remove extra solvent, air dried and stored in glass bottles for further analysis. So, total six extracts were prepared and analyzed.

Phytochemical analysis

Various phytochemical tests were carried out to analyze the alkaloids, sterols, carbohydrates, tannins, flavonoids, phenols, saponins, terpenes, amino acids and proteins in the extract.

Test for alkaloids

Wagner's test : Wagner's reagent is the combination of 2 g of potassium iodide and 1.27 g of iodine in 100 ml water. 1 ml of Wagners reagent was added to 2 mg of the extract. The appearance of reddish brown colored precipitate indicates the presence alkaloids.

Dragendorff's test : Dragendorff's reagent is the combination of freshly prepared solution A and solution B. Solution A is composed of 17 g bismuth nitrite and 200 g tartaric acid dissolved in 800 ml distilled water, and solution B is composed of 160 g potassium iodide in 400 ml distilled water. 5 ml of 1.5 % v/v of hydrochloric acid was added to 3 mg of the extract and filtered. The Dragendroff's reagent was applied to the Whatman filter paper. The filtrate alkalized with ammonia was extracted with chloroform and the remaining extract was applied to the test paper with the help of capillary tube. Red color observation of the test paper indicated the presence of alkaloids.

Test for sterols

Salkowski's test: In a test tube, 5 mg of the extract was dissolved in 2 ml chloroform, and 2 ml of sulfuric acid was added thereto. The test tube was shaken until the formation of red color in the chloroform layer indicated the presence of sterols.

Lieberman Burchard test

About 5 to 6 mg of the extract was dissolved in 5 ml of chloroform in a test tube, and about 2 to 3 ml of acetic anhydride was added to it. By tilting the test tube slightly, 3 to 4 drops of concentrated sulfuric acid were added from the side, and observed a green color precipitate.

Test for Carbohydrates

Benedicts test : In a test tube, about 5 to 6 drops of Benedicts reagent were added to 5 mg of the residue. Further, this test tube was placed in a water bath for 5 to 7 minutes, cooled and observed for the reddish precipitate[30].

Molisch's test : Molisch's reagent is composed of 10 g alpha naphthol in 100 ml of alcohol (90%).
About 2 to 3 mg of the extract was treated with 2 to 3 drops of Molisch's reagent in a test tube and about 1 ml concentrated sulfuric acid was added to it from the side of the test tube until a red ring was formed at the surface of liquids indicating the presence of carbohydrates.

Test for Tannins (Braymer's test): About 2 mg of the extract was treated with 10 % $FeCl_3$ solution, and the formation of a blue or green solution was observed [30].

Test for Flavonoids

Alkaline reagent test: 5 to 6 drops of 20% sodium hydroxide were added to 2 mg of extract. After adding dilute hydrochloric acid, it turned yellow and became colorless [31].

Shinoda test: About 2 mg of the test extract was dissolved in 5 ml of ethanol (95% v/v),and further treated with 5 to 6 drops of concentrated hydrochloric acid and 0.5 g of magnesium metal. The appearance of pink or magenta color indicates the presence of flavonoids.

Test for Phenols (Ferric Chloride test): 1 ml of extract was treated with 5 % $FeCl_3$ solution and observed the formation of a deep blue or black color [31].

Test for Saponins (Foam test): In a test tube, about 2 to 3 mg of the extract and 10 ml water was taken, shaken vigorously,and observed the formation of stable and long lasting foam.

Test for Terpenes (Salkowski's test): About 5 mg of the extract was treated with 2 ml chloroform, and 3 ml concentrated sulfuric acid was added carefully to form a layer. Red- brown precipitates or golden yellow color observed at the interface indicating the presence of terpenes [32].

Test for amino acids and proteins: 4 to 5 drops of freshly prepared ninhydrin solution were added to 2 ml of the extract, placed it in aboiling water bath for 2 to 3 minutes, and observed the formation of a purple color [33].

RESULTS AND DISCUSSION

The phytochemical analysis of extracts of *Piper nigrum* Linn. and *Nigella sativa* Linn. Indicates the presence of various biologically active constituents or secondary metabolites. Table 1 shows the results of the percentage yield of the extracts. In *Piper nigrum* Linn., the percentage yield (% w/w)of the obtained extracts is water (5.71), which is higher than methanol (5.38) and petroleum ether (2.07).The petroleum ether, methanol and aqueous extracts showed the presence of sterols and terpenes. The methanol and water extracts tested positive for all the phytochemicals, indicating the presence of all phytochemicals, including alkaloids, sterols, carbohydrates, tannins, phenols, flavonoids, saponins, terpenes, amino acids and proteins. In *Nigella sativa* Linn., the percentage yield (% w/w) of the obtained extracts is as water (5.33), which is higher than methanol (4.92) and petroleum ether (3.61). The petroleum ether, methanol, and aqueous extracts show the presence of sterols, terpenes, phenols, and tannins. The methanol extract shows almost all phytochemicals except saponins. Whereas, water extract showed the presence of all the phytochemicals and tested positive for alkaloids, sterols, carbohydrates, tannins, flavonoids, phenols, saponins, terpenes, amino acids and proteins. These biologically active constituents are responsible for various medicinal and pharmacological activities of *Piper nigrum* Linn. and *Nigella sativa* Linn. Table 2 shows the results of phytochemical analysis of the two plant extracts.

CONCLUSION

Piper nigrum Linn. and *Nigella sativa* Linn. are the richest source of secondary metabolites such as alkaloids, sterols, flavonoids, saponins, tannins, phenols, carbohydrates, proteins and amino acids. It can be used in herbal drug manufacturing industries as well as in food industries.

REFERENCES

1. Dewick PM. Tumor inhibition of plant. Trease and Evans Pharmacognosy.14th ed. London: W C Evans. WB Saunders Company; 1996.
2. Phillipson JD, Wright CW. Plants with Antiprotozoal activity. Trease and Evans Pharmacognosy.14th ed. London: WB Saunders Company;1996.
3. Arunkumar S, Muthuselvam. Analysis of phytochemical constituents and antimicrobial activities of *Aloe vera* L. against clinical pathogens. World J Agril Sci 2009;5(5): 572-576.
4. Criagg GM, David JN. Natural product drug discovery in the next millennium. J Pharm Biol 2001;39: 8-17.
5. Edoga HO, Okwu DE, Mbaebie BO. Phytochemical constituents of some Nigerian medicinal plants. Afr J Biotechnol 2005; 4(7): 685-688.
6. Mann J. Secondary Metabolism. Oxford University Series, London: Clarendon press; 1978. p. 154.
7. Vasu K, Goud JV, Suryam A, Singara Chary MA. Biomolecular and phytochemical analyses of three aquatic angiosperms. Afr J Microbiol Res 2009; 3(8):418-421.
8. Cowan MM. Plant products as antimicrobial agents. Clin Microbiol Rev 1999; 12: 564-582.
9. Khan S, Mirza KJ, Anwar F, Abdin MZ. Development of RAPD markers for authentication of Piper nigrum (L),Environ we Int J Sci Tech 2010; 5: 47-56.
10. Indian herbal pharmacopoeia.Revised new ed, Mumbai:Indian Drug Manufacturers' Association; 2002.
11. Hamrapurkar PD, Jadhav K, Zine S. Quantitative Estimation of Piperine, in Piper nigrum and Piper longum using High Performance Thin Layer Chromatography. J App Pharmaceut Sci 2011; 1(3): 117-120.

12. Wongpa S, Himakoun L, Soontornchai S, Temcharoen P.Antimutagenic effects of piperine on cyclophosphamideinduced chromosome aberrations in rat bone marrow cells. Asian Pacific Journal of Cancer Prevention 2007; 8 (4): 623-627.
13. Ahmad N, Fazal H, Abbasi BH, Rashid M, Mahmood T, Fatima N.Efficient regeneration and antioxidant potential in regenerated tissues of Piper nigrum L. Plant Cell Tissue and Organ Culture 2010; 102: 129-134.
14. Pathak N, Khandlewal S.Cytoprotective and immunomodulating properties of Piperine on murine splenocytes: an in vitro study. Eur J Pharmacol 2007; 576 (1-3): 160-170
15. Pathak N, Khandlewal S.Role of oxidative stress and apoptosis in cadmium induced thymic atrophy and splenomegaly in mice. Toxicol Lett 2007; 169(2): 95-108.
16. Gulcin I.The antioxidant and radical scavenging activities of black pepper (*Piper nigrum*) seeds. Int J Food Sci Nutr 2005; 56 (7): 491-499
17. Saxena R, Venkaiah K, Anitha P, Venu L, Raghunath M. Antioxidant activity of commonly consumed plant foods of India: contribution of their phenolic content. Int J Food Sci Nutr 2007; 58 (4): 250-260.
18. Umit A, Kadir I, Akgun KO. Antifungal activity of aqueous extracts of spices against bean rust (Uromyces appendiculatus). Allelopathy Journal 2008; 24: 0973-5046.
19. Ibrahim M, Nane KM, Anjum A, Khan AA, Habeeb MA, Devi YP, *et al*. Hepatoprotective activity of Sapindus mukorossi and rheum emodi extracts: *In vitro* and *in vivo* studies. World J Gastroenterology 2008;14(16): 2566-2571.
20. Panda S, Kar A.Piperine lowers the serum concentrations of thyroid hormones, glucose and hepatic 5D activity in adult male mice. Horm MetabRes 2003; 35 (9): 523-526.
21. Parmar VS, Jain SC, Bisht KS, Jain R, Taneja P, Jha A, *et al*.Phytochemistry of the genus Piper. Phytochemistry 1997; 46 (4): 597-673.
22. El-Hamss R, Idaomar M, Alonso-Moraga A, Munoz-Serra A.Antimutagenic properties of bell and black peppers. Food Chem Toxico 2003; 41 (1): 41-47.
23. Teuscher E. Pepper.Medicinal spices.Stuttgart (Germany): GmbH Scientific Publishers; 2006.
24. Kang MJ, Cho JY, Shim BH, Kim DK, Lee J. Bioavailability enhancing activities of natural compounds from medicinal plants. J Med Plants Res 2009; 3 (13): 1204-1211.
25. Khare CP.Encyclopedia of Indian Medicinal plants. New York: Springer-Verlag Berlin Heidelberg; 2004
26. Duthie JF.Flora of the Upper Gangetic Plain and of the Adjacent Siwalik and Sub-Himalayan Tracts.Vol. I.Calcutta: Superintendent of Government printing; 1960.p.19-20.
27. Ng WK, Yazan LS, Ismail M.Thymoquinone from Nigella sativa was more potent than cisplatin in eliminating of SiHa cells via apoptosis with down-regulation of Bcl-2 protein. Toxicol *In Vitro*2011; 25(7): 1392-1398.
28. Ghonime M, Eldomany R, Abdelaziz A, Soliman H. Evaluation of the immunomodulatory effect of three herbal plants growing in Egypt. Immunopharmacol Immunotoxicol 2011; 33(1): 141-145.
29. Bakathir HA,Abbas NA.Detection of the antimicrobacterial effect of Nigella sativa ground seeds with water. Afr J Tradit Compl Altern Med 2011;8(2):159-164.
30. Jayanthi P, Lalitha P, Sripathi SK. Phytochemical investigation of the extracts of Eichhornia crassipes and its solvent fractionates. Journal of Pharmacy Research 2011; 4 (5):1405-1406.
31. Singh KL, Singh LR, Devi PG, Devi NR, Singh LS, Bag GC. Comparative study of phytochemical constituents and total phenolic content in the extracts of three different species of genus Hedychium. International Journal of PharmTech Research 2013; 5 (2): 601-606.
32. Sharma AK, Gangwar M, Tilak R, Nath G, Sinha ASK, Tripathi YB, *et al*. Comparative *in vitro* antimicrobial and phytochemical evaluation of methanolic extract of root, stem and leaf of *Jatropha curcas* Linn. Pharmacognosy Journal 2012; 4 (30): 34-40.
33. Sama K, Sivaraj R. Pharmacognostical and phytochemical screening of fruits and leaves of *Cissus arnottiana*. Asian J Pharm Clin Res 2012; 5 : 64-66.

Table 1: Percentage yield of *Piper nigrum* Linn. and *Nigella sativa* Linn. extract in different solvents

Crude Extracts	Percentage Yield (%w/w)	
	***Piper nigrum* Linn.**	***Nigella sativa* Linn.**
Petroleum ether extract	2.07	3.61
Methanol extract	5.38	4.92
Aqueous extract	5.71	5.33

Table 2: Results of phytochemical analysis of various extracts of *Piper nigrum* Linn. and *Nigella sativa* Linn.

Phytochemicals	***Piper nigrum* Linn.**			***Nigella sativa* Linn.**		
	PE	**Met**	**Aq**	**PE**	**Met**	**Aq**
Alkaloids	-	++	++	-	+	+
Sterols	+	+	+	+	+	+
Carbohydrates	-	+	+	-	+	+
Tannins	-	+	+	+	+	+
Flavonoids	-	+	+	-	+	+
Phenols	-	+	+	+	+	+
Saponins	-	+	+	-	-	+
Terpenes	++	+	+	+	+	+
Amino acids and Proteins	-	+	+	-	+	+

(PE: Petroleum ether extract, Met: Methanol extract, Aq: Aqueous extract)
(Note: ++ indicates highly present, + indicates present and – indicates absent)

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RESEARCH ARTICLE

Microwave Assisted Organic Synthesis of C-Mannich Bases of Thiazolo [3,2-a] Pyrimidine Derivatives

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ABSTRACT

An effective synthesis of C-Mannich Bases of thiazolo[3,2-a] pyrimidine derivatives from formaldehydes, thiazolo [3,2-a] pyrmidine and seven distinctive heterocyclic 2^0 amines under the irradiation of microwave is described. Stood out from old style Mannich reaction conditions, this new technique has the upside of incredible yields and shorter reaction times.

Keywords: dihydropyrimidin-2-(1*H*)-ones, Biginelli reaction, thiazolo [3,2-a] pyrimidine, C-Mannich Bases, Microwave.

INTRODUCTION

Pyrimidine ring frameworks are significant classes of compounds owing to their wide-range of biological exercises. Nitrogen aromatic pyrimidine, pyridine, and their analogs occurs in nature and they show enthusiastic job in the pitch of engineered heterocyclic science [1]. Such heterocyclic compounds are widely utilized for numerous applications in pharmaceutical science. A considerable lot of their derivatives are utilized as antimicrobial [2-10], antiviral [11-13], antitumor [14-21] and against oxidant [22, 23] agents in veterinary medicinal. Dihydropyrimidinones (DHPMs) subsidiaries have exhibited important pharmacological properties, for example, antiviral, against bacterial, antitumor and antihypertensive exercises [24], Thiazolidone derivatives condensed with the pyridine cycle, in particular thiazolo pyridine, are of high need in current therapeutic chemistry, because these compounds display various kinds of biological activity. Among them were identified substances with herbicidal [25], cancer prevention agent [26-29], antimicrobial [30], antifungal [31], and anti-mitotic[32], exercises. Likewise, this class of compound is show strong inhibitory activity for A42 fibrillization for Alzheimer's infection treatment [33]. It was built up that these subsidiaries display against tuberculosis [34] and mitigating [35-37] activities. In the most recent decade, the Mannich reaction has been exceptionally used as one of the potential multi component reactions (MCRs) because of its presentation in the structure of carbon–nitrogen (C–N) and carbon–carbon (C–C) single bonds

[38]. It is notable that compounds with one active hydrogen atom experience a solitary Mannich reaction, while compounds with two neighboring active hydrogen atoms experience a twofold Mannich reaction [39-41]. Mannich reaction has been seeing nonstop development in the field of organic chemistry and the resultant β-amino carbonyl compounds deliver differing auxiliary highlights by showing a wide scope of intense biological activities in medicinal chemistry [42,43].However, this reaction experiences the harsh conditions, high reaction times and regularly low yields. In this manner, the revelation of milder and practical routes for the synthesis of C-Mannich Bases by the Mannich reaction keeps on drawing in the consideration of researchers. Microwave assisted synthesis comparatively beneficial than conventional synthesis, in conventional method need of large solvent, long time taken to get heated, spread bad odour where these can be reduced in microwave assisted synthesis [54]. Microwave-assisted organic synthesis (MAOS) exploits dielectric volumetric heating as an alternative heat source, which results in faster and more selective reactions due to the uniform heat distribution. Accordingly, there is a need to build upan efficient method for the synthesis of C-Mannich Bases. In this way in continuation of our work related to Mannich reaction, we wish to report here the utilization of microwave irradiation method for the one-pot multicomponent synthesis of C-Mannich Bases through Mannich reaction approach with the hope of obtaining compounds will help in the building of medicinally active framework and possess diverse biological activities.

MATERIAL AND METHODS

In the synthesis of C-Mannich Bases, laboratory grade ethyl acetoacetate, thiourea, different aldehydes, chloroacetic acid and other solvents were used after purifying as and when required. The entire heterocyclic secondary amino components namely benzimidazole, 2-methyl benzimidazole, 2-benzyl benzimidazole, benzotriazole, phthalimide and tetrahydro carbazole used were synthesized by the literature method except morpholine [55]. The melting points of C-Mannich bases is determined by open capillary method. Elemental analysis for C, H, N content were carried out on Perkin-Elmer (USA) 2400 instrument. Infrared absorption spectra (IR) were scanned on a NICOLET-400 D FTIR spectrophotometer using KBr pellets and ^{1}H NMR spectra were scanned in $CDCl_3$on Brucker 400 MHz Ft-NMR instrument using TMS as an internal standard. o-hydroxybenzaldehyde and p-hydroxybenzaldehyde (1a & 1b) reacts with ethylacetoacetate (2) and thiourea(3) via Biginelli reaction to give3,4-dihydropyrimidine-2(*1H*)-thione (DHPMs)(4a & 4b) (Scheme I) followed by the cyclization reaction with chloroacetic acid (5) gives Ethyl 5,7-dimethyl-3-oxo-2,3-dihydro-5H-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (6a & 6b)(Scheme II) which upon mannich reaction with formaldehyde **7** and different heterocyclic 2^0-amines (8a-g) gives two series of C-Mannich bases namely, Ethyl 5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivatives (9a-g) and Ethyl 5-(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivatives (10a-g). Scheme III show the synthetic protocol of the final compounds (9a-g & 10a-g). Procedure for the synthesis of ethyl 4-(2-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4a) A mixture of o-hydroxybenzaldehyde(1a) (0.05 mol), ethylacetoacetate(2) (0.05 mol), and thiourea(3) (0.05 mol) and a few drops of 37% HCl as catalyst was irradiated under microwave at 280 W for 30 seconds. The progress of reaction was monitored continuously by TLC. After cooling at room temperature, the resulting mixture was washed with ice cold water. The product was further washed with ether, and purified by recrystallization from methanol. Likewise the different DHPMs, ethyl 4-(4-hydroxyphenyl)- 6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b) were set up by utilizing 4-hydroxybenzaldehyde (1b).

Procedure for the synthesis of ethyl 5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidine-6-carboxylate (6a) : A blend of (0.011 mol) of chloroacetic acid (5), (0.01 mol) of ethyl 4-(2-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate(4a), and 10 ml of DMF was refluxed under microwave illumination at 280W for 45 sec. The blend was permitted to remain at room temperature for an hour and cooled to 0-5°C. The solid separated was filtered off, washed with chilled water and recrystallized from ethanol. Along these lines the other ethyl 5-(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate

(6b) were set up by utilizing ethyl 4-(4-hydroxyphenyl)- 6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b).

Synthesis of C-Mannich Bases of ethyl 5-(2-hydroxyphenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazol-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate (9a): A mixture of ethyl 5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6a) (0.05 mol), 37% formaldehyde **(7)** (0.05 mol), benzimidazole (8a) (0.05 mol) and 10 ml of ethanol was refluxed under microwave irradiation at 420W for 90 seconds in presence of catalytic amount of HCl. The reaction was observed persistently by TLC. After completion of reaction, the resulting mixture was cooled to room temperature and poured into crushed ice with continuous stirring. The solid obtained was filtered off, washed thoroughly with hot water, air-dried and recrystallized from appropriate solvent to give ethyl 5-(2-hydroxyphenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazol-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate(9a). Further, Mannich reaction of ethyl 5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6a) was done individually with other heterocyclic secondary amines specifically 2-methyl benzimidazole (8b), 2-benzyl benzimidazole (8c), benzotriazole (8d), morpholine (8e), phthalimide (8f) and tetrahydro carbazole (8g) for synthesis of C-Mannich bases to yield a series of C-Mannich bases (9b-g). Similarly, other series of C-Mannich bases (10a-g) were prepared by MAOS of ethyl 5-(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6b) as substrate via Mannich reaction.IUPAC names of all these Mannich bases are given in Table IV.

Ethyl4-(2-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate(4a) :Yellow solid, mp 200-202^{0}C, Yield 75%, Anal. cacld for $C_{14}H_{16}N_2O_3S$ M.W.:292 Calc.C, 57.52; H, 5.52; N, 9.58; found: C, 57.34; H, 5.81; N, 9.51.IR (υ cm^{-1}): 3420 (O-H stretching), 3107 (Aromatic C-H str), 1226 (-COOCH$_2$CH$_3$), 1230 and 1163 (C-O-C), 1710 (C=O), 1275 (NH-C=S-NH), 1100 (C=S), 3315 (N-H). ^{1}H NMR:δ 1.1 (3H,t,-OCH$_2$CH$_3$), 1.9 (3H,s,CH$_3$), 3.1 (2H,q,-OCH$_2$CH$_3$), 4.4 (1H,s,H), 6.8-7.1 (4H,m,aromatic rings), 8.8 (1H,s,NH), 9.1 (1H,s,OH), 9.3 (1H,s, NH);^{13}C NMR: 13.8, 17.2, 54.3, 61.0, 103.7, 115.8, 122.5, 134.3, 144.8, 146.3,154.0, 158.7, 166.9, 175.3.

Ethyl4-(4-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b) Cream white solid, mp 187-189^{0}C, Yield 73%, Anal. cacld for $C_{14}H_{16}N_2O_3S$ M.W.:292 Calc.C, 57.52; H, 5.52; N, 9.58; found: C, 57.58; H, 5.41; N, 9.78.IR (υ cm^{-1}): 3398 (O-H stretching), 3100 (Aromatic C-H str), 1220 (-COOCH$_2$CH$_3$), 1228 and 1148 (C-O-C), 1705 (C=O), 1265 (NH-C=S-NH), 1109 (C=S), 3308 (N-H). ^{1}H NMR:δ 1.1 (3H,t,-OCH$_2$CH$_3$), 1.8 (3H,s,CH$_3$), 3.1 (2H,q,-OCH$_2$CH$_3$), 4.4 (1H,s,H), 6.7-7.1 (4H,m,aromatic rings), 8.7 (1H,s,NH), 9.2 (1H,s,OH), 9.5 (1H,s,NH);^{13}C NMR: 14.1, 17.5, 54.7, 61.0, 101.4, 113.6, 121.7, 132.1, 143.7, 145.2,156.5, 158.4, 167.2, 174.8.

Ethyl 5-(2-hydroxyphenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate(6a) Brown solid, mp 185-187^{0}C, Yield 73%, Anal. cacld for $C_{16}H_{16}N_2O_4S$ M.W.: 332 Calc. C, 57.82; H, 4.85; N, 8.43; found: C, 58.05; H, 4.54; N, 8.70.IR (υ cm^{-1}): 3348 (O-H stretching), 3115 (Aromatic C-H str), 1232 and 1138 (C-O-C str), 1711 (-COOCH$_2$CH$_3$), 1748 (C=O), 1235, 1201 (C-N str), 748 (C-S-C str).^{1}H NMR: δ 1.1 (3H,t,-OCH$_2$CH$_3$), 1.8 (3H,s,CH$_3$), 3.2 (2H,q, CH$_2$ thiazole ring), 4.1 (2H,q,-OCH$_2$CH$_3$), 4.4 (1H,s,H), 6.8-7.1 (4H,m,aromatic rings), 8.2 (1H,s,OH).^{13}C NMR: 14.4, 17.6, 35.2, 55.5, 60.0, 101.4, 114.3, 122.2, 128.1, 136.2, 142.4, 152.3, 154.7, 159.2, 165.3, 174.5.

Ethyl 5-(4-hydroxyphenyl)-7-methyl-3-oxo-3,5-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate(6b) White solid, mp 212-214^{0}C, Yield 76%, Anal. cacld for $C_{16}H_{16}N_2O_4S$ M.W.: 332 Calc. C, 57.82; H, 4.85; N, 8.43; found: C, 57.65; H, 5.06; N, 8.27.IR (υ cm^{-1}): 3402 (O-H stretching), 3109 (Aromatic C-H str), 1228 and 1126 (C-O-C str), 1701 (-COOCH$_2$CH$_3$), 1745 (C=O), 1247, 1210 (C-N str), 731 (C-S-C str).^{1}H NMR: δ 1.1 (3H,t,-OCH$_2$CH$_3$), 1.7 (3H,s,CH$_3$), 3.2 (2H,q, CH$_2$ thiazole ring), 4.2 (2H,q,-OCH$_2$CH$_3$), 4.5 (1H,s,H), 6.8-7.2 (4H,m,aromatic rings), 8.1 (1H,s,OH).^{13}C NMR: 13.8, 17.4, 34.5, 56.1, 61.7, 103.1, 111.8, 121.5, 128.6, 135.9, 142.8, 152.7, 155.3, 160.6, 166.7, 177.2.

Ethyl2-((1H-benzo[d]imidazol-1-yl)methyl)-5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidine -6-carboxylate (9a) Lightbrown solid, mp 131-133^{0}C, Yield 70%, anal. cacld for $C_{24}H_{22}N_4O_4S$M.W.: 462 Calc. C, 62.32;

H, 4.79; N, 12.11; found: C, 62.04; H, 4.60; N, 11.98. IR (υ cm^{-1}): 3030(C-H str), 3010 and 2860 (-CH_2str), 1455 (-CH_2 bending), 1260 and 1130 (C-O-C str), 1775 (-C=O str), 1740 (C=O str), 1425 (ring str), 1315 (C-N str), 1590, 1545 and 1480 (ring str), 12250, 1010 (ring breathing), 721 (C-S-C str).^{1}H NMR:δ 1.9 (3H,t,CH_3 of -OCH_2CH_3), 2.2 (3H,s,CH_3 of pyrimidine ring), 4.2 (2H,q,CH_2 of-OCH_2CH_3), 4.6 (2H,d,CH_2 of methylene bridge),4.9 (1H,q,CH of thiazole ring), 5.9 (1H,s,H on pyrimidine ring), 7.5 (1H,s,H on imidazole ring at2-position), 7.2-8.1(8H,m,two aromatic rings), 8.8 (1H,s,OH);^{13}C NMR: 13.8, 26.4, 48.9, 55.4, 58.4, 60.7, 110.0, 118.1, 119.1, 121.8, 122.4, 130.4, 130.7, 131.2, 136.5, 139.1, 143.3, 143.4, 151.6, 155.7, 167.2, 171.3, 172.2, 177.1.

Ethyl 5-(2-hydroxyphenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazol-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidine -6-carboxylate (9b) Brown solid, mp 174-176^{0}C, Yield 71%, anal. cacld for $C_{25}H_{24}N_4O_4S$M.W.: 476 Calc. C, 63.01; H, 5.08; N, 11.76;found: C, 62.84; H, 4.98; N, 12.00. IR (υ cm^{-1}): 3030(C-H stretching), 2910 and 2830 (-CH_2 str), 1452 (-CH_2 bending), 1280 and 1140 (C-O-C str), 1730 (-C=O str), 1700 (C=O str), 1345 (C-N str), 1600, 1575 and 1530 (ring str), 1210, 1030 (ring breathing), 748 (C-S-C str).^{1}H NMR:δ 1.9 (3H,t,CH_3 of -OCH_2CH_3), 2.2 (3H,s,CH_3 of pyrimidine ring), 2.6 (3H,s,CH_3 of imidazole ring at 2-position), 4.0 (2H,q,CH_2 of -OCH_2CH_3), 4.4 (2H,d,CH_2 of methylene bridge), 5.3 (1H,q,CH of thiazole ring), 6.0 (1H,s,H on pyrimidine ring), 6.8-7.7 (8H,m,two aromatic rings), 8.5 (1H,s,OH); ^{13}C NMR: 12.6, 13.3, 26.4, 50.1, 53.2, 58.3, 60.7, 109.2, 118.0, 118.5, 121.3, 122.3, 123.5, 130.1, 130.5, 131.2, 138.1, 139.0, 150.4, 151.8, 151.7, 156.2, 167.5, 171.3, 172.1.

Ethyl 2-((2-benzyl-1H-benzo[d] imidazol-1-yl)methyl)-5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo [3,2-a]pyrimidine-6-carboxylate (9c) Dark grey solid, mp 230-232^{0}C, Yield 66%, anal. cacld for $C_{31}H_{28}N_4O_4S$M.W.: 552 Calc. C, 67.37; H, 5.11; N, 10.14; O, 11.58; S, 5.80; found: C, 67.51; H, 5.34; N, 9.92. IR (υ cm^{-1}): 3045 (C-H str), 3010 and 2910 (-CH_2 str), 1450 (-CH_2 bending), 1265 and 1110 (C-O-C str), 1705 (-C=O str), 1670 (C=O str), 1365 (ring str), 1310(C-N str), 1590, 1540 and 1465 (ring str), 1210, 1060 (ring breathing), 732 (C-S-C str). ^{1}H NMR: δ 1.8 (3H,t,CH_3 of -OCH_2CH_3), 2.1 (3H,s,CH_3 of pyrimidine ring), 3.3 (2H,s,CH_2 of benzyl group on imidazole ring), 4.0 (2H,q,CH_2 of-OCH_2CH_3), 4.5 (2H,d,CH_2 of methylene bridge), 4.9 (1H,q,CH of thiazole ring), 5.9 (1H,s,H on pyrimidine ring), 6.9-7.7 (13H,m,three aromatic rings), 8.6 (1H,s,OH); ^{13}C NMR: 13.9, 26.1, 28.3, 50.3, 53.9, 58.4, 60.7, 109.5, 118.3, 118.4, 120.7, 121.1, 122.9, 124.6, 126.4, 128.5, 129.2, 130.1, 130.5, 131.2, 134.5, 139.2, 151.2, 151.7, 153.3, 167.0, 171.4, 172.1.

Ethyl 5 - (4 – hydroxyphenyl) - 7 – methyl -2- (morpholinomethyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate (10e) White solid, mp 142-144^{0}C, Yield 68%, anal. cacld for $C_{21}H_{25}N_3O_5S$ M.W.: 431 Calc. C, 58.45; H, 5.84; N, 9.74; found: C, 58.64; H, 6.12; N, 9.49. IR (υ cm^{-1}): 3010(C-H str), 2860 and 2800 (-CH_2str), 1445 (-CH_2 bending), 1230 and 1155 (C-O-C str), 1730 (-C=O str), 1660 (C=O str), 1370 (ring str), 1285 (C-N str), 1610, 1540 and 1470 (ring str), 1080, 1030 (ring breathing), 758 (C-S-C str), 1140 (C-O str of morpholine ring). ^{1}H NMR: δ 2.1 (3H,t,CH_3 of -OCH_2CH_3), 2.3 (3H,s,CH_3 of pyrimidine ring), 2.5-2.7 (4H,m,CH_2 of morpholine ring adjacent to nitrogen), 2.8 (2H,d,CH_2 of methylene bridge), 3.6-3.9 (4H,m,CH_2 of morpholine ring adjacent to oxygen), 4.2 (2H,q,CH_2 of -OCH_2CH_3), 4.7 (1H,q,CH of thiazole ring), 5.9 (1H,s,H on pyrimidine ring), 7.3-7.7 (4H,m,onearomatic rings), 8.3 (1H,s,OH). ^{13}C NMR: 13.7, 26.2, 48.1, 51.6, 54.0, 58.6, 60.9, 66.1, 67.0, 115.4, 118.1, 122.6, 130.2, 130.5, 131.2, 139.4, 151.7, 156.1, 167.4, 172.1, 172.7

Ethyl 2 - ((1,3 - dioxoisoindolin – 2 - yl) methyl) – 5 -(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo [3,2-a]pyrimidine-6-carboxylate (10f) Light green solid, mp 210-212^{0}C, Yield 65%, anal. cacld for $C_{25}H_{21}N_3O_6S$ M.W.: 491 Calc. C, 61.09; H, 4.31; N, 8.55; found: C, 60.90; H, 4.05; N, 8.47; IR (υ cm^{-1}): 3080(C-H str), 3010 and 2860 (-CH_2 str), 1445 (-CH_2 bending), 1280 and 1150 (C-O-C str), 1765 (-C=O str), 1720 (C=O str), 1380 (ring str), 1310 (C-N str), 1585, 1510 and 1370 (ring str), 1190, 1070 (ring breathing), 762 (C-S-CStr), 1710 (C=O str of phthalimide).^{1}H NMR: δ 2.0 (3H,t,CH_3 of-OCH_2CH_3), 2.2 (3H,s,CH_3 of pyrimidine ring), 4.2 (2H,q,CH_2 of -OCH_2CH_3), 4.8 (2H,d,CH_2 of methylene bridge), 5.3 (1H,q,CH of thiazole ring), 5.9 (1H,s,H on pyrimidine ring), 7.1-7.8 (8H,m,two aromatic rings), 8.5 (1H,s,OH); ^{13}C NMR: 13.9, 26.2, 37.2, 48.7, 58.3, 60.9, 118.1, 121.5, 122.9, 130.2, 130.8, 131.2, 131.8, 133.9, 139.2, 151.6, 153.9, 167.1, 167.4, 168.8, 172.1.

Ethyl 5-(4-hydroxyphenyl)-7-methyl-3-oxo-2-((1,2,3,4-tetrahydro-9H-carbazol-9-yl)methyl)-2,3-dihydro-5H-thiazolo [3,2-a] pyrimidine-6-carboxylate (10g) Graysolid, mp 240-242^{0}C, Yield 67%, anal. cacld for $C_{29}H_{29}N_3O_4S$ M.W.: 515 Calc. C, 67.55; H, 5.67; N, 8.15; found: C, 67.24; H, 5.88; N, 8.29. IR (υ cm^{-1}): 3020(C-H str), 2910 and 2850 (-CH_2 str), 1450 (-CH_2 bending), 1260 and 1145 (C-O-C str), 1710(-C=O str), 1680 (C=O str), 1390 (ring str), 1360 (C-N str), 1620, 1550 and 1520 (ring str), 1130, 1010 (ring breathing), 728 (C-S-CStr). ^{1}H NMR: δ 1.7-1.9 (4H,m,-CH_2 of carbazole ring), 2.0 (3H,t,CH_3 of -OCH_2CH_3), 2.3 (3H,s,CH_3 of pyrimidine ring), 2.4-2.8 (4H,m,-CH_2 of carbazole ring adjacent to double bond), 4.2 (2H,q,CH_2 of -OCH_2CH_3), 4.7 (2H,d,CH_2 of methylene bridge), 5.3 (1H,q,CH of thiazole ring), 5.8 (1H,s,H on pyrimidine ring), 6.8-7.8 (8H,m,two aromatic rings), 8.1 (1H,s,OH);^{13}C NMR: 13.9, 21.5, 22.5, 22.9, 26.2, 51.8, 54.2, 58.4, 60.9, 96.7, 108.0, 118.1, 118.2, 118.4, 120.1, 121.8,123.5, 128.4, 130.0, 130.8, 131.1, 133.8, 139.1, 141.3, 151.7, 154.2, 167.4, 172.1, 172.3.

RESULT AND DISCUSSION

Microwave assisted organic synthesis (MOAS) of C-Mannich bases via Mannich reactions of thiazolopyrimidines with seven heterocyclic secondary amines were studied in the two steps. Prior to this, the optimization of power level and reaction time period was carried out with reference to yield of the product. The data of this optimization are shown in the Table I, II & III revels that the power level of MAOS of Biginelli, cyclization reaction and that of Mannich reaction was 280, 280 and 420W respectively for maximum yield. The first step of MAOS is a Biginelli reaction of aromatic ldehydes, β-diketoester and thiourea under solvent free conditions (Scheme I). In the second step, cyclization reaction carried out using dihydropyrimidin-2-(1*H*)-ones (DHPMs) (4a-b) respectively with choloroacetic acid **5** in DMF gave thiazolopyrimidines (6a & 6b) (Scheme II). Solvent free conditions was used in preparation of (DHPMs) where as that of cyclization was carried out using N,N-dimethylformamide (DMF) as solvent because under solvent free conditions, the product obtained was of gummy nature.

Microwave-assisted cyclocondensation of DHPMs with chloroacetic acid, like the corresponding conventional heating method, take place efficiently albeit in much less time. 4a-b and 6a-b were crystallized from appropriate solvent and their purity was checked by mp and TLC. The yield of the products was increased to 90 % as compared to classical method (57-70 %). Mannich reaction of thiazolopyrimidines 6a-b with various heterocyclic secondary amines 8a-g and formaldehyde **7** at ambient temperature in microwave yielded two series of Mannich bases (9a-g and 10a-g) (Scheme III). They have analyzed for their melting points and purity. Further the comparisons of their elemental and spectral data (IR, ^{1}H NMR and ^{13}C NMR) are in good agreement with corresponding samples prepared by the conventional methods. Spectral data and elemental analysis (C, H, N) supported the structure assigned. The physical data of 9a-g and 10a-g are summarized in preceding section. It was seen that the reaction rates and yield showed by microwave technique were better contrasted with the conventional technique. Thus, prominent feature of most microwave conditions is the in situ quick conversion of microwaves to heat and the possible more homogeneous thermal profile than conventional heating methods. Spectral studies of C-Mannich bases have shown the following characteristic features:

The characteristic absorption bands of DHPMs component in IR spectra of thiazolo[3,2-a] pyrimidine(6a-b)resemble pattern observed for parent DHPMs substrate(4a-b) reported in experimental section with the exception that the absorption bands at 1550 and 700 cm^{-1} (-NH) in plane and out of plane bending due to secondary (-NH) group of DHPM substrate disappeared in the IR spectra of both thiazolo[3,2-a]pyrimidine (6a-b). Two strong band respectively in the region 2780-2770 and 1430-1420 cm^{-1} are expected to –CH stretching and bending vibration of methylene linkages between thiazolopyrimidine substrate and heterocyclic 2° amino component. In ^{1}H NMR spectra of the thiazolo[3,2-a]pyrimidine(6a-b)have shown the absence of two (1H, -NH) 2° amino group of DHPMs ring systems. This suggest that the hydrogen atom of two 2° amino group of DHPMs have reacted with chloroacetic acid ang gets cyclized to thiazolo [3,2-a]pyrimidine. Resulted thiazolo [3,2-a]pyrimidine compound under goes Mannich reaction with formaldehyde and heterocyclic 2° amino compounds to form substituted C-Mannich bases. This can be

further confirmed by the appearance of the new ^{1}H NMR signal in the range δ 4.20-6.10 due to (2H, -CH_2) of methylene linkage formed between to thiazolo [3,2-a]pyrimidineand heterocyclic 2° amino compounds. The – CN stretching vibration frequencies due to 3° amino group in C-Mannich bases appeared as a strong absorption band in the region 1360-1310 cm^{-1} in IR spectra of C-Mannich bases. The characteristic bands of aromatic ring observed at 1600, 1580 and 1450 cm^{-1} due to skeletal vibration of the benzene ring and corresponding ^{1}H NMR signals for aromatic protons have been obtained as a multiplet in the region of δ 6.50-8.10. The characteristic ^{1}H NMR signals of heterocyclic secondary aminomoieties in C-Mannich bases were for benzimidazole (8.2 δ, 1H,singlet),2-methylbenzimidazole (2.5 δ, 3H,singlet), 2-benzylbenzimidazole (3.7 δ 2H,singlet), morpholine (2.6-2.7 δ, 4H,multiplet and 3.5-3.6 δ, 4H,multiplet), tetrahydrocarbazole (1.8-2.0 δ, 4H,multiplet and 2.6-2.7 δ, 4H,multiplet) in 9a, 9b, 9c, 9e and 9g respectively. In addition to these the ^{13}C NMR signals of heterocyclic secondary amines are at δ 13.1 and 13.8 ppm (-CH_3 of 2-methylbenzimidazole), δ 28.1 and 28.3 ppm(-CH_2 of 2-benzylimidazole), δ 58.8 and 58.5 ppm (-CH_2 of morpholine ring),δ 167.5 and 167.6 ppm (C=O of phthalimide ring), δ 21.8, 22.2 and 23.0 ppm (-CH_2 of tetrahydrocarbazole). All these inferences support the predicted chemical structure of novel C-Mannich bases as shown in Scheme III.

CONCLUSION

In conclusion, we have portrayedthe microwave irradiation as an efficient method for the synthesis of C-Mannich Bases of thiazolo [3,2-a] pyrimidine by multi component Mannich reactions under micro-wave irradiation. This technique offers a few points of interest including high yields, very short reaction time and a simple experimental workup procedure, which makes it a useful process for the synthesis of C-Mannich Bases of thiazolo[3,2-a]pyrimidine. We believe, our method will discover significant applications in the synthesis of C-Mannich Bases of thiazolo[3,2-a] pyrimidine to cater there quirements of academia as well as pharmaceutical industries.

REFERENCES

1. T. Eicher, S. Hauptmann, A. Speicher, The Chemistry of Heterocycles, *Wiley*, (2003).doi:10.1002/352760183X
2. N.S. El-gohary, M.T. Gabr, M.I. Shaaban, *Bioorg. Chem.*, 89, (2019) 102976–102989.
3. A. Ali, et al, *J. Med. Chem.*,46, (2003)1824–1830.
4. S. Cherukupalli, et al, *Bioorg. Med., Chem*. 26, (2018) 309–339.
5. S. Garg, et al, *Bioorg. Med., Chem.* 24, (2016) 5521–5533.
6. B.S. Holla, M. Mahalinga, M.S. Karthikeyan, P.M. Akberali, N.S. Shetty, *Bioorg. Med., Chem*. 14, (2006) 2040–2047.
7. F. Varano, et al, *Bioorg. Med., Chem.* 26,(2018) 3688–3695.
8. Y.N. Mabkhot, F. Alatibi, N.N.E. El-Sayed, N.A. Kheder, S.S. Al-Showiman,*Molecules*., 21, (2016) 1–9.
9. M. Alrobaian, S. Al Azwari, A. Belal, H.A. Eldeab, *Molecules*, 24, (2019) 1969-1983.
10. A. Karunanidhi, et al, *Molecules*,24, (2019) 1–12.
11. A. Varizhuk, A. Chizhov, V. Florentiev, *Bioorg. Chem*., 39, (2011) 127–131.
12. G. Wang, et al, *J. Med. Chem*., 59, (2016)4611–4624.
13. H. Kumamoto, et al, *ACS Med. Chem. Lett*., 9,(2018) 1211–1216.
14. A. Rahmouni, et al, *Bioorg. Chem*., 66, (2016)160–168.
15. M.T. El Sayed, et al, *Bioorg. Chem*., 78, (2018) 312–323.
16. S. Cherukupalli, et al, *Bioorg. Chem*., 79, (2018) 46–59.
17. Y.A.Elshaier, et al, *Bioorg. Med., Chem.*25, (2017) 2956–2970.
18. A.G.E. Amr, A.M. Mohamed, S.F. Mohamed, N.A. Abdel-Hafez, A.E. Hammam,*Bioorg. Med. Chem.*, 14, (2006) 5481–5488.
19. A.M. Al-Majid, et al, *Molecules*., 24 (2019) 1–12.
20. A .Basnet, et al, *Bioorg. Med., Chem*. 15, (2007) 4351–4359.

21. M.H. Helal, et al, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc*., 135, (2015) 764–773.
22. S. Riaz, et al, *Bioorg. Chem*., 57, (2014)148–154.
23. E.M. Flefel, W.I. El-Sofany, M. El-Shahat, A. Naqvi, E. Assirey, *Molecules*., 23, (2018) 2548–2563.
24. Atwal, K.S., Rovnyak, G.C., Kimball, S.D., Floyd, D.M., Mereland,S., Swanson, B.N., Gougoutas, J.Z., Schwartz, J., Smillie, K.M.,Malley, M.F., *J. Med. Chem.,* 33,(1990) 2629–2635.
25. Hegde, S.G.; Mahoney, M.D. *J Agric Food Chem*., 41, (1993) 2131–2134.
26. Klenina, O.; Drapak, I.; Chaban, T.; Ogurtsov, V.; Chaban, I.; Golos, I. *Chem. & Chem. Techn.,* 7, (2013) 397-404.
27. Chaban, T.I.; Ogurtsov, V.V.; Chaban, I.G.; Klenina, O.V.; Komarytsia, J.D. *Phosphorus, Sulfur Silicon Relat. Elem.*, 188, (2013) 1611-1620.
28. Klenina, O.; Chaban, T.; Zimenkovsky, B.; Harkov, S.; Ogurtsov, V.; Chaban, I.; Myrko, I. *Pharmacia*, 64, (2017) 49-71.
29. Chaban, T.; Ogurtsov, V.; Mahlovanyy, A.; Sukhodolska, N.; Chaban, I.; Harkov, S.; Matiychuk, V. *Pharmacia*, 66, (2019) 171-180.
30. Saeyd, H.H.; Morsy, E.M.; Kotb, E.R., *Sci Commun.,* 40, (2010) 2712-2722.
31. Al-Thebeiti; Marzoog, S. *Farmaco.,* 55, (2000) 109-118.
32. Victor, V.; Semenov, B.; Lichitsky, V.A.; Komogortsev, N.A.; Dudinov, A.M.; Krayushkin, M.M. *Eur. J. Med. Chem.,* 125, (2017) 573-58.
33. Lee, Y.R.; Yoo, S.S. *Bull. Korean Chem. Soc.* 1, (2008) 234-236.
34. Chaban, T.; Klenina, O.; Drapak, I.; Ogurtsov, V.; Chaban, I.; Novikov, V. *Chem. & Chem. Techn*., 89, (2014) 287-292.
35. Chaban, T.; Klenina, O.; Zimenkovsky, B.; Chaban, I.; Ogurtsov, V.; Shelepeten, L. *Der Pharma Chemica,* 8, (2016) 534-542.
36. Chaban, T.; Klenina, O.; Harkov, S.; Ogurtsov, V.; Chaban, I.; Nektegaev I. *Pharmacia*, 64, (2017) 16-30.
37. Chaban, T.; Matiychuk, V.; Ogurtsov, V.; Chaban, I.; Harkov, S.; Nektegaev, I. *Pharmacia,* 65, (2018) 51-62.
38. M. Arend, B. Westermann and N. *Angew. Chem*., 110(8), (1998) 1096–1122.
39. A. F. M. El-Mahdy and S.-W. Kuo, *Polym. Chem*., 9, (2018) 1815–1826.
40. A. M. Mahmoud, H. A. H. El-Sherif, O. M. A. Habib and A. A. O. Sarhan, *Phosphorus Sulfur Relat. Elem.*, 182(8), (2007) 1757–1766.
41. H. R. Abuzeid, A. F. M. EL-Mahdy, M. M. M. Ahmed and S. Kuo, *Polym. Chem*., 10, (2019) 6010–6020.
42. B. Pacorel, S. C. Leung, A. V. Stachulski, J. Davies, L. Vivas, H. Lander, S. A. Wards, M. Kaiser, R. Brun and P. M. O. Niell, *J of Med. Chem.*, 53, (2010) 633.
43. M. S. Khan, A. Husain and S. Sharma, *Acta Poloniae Pharmaceuticals*, 67, (2010) 261.
44. L. Popiolek, J. Rzymowska, U. Kosikowska, A. Hordyjewska, M. Wujec and A. Malm, *J of Enzyme Inhibition and Med. Chem.*, 29, (2014) 786.
45. S. Joshi, N. Khosla, D. Khare and R Sharda, *Bioor. Med.l Chem. Lett*., 15, (2005)221.
46. B. L. Khalil, M. A. Younus, T. M. Salih, R. M. Rumez and B. W. Khamma, *Chem. and Materials Research*, 6, (2014)55.
47. N. H. Jainab, P. Sivachidambaram, J. Yuvaraju, K. J. Beyatricks and B. Raj, *Asian J. of Research in Chem.*, 7, (2014)176.
48. G. Cihan-Ustundag, B. Simsek, E. Ilhan and G. Capan, *Letters in Drug, Design and Discovery*, 11, (2014)290.
49. R. P. Purushottam, S. M. Vishal, V. K. Deshmukh and S. R. Chaudhari, *International Journal of Pharmaceutical Science Review and Research*, 21, (2013)199.
50. A. Zalai, in 5th Int. Koll. Addit. Schmierst. Arbeits Flussigkeiton, Budapest, 2, (1986)91411.
51. H. X. Feng, J. Li and X. H. Gao, *Advanced Materials Research*, 538, (2012)2329.
52. T. B. Shah, A. Gupte, M. R. Patel, V. S. Chaidhari, V. C. Patel, *Indian Journal of Chemistry-Sec. B*, 48B(1), (2009) 88-96.
53. T. B. Shah, A. Gupte, M. R. Patel, V. S. Chaidhari, V. C. Patel, *Indian Journal of Chemistry-Sec. B*, 49B(5), (2010) 578-586.
54. Ajmer Singh Grewal, Karunesh Kumar, Karunesh Kumar, Sonika Redhu. Microwave-ssisted synthesis: a green chemistry approach. *Int Res J Pharm Appl Sci*, 3, (2013) 278-85.
55. H El-Marry A, Fahmy H H & Abdelwahed S H, *Molecules*, 5, (2000) 1429.

Table I: Comparison of reaction parameters for conventional and MAOS of dihydropyrimidines (4a & 4b).
Powe Level: 280W

Code	Aldehydes	Conventional method		Microwave irradiation 280W	
		Time in Minutes	% Yield	Time in Seconds	% Yield
4a	o-hydroxy benzaldehyde	120	69	30	86
4b	p-hydroxy benzaldehyde	145	61	30	92

Table II:Comparison of reaction parameters for conventional and MAOS of Thiazolo[3,2-a] pyrimidines(6a & 6b).
Power level: 280W

Code	Conventional method		Microwave irradiation 280W	
	Time in Minutes	% Yield	Time in Seconds	% Yield
6a	142	61	45	88
6b	160	58	45	79

Table III: Comparison between the conventional and microwave assisted synthesis of C-Mannich bases (9a-g & 10a-g).

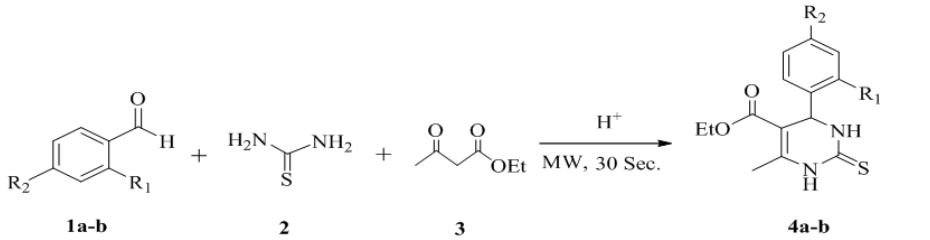
Code	Heterocyclic 2^0-amines (8a-g)	Conventional method*		Microwave irradiation*420W	
		Time in Minutes	% Yield	Time in Seconds	% Yield
9a	Benzimidazole	6	66	90	81
9b	2-Methyl benzimidazole	6	61	90	71
9c	2-Benzyl benzimidazole	7	67	120	66
9d	Benzotriazole	6.5	70	100	70
9e	Morpholine	6	64	120	87
9f	Phthalimide	6	57	90	65
9g	Terahydro carbazole	7.5	60	130	67
10a	Benzimidazole	5.5	60	70	83
10b	2-Methyl benzimidazole	6	67	90	69
10c	2-Benzyl benzimidazole	6	70	90	74
10d	Benzotriazole	6.5	58	100	70
10e	Morpholine	6	66	90	90
10f	Phthalimide	6	69	90	68
10g	Terahydro carbazole	7	61	120	63

***Catalyst: Conc. HCl**

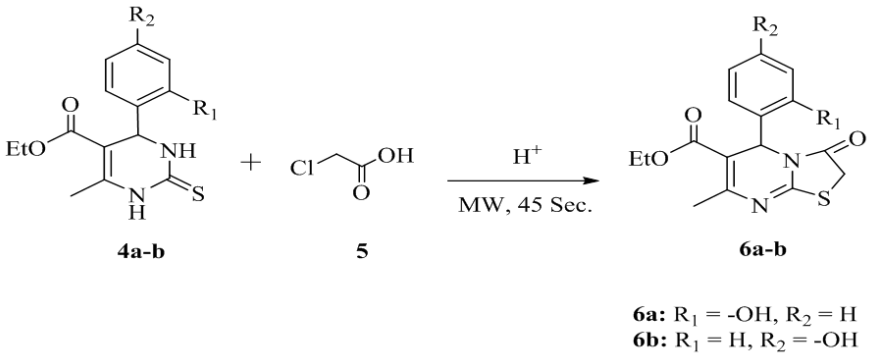
Table IV: IUPAC name of C-Mannich Bases (9a-g & 10 a-g).

Entry	Heterocyclic 2^0-amines (8a-g)	IUPAC Name	Mole. formula	m.p ^{0}C	Yield %
9a	Benzimidazole	ethyl 2-((1H-benzo[d]imidazol-1-yl)methyl)-5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{24}H_{22}N_4O_4S$	193-195	67

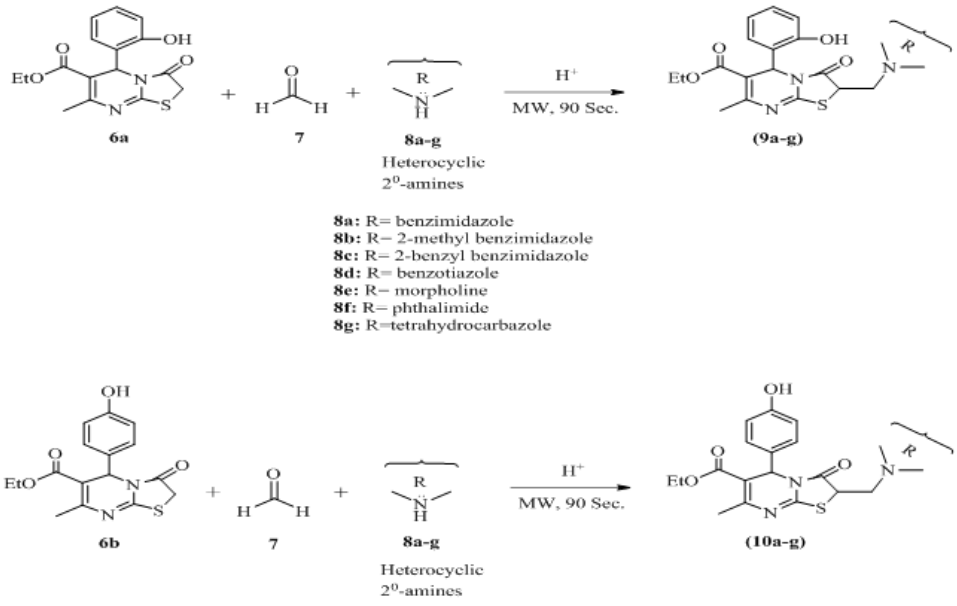
9b	2-Methyl benzimidazole	ethyl 5-(2-hydroxyphenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazol-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{24}N_4O_4S$	210-212	61
9c	2-Benzyl benzimidazole	ethyl 2-((2-benzyl-1H-benzo[d]imidazol-1-yl)methyl)-5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{31}H_{28}N_4O_4S$	234-236	57
9d	Benzotriazole	ethyl 2-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{23}H_{21}N_5O_4S$	175-177	55
9e	Morpholine	ethyl 5-(2-hydroxyphenyl)-7-methyl-2-(morpholinomethyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{21}H_{25}N_3O_5S$	202-204	71
9f	Phthalimide	ethyl 2-((1,3-dioxoisoindolin-2-yl)methyl)-5-(2-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{21}N_3O_6S$	144-146	60
9g	Terahydro carbazole	ethyl 5-(2-hydroxyphenyl)-7-methyl-3-oxo-2-((1,2,3,4-tetrahydro-9H-carbazol-9-yl)methyl)-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{29}H_{29}N_3O_4S$	191-193	52
10a	Benzimidazole	ethyl 2-((1H-benzo[d]imidazole-1-yl)methyl)-5-(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{24}H_{22}N_4O_4S$	224-226	61
10b	2-Methyl benzimidazole	ethyl 5-(4-hydroxyphenyl)-7-methyl-2-((2-methyl-1H-benzo[d]imidazole-1-yl)methyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{24}N_4O_4S$	167-169	67
10c	2-Benzyl benzimidazole	ethyl 2-((2-benzyl-1H-benzo[d]imidazole-1-yl)methyl)-5-(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{31}H_{28}N_4O_4S$	230-232	58
10d	Benzotriazole	ethyl 2-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-5-(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{23}H_{21}N_5O_4S$	207-209	63
10e	Morpholine	ethyl 5-(4-hydroxyphenyl)-7-methyl-2-(morpholinomethyl)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{21}H_{25}N_3O_5S$	201-203	77
10f	Phthalimide	ethyl 2-((1,3-dioxoisoindolin-2-yl)methyl)-5-(4-hydroxyphenyl)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{25}H_{21}N_3O_6S$	176-178	61
10g	Terahydro carbazole	ethyl 5-(4-hydroxyphenyl)-7-methyl-3-oxo-2-((1,2,3,4-tetrahydro-9H-carbazol-9-yl)methyl)-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate	$C_{29}H_{29}N_3O_4S$	241-243	59



Scheme I: Synthetic protocol for DHPMs



Scheme II: Synthetic protocol for Thiazolo [3,2-a] pyrimidine



Scheme III: Synthetic protocol for C-Mannich Bases

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RESEARCH ARTICLE

Morphological Analysis of Corrosion Inhibition by 2-Carboxyethyl Phosphonic Acid and Zn^{2+} System on Carbon Steel in Seawater

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ABSTRACT

The corrosion-inhibitive properties of 2-carboxyethyl phosphonic acid (2-CEPA) and Zn^{2+}on carbon steel in seawater has been investigated using weight loss and electrochemical measurements. The results show that 98% inhibition efficiency is achieved with binary system consisting of 250 ppm of 2-CEPA and 50 ppm of Zn^{2+}. Cyclic voltammetry study reveals that the protective film is more compact and stable even in 3.5% NaCl environment. Surface evaluation techniques like FTIR and SEM were used to determine the nature of the protective film formed on the metal surface.

Keywords: Corrosion in hibition ,carbon steel, seawater, cyclic voltammetry, FTIR, SEM.

INTRODUCTION

Corrosion is a slow and steady destruction of a material, typically metal, by chemical reaction with its environment. In seawater, corrosion is severe due to the presence of chloride ions and dissolved oxygen [1-3]. Seawater has been used as cooling fluid in various industries. It has been estimated that some 20% of the corrosion cost is due to microbial corrosion and degradation [4-5]. Metals obtain stability when their surfaces are separated from the normal terrestrial environment [6]. Carbon steel is widely used in infrastructure in marine environments [7]. Corrosion inhibition as a protective method is of great importance. Inhibitors often work by adsorbing themselves on the metallic surface, protecting it by forming a film. The strength of the adsorption bond is the dominant factor for organic inhibitors. Their effectiveness depends on the chemical composition, their chemical structure, and their affinity towards the metal surface. Inhibition of corrosion and scaling can be done by the application of inhibitors. Most of the organic inhibitors containing nitrogen, oxygen, sulfur atoms, and multiple bonds in their molecules

facilitate adsorption on the metal surface [8]. Several phosphonic acids have been used as corrosion inhibitors [9-13]. The inhibition efficiency of phosphonates depends on the number of phosphono groups in a molecule and also on different sub stituents. Compounds with a phosphonic functional group are considered to be the most effective chemical for inhibiting the corrosion process and it is well known that short-chain-substituted phosphonic acids are good corrosion inhibitors for iron and low-alloyed steels [14]. An environmental-friendly compound, 2-carboxyethylphosphonic acid, contains not only phosphono groups, but also carboxyl and ethyl groups, which can decrease corrosion. The present study aims a) to find out the corrosion-inhibition effects of 2-CEPA and Zn^{2+} system on carbon steel in seawater medium using weight-loss method b)to investigate the nature of the protective film in 3.5% NaCl environment c)to analyze the protective film by Fourier Transform Infrared Spectroscopy (FTIR) d**)**to study the surface morphological changes during iron corrosion by Scanning Electron Microscopy (SEM)**e)** to propose a suitable mechanism of corrosion inhibition based on the results from the above studies.

EXPERIMENTAL

Preparation of Specimen

Carbon steel specimen [0.0267 % S, 0.06 % P, 0.4 % Mn, 0.1 % C and the rest iron] of dimensions 1.0 cm x 4.0 cm x 0.2 cm was polished to a mirror finish and degreased with trichloroethylene.

Weight-Loss Method

Carbon steel specimens in triplicate were immersed in 100 mL of the solutions containing various concentrations of the inhibitor in the presence and absence of Zn^{2+} for one day. The weight of the specimens before and after immersion was determined using a Shimadzu balance, model AY62. The corrosion products were cleaned with Clarke's solution [15]. The inhibition efficiency (IE) was then calculated using the equation: $IE = 100\ [1- (W_2/W_1)]$ % where W_1 is the weight loss value in the absence of inhibitor and W_2 *is the* weight loss value in the presence of inhibitor.

Cyclic Voltammetry

Cyclic voltammograms were recorded in Versa STAT MC electrochemical system. A three-electrode cell assembly was used. The working electrode was carbon steel. The exposed surface area was 1 cm^2. A saturated calomel electrode (SCE) was used as the reference electrode and a rectangular platinum foil was used as the counter electrode. The cyclic voltammetry curves were recorded in the scan range of −1.8 to −1.8 V (SCE) with a scan rate of 20 mV s^{-1}.

Surface Examination Study

The carbon steel specimens were immersed in various test solutions for a period of one day. After one day, the specimens were taken out and dried. The nature of the film formed on the surface of the metal specimen was analyzed by various surface analysis techniques.

Fourier Transform Infrared Spectra (FTIR)

The FTIR spectra were recorded in a Perkin-Elmer-1600 spectrophotometer. The film formed on the metal surface was carefully removed and mixed thoroughly with KBr making the pellet.

Scanning Electron Microscopic Studies (SEM)

The carbon steel samples immersed in the blank solution and in the inhibitor solution for a period of one day were removed, rinsed with double-distilled water, dried, and observed under a scanning electron microscope to examine the surface morphology. The surface morphology measurements of carbon steel were examined using JEOL-MODEL 6390 computer-controlled scanning electron microscope.

RESULTS AND DISCUSSION

Weight-Loss Method

The physicochemical parameters of seawater are given in Table 1. Table 2 gives values of the corrosion-inhibition efficiencies and the corresponding corrosion rates of 2-carboxyethyl phosphonic acid (2-CEPA) –Zn^{2+} in controlling corrosion of carbon steel in seawater for a period of 24 hours at room temperature. The 2-CEPA alone has high rate of corrosion. The inhibition efficiency of 2-CEPA is improved by adding various concentrations of Zn^{2+} [16]. However, by increasing the concentration of 2-CEPA as well as Zn^{2+}, the maximum inhibition is achieved and the corrosion rate is decreased. It is found that 250 ppm of 2-CEPA and 50 ppm of Zn^{2+} have 98% inhibition efficiency. Therefore, it can be determined that inhibition efficiency increases with the increase of concentration of inhibitors. This behavior could be attributed to the increase of the surface area covered by the adsorbed molecules of phosphonic acid with the increase of its concentration. It is generally assumed that the adsorption of the inhibitor at the metal/solution interface is the first step in the mechanism of inhibition in aggressive media.

CYCLIC VOLTAMMETRY

Cyclic voltammograms have been used to investigate the corrosion behaviour of metals [17-19]. Deyab and Keera [19] have analysed the influence of sulphide, sulphate, and bicarbonate anions on the pitting corrosion behaviour of carbon steel in formation water containing chloride ions by means of cyclic voltammetry technique. The cyclic voltammograms were recorded in the presence of increasing amounts (0.1 to 0.3 M) of NaCl at a scan rate of 10 mV s^{-1}. The anodic response exhibits a well-defined anodic peak followed by a passive region. The anodic peak is due to active metal dissolution and formation of ferrous hydroxide [20]. The cathodic sweep shows two cathodic peaks. The appearance of cathodic peak around -1.1 V is due to reduction of corrosion product, namely iron oxide to iron. The appearance of cathodic peak around -0.7 V is due to the reduction of pitting corrosion products precipitate on the electrode surface. In the present study, cyclic voltammograms were recorded by immersing the working electrode, carbon steel, in 3.5% NaCl solution. The cyclic voltammogram of carbon steel immersed in 3.5% NaCl is shown in Figure1a. It is observed that during anodic scan, no peak is observed but a passive state is noticed. This can be explained as follows: When the metal dissolves, ferrous hydroxide is formed. When the concentration of ferrous oxide at the anodic surface exceeds its solubility product, precipitation of solid oxide occurs on the electrode surface. When the surface is entirely covered with oxide passive film, anodic current density does not increase indicating onset of passivation [19]. In the passive state, the Cl^- ion can be adsorbed on the bare metal surface in competition with OH^- ions. As a result of high polariz ability of the Cl^- ions, the Cl^- ions may adsorb preferentially [21].

The cathodic sweep shows only one peak at -1.12 V. This is due to the reduction of corrosion product, iron oxideto iron. The peak due to reduction of pitting corrosion product is absent. The cyclic voltammogram of carbon steel electrode, which has been immersed in seawater for one day and dried is shown in Figure1b. (brown iron oxide is observed on the carbon steel electrode). It is observed that during anodic sweep, no peak appears, but a passive region is observed. During the cathodic sweep, the peak due to reduction of pitting corrosion product appears at -528 mV indicating pitting corrosion takes place. However, the peak due to reduction of corrosion product, iron oxide, appears at -1.133 V. The current density increases from -1.148 $x10^{-3}$ A/cm^2 to -1.172 $x10^{-3}$ A/cm^2. This indicates that when carbon steel electrode is immersed in seawater for one day, a protective film of iron oxide is formed on the electrode surface. It is stable in 3.5% NaCl solution. The increase in current density is explained as follows: Chloride ion is adsorbed on the passive film. The adsorbed chloride ion penetrates the oxide film, especially at the flaws and defects in the oxide film [22]. When the penetrated chloride ion reaches the metal surface, it promotes local corrosion. When the carbon steel electrode is immersed in seawater containing 250 ppm of 2-CEPA and 50 ppm of Zn^{2+} for one day, a protective film is formed. It consists of Fe^{2+} – 2-CEPA complex, Zn^{2+} – 2-CEPA complex, and $Zn(OH)_2$ as revealed by FTIR spectroscopy. The cyclic voltammogram of carbon steel electrode deposited with the above protective film is shown in Figure 1c. It is observed that during anodic sweep, dissolution of metal does not take place. This indicates that the protective film is stable and compact. Electrons are not transferred from the metal

surface, and a passive region is observed. During cathodic sweep, the peak corresponding to reduction of pitting corrosion product appears at -525 mV. However, the peak due to reduction of iron oxide to iron appears at -1.187 V. The current density increases from -1.148 $x10^{-3}$ A/cm^2 to -1.286 $x10^{-3}$ A/cm^2. The increase in current density has been explained as above. It is observed from the Figures 1a, 1b, and1c that the pitting potentials for the three systems are at -644.4 mV, -755.5 mV and -594.1 mV respectively. That is when carbon steel electrode is immersed in the seawater medium, the pitting potential is shifted to more negative side (active side, i.e., -755.5 mV). It accelerates corrosion because the protective film formed is porous and amorphous. When the electrode is immersed in the inhibitor medium, the pitting potential is shifted to the noble side, i.e., -594.1 mV. This indicates that the passive film found on the metal surface in the presence of inhibitors is compact and stable. It can withstand the attack of chloride ion present in 3.5 % Na Cl. This indicates that the passive film found on the metal surface in the presence of inhibitors is compact and stable. It can withstand the attack of chloride ion present in FTIR Spectra FTIR Spectra have been used to analyze the protective film found on the metal surface [23-25].

The FTIR spectrum (KBr) of pure 2-CEPA is shown in Figure 2a. The P-O stretching frequency appears at 1017.75 cm^{-1} and the C=O stretching frequency of the carboxyl group appears at 1721.86 cm^{-1}. The FTIR spectrum of the film formed on the metal surface after immersion in seawater containing 250 ppm of 2-CEPA and 50 ppm of Zn^{2+} is shown in Figure 2b. The P-O stretching frequency has shifted from 1017.75 to 1054.41 cm^{-1} and the C=O stretching frequency has shifted from 1721.86 to 1632.84 cm^{-1}. It is inferred that oxygen atom of the carboxyl group has coordinated with Fe^{2+} resulting in the formation of Fe^{2+}– 2-CEPA complex formed on the anodic sites of the metal surface. The peak at 3434.81 cm^{-1} is due to –OH stretching. The band due to Zn-O appears at 1407.02 cm^{-1}. These results confirm the presence of $Zn(OH)_2$ deposited on the cathodic sites of the metal surface. Thus, FTIR spectral study leads to the conclusion that the protective film consists of Fe^{2+}– 2-CEPA complex and $Zn(OH)_2$.

SEM Investigation

The scanning electron micrographs of carbon steel are shown in Figure.3. The SEM micrograph of polished carbon steel surface (control) is shown in Figure.3a. This shows the smoothness of the metal surface. This implies the absence of any corrosion product formed on the metal surface. The SEM micrograph of carbon steel immersed in seawater is shown in Figure 3b. This shows the roughness of the metal surface by the corrosive environment and the porous layer of corrosion product is present. Pits are observed on the metal surface. Figure 3c shows that the presence of 250 ppm of 2-CEPA and 50 ppm of Zn^{2+}in seawater gives the formation of thick films on the carbon steel surface. This may be interpreted as due to the adsorption of the inhibitor on the metal surface incorporating into the passive film in order to block the active site present on the carbon steel surface [26,27].

Mechanism of Corrosion Inhibition

The results of the weight loss study show that the formulation consisting of 250 ppm of 2-CEPA and 50 ppm of Zn^{2+} has 98% of inhibition efficiency in controlling corrosion of carbon steel in seawater. FTIR spectra reveal that the protective film consists of Fe^{2+}– 2-CEPA complex and $Zn(OH)_2$. In order to explain these facts, the following mechanism of corrosion inhibition is proposed.

When carbon steel is immersed in an aqueous solution, the anodic reaction is:
$Fe \rightarrow Fe^{2+} + 2e^-$.

The corresponding cathodic reaction is reduction of oxygen to hydroxyl ions:
$O_2 + 2H_2O + 4e^- \rightarrow 4OH^-$.

When the formulation consists of 250 ppm of 2-CEPA and 50 ppm Zn^{2+} in seawater, there is formation of 2-CEPA – Zn^{2+} complex in solution. When carbon steel is immersed in this environment, the 2-CEPA – Zn^{2+} complex diffuses from the bulk of the solution to the metal surface. When 2-CEPA – Zn^{2+} complex is converted into 2-CEPA – Fe^{2+}

complex on the anodic sites of the metal surface, the stability of Fe^{2+}– 2-CEPA complex is higher than the corresponding Zn complex.

Zn^{2+}– 2-CEPA + Fe^{2+} → Fe^{2+}– 2-CEPA + Zn^{2+}.

The released Zn^{2+} combines with OH^- to form $Zn(OH)_2$ on the cathodic sites of the metal surface.

$Zn^{2+} + 2OH^- \rightarrow Zn(OH)_2$.

The protective nature of the film is due to the presence of metal inhibitor complex and zinc hydroxide. Formation of the metal inhibitor complex fills the pores of the otherwise porous film and makes it a protective film. Thus, the protective film consists of Fe^{2+}– 2-CEPA complex and $Zn(OH)_2$.

CONCLUSIONS

The conclusions drawn from the results may be given as, The formulation consists of 250 ppm of 2-CEPA and 50 p pm of Zn^{2+} has 98% IE. Cyclic voltammetry study reveals that the protective film is more compact and stable even in 3.5% Na Cl environment. FTIR spectra show that the protective film consists of Fe^{2+}– 2-CEPA complex and $Zn(OH)_2$. The SEM micrographs confirm the formation of protective layer on the metal surface.

Conflict of Interest

We have no conflict of interest to declare including any financial, personal, or other relationships with other people or organizations that can influence their work.

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REFERENCES

1. Satyanarayana, M. G. V.; Kalpana, Y.; Himabindu, V.; Kumar, K. *Corros. Eng. Sci. Technol*. 2012, 47(1), 38-44.
2. Al-Baker, N.; Shawabkeh, R.; Rihan, R. *Corros. Eng. Sci. Technol*. 2011, 46(7), 767-776.
3. Durodola, B. M.; Olugbuyiro, J. A. O.; Moshood, S. A.; Fayomi, O. S.; Popoola, A. P. I. Int. J. Electrochem. Sci. 2011, 6, 5605-5616.
4. Duan, J.; Wu, S.; Zhang, X.; Huang, G.; Du, M.; Hou, B. *Electrochim. Acta*. 2008, 54, 22.
5. El-Shamy, A. M.; Soror, T. Y.; El-Dahan, H. A.; Ghazy, E. A.; Eweas, A. F. *Mater. Chem. Phys*. 2009, 114, 156.
6. Bockris J. O. M.; Reddy, A. K. N. *Modern Electrochemistry, Plenum Press, New York.*1977, 2, 861.
7. Zou, Y.; Wang, J.; Zheng, Y. Y. *Corros. Sci.* 2011, 53, 208.
8. Mohamed, H. A.; Farag, A. A.; Badran, B. M. *J. Appl. Polym. Sci*. 2010, 117, 1270-1278.
9. Amar, H.; Benzakour, J.; Derja, A.; Villemin, D.; Moreau, B. *J. Electroanal. Chem.*2003, 558, 131.
10. Amar, H.; Benzakour, J.; Derja, A.; Villemin, D.; Moreau, B.; Braisaz, T.; Tounsi, A. *Corros. Sci.* 2008, 50, 124.
11. Gopi, D.; Manimozhi, S.; Govindaraju, K. M. *J. Appl. Electrochem.*2007, 37, 439.
12. Apparao, B. V.; Christina, K. *Indian J. Chem. Technol.*2006, 13, 275.
13. Labjar, N.; Lebrini, M.; Bentiss, F.; Chihib, N. E.; El Hajjaji, S.; Jama, C. *Mater. Chem. Phys.* 2010, 119, 330.
14. Fang, J. L.; Li, Y.; Ye, X. R.; Wang, Z. W.; Liu, Q. *Corrosion*.1993, 49, 266.
15. Wranglen, G. *Introduction to corrosion and protection of Metals. London: Chapman & Hall*.1985, 236.
16. Gunasekharan, G.; Palaniswamy, N.; Apparao, B. V. *Bull. Electrochem*. 1996, 12(1-2), 59-63.

17. Dutra, C. A. M.; Codaro, E. N.; Nakazato, R. Z. *Mater. Sci. Appl*. 2012, 3, 348.
18. Li, Y.; Kumar, P.; Shi, X.; Nguyen, T. A.; Xiao, Z.; Wu, J. *Int. J. Electrochem. Sci*. 2012, 7, 8151.
19. Deyab, M. A.; Keera, S. T. *Egypt. J. Petrol.*2012,21, 31.
20. Gouda, V. K. in: *Proc. 12th Int. Corrosion Cong., Houston, TX, USA*.1993, 19.
21. Refaey, S. A. M.; Abd El-Rehim, S. S.; Taha, F.; Saleh, M. B.; Ahmed, R. A. *Appl. Surf. Sci.*2000,158, 190-196.
22. Kannagara, D. C. W.; Conway, B. E. *J. Electrochem. Soc.* 1987, 134. 894.
23. Selvi, J.A.; Rajendran, S.; Sri, V. G.; Amalraj, A. J.; Narayanasamy B. *Port. Electrochim. Acta*. 2009, 27(1), 1.
24. Sathiyabama, J.; Rajendran, S.; Selvi, J. A.; Jeyasundari, J. *Open Corros. J.*2009, 2, 77-82.
25. Kavipriya, K.; Sathiyabama, J.; Rajendran, S. *Eur. Chem. Bull*. 2013, 2(9), 657-661.
26. Amar, H.; Braisaz, T.; Villemin, D.; Moreau, B. *Mater. Chem. Phys*. 2008, 110(1), 1-6.
27. Anbarasi, C.M.; Rajendran, S.; Narayanasamy, B.; Krishnaveni, A. *Asian J. Chem*. 2012, 24, 5029.

Table 1: The physicochemical parameters of natural seawater collected in Mandapam, Tamilnadu, India.

Parameter	Value
Total dissolved salts (mg/L)	78136
Electrical conductivity (micro mhos/cm)	70788
pH	7.82
Total hardness ($CaCO_3$ equivalent)	24500
Calcium as Ca (mg/L)	2200
Magnesium as Mg (mg/L)	1800
Sodium as Na (mg/L)	9600
Chloride as Cl (mg/L)	23100
Fluoride as F (mg/L)	1.2
Free ammonia as NH_3 (mg/L)	900
Sulphate as SO_4 (mg/L)	2350

Table 2: The inhibition efficiency (IE%) and the corrosion rate (mdd) of 2-CEPA –Zn^{2+} system determined by weight-loss method.

2-CEPA ppm	Zn^{2+} ppm					
	0		25		50	
	IE%	CR (mdd)	IE%	CR (mdd)	IE%	CR (mdd)
0	-	36.36	15	30.91	23	27.99
50	15	30.91	45	19.99	71	10.54
100	21	28.72	50	18.18	84	5.82
150	26	26.91	58	15.27	90	3.64
200	30	25.45	63	13.45	95	1.82
250	35	23.63	70	10.91	98	0.73

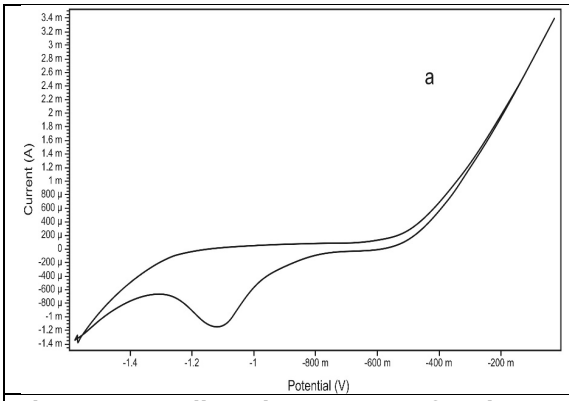

Figure 1a: Cyclic voltammogram of carbon steel electrode immersed in 3.5% NaCl

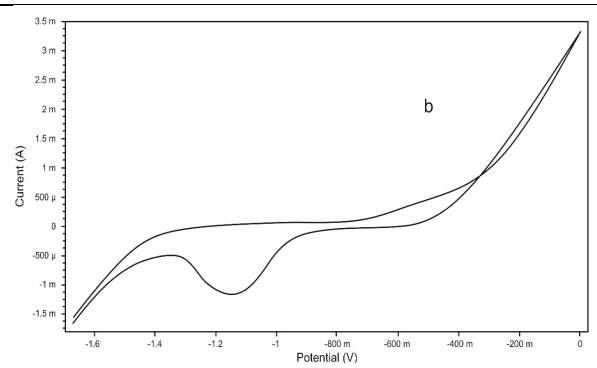

Figure 1b: Cyclic voltammogram of carbon steel electrode submerged in 3.5% NaCl solution after its immersion in seawater for one day

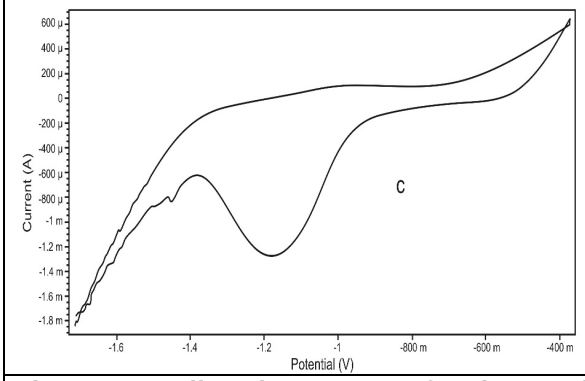

Figure 1c: Cyclic voltammogram of carbon steel electrode submerged in 3.5% NaCl solution after its immersion in seawater containing 250 ppm of 2-CEPA and 50 ppm of Zn^{2+} for one day

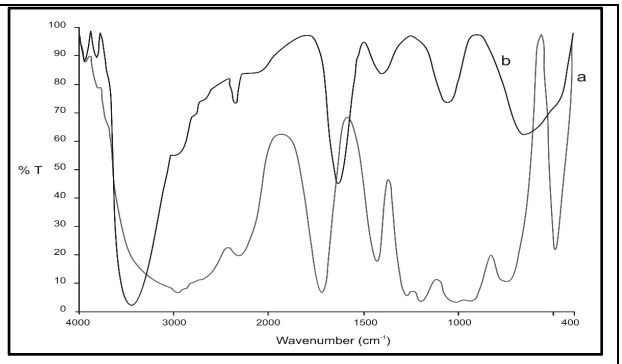

Figure 2: FTIR Spectra: a) Pure 2-CEPAb)Film formed on metal surface after immersion in seawater containing 250 ppm of 2-CEPA *and* 50 ppm of Zn^{2+}

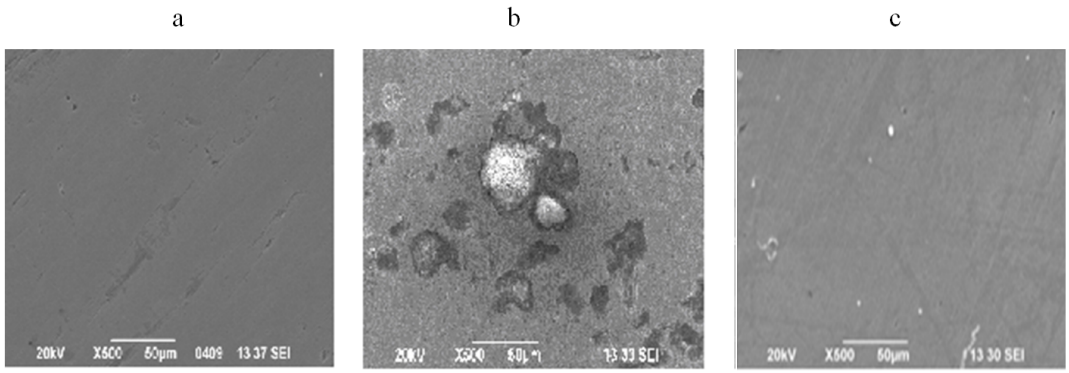

Figure 3: SEM micrographs (magnification-x500) of a) polished carbon steel (control) b) carbon steel immersed in seawater c) carbon steel immersed in seawater containing 250 ppm of 2-CEPA and 50 ppm of Zn^{2+}

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RESEARCH ARTICLE

Antiparkinson Effect of Hydro-Alcoholic Extract of Leaves of *Cassia marginata* Roxb

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ABSTRACT

People are now a days filled with stress which contribute to many neurodegenerative diseases such as Depression, Alzheimer's disease and Parkinson's disease. The present study was aimed to evaluate the antiparkinson's effect of hydro-alcoholic extract of leaves of *Cassia marginata* Roxb on Chlorpromazine induced Parkinsonism in rats. Parkinsonism was induced by chlorpromazine (3mg/kg/day,i.p) for a period of 21 days. The anti parkinson's effect was assessed by catalepsy bar test, locomotor and Rota-rod test. Oxidative stress was assessed by measuring the brain homogenate levels of Super oxide dismutase, Catalase, Reduced glutothione and Malondialdehyde in rats. The hydro-alcoholic extract of leaves of *Cassia marginata* Roxb at 200 and 400 mg/kg/day pretreated groups significantly increased the locomotor and musclegrip activity ($p<0.001$), and decreased the catalepsy time ($p<0.001$) when compared to Chlorpromazine treated animals.It also showed significant reduction in oxidative stress by increasing the levels of Superoxide dismutase, Catalase, Reduced glutathione ($p<0.001$) and decrease in the level of Malondialdehyde ($p<0.001$) in the brain. Thus the results of the present study concluded that the hydro-alcoholic extract of leaves of *Cassia marginata* Roxb has significant neuro protective property against Chlorpromazine induced Parkinsonism in rats.

Keywords: *Cassia marginata* Roxb, Chlorpromazine, Antiparkinson, Catalepsy, Locomotor activity, Muscular rigidity.

INTRODUCTION

Parkinson's Disease (PD) is a chronic, progressive, neurodegenerative disorder caused by the degeneration of nerve cells in the part of the brain called Substantia Nigra pars compacta (SNpc) [1] and also the extensive presence of an intracellular protein called alpha synuclein (aSyn). The dopamine deficiency in the basal ganglia leads to classical parkinsonian motor symptoms such as bradykinesia, tremor, rigidity and later postural instability [2]. It also shows non-motor symptoms like tiredness, depression and pain [3]. Parkinson's disease is the second most common age-related neurodegenerative disorder next to Alzheimer's disease [4]. In India,the prevalence was around 10 percent of the global burden, 5.8 lakhs [5]. Many studies report that the Free radicals are produced within the basal ganglia and damage the subtantia nigral neurons, which results in pathogenesis of parkinson's disease. Plants and their extracts are the richest source of natural antioxidants. The antioxidant activity of plants is due to the presence of many vital phytoconstituents like phenolic compounds such as flavonoids, alkaloids, saponins and tannins. Several studies reported that the flavonoids have neuro protective effects. Current therapy approaches couldn't cure PD. It mainly involves the use of medications that can help to control the symptoms of PD [6, 7] which exert more side effects. Hence, there is a continuous search for drugs from medicinal plants is being increased because of its less side effects and easy availability and low cost. So, there is a demand for the utilization of plant derived drugs for the treatment of parkinson's disease. *Cassia marginata* Roxb belonging to the family fabaceae, commonly known as red cassia is widely distributed in South India and Sri Lanka. The plant is used in the treatment of Gastric problems, muscle spasms, nausea, vomiting, blotches, infections, diarrhea, cold and stomach spasms and diabetics by the tribal people of Andhra Pradesh and Tamilnadu [8]. Hence, the present study was focused on the screening of antiparkinson's effect of hydro-alcoholic extract of leaves of the plant *Cassia marginata* Roxb against chlorpromazine-induced Parkinsonism in rats.

MATERIALS AND METHODS

Plant material

Cassia marginata Roxb was commonly known as red cassia or Ceylon senna. The leaves of *Cassia marginata* Roxb were collected from Kanjeepuram District, Tamilnadu in the month of March 2019. The collected leaves of *Cassia marginata* Roxb were authenticated by Botanist Dr. A. Balasubramaniam, ABS Botanical garden, Karipatty, Salem. A voucher specimen (KCM-1) was deposited in the museum, Vinayaka Mission's College of Pharmacy, Salem, Tamilnadu for future reference. The collected leaves were dried in shade and stored in airtight container.

Extraction

About 500g of the powdered leaves of *Cassia marginata* Roxb were extracted using cold maceration method. Plant material was placed in a closed vessel and the solvent was added (ethanol and water in 70:30 ratio) in sufficient quantity to make the hydro-alcoholic extract. The preparation was allowed to stand for 3 days. After the specified time, the extract was filtered and the liquid was strained off. Then the filtered liquid was evaporated, concentrated and stored in an airtight container.

Animals

Healthy adult male wistar rats, weigh 150–200 g, and female albino mice weighing 22–35 g was used for the study and acclimatized to laboratory conditions for one week. The animals were kept in a well-ventilated polypropylene cages at 12h light and 12 h dark schedule at 25°C and 55–65% e humidity levels. The rats had been given a normal diet of pellets and free access to water. The experimental proposal was submitted to Institutional Animal Ethical Committee clearance and was approved by the same (P.col/21/2019/IAEC/VMCP).

Phytochemical evaluation of *Cassia marginata* Roxb

The hydro-alcoholic extract of *Cassia marginata* Roxb was screened for phytoconsitutents by using standard procedures to test for the presence of alkaloids, carbohydrates, flavonoids, glycosides, proteins and free amino acids, gums and mucilages, saponins, sterols, fixed oils, tannins, and phenolic compounds.

Acute toxicity studies of *Cassia marginata* Roxb

LD_{50} of the extract was determined by following OECD guidelines no. 423. This test involves the administration of a single bolus dose of test substance to fasted healthy female mice by oral gavage and observed the animals for signs of toxicity and mortality for 14 days. Any one animal had shown death, a restart of the same dose confirmed the toxic dose then. If mortality had not been found, and the same protocol for higher doses was performed.

Chlorpromazine-induced model

Chlorpromazine (CPZ)is a first generation neuroleptic drug which on prolonged use can cause tardive dyskinesia, hypolocomotion and muscular rigidity. Thus, chronic treatment of CPZ for 21days model was been selected for the present study [9]. Chlorpromazine injection (largactil) was received from hospital pharmacy, Ammani hospitals, Salem, Tamilnadu, India. Rats were randomly assigned to 5 groups. Each group consists of 6 animals. Group I animals were administered with vehicle and served as normal control group. Group II animals were administered with chlorpromazine (3 mg/kg, i.p.) daily for a period of 21 days and served as the negative control group. Group III animals received Syndopa (levodopa + carbidopa) (6 mg/kg, p.o. for 21 days) and served as standard group. Group IV and Group V animals were administered with hydro-alcoholic extract of leaves of *Cassia marginata* Roxb (HAECM) 200 mg/kg and 400 mg/kg p.o, respectively for 21 days. CPZ was given 30 minutes prior to standard and test drug administration. Bodyweight changes and behavioral assessments were carried out before the start of the treatment. Behavioral assessments include catalepsy bar test, locomotor activity test, muscular rigidity test were done before start of the experiment, on day 7, day 14, and day 21. After completion of the experiment, biochemical parameters such as MDA, CAT, SOD and GSH levels were calculated from the rat brain homogenate.

Evaluation of Behavioral Properties

Catalepsy bar test

Catalepsy is characterized by muscle rigidity associate with failure to correct an externally induced oblique posture for a protracted amount of time. The standard bar test was used for the assessment of catalepsy [10]. In this method, the rats were placed in a position with its front legs resting on a bar suspended on top of the ground. The intensity of catalepsy was measured by the length of time that the subject maintains this externally induced abnormal posture. Each animal was observed, after administration of chlorpromazine. The scoring of this method was given below.

Phase I-0.5	The rat only moves upon touched / pushed.
Phase II-0.5	The rats' front paws were conversely positioned on a 3 cm stone bar. If the rat unable to fix the pose in 15sec, a score of 0.5 was add upto the score of phase 1 for each paw.
Phase III-1.0	The rat's front paws were positioned conversely on a stone bar of 9 cm high. If the rat unable to fix the Pose in 15sec, a score of 1 was given to the scores of phase I and phase II for each paw. Thus, the maximum was 3.5 score was normally given to the animals.

Locomotor activity test

Actophotometer is used to assess the locomotor activity in animals. Rats were individually placed in actophotometer and the total locomotor activity count was measured for 10 minutes 11. Each animal was observed following the administration of standard and test substance and values were expressed as counts/10 min.

Rotarod activity test

Rotarod test is used to assess the muscle coordination and muscle rigidity of an animal. Rotarod apparatus has a horizontal grooved rod rotating at a fixed speed. Each rat is subjected to balance on this rod [12]. The floor of each compartment has sensors that deactivate the timers when the rat fall- off and the exact fall off time for each rat is displayed on the respective display. A cut-off time of 180 seconds was fixed and followed over the entire test. The mean effects of the study were reported as the fall of time. Each animal following the administration of standard and test substance, the fall off time was recorded.

Biochemical estimation

After the treatment period, all the animals were scarified by decapitation under mild anesthesia. The brains were immediately removed, forebrain was dissected out, and cerebellum was discarded. The isolated brains were put on ice and then rinsed in an ice-cold isotonic saline to remove blood. Tissue homogenate (10%) was prepared in 0.1 M phosphate buffer (pH 7.4). The homogenate was centrifuged at 10,000 g for 15 minutes and aliquots of supernatant obtained were used for biochemical estimation. From the above brain homogenate, following biochemical levels were estimated.

Malondialdehyde

Malondialdehyde (MDA) level is considered as an indirect measure of lipid peroxidation and was usually measured by the reaction of thiobarbituric acid [13]. In a test tube, 1 ml of supernatant homogenate and 3 ml of thiobarbituric acid was taken. The above solution was stirred and kept for 15 min. then cooled the solution by kept it an ice bath. Followed cooling, solution was centrifuged to 3500g for 10 min. The upper portion was separated and analyzed with a UV-spectrophotometer at 532 nm. The experiment was repeated for three times. The enzyme level was expressed as nanomoles per mg of protein.

Superoxide dismutase

Superoxide dismutase (SOD) is an antioxidant enzyme which catalyses' the dismutation of superoxide to nonreactive oxygen species, and hydrogen peroxide. SOD function was calculated by the method of Beyer and Fridovich [14]. In a test tube, 0.1 mL of supernatant tissue homogenate, 0.1 mL EDTA (1×10^{-4} M), 0.5 mL of carbonate buffer (pH 9.7), and 1 mL of epinephrine (1 mM) was taken and mixed well. The optical density of the red coloured mixture formed was analyzed at 480 nm on a spectrophotometer for 3 minutes. One unit of the enzyme activity means the concentration required to inhibit chromogen production by 50% in 1 minute, at specific assay conditions. The enzyme level was expressed as units/min/mg of protein.

Catalase

Oxidative stress may lead to decreased levels of catalase. The catalase function was investigated by following Aebi method [15]. 0.05 ml of supernatant of tissue homogenate and 1.95 ml of phosphate buffer (50 mM) was mixed and taken in a 3 ml cuvette. Then add 1 ml of hydrogen peroxide and measure the absorbance at 240 nm at 15 sec intervals. The catalase level was measured by calculating the H_2O_2 millimolar extinction coefficient. The enzyme level was indicated as micromoles of H_2O_2 utilized /minute/ mg of protein.

Reduced Glutathione

GSH is an enzyme/antioxidant present in plants, animals, fungi, and some bacteria. A primary function of glutathione is to reduce the oxidative stress. Reduced GSH level was measured by precipitating 1 ml of tissue homogenate with 1 ml of 10% trichloroacetate. To an aliquot of the supernatant, 4 ml of phosphate solution is added. Then 0.5 ml of 5, 5′-dithiobis-(2-nitrobenzoic acid) (DTNB) reagent were added and the reading was taken at 412 nm [16]. The results were indicated by nM per mg of protein.

Statistical Analysis

All the readings were expressed as mean ± SEM and were analyzed by one-way ANOVA followed by Dunnett's *t*-test for multiple comparisons. p values < 0.05 was considered to be significant.

RESULTS

Acute toxicity studies of *Cassia marginata* Roxb

The LD_{50} determination was done in mice as per OECD Guidelines 423. The HAECM was found to be safe and non-toxic upto 2000 mg/kg. No morbidity and mortality was observed in all the doses tested. Hence, 200 mg/kg was fixed as the therapeutic dose and 400 mg/kg was fixed as higher dose for present study.

Phytochemical evaluation of *Cassia marginata* Roxb.

Phytochemical screening of *Cassia marginata* Roxb showed the presence of carbohydrates, sterols, phenolic compounds, tannins, flavonoids, and glycosides in the HAECM.

Chlorpromazine-induced catalepsy

Effect of HAECM on chlorpromazine-induced catalepsy in rats

All the animals were evaluated for the assessment of catalepsy for a period of 21 days. The animals were evaluated on day 0, day 7, day 14 and day 21 after treatment. The control animals were shown a catalepsy time of about 1.83-2.33 seconds during their entire observation period. On day21, Chlorpromazine treated animals showed significant increase of catalepsy time compared to control groups. Whereas Group-III, Syndopa treated animals significantly reduced ($p < 0.001$) the catalepsy time as compared to Group-II on day 21. Similarly, group IV and V animals treated with 200mg/kg and 400 mg/kg showed a significant reduction ($p < 0.001$) in the catalepsy time in a dose dependent manner shown in table no.1

Effect of HAECM on chlorpromazine-induced hypolocomotion in rats

The locomotor activity was significantly reduced in Chlorpromazine treated group when compared to normal group. Syndopa treated animals significantly increased the locomotor activity ($p < 0.001$). Administration of HAECM 200 and 400 mg/kg showed significant increase in locomotor activity on day 21 in a dose dependent manner was shown in table no.2.

Effect of HAECM on chlorpromazine -induced muscular rigidity in rats

Muscular rigidity of the animals was evaluated by using a Rota rod apparatus. The mean fall-off time was considered to be an indicator of muscular rigidity. chlorpromazine treated group showed significant reduction ($p < 0.001$ in fall of time compared to normal group animals. While the HAECM treated animals also showed increase in fall of time ($p < 0.001$) compared to chlorpromazine treated animals are shown in table no.3.

Effect of HAECM on biochemical parameters of Chlorpromazine-induced model

Administration of chlorpromazine showed a significant elevation of MDA and reduction of SOD, CAT and GSH when compared to normal control animals. Treatment with HAECM (200 and 400mg/kg) showed significant reversal of these levels ($p < 0.001$) when compared to chlorpromazine treated animals. While, Syndopa treated groups significantly prevents the reduction ($p < 0.001$) in the levels of CAT, SOD and GSH and rise in the level of MDA shown in table no.4.

DISCUSSION

Parkinsonism is a neurodegenerative disorder described by the progressive destruction of dopamine neurons. The factors that are responsible for dopaminergic neurons loss is still unclear. Current therapy approaches couldn't cure PD, it involves dopamine replacement therapy which leads to durable complications. Herbal products are now used as a healthier alternative to treat PD. The World Health Organization has also stressed the potential of herbal medicine, and has established botanical medicine approaches, regulations and procedures. Hence, in the present study, the hydro-alcoholic extract of *Cassia marginata* Roxb was screened for its neuroprotective activity.

Chlorpromazine is one of the first generation typical anti-psychotic drugs recommended by WHO for the for the treatment of psychosis[17]. Chronic treatment with Chlorpromazine blocks dopamine receptors in brain. Reduction in the dopaminergic neurotransmission results in motor defects such as catalepsy, akinesia, bradykinesia, tremor, and muscular rigidity and also reduces in the levels of antioxidant enzymes in the brain. Thus schizophrenic and psychiatric patients taking chlorpromazine for long time suffers from parkinsonism. In the present study, chlorpromazine(3mg/kg, i.p) for 21 days was used for the induction of parkinson's disease. It also produces reduction in the levels of antioxidant enzymes such as SOD, CAT, GSH, and level of MDA is increased. In the present work, it was observed that chlorpromazine (3mg/kg, i.p) treatment produced catalepsy in Group II animals. All the groups i.e Syndopa, Hydroalcoholic extracts of leaves of *Cassia marginata* at 200 and 400 mg/kg showed significant reduction in catalepsy time. Decrease in catalytic time indicates the activity of HAECM against parkinsonism. they also restored the locomotor activity and muscle grip properties. Further, chlorpromazine treated animals showed decreased levels of SOD, GSH, CAT and elevated levels of MDA in brain tissue contrast to the normal animals. Active marker of oxidative stress is lipid peroxidation. Excessive lipid peroxidation product levels were observed in the substantia nigra of people who suffer from Parkinson's disease. In our study, same finding was observed in the brain homogenates of control animals treated with chlorpromazine. Normally the brain was protected from free radicals by the antioxidant enzymes like SOD, CAT and GSH. Glutathione peroxidase protects the brain against neurodegeneration by scavenging H_2O_2 from cellular metabolism and balance the formation and decomposition of H_2O_2 in normal conditions[18,19]. This clearly indicates that the reduced glutathione is the limiting factor in eliminating H_2O_2. These factors depict the oxidative stress of chlorpromazine. administration of HAECM treated animals showed significant reduction of MDA levels and increased levels of antioxidant enzymes. Similarly, Syndopa treated animals reversed these levels to normal level. Thus, it was observed from the present study that the administration of HAECM in two doses significantly reduced the catalepsy time and increased the locomotor, muscle grip and LPO levels against chlorpromazine induced parkinsonism.

CONCLUSION

The hydro-alcoholic extract of leaves of *Cassia marginata* Roxb. was screened for its anti-parkinsonism activity against chlorpromazine model. The results of the present study showed that HAECM possess neuroprotective effect by delaying the onset of PD and also reduces the manifestations of PD. In future, *Cassia marginata* Roxb will provide a scientific basis for further studies.

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REFERENCES

1. Bhangale, J.O. and S.R. Acharya. Anti-Parkinson Activity of Petroleum Ether Extract of Ficus religiosa (L.) Leaves. Advances in pharmacological sciences 2016; 1-9.
2. Beal, M.F., Mitochondrial dysfunction in neurodegenerative diseases. Biochim Biophys Acta 1998; 1366(1-2): 211-23.
3. Radhakrishnan, D.M. and V. Goyal, Parkinson's disease: A review. Neurol India 2018; 66(Suppl) S1:26-s35.
4. Cacabelos, R., Parkinson's Disease: From Pathogenesis to Pharmacogenomics. International journal of molecular sciences 2017; 18(3): 551.1-28
5. Oliveira de Carvalho A, Filho ASS, Murillo-Rodriguez E, Rocha NB, Carta MG, Machado S. Physical Exercise For Parkinson's Disease: Clinical And Experimental Evidence. *Clin Pract Epidemiol Ment Health* 2018 Mar;14:89-98.
6. Wolfgang H. Oertel, Recent advances in treating Parkinson's disease. F1000Research 2017; 6: 260-260.
7. Hurtig, H.I., Problems with current pharmacologic treatment of Parkinson's disease. Exp Neurol 1997; 144(1): 10-6.
8. K.S. Murugesa Mudaliyar, Siddha Materia Medica, Directorate of Indian Medicine & Homeopathy. Chennai.2008.
9. Souravh Bais, N. S. Gill, Nitan Kumar, "Neuroprotective Effect of Juniperus communis on Chlorpromazine Induced Parkinson Disease in Animal Model", Chinese Journal of Biology 2015; vol. 2015, 1-7.
10. Barbara Bricker, Dinithia Sampson, and Seth Y. Ablordeppey, Evaluation of the potential of antipsychotic agents to induce catalepsy in rats: assessment of a new, commercially available, semi-automated instrument. Pharmacol Biochem Behav 2014; 120: 109-16.
11. Uma Bhosale, Radha Yegnanarayan, Pophale Prachi, Mandar Zambare, R.S. Somani,,Study of CNS depressant and behavioral activity of an ethanol extract of Achyranthes Aspera (Chirchita) in mouse model. Annals of neurosciences 2011; 18(2): 44-47.
12. Shiotsuki, H., et al.,A rotarod test for evaluation of motor skill learning. J Neurosci Methods 2010; 189 (2): 180-5.
13. Ohkawa, H., N. Ohishi, and K. Yagi, Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem 1979; 95(2): 351-8.
14. W. F. Beyer Jr. and I. Fridovich, "Assaying for superoxide dismutase activity: some large consequences of minor changes in conditions," Analytical Biochemistry 1987; 16 (2): 559– 566.
15. Aebi. H. "Catalase in vitro," Methods in Enzymology, Academic Press, New York, 1984. vol. 105. 121–126,
16. S. K. Srivastava and E. Beutler, "Accurate measurement of oxidized glutathione content of human, rabbit, and rat red blood cells and tissues," Analytical Biochemistry 1968. 25: 70– 76.
17. PradeepPal, Ghosh AK. Antioxidant, Anti-alzheimer and Anti-parkinson activity of *Artemisia nilagirica* Leaves with Flowering Tops. UKJPB 2018; 6(2):12-23.
18. Dexter DT, Holley AE, Flitter WD. Increased levels of lipid hydroperoxides in the Parkinsonian substantia nigra: an HPLC and ESR study. Movement Disorders 1994; 9(1): 92–97.
19. Parikh V, Khan MM, Mahadik SP. Differential effects of antipsychotics on expression of antioxidant enzymes and membrane lipid peroxidation in rat brain. Journal of Psychiatric Research 200;37(1): 43–51.

Table.no.1. Effect of HAECM on Chlorpromazine-induced Catalepsy in rats.

S.No	Group	Treatment	Catalepsy Time (Sec)			
			Day 0	Day 7	Day 14	Day 21
1	Group-I	Normal saline (0.1 ml, p.o.)	1.83±0.34	1.66±0.23	1.5± 0.24	2.33± 0.23
2	Group-II	Chlorpromazine (CPZ) (3mg/kg, i.p)	2.33±0.23	9± 0.8*	15± 0.37*	23.67±1.05*
3	Group-III	CPZ (3mg/kg, i.p) + Syndopa(6mg/kg, p.o.)	2± 0.28	4± 0.28*	5.17±0.31*	6± 0.26*

4	Group-IV	CPZ (3mg/kg, i.p) + HAECM(200mg/kg,p.o.)	1.83±0.34	6± 0.28*	10.17±0.31*	15.33±0.67*
5	Group-V	CPZ (3mg/kg, i.p) +HAECM(400mg/kg, p.o.)	2± 0.28	5.5±0.47*	7± 0.4*	10± 0.26*

All the values were expressed as mean± SEM and n=6 in each group. All the data were analyzed by One-way ANOVA method. P values < 0.05 are considered to be significant. (* = P value < 0.001)

Table.no.2. Effect of HAECM on Chlorpromazine-induced Hypolocomotion in rats.

S.No	Group	Treatment	Locomotor Activity Score (Counts/10min)			
			Day 0	Day 7	Day 14	Day 21
1	Group-I	Normal saline (0.1 ml, p.o.)	262± 5.85	284.17±6.54	266.5± 7.40	275.83±7.58
2	Group-II	Chlorpromazine (CPZ)(3mg/kg, i.p)	264.5± 6.01	43.17± 2.69*	29.33± 2.24*	15.33± 1.98*
3	Group-III	CPZ (3mg/kg, i.p) + Syndopa (6mg/kg, p.o.)	262.83±6.56	168.33±3.70*	190± 7.10*	220.17±4.15*
4	Group-IV	CPZ (3mg/kg, i.p) +HAECM (200mg/kg, po)	272.67±7.89	96± 4.27*	122.83±4.65*	139.17±7.04*
5	Group-V	CPZ (3mg/kg, i.p) +HAECM (400mg/kg,p.o)	263.5± 7.73	123± 6.32*	156.17±5.96*	196.17±5.94*

All the values were expressed as mean± SEM and n=6 in each group. All the data were analyzed by One-way ANOVA method. P values < 0.05 are considered to be significant. (* = P value < 0.001)

Table.no.3. Effect of HAECM on Chlorpromazine-induced Muscular rigidity in rats.

S.No	Group	Treatment	Retention Time (Sec)			
			Day 0	Day 7	Day 14	Day 21
1	Group-I	Normal saline (0.1 ml, p.o.)	112.5± 6.63	112.83±5.72	111± 4.83	111.5± 6.75
2	Group-II	Chlorpromazine (CPZ) (3mg/kg, i.p)	113.33±6.26	59.5± 3.04*	30.67±4.35*	19.67± 3.02*
3	Group-III	CPZ (3mg/kg, i.p) + Syndopa(6mg/kg, p.o.)	116.17±6.85	75± 3.15*	90.67±3.30*	105.83±5.10*
4	Group-IV	CPZ (3mg/kg, i.p) +HAECM(200mg/kg,p.o.)	119.67±4.70	61± 3.20*	71.17±2.97*	81± 3.78*
5	Group-V	CPZ (3mg/kg, i.p) +HAECM(400mg/kg,p.o.)	118.83±4.85	72.17± 3.18*	81.17±4.13*	92.67± 2.91*

All the values were expressed as mean± SEM and n=6 in each group. All the data were analyzed by One-way ANOVA method. P values < 0.05 are considered to be significant. (* = P value < 0.001)

Table.no.4. Effect of HAECM on Biochemical Parameters of Chlorpromazine-induced model.

S.No	Group	Treatment	MDA Level (nM/mg of protein)	CAT Level (μmoles of H_2O_2 used/ min/ mg of protein)	SOD Level (units/mg of protein)	GSH Level (nM/mg of protein)
1	Group-I	Normal saline (0.1 ml, p.o.)	1.455±0.061	5.679±0.103	3.226±0.06	4.564±0.12
2	Group-II	Chlorpromazine (CPZ) (3mg/kg, i.p)	2.489±0.093*	3.444±0.107*	2.0±0.079*	2.963±0.084*
3	Group-III	CPZ (3mg/kg, i.p) +Syndopa (6mg/kg, p.o.)	1.694±0.041*	5.422±0.092*	2.80±0.048*	4.237±0.09*
4	Group-IV	CPZ (3mg/kg, i.p) + HAECM (200mg/kg, p.o.)	2.14±0.05*	4.430±0.082*	2.306±0.045*	3.469±0.085*
5	Group-V	CPZ (3mg/kg, i.p) + HAECM (400mg/kg, p.o.)	1.876±0.081*	4.807±0.042*	2.682±0.041*	3.736±0.068*

All the values were expressed as mean± SEM and n=6 in each group. All the data were analyzed by One-way ANOVA method. P values < 0.05 are considered to be significant. (* = P value < 0.001)

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RESEARCH ARTICLE

Impact of Change Management on the Performance of College Students in Odisha

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ABSTRACT

Change is all around us and it's a procedure, not an incident. Change can turn an emergency into a prospect and change meet head-on the status quo. An organization is an open system which depends upon environment for its continued existence and survival. So, adopting the change is not a lavishness, but need and requirement of the industries. The speed and complexity of changes in the organizations have forced the education system to be modified. Any change in the organization is not possible without the change in people. The students must be ready for adopting the change; the academicians should focus on quality and updated knowledge in order to impart the quality education to the students and the companies must adopt the change in order to win in the dynamic competitive environment. Academicians have the responsibility to create the talented & dynamic professionals in order to make the nation's progress in the era of liberalization, globalization and privatization. The prospects of teaching highlight the enormous requirement deliberately make most of the "Internet of Things" to organize the future employees to face confronts ahead. There is a great need of modifications in the present education system in order to make the organizational, societal and nation's progress. It is the obligation of the educationists to maintain the real facts of life by linking bookish knowledge with the practical knowledge.This research paper is an attempt to find out the students' attitude towards technology, various technological tools adopted by students, the awareness and use of different skill based schemes of Government amongst students. This study is based on the online questionnaires designed for Students. The sample size includes 200 students from different colleges of Odisha.

Keywords: Change Management, Schemes of Government, technology, performance.

INTRODUCTION

Change management is a united word for all tactics to formulate and upkeep persons, groups, and administrations in creation of organizational change. The greatest collective transformation drivers comprise: technical development, procedure evaluations, disaster, and customer practice variations; stress from innovative marketable participants, strategy formulation, and company reformation. It comprises approaches that transmit or redefine the practice of possessions, commercial procedure, financial plan distributions, or additional styles of process that meaningfully transform a company. Organizational change management should be proactive, not reactive and indifferent. Structural change management reflects the full business and what wants to modify, while change management may be used exclusively to mention to how persons and groups are affected by such administrative alteration. It compacts with plentiful poles apart disciplines, social sciences to information technology and commercial answers.

Schemes of Government for Change Management
PMKVY (Pradhan Mantri Kaushal Vikas Yojana)

The goal of learning in Pradhan Mantri Kaushal Vikas Yojana system is deliver expertise working out to the new persons through all countries and parts of India in numerous subdivisions and work characters.

Digital India

Digital India is a movement propelled by the Administration of nation to safeguard the Government services are prepared accessible to people automatically by enhanced online arrangement and by growing online connectivity or by creating the nation numerically invested in the arena of expertise.

Entrepreneurship and Skill Development

The Ministry of Skill Development and Entrepreneurship is a Ministry of Government of India has organised on 9 November 2014 to synchronise all skill development determinations through the nation. Industrialised training, internship and additional expertise improvement accountabilities were transferred from the Ministry of Labour and Employment to this newly-made Ministry on 16 April 2015.

Pradhan Mantri Yuva Yojana

Pradhan Mantri YUVA Yojana (Yuva Udyamita Vikas Abhiyan) is nationwide sponsored Scheme on entrepreneurship education and training being applied by the Ministry of Skill Development and Entrepreneurship, Government of India.

Start Up India

Start-up India is a great scheme of the Government of India. The achievement strategy of this advantage is founded on the following three pillars Simplification and Handholding, funding Support and Incentives.
Industry-Academia Partnership and Incubation

Review of Literature

According to Burnes (2004) change is a ubiquitous characteristic of managerial lifetime, both at a functioning and tactical level. Consequently, there must be no uncertainty concerning the significance to any establishment of its capability to recognize where it requirements to be in the forthcoming, and how to achieve the modifications indispensable getting there. Zorn et al., (2000). The capability to transformer currently and positively is well-thought-out to be vital to any establishment' sexistence. The necessity for ongoing alteration necessitates a structural

capability to acquire on a persistent foundation in a synchronised and broad minded scheme. According to Clarke (1999), despite the fact that supreme workforces may have been given restricted chances to be convoluted in the improvement of managerial change practices, it has not necessarily hindered them from observing and thereby formulating their own views regarding change and change management in their work environment. A striking opinion of Seijts and O'Farrell (2003) is that leadership "includes establishing a new direction for the organization, inspiring people to change their behaviours and routines consistent with the new direction, and coaching them on how to overcome barriers to change". As per M. Radovic (2008).

The degree of managerial transformation has not slackened in new years, and might even be growing. The speedy and recurrent revolution in expertise is lashing variations to managerial schemes and procedures. Headship and administration expertise, such as visioning, arranging, scheduling, providing response and gratifying accomplishment, are crucial aspects in any popular transformation resource fullness. Swarnalatha and Prasanna (2013) There are many research studies proposing various approaches for popular change management but furthermost share the shared subject that effective employee engagement is measured a main forerunner to prosperous change management. In totaling, it appears that employee engagement and change management share numerous of the similar purposes thought an obligation for popular application. Change management is a set of procedures that is engaged to confirm that note worthy variations are applied in an methodical, organized and organized style to influence organizational change (Mullins, 1999).

Beaudoin (2002) states that developing leaders in distance education prerequisite an assortment of abilities that are continually sophisticated and those comprise resource utilization, prerequisites calculation, matching expertise to requirements, program assessment and authorisation, strategy origination, deliberate planning, operative dynamism thoughts, market investigation, executing connected substructure, work together with associates, teaching and provision for academicians, and mentoring the next generation of leaders The current financial meltdown has terrified numerous encounters to commercial administrators and leaders through the domain. Everyone under way accusing B-schools for the current mess. Is it right to blame them? If not, then who is accountable for the present world-wide confusion? Is it the Colleges or academicians or scholars or parents or all to be blamed? Robbins (2004) mainly designated that organizational behaviour which emphasis on individual group, arrangement and association between them, is identifier for organizational change and persons mental state must be occupied into deliberation for the achievement of organizational change. Leaders also must persuade the workforces who are not accepting the change. This is the other role of leaders in change procedure. Banker (2012) suggested five features to comprehend and aid company's change process like executive sense-giving and middle managers sense making in process, accepting routines and trial and error method in OD, philosophical alterations in organization, financial crises bare in organization and demographic depletion.

Objectives of the study

To study the interest in latest technologies adopted by students. To check the awareness and use of different skill based schemes of Government amongst students Like Pradhan Mantri Kaushal Vikas Yojana, Digital India, Entrepreneurship & Skill India, Pradhan Mantri YUVA Yojana, and Startup India in addition to their base education. To study the incorporation of contemporary issues/recent trends into learning by the students.

RESEARCH METHODOLOGY

Sampling Method: Convenience Sampling

Data Collection Method

Primary Data

- Online questionnaire as well as Schedules and Printed Questionnaires are used for data collection from Students.
- Online questionnaire links sent to E-mail Ids of the target groups.

Secondary Data: Journals, Magazines & Internet

Link for the questionnaire:

https://docs.google.com/forms/d/e/1FAIpQLSe-lKAgE5vnUZyt481QD61wWQFcROsuSpdibfAQqdSi6rN6oA/viewform

Data Analysis and Interpretation

Interest in latest technologies adopted by students

Figure 1 shows that 91% of students use technology for research where as 9% do not use.70% of students use video conferencing as an important tool for learning where as 30% do not use. 71% of students use websites which are made for learning languages and online teachers are there to help students. 28% of students play online management games where as 72% do not play. Only 45% of students attend web seminars where as 55% do not attend. 78% of students use applications in mobiles for building their career where as 22% do not use.43% of students use BUSUU APP to learn different languages online and to get access to grammar guides provided by experienced publishers where as 57% does not use the app. It shows that most of the students are adopting latest technology for their studies and research.

Awareness of schemes of Government amongst students PMKVY

Figure 2 explains that 91% of students are aware about short term trainings regarding PMKVY, whereas 9% are not aware.85% of students are aware about special projects regarding PMKVY, whereas 15% are not aware. 94% of students are aware about placement guidelines regarding PMKVY, whereas 6% are not aware.76% of students are aware about monitoring guidelines regarding PMKVY, whereas 24% are not aware. It shows that maximum students are aware of PMKVY. It is a very good sign that the students are aware.

Use of PMKVY

Figure 3 shows that 30% of students use short term trainings regarding PMKVY, whereas 70% do not use.20% of students use special projects regarding PMKVY, whereas 80% do not use.35% of students use placement guidelines regarding PMKVY, whereas 65% do not use.30% of students use monitoring guidelines regarding PMKVY, whereas 70% do not use. It shows that even if the students are aware they are not using it. So steps should be taken to motivate more students to use it. Because only knowing the things will not solve the problem. It has to be properly implemented.

Awareness about Digital India

Figure 4 shows that 81% of students are aware about Digi Locker, whereas 19% are not aware.86% of students are aware about My Gov.in, whereas 14% are not aware. 81% of students are aware about Sign Framework, whereas 19% are not aware.91% of students are aware about Swach Bharat Mission Mobile App, whereas 9% are not aware.98% of students are aware about National Scholarship Portal, whereas 2% are not aware.61% of students are aware about EHospital, whereas 39% are not aware. 97% of students are aware about Digitize India Platform, whereas 3% are not aware. 81% of students are aware about Bharat Net, whereas 19% are not aware.89% of students are aware about Centre of Excellence on Internet of Things (IoT), whereas 11% are not aware.92% of students are aware about Digi Locker, whereas 8% are not aware. The analysis shows that most of the students are aware about digital India. It is a very good sign for the development of our students which will lead our country to developed country from developing country.

Use of Digital India Scheme

Figure 5 shows that 11% of students use Digi Locker, whereas 89% do not use.39% of students use MyGov.in, whereas 61% do not use.31% of students use eSign Framework, whereas 69% do not use.41% of students use Swach Bharat Mission Mobile App, whereas 59% do not use.57% of students use National Scholarship Portal, whereas 43%

do not use.9% of students use eHospital, whereas 91% do not use.17% of students use Digitize India Platform, whereas 83% do not use.21% of students use Bharat Net, whereas 79% do not use.27% of students use Centre of Excellence on Internet of Things (IoT), whereas 73% do not use.21% of students use Digi Locker, whereas 79% do not use. The analysis shows that even if most of the students know about the digital India, they are not using it. So it requires proper motivation and training to use it. The teachers can motivate the students for digital India.

Awareness of Entrepreneurship and Skill Development

Figure 6 shows that 91% of students are aware of Entrepreneurship Hub, whereas 9% are not aware. 96% of students are aware of Atal Innovation Mission (AIM), whereas 4% are not aware.81% of students are aware of Self Employment Talent Utilisation (SETU), whereas 19% are not aware.86% of students are aware of Entrepreneurship Hubs, whereas 14% are not aware. The analysis shows that most of the students are aware about the entrepreneurship and skill development. It is a positive sign that many of the students are aware.

Application of Entrepreneurship and Skill Development

Figure 7 shows that 41% of students use Entrepreneurship Hub, whereas 59% do not use.46% of students use Atal Innovation Mission (AIM), whereas 54% do not use. 31% of students use Self Employment Talent Utilisation (SETU), whereas 69% do not use.32% of students use Entrepreneurship Hubs, whereas 68% do not use. This analysis shows even most of the students know they are not using. So it requires to motivate and give them training to use.

Awareness of Pradhan Mantri Yuva Yojana (PMYY)

Figure 8 shows that 85% of students are aware about massive open On-line Courses (MOOCs), whereas 15% are not aware.96% of students are aware about Learning Management System (LMS), whereas 4% are not aware. The analysis shows that most of the students are aware about the open on line courses. This is very much required and also useful at this time of Covid-19. As the physical classroom teaching is not possible, most of the colleges are using online teaching.

Application of Pradhan Mantri Yuva Yojana (PMYY)

Figure 9 shows that 41% of students use Massive open On-line Courses (MOOCs), whereas 59% do not use.46% of students use Learning Management System (LMS), whereas 54% do not use. It shows nearly half of the students are using on line courses. No doubt the use of online teaching and on line courses have been increased due to Covid-19.

Awareness of Start-up India

Figure 10 shows that 81% of students are aware about Simple Compliance Regime for startups based on Self-certification, whereas 19% are not aware.82% of students are aware about Legal support and fast-tracking patent examination at reduced costs, whereas 18% are not aware.86% of students are aware about credit guarantee fund for start-ups, whereas 14% are not aware.91% of students are aware about innovation focused programs, whereas 9% are not aware.92% of students are aware about Startup Fests to showcase innovations and providing collaboration platforms, whereas 8% are not aware. It shows that most of the students are aware about start up India. It is a very good sign for the development of our students and so also for our country.

Incorporation of contemporary issues / recent trends into learning by the students

62% of students can handle diversity at workplace, whereas 38% cannot handle. 72% of students can handle multigenerational challenges at workplace, whereas 28% cannot handle.66% of students are aware about the recent government schemes, whereas 34% are not aware.76% of students know Finance/Marketing/HR strategies are formed and developed in reaction to factors related to internal and external environmental factors, whereas 24% don't know.67% of students know how to formulate strategies in the era of globalization, digitization and modernization, whereas 33% don't know.67% of students can minimize risk in the dynamic changing business

environment, whereas 33% can't.75% of students can do sustainable management in terms of HR/Marketing/Finance, whereas 25% can't do.63% of students know how to incorporate technology in the industries, whereas 37% don't know.93% of students feel that they are employable, whereas 7% don't. The analysis explains that most of the students are aware about the contemporary issues. It is a positive and encouraging sign for the students.

CONCLUSION

In the words of Mark Sanborn, "Your success in life isn't based on your ability to simply change. It is based on your ability to change faster than your competition, customers, and business." For the growth and development of nation, there must be rapid industrialization imperative for generating employment opportunities and in order to get the good placements, a teacher must create talented human resources for the organizations in order to get the optimum use of all other physical, financial and material resources. Due to crisis, mergers, acquisitions, reaction to internal and external pressure, technology up gradation, modernization and various other factors, it is imperative for the organizations to change its Vision, Mission, Strategies, Technology, People, organization structure, culture and work processes. If the academicians will train the students about how to handle change, then in the organizations, these people can proactively anticipate and handle the change rather than being reactive and indifferent towards the change.There is a great need for more innovation in the education system in order to create youth empowerment. Academicians are change agents in order to make the students fit to the organization. Updating the knowledge with the changes in technology is hard as compared to other changes in the organization. So, the educational system must be properly linked with the recent/contemporary changes especially with the technology.

Limitation and Future Research

The sampling technique used in this research study is convenient sampling is devising certain limitations like it does not signify normalize distribution as compare to other sampling techniques like random sampling and stratified sampling.
The data was collected only from the students of Odisha so the consequence cannot be widespread for other states.
Sample size is too small which does not signify the comprehensive population of students.

REFERENCES

1. Burnes, B. (2004) Managing Change: A Strategic Approach to Organisational Dynamics, 4th edition (Harlow: Prentice Hall).
2. Zorn, T., Page, D. & Cheney, G. (2000). Nuts about change: Multiple perspectives on change oriented communication in a public sector organization. Management Communication Quarterly, 13(4), 515-566.
3. Clarke, M. (1999). Creating change from below: Early lessons for agents of change. The Leadership & Organization Development Journal, 20(2), 70-80.
4. Seijts, G.H. & O'Farrell, G. (2003). Engage the heart: Appealing to the emotions facilitates change. Ivey Business Journal, January/February 2003, 1-5.
5. Radovic M. (2008). Effective Organizational Change Management. Serbian Journal of Management, 3(1), 119 – 125.
6. Swarnalatha C. And Prasanna T.S. (2013). Employee Engagement and Change Management. 2(6). 01-06.
7. Mullins L.J (1999), Management and Organizational Behaviour. (5th Ed.): In Marrow, A.J (1969), The Practical Theorist: The Life and Work of Kurt Lewin Teachers College Press.1977 Ed. New York.
8. Beaudoin MF. Distance education leadership: An essential role for the new century [Electronic version]. Journal of Leadership Studies 2002; 8(3): 131-145.
9. Robbins, S.P. (2004). OrganisationalBehaviour. Pearson: Frenchs Forest, NSW.
10. Banker, Darshna. (2012). Organizational Change: Pragmatic Approaches to Organizational Change Management. Amity Global Business Review, February,63-69.

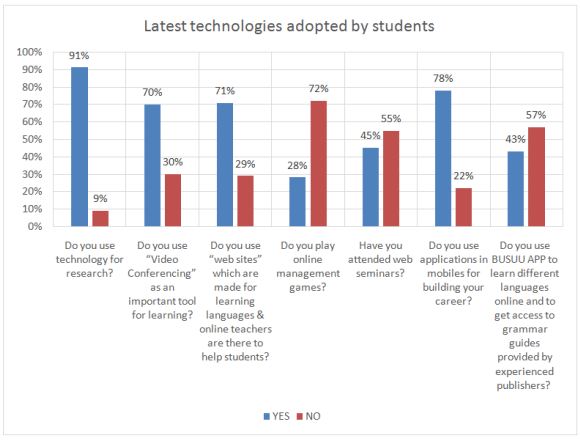

Figure 1: Proportion of latest technologies adopted by students

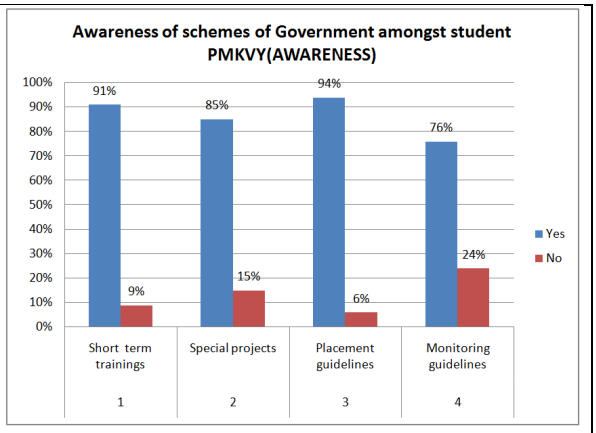

Figure 2: Proportion of to check the awareness of schemes of Government amongst student PMKVY (AWARENESS)

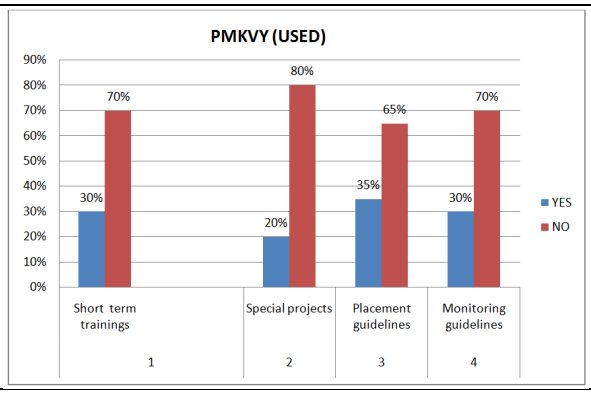

Figure 3: Proportion of PMKVY (Used)

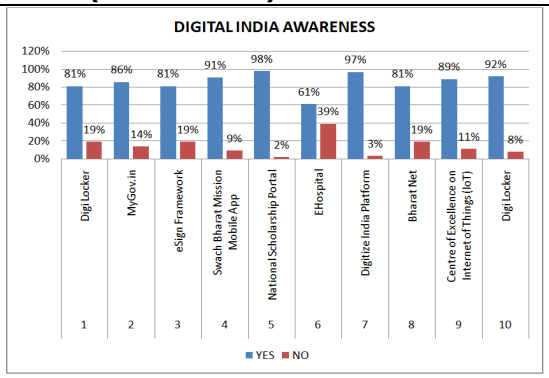

Figure 4: Proportion of digital India awareness

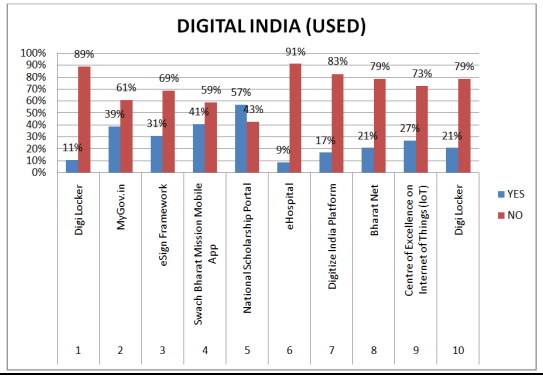

Figure 5:Proportion of Digital India used

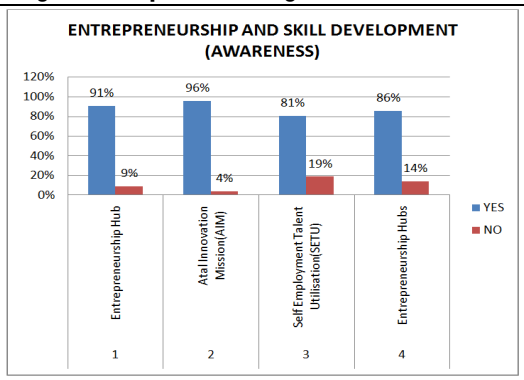

Figure 6: Proportion of Entrepreneurship and skill development awareness

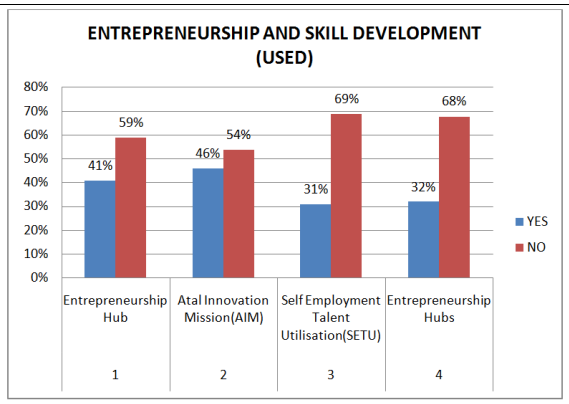

Figure 7: Proportion of Entrepreneurship and Skill Development (Used)

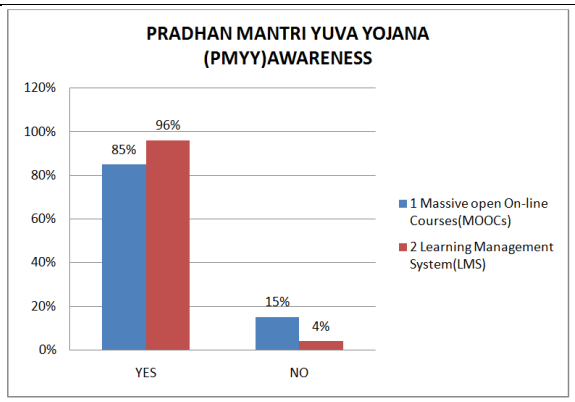

Figure 8: Proportion of Pradhan Mantri Yuva Yojana (PMYY) Awareness

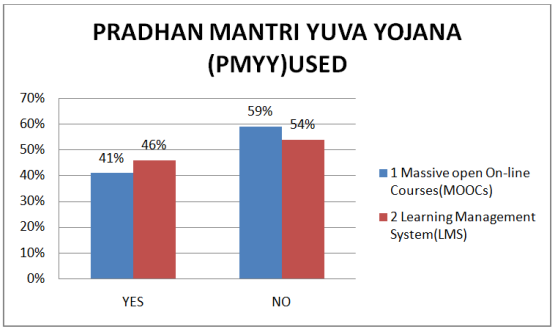

Figure 9: Proportion of Pradhan Mantri Yuva Yojana (PMYY) Used

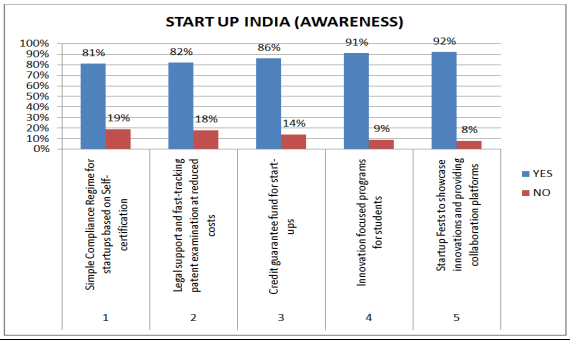

Figure 10: Proportion of Start Up India (Awareness)

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RESEARCH ARTICLE

Generic Decision Problem Concerning Aircraft Landings

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ABSTRACT

In this paper, we define a generic decision problem - the displacement problem. The displacement problem arises when we have to make a sequence of decisions and each new decision that must be made has an explicit link back to the previous decision that was made. This link is quantified by means of the displacement function. One situation where the displacement problem arises is that of dynamically scheduling aircraft landings at an airport. Here decisions about the landing times for aircraft (and the runways they land on) must be taken in a dynamic fashion as time passes and the operational environment changes. We illustrate the application of the displacement problem to the dynamic aircraft landing problem. Computational results are presented for a number of available test problems.

Keywords: operations research, generic decision problem- displacement problem, aircraft landing problem , statistics.

Displacement Problem

In many decision problems we assume a static operational environment. However, often in applications the operational environment changes, typically as time passes new information makes it necessary to revise the previous decisions that have been made. Such situations are dynamic in the sense that planned decisions continually have to be revisited as the operational environment changes. However it is clear that, from an operational viewpoint, it may often be undesirable to perturb (change, displace) the previous decision 'too much' in making a new decision. Typically therefore in making a new decision we have to consider explicitly the previous decision that was made as we have some degree of commitment to it and are reluctant to change it too much. Hence we have a generic decision problem, the displacement problem, which arises when we have to make a sequence of decisions and each successive decision that is made involves an explicit link back to the previous decision. Let the original (static) problem (SP) consist of N decision variables xi, i = 1, ..., N (where we use x to denote the vector of decision variables). Then a general mathematical description of SP is given by minimise $Z(x)$ subject to $C(x)$, where $Z(x)$ is the objective function and $C(x)$ represents the constraints of the problem. Z and C can be linear or nonlinear functions, and x can be a mix

of both integer and continuous variables. Suppose that we solve SP and let Xi, i = 1, ..., N be a feasible solution (as found by some algorithm) to SP. We use X to denote this vector. Note here that X need not be the optimal solution to SP, for example, X may be obtained via a heuristic solution algorithm. Consider now that something in the original problem changes, for example: a piece of data (a number, involved in Z or C) changes; a new variable (decision) appears; a new constraint is added. Such changes will occur because when we action the decisions X derived from solving SP we will find that something in the operational environment is different from what we had previously assumed in arriving at those decisions. As a result of this changing operational environment, we need to resolve the original problem, incorporating any changes, but with some additional restriction (link) back to the original (previous) solution X. In our approach, we define a displacement function $D(X, x)$ that quantifies the effect of displacing each decision variable i from its previous (known) solution value Xi to its new (currently unknown) value xi. The exact mathematical form of the displacement function $D(X, x)$ is our choice, and it can be a linear or nonlinear function. It is convenient, however, both for conceptual and for modelling reasons, to impose three restrictions upon the displacement function $D(X, x)$:

1. $D(X, x) \geq 0 \; \forall X, x$, so that displacement is non-negative.
2. $D(X, x)$=0 if $xi = Xi$, i = 1, ..., N, so that displacement takes the value zero if the new decisions [xi] are the same as the old decisions [Xi].
3. $D(X, x)$ is a separable function into a summation of terms involving only Xi and xi, so that the contribution to total displacement of a change in decision variable i, from Xi to xi, can be identified separately from the effect of all other changes in decision variables.

Let:

$D(X,$ x) represent the contribution to total displacement of a change in decision variable from Xi to xi (eg. if $D(X,$ x) = $\sum_{i=1}^{N}(X_i - x_i)^2$ then $Di(X, x) = (Xi - xi)^2$).

p_i be the objective function weighting (≥ 0) per unit of displacement in variable i (i = 1, …, N).

Δ_i be the maximum displacement (≥ 0) that we are prepared to accept in variable i (i = 1, …, N).

Then the general form of the displacement problem is:

minimise

$$\lambda_{\text{cost}} Z^*(X) + \lambda_{\text{disp}} \sum_{i=1}^{N}(X, x)\lambda_{\max} D_{\max} \quad (1.1)$$

Subject to $C^*(x)$ (1.2)

$D_i(X, x) \leq \Delta_i, \quad i = 1, ..., N$ (1.3)

$D_{\max} = \max[D_i(X, x) \mid i = 1, ..., N]$ (1.4)

Here, Z^* and C^* represent the original objective and constraints (Z and C) but amended to reflect any changes that have occurred (eg the addition of new decision variables). In the objective function, Equation (1.1), λcost, λdisp and λmax (≥ 0) are the weights (respectively) attached to: total cost of solution $Z^*(x)$; total cost of displacement $\Sigma_i = 1^N$ $p_i D_i(X, x)$; and maximum displacement $D_{\max}$. Equation (1.3) limits the displacement for any variable, while Equation (1.4) defines the maximum displacement $D_{\max}$.

Aircraft Landing

In this section, we first briefly review the aircraft landing problem (henceforth ALP) and then go on to define an example of displacement function for the dynamic ALP.

Aircraft Landing Problem

The ALP is the problem of deciding a landing time on an appropriate runway for each aircraft in a given set of aircraft such that each aircraft lands within a predetermined time window; and separation criteria between the

landing of an aircraft, and the landing of all successive aircraft, are respected. In order to formulate the problem define:

P the number of aircraft
E_i the earliest landing time for aircraft i
L_i the latest landing time for aircraft i
T_i the target (preferred) landing time for aircraft i
g_i the penalty cost (≥ 0) per unit of time for landing before target T_i for aircraft i
h_i the penalty cost (≥ 0) per unit of time for landing after target T_i for aircraft i
S_{ij} the required separation time (≥ 0) between aircraft i landing and aircraft j landing (where aircraft i lands before aircraft j)
x_i the landing time (≥ 0) for aircraft i, a decision variable
δ_{ij} = 1 if aircraft i lands before aircraft j
= 0 otherwise

then the (single runway) static ALP has

$$Z(\underline{x}): \sum_{i=1}^{P} (g_i \max[0, T_i - x_i] + h_i \max[0, x_i - T_i]) \tag{1.5}$$

$$C(\underline{x}): \delta_{ij} + \delta_{ij} = 1, \quad i = 1,...,P; \quad j = 1,...,P; \quad j > i \tag{1.6}$$

$$x_j \geq x_i + S_{ij}\delta_{ij} - (L_i - E_j)\delta_{ij}, \quad i = 1,...,P; \quad j = 1,...,P; \; i \neq j \tag{1.7}$$

$$E_i \leq x_i \leq L_i; \quad i = 1,...,P \tag{1.8}$$

Equation (1.6) ensures that for each pair of aircraft one lands before the other, Equation (1.7) enforces separation between aircraft and Equation (1.8) ensures that each aircraft lands within its time window. The first/second maximisation terms in Equation (1.5) account for aircraft that land before/after target. This cost function is illustrated diagrammatically in Figure 1. Colloquially g_i and h_i are the slope of the cost function before and after the target time T_i respectively. Extending the above single runway formulation to the multiple runway case is easily done and, for reasons of space, will not be presented here. Note here that given a fixed landing sequence (equivalently values for the zero–one variables δ_{ij} above), an effective approach to deciding optimal landing times that minimise cost with respect to that given sequence is to solve the LP that results from Equations (1.5), (1.6), (1.7) and (1.8) when the zero–one variables are eliminated. For convenience, we refer to this LP as ALP^F indicating that it is the ALP with a fixed landing sequence. Beasley et al. [4] first formulated the static ALP as a mixed-integer zero–one linear program and solved it numerically for a number of test problems involving up to 50 aircraft and four runways. Beasley et.a. [5] studied the single runway static ALP and presented a population heuristic (genetic algorithm) for the problem. Other work relating to the static ALP is described in Beasley et.al. [4] and, for reasons of space, that description will not be repeated here. In this Paper, we deal with the dynamic, or on-line, ALP, where decisions about the landing times (and runways) for aircraft must be made as time passes and as the operational environment changes (aircraft land,

new aircraft appear, etc). Current air traffic control practice [16, 18, 19] for dealing with this problem is to schedule aircraft to land in a first-come, first-served (FCFS) manner.

Previous Work

There appears to have been relatively little work published with regard to the dynamic ALP. Andreussi et.al. [1] referred to the problem as the aircraft sequencing problem and presented a paper concerned with developing a discrete-event simulation model to evaluate different sequencing strategies. Computational results were presented for a number of simulated scenarios involving three runways. Dear and Sherif [14, 15] discussed both the static and dynamic ALP and presented a heuristic algorithm for the single runway dynamic ALP based upon constrained position shifting. This involves finding, for a small set of aircraft, the best possible positions for them in the landing queue subject to the constraint that no aircraft can be moved more than a pre-specified number of positions away from the position it had in the landing queue based on FCFS, see also Dear [13] Computational results were presented for three simulated scenarios involving 500 aircraft and one runway. Brinton [7] presented a tree search approach for the ALP. In his approach, the tree represents the sequence in which aircraft should be landed. The dynamic ALP is dealt with via freezing the position of an aircraft in the landing sequence and via costs associated with changes in the scheduled landing time. No detailed computational results were presented however. Venkata krishnan et al [22] observed separation times adopted on landing at Logan Airport Boston. Using these observed separation times they applied the work of Psaraftis, [20, 21] which they modified in a heuristic manner to take account of aircraft time windows, to see the improvement that could result from better sequencing. They presented two approaches to the dynamic ALP. In both approaches aircraft are frozen in the landing sequence once they are near to landing. The difference between their approaches is that one leaves the aircraft time window unchanged, while the other gradually reduces the size of the time window as an aircraft approaches landing. Computational results were presented for six data sets involving up to 92 aircraft and two runways.

Ciesielski and Scerri [11, 12] presented a genetic algorithm for the problem. In their approach, landing times are allocated by specifying a 30s time slot. Their approach consists of finding the best solution they can within 3 min of elapsed time, updating the situation with respect to aircraft that have landed/appeared and resolving a new problem. Unlike the work presented in his paper, they include no link between the previous set of landing time decisions and the new set. Computational results were presented for two data sets involving 28 and 29 aircraft and two runways. Milan [18] considered the problem of assigning priorities for landing to aircraft in arrival batches (a batch comprising aircraft due to arrive at approximately the same time). Priorities were based upon factors such as number of passengers, cost of passenger delays and proportion of transfer passengers. Once priorities had been assigned the aircraft in a batch were landed in priority order. Computational results were presented for one example with 30 aircraft and one runway. Carr et al [8, 9, 10] presented papers concerned with modifying the standard FCFS approach to allow individual airlines to express priorities with regard to the landing of their aircraft. Computational results were presented for a number of simulated scenarios involving three runways. Bolender and Slater [6] approached the dynamic ALP via queueing theory and discrete-event simulation. They assumed that aircraft appear according to a Poisson process so that aircraft inter arrival times follow a negative exponential distribution. Their analysis focuses on differing ways of allocating a newly appeared aircraft to a runway for landing (when multiple runways are present). Once allocated to a runway aircraft land in FCFS order. Computational results were presented for a number of problems involving up to three runways. Wong [23] discusses the algorithms underlying the CTAS (Center TRACON (terminal radar approach control) Automation System) system developed at the NASA Ames Research Center. For the dynamic ALP, an FCFS approach is used with aircraft being frozen once they are close to landing.

Displacement Function

In order to deal with the dynamic ALP as a displacement problem, we need to define an appropriate displacement function. Considering Figure 1 suppose that aircraft i has been assigned a landing time X_i from the solution to the original static ALP and further suppose that this time is later than its desired target time (i.e. $X_i > T_i$). When we come to solve the displacement problem the effect of the cost component ($g_i \max[0, T_i - x_i] + h_i \max[0, x_i - T_i]$) associated

with aircraft i in the displacement problem objective function will be to try and move the new landing time for aircraft i (x_i) closer to the desired target time T_i (i.e. to have $x_i < X_i$). This will be a desirable displacement from the current landing time X_i. It may be however that other factors (eg. newly appeared aircraft that must be scheduled for landing) will mean that aircraft i has its landing time further increased (i.e. $x_i > X_i$). This will not be a desirable displacement and so should incur an extra cost, such as shown by the dotted displacement function line in Figure 1. For the sake of illustration we shall assume, as Figure 1, that this extra cost is also hi for each unit of time the aircraft is displaced later than Xi, that is, that the displacement function is h_i max[0, x_i-X_i] if $X_i > T_i$. Similarly, if the assigned landing time X_i is less than the target time T_i, then when the displacement problem is solved, aircraft i will not wish to move further away from its desired target time T_i and any such movement should be penalized by an additional cost. Again for the sake of illustration we shall assume, as in Figure 1, that this extra cost is g_i for each unit of time the aircraft is displaced earlier than X_i, that is, that the displacement function is g_i max[0, X_i - x_i] if $X_i < T_i$. Hence our displacement function is:

$$D_i(X, x) = g_i \max[0, X_i - x_i] \text{ if } X_i < T_i$$
$$h_i \max[0, x_i - X_i] \text{ if } X_i > T_i$$
$$g_i \max[0, X_i - x_i] + h_i \max[0, x_i - X_i] \quad (1.9)$$

where for the case $X_i = T_i$ we ensure that deviations from target (in either direction) are further penalised. This displacement function satisfies the restrictions ($D(X, x)$ non-negative, zero if $xi = Xi$ and a separable function) mentioned previously.

Solving the Displacement Problem

In order to solve the displacement problem we adapted three solution approaches, one optimal [4] and two heuristic, [4, 5] given previously in the literature for the static ALP. We believe it to be a natural state of affairs that solution approaches (both heuristic and optimal) developed for the static ALP can with suitable amendment be applied directly to the dynamic ALP. One should reasonably expect that solution approaches developed for the original static decision problem have an important role to play in solving the displacement problem defined from the original static decision problem. The adaptations we made were as briefly outlined below. Beasley et al [4] presented an optimal solution algorithm based upon linear programming (LP)-based tree search for the static ALP. Although the displacement function (Equation (1.9)) defined above for the dynamic ALP is nonlinear, by utilising the definition of the displacement problem (Equations (1.1), (1.2), (1.3) and (1.4)) together with the definition of the static ALP (Equations (1.5), (1.6), (1.7) and (1.8)), it is possible to show that the dynamic ALP as formulated above can be transformed into a mixed-integer zero–one linear program. Hence, LP-based tree search can be directly applied in order to find the optimal solution to each successive displacement problem. We refer to this algorithm as DALP-OPT.

The heuristic solution algorithm presented in Beasley et al [4] for the static ALP used two steps: firstly a simple constructive step to decide the sequence in which aircraft are to land (and on which runway), based upon sorting aircraft into target time order; and secondly solving ALP to decide the landing times for each aircraft. With respect to adapting this heuristic for the solution of the displacement problem we found that, computationally, directly applying this heuristic to the displacement problem could lead to infeasibility, that is, we could end up with a displacement problem for which the heuristic could not find a feasible solution. We found that, for the particular test problems we considered, this issue of infeasibility did not arise if we also generated a landing sequence based upon first sorting aircraft using their landing time as decided at the solution to the previous displacement problem and then including any newly appeared aircraft in target time order. Again given a landing sequence we solved ALP^F to decide landing times. In the computational results presented below we applied both of these heuristics and took the best solution found. We refer to this algorithm as DALP-H1. In order to adapt the population heuristic (genetic algorithm) presented by Beasley et al [5] for the single runway static ALP to the multiple runway dynamic ALP, we:

- extended the representation, together with the crossover and mutation operators, to include runway choice;
- incorporated maximum displacement by time window modification;
- seeded the initial population with suitable individuals based upon the landing sequences given by sorting aircraft into earliest/target/latest time order;
- applied the population heuristic after first using DALP-H1 and seeding the initial population with the best solution found by DALP-H1
- took the best solution as found by the population heuristic and solved ALPF to decide landing times.

We refer to this algorithm as DALP-H2.

Computational Results

The algorithms DALP-H1, DALP-H2 and DALP-OPT for the dynamic ALP outlined in this chapter were programmed in FORTRAN and run on a Silicon Graphics Indigo workstation (R4000, 100 MHz, 64 MB main memory) for a number of test problems involving up to 500 aircraft and five runways. This machine is approximately 25 times slower than a 2.5 GHz Pentium pc. In order to solve the mixed-integer zero–one formulation of the displacement problem to optimality using LP-based tree search, and also to solve ALP^F, we used the CPLEX (version 6.5) software package.

Methodology

The methodology we adopted was as follows:

1. Each aircraft i (i = 1, ..., P) had an appearance time A_i, the time at which it was first available to be assigned a landing time. We also defined a freeze time t^* such that any aircraft assigned a landing time within t^* of the current time had its landing time (and runway) frozen. Set the landing times $X_i = \infty$, i = 1, ..., P. Let:

$F_0(i)$ represent the set of aircraft that have not yet appeared by time t, that is, $F_0(i) = [i \mid A_i > t, i = 1, \ldots, P]$
$F_1(t)$ represent the set of aircraft that have appeared by time t, but have not yet landed (or had their landing times frozen), that is, $F_1(t) = [i \mid A_i \le t$ and $X_i > t + t^\circ, i = 1, \ldots, P]$
$F_2(t)$ represent the set of aircraft that have appeared by time t and have landed (or have had their landing times frozen), that is, $F_2(t) = [i \mid A_i \le t$ and $X_i > t + t^\circ, i = 1, \ldots, P]$
γ be the iteration counter
Z_{disp} be the accumulated displacement cost

2. Set $\gamma = 0$ and $Z_{disp} = 0$. Set the current time $t_0 = \min [A_i | I = 1, ..., P]$ and solve the original static ALP involving just those aircraft in $F_1(t_0)$. The solution to this static ALP gives the initial landing times X_i $\forall i \in F_1(t_0)$.
3. If aircraft are still to appear ($|F_0(t\gamma)| \ge 1$) then go to step (4), otherwise ($|F_0(t\gamma)| = 0$) all aircraft have appeared in which case go to step (5).
4. Set $\gamma = \gamma + 1$. Advance the time to $t\gamma = \min[A_i | i \in F_0(t_{\gamma - 1})]$ and solve the displacement problem involving just those aircraft in $F_1(t_\gamma) \bigcup F_2(t_\gamma)$, where the aircraft in $F_2(t_\gamma)$ are constrained to land at the landing times X_i ($\forall i \in F_2(t_\gamma)$), and on the appropriate runways, as were obtained from the previous displacement solution. Add the displacement cost component $\lambda_{disp} \sum_{i \in F_1 \cap F_1(t_\gamma) \cap F_1(t_\gamma - 1)} p_i D_i(X, x) + \lambda_{disp} D_{disp})$ of this solution to Z_{disp} and go to step (3).
5. All aircraft in $F_1(t_\gamma)$ are now deemed to land at the landing times (and on the appropriate runways) as were obtained from the last displacement solution. Compute $Z_{sol} = \sum_{i=1}^{P} (g_i \max[0, T_i - X_i] + h_i \max[0, X_i - T_i])$ which is the cost of the final solution in terms of the cost function associated with the original (static) ALP.

RESULTS

We considered two sets of test problems. The first set, involving up to 50 aircraft, were those previously considered in Beasley et al [4] for which optimal static solutions are known. The second set we considered were larger, involving between 100 and 500 aircraft, and were generated in the following manner:

- aircraft appeared according to a negative exponential distribution with a mean inter arrival distance of 6.5 nautical miles, converted into an earliest time by assuming a speed of 210 knots (nautical miles per hour)
- the appearance time for each aircraft was 10 min before its earliest time; the target time was randomly generated between 1 and 10 min after the earliest time; the latest time was 30 min after the earliest time
- costs for appearing before/after target were real numbers randomly generated from the interval [1, 2] and a freeze time of 12 min was adopted
- aircraft were classified by four types: heavy, upper-medium, lower-medium and small, with the type being randomly generated with probabilities of 0.4, 0.3, 0.2 and 0.1 respectively. Separation distances/times on landing were calculated as in [5].

For the largest problem solved this corresponds to scheduling the landing of 500 aircraft over a 15-h time period. All of the test problems solved in this chapter are publicly available from OR-Library, [2, 3]. Table 1 gives the results for the smaller problems with $\lambda_{cost} = \lambda_{disp} = 1$, $\lambda_{max} = 0$ and $p_i = 1$, $\Delta_i = \infty \forall i$. In that table we, in order to provide some insight into the quality of our results, have given the solution value associated with the optimal static approach (from Beasley et al1). This value provides a benchmark since (in terms of the original cost, Equation (1.5)) the best possible sequence of decisions (landing times and runways) we can make, over a succession of displacement problem solutions, correspond to the decisions (landing times and runways) arrived at by solving, just once, the static ALP involving all aircraft. We also show in Table 1 the solution value found by taking the best solution from two FCFS approaches: schedule each aircraft as early as possible; and schedule each aircraft at its target time (if that is feasible) but as early as possible if the target time is not feasible. Summarizing then we have that Table 1 shows, for each problem: the number of aircraft; the number of runways; the optimal static solution value (Z_{static}); the FCFS solution value (Z_{FCFS}); the solution values (Z_{sol}, Z_{disp}) and the total time taken when each successive displacement problem is solved heuristically/optimally. Table 2 shows similar information as Table 1 for the larger problems. Table 3 also shows results for these problems but where, compared to Table 2, we have increased λ_{disp} to 2, λ_{max} to 5, and have set $\Delta_i = 10 \ \forall i$. This corresponds to a scenario in which we are trying to further discourage displacement and also explicitly limit displacement. We only show in Table 3 those test problems that exhibited some displacement in Table 2. Examining Tables 1, 2 and 3 we would make the following observations:

- Excluding from Table 1 those problems for which $Z_{static} = 0$, the average percentage cost increase over and above the static solution is 591.1% for FCFS ($100(Z_{FCFS} - Z_{static}) / Z_{static}$) 55.1% for DALP-H1 ($100(Z_{sol} + Z_{disp} - Z_{static})/Z_{static}$), 50.9% for DALP-H2, but only 36.4% for DALP-OPT.
- Of the 39 larger problems shown in Tables 2 and 3, we have that the best solution value ($Z_{sol} + Z_{disp}$) is given by DALP-OPT 37 times. This compares with 15 times for DALP-H2 and eight times for DALP-H1 and indicates the value of resolving each successive displacement problem optimally rather than heuristically. Note here that normally one expects an optimal algorithm (by its very nature) to always produce a solution superior (or equal) to that produced by a heuristic algorithm. Here however for two of these 39 problems (problem 12 with three runways in Tables 2 and 3), our heuristic DALP-H2 produces a better solution than DALP-OPT. The reason for this is a generic one in that we are solving a succession of displacement problems as time passes (aircraft land, new aircraft appear) and the values shown in Tables 2 and 3 are summary statistics of the overall effect of these solutions in cost terms. It can happen, as here, that solving a displacement problem heuristically leads to decisions that are better (in terms of aircraft yet to appear - which are unknown) than the decisions made by solving the same displacement problem optimally. As such, the overall solution produced by successive

applications of a heuristic algorithm can be superior to the overall solution produced by successive applications of an optimal algorithm.

- It is clear that the benefit gained by DALP-H2, compared to DALP-H1, is more marked for larger problems. DALP-H2 improves upon the DALP-H1 solution ($Z_{sol} + Z_{disp}$) for only three of the 25 problems in Table 1, but for 31 of the 39 problems in Tables 2 and 3.

In order to investigate problems where DALP-OPT becomes computationally ineffective we show in Table 4 the results for the same problems as in Table 2 but with the freeze time reduced to zero. Reducing the freeze time increases the number of aircraft that are available to have their landing times rescheduled and hence increases the size of the displacement problem that has to be solved optimally by DALP-OPT. It is clear from Table 4 that while for some problems DALP-OPT is still computationally effective, there are a number of problems (in particular those that terminated without a solution due to time limit considerations) for which DALP-OPT is computationally ineffective. Note here, however, that both DALP-H1 and DALP-H2 are computationally effective for all of the problems shown in Table 4.

REFERENCES

1. Beasley, J.E.; Krishnamoorthy, M.; Sharaiha, Y.M. and Abramson, D. (2000) : Scheduling aircraft landings - the static case. Transport Sci 34: 180–197.
2. Beasley, J.E.; Sonander, J. and Havelock, P. (2001) : Scheduling aircraft landings at London Heathrow using a population heuristic. J Opl Res Soc 52: 483–493.
3. Odoni, A.R.; Rousseau, J.M. and Wilson, N.H.M. (1994) : Models in urban and air transportation. In: Pollock, S.M., Rothkopf, M.H. and Barnett, A. (eds) Operations Research and the Public Sector: Handbooks in Operations Research and Management Science, Vol 6. North-Holland: Amsterdam, The Netherlands, pp 107–150.
4. Erzberger, H. (1995) : Design principles and algorithms for automated air traffic management: In: Knowledge-based Functions in Aerospace Systems. AGARD Lecture Series no. 200. NATO Neuilly-Sur-Seine, France, 7:1–7:31.
5. Milan, J. (1997) : The flow management problem in air traffic control: a model of assigning priorities for landings at a congested airport. Transport Plann Technol 20: 131–162.
6. Andreussi, A.; Bianco, L. and Ricciardelli, S. (1981) : A simulation model for aircraft sequencing in the near terminal area. Eur. J. Opl. Res. 8: 345–354.
7. Dear, R.G. and Sherif, Y.S. (1989) : The dynamic scheduling of aircraft in high density terminal areas. Microelectron Reliab 29: 743–749.
8. Dear, R.G. and Sherif, Y.S. (1991) : An algorithm for computer assisted sequencing and scheduling of terminal area operations. Transport Res A 25A: 129–139.
9. Dear, R.G. (1976) : The dynamic scheduling of aircraft in the near terminal area, Report R76-9 Flight Transportation Laboratory, MIT, Cambridge, MA, USA.
10. Brinton, C.R. (1992) : An implicit enumeration algorithm for arrival aircraft scheduling. In: Proceedings of the 11th IEEE/AIAA Digital Avionics Systems Conference Seattle, WA. IEEE, NY, USA, pp 268–274.
11. Venkatakrishnan, C.S.; Barnett, A. and Odoni, A.R. (1993) : Landings at Logan Airport: describing and increasing airport capacity. Transport Sci 27: 211–227.
12. Psaraftis, H.N. (1978) : A dynamic programming approach to the aircraft sequencing problem, Report R78-4 Flight Transportation Laboratory, MIT, Cambridge MA, USA.
13. Psaraftis, H.N. (1980) : A dynamic programming approach for sequencing groups of identical jobs. Opns. Res. 28: 1347–1359.
14. Ciesielski, V. and Scerri, P. (1997) : An anytime algorithm for scheduling of aircraft landing times using genetic algorithms. Aust. J. Intell. Inf. Process Systems 4: 206–213.

15. Ciesielski, V. and Scerri, P. (1998) : Real time genetic scheduling of aircraft landing times. In: Fogel, D. (ed) Proceedings of the 1998 IEEE International Conference on Evolutionary Computation (ICEC98). IEEE, NY, USA, pp 360–364.
16. Carr, G.C.; Erzberger, H. and Neuman, F. (1998) : Airline arrival prioritization in sequencing and scheduling. Paper presented at the second USA/Europe Air Traffic Management R&D Seminar, Orlando. Available from. http://www.ctas.arc.nasa.gov/publications.
17. Carr, G.C.; Erzberger, H. and Neuman, F. (1999) : Delay exchanges in arrival sequencing and scheduling. J. Aircraft 36: 785–791.
18. Carr, G.C.; Erzberger, H. and Neuman, F. (2000) : Fast-time study of airline-influenced arrival sequencing and scheduling. J. Guidance Control Dyn. 23: 526–531.
19. Bolender, M.A. and Slater, G.L. (2000) : Evaluation of scheduling methods for multiple runways. J. Aircraft 37: 410–416.
20. Wong, G.L. (2000) : The dynamic planner: the sequencer, scheduler, and runway allocator for air traffic control automation, Report NASA/TM-2000-209586, NASA Ames Research Center, Moffett Field, CA, USA, Available from. http://www.ctas.arc.nasa.gov/publications.
21. ILOG Inc. (1999) : ILOG CPLEX 6.5 User's Manual. ILOG Inc.: Mountain View, CA, USA.
22. Beasley, J.E. (1990) : OR-Library: distributing test problems by electronic mail. J. Opl. Res. Soc. 41: 1069–1072.
23. Beasley, J.E. (1996) : Obtaining test problems via Internet. J. Global Optim. 8: 429–433.

Table 1: Computational Results: Small Problems

Problem number	Number of aircraft	Number of runways	Optimal static solution Z_{static}	FCFS solution Z_{FCFS}	Heuristic solution to each successive displacement problem						Optimal solution to each successive displacement problem DALP-OPT		
					DALP-H1			DALP-H2					
					Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)
1	10	1	700	1790	740	260	0.1	Same		0.1	740	260	0.1
		2	90	120	120	0	0.1	Same		0.1	90	30	0.1
		3	0	0	0	0	0.1	Same		0.1	0	0	0.1
2	15	1	1480	2610	1870	110	0.1	Same		0.2	1730	250	0.5
		2	210	210	210	0	0.2	Same		0.2	210	0	0.3
		3	0	0	0	0	0.1	Same		0.1	0	0	0.1
3	20	1	820	2930	1440	290	0.2	Same		0.4	940	230	0.5
		2	60	60	60	0	0.2	Same		0.3	60	0	0.3
		3	0	0	0	0	0.1	Same		0.1	0	0	0.1
4	20	1	2520	6290	2670	960	0.2	Same		0.3	2700	420	0.9
		2	640	1560	680	170	0.2	Same		0.3	680	80	2
		3	130	330	130	10	0.2	Same		0.3	130	10	0.6
		4	0	60	0	0	0.1	Same		0.1	0	0	0.1
5	20	1	3100	8370	6130	490	0.3	6130	250	0.4	3810	630	1.3
		2	650	1440	1070	60	0.2	1050	120	0.3	680	170	4
		3	170	240	240	0	0.2	Same		0.3	240	0	0.9
		4	0	0	0	0	0.1	Same		0.1	0	0	0.1
6	30	1	24442	24442	24442	0	0.4	Same		0.6	24442	0	0.6
		2	554	882	882	0	0.4	Same		0.4	809	98	0.5
		3	0	0	0	0	0.2	Same		0.2	0	0	0.2
7	44	1	1550	1550	3974	0	1	Same		1.4	3974	0	1.5
		2	0	0	0	0	0.6	Same		0.6	0	0	0.6
8	50	1	1950	26835	2915	735	1.3	2710	430	2	2000	455	3.1
		2	135	10140	255	15	1.1	135	75	1.2	135	75	1.2
		3	0	4825	0	0	0.7	Same		0.7	0	0	0.7

Note: 'Same' means that the solution values for both Z_{sol} and Z_{disp} for DALP-H2 were identical to those for DALP-H1.

Table 2 : Computational Results: Large Problems

Problem number	Number of aircraft	Number of runways	FCFS solution Z_{FCFS}	Heuristic solution to each successive displacement problem						Optimal solution to each successive displacement problem DALP-OPT		
				DALP-H1			DALP-H2					
				Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)
9	100	1	36839.36	13554.77	1213.12	3.7	12553.87	1041.4	4.7	7848.42	1171.12	5.7
		2	10661.92	578.71	57.94	3	577.57	33.12	2.8	573.25	33.12	3.4
		3	4142.07	88.72	33.28	2.6	Same		2.6	88.72	33.28	2.6
		4	1518.04	0	0	2.3	Same		2.3	0	0	2.3
10	150	1	54113.54	31945.03	1602.79	7.6	31034.04	1220.52	9.7	17726.06	2164.97	13.5
		2	13 318.09	1903	428.36	6.9	1417.82	307.82	6.8	1372.21	53.7	8.7
		3	5290.35	219.44	34.68	5.7	216.25	34.68	5.4	246.15	1.14	6
		4	3203.35	47.2	0	5.6	34.22	0	5.1	34.22	0	5.1
		5	770.9	0	0	4.9	Same		4.9	0	0	4.9
11	200	1	66427.28	27417.23	2714.15	16.6	23963.48	2150.87	18.5	19327.45	1954.41	22.6
		2	17381.29	1671.13	455.31	12.3	1692.97	245.84	12.1	1683.75	91.32	15.9
		3	5901.27	347.37	0	10.2	333.53	0	9.4	333.53	0	13.2
		4	2040.41	69.66	0	8.9	Same		8.9	69.66	0	9.3
		5	516.84	0	0	8.6	Same		8.6	0	0	9.1
12	250	1	81916.40	34246.39	2599.64	22.3	31439.77	1792.73	28.2	25049.24	1941.88	43.2
		2	22 790.99	2848.87	718.05	18.6	2497.06	545.68	19.3	2204.96	155.31	43.2
		3	8883.11	265.24	44.1	15.8	252.52	44.1	15.7	430.5	37.74	17.1
		4	3261.29	2.86	0	14.1	Same		14.1	2.86	0	14.1
		5	1053.63	0	0	13.5	Same		13.5	0	0	13.5
13	500	1	178725.16	80551.35	6001.64	90.7	78008.48	4320.72	113.3	58392.69	5107.4	249.5
		2	52714.51	24275.34	1359.87	67.1	6006.65	588.42	84.6	4897.92	312.28	105.5
		3	19871.45	1098.25	195.75	65.8	921.76	138.87	72.2	821.82	30.62	84.5
		4	8132.8	152.5	49.01	74.2	134.37	0	58.4	123.3	4.62	57.5
		5	2942.23	0	0	56.8	Same		56.8	0	0	56.8

Note: 'Same' means that the solution values for both Z_{sol} and Z_{disp} for DALP-H2 were identical to those for DALP-H1

Table 3 : Computational Results: Large Problems with Displacement Limit

Problem number	Number of aircraft	Number of runways	Heuristic solution to each successive displacement problem						Optimal solution to each successive displacement problem DALP-OPT		
			DALP-H1			DALP-H2					
			Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)
9	100	1	25 807.86	128.88	3.6	19 606.45	0	5.2	9971.66	325.86	5.7
		2	940.6	63.34	3.2	599.6	40.98	3.1	599.6	40.98	3.6
		3	160.32	0	2.4	126.88	0	2.6	126.88	0	2.7
10	150	1	39746.07	0	8.1	38939.21	0	10	33777.61	0	12.6
		2	6661.18	26.82	7.4	1708.01	34.76	7.1	1471.39	34.76	8.5
		3	329.05	7.28	6.4	325.86	7.28	5.8	246.15	7.28	6.2
11	200	1	42516.85	0	14.3	35976.61	0	17.5	31450.44	52.3	22.1
		2	3766.69	38.76	17	2421.64	93.6	13.1	1910.73	52.1	15.3
12	250	1	48514.77	0	24.6	42652.68	19.38	28.7	32744.58	76.92	37.1
		2	4186.92	64.86	20.5	3536.68	0	20.6	2391.19	34.94	24.1
		3	711.79	0	24	339.77	0	16.9	579.91	0	19.7
13	500	1	135592.03	145.42	91.4	107899.41	145.82	118.6	80714.10	257.7	160.8
		2	28 616.54	39.82	85.8	8064.53	41.18	90.1	6167.2	63.04	105.1
		3	1587.48	183.5	72.6	1001.94	156.24	78.4	894.75	81.88	79
		4	230.74	0	70.7	128.58	0	63	128.58	0	63

Table 4 : Computational Results: Large Problems, Zero Freeze Time

Problem number	Number of aircraft	Number of runways	Heuristic solution to each successive displacement problem						Optimal solution to each successive displacement problem DALP-OPT		
			DALP-H1			DALP-H2					
			Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)	Z_{sol}	Z_{disp}	Total time (min)
9	100	1	8185.25	3762.06	4.1	7800.93	2947.55	5.5	6219.54	1371.35	77.1
		2	510.4	205.44	3.8	480	117.12	4.6	480.58	83.4	9.7
		3	88.72	33.28	3.2	Same		3.2	88.72	33.28	4
		4	0	0	2.3	Same		2.3	0	0	2.4
10	150	1	23569.43	4105.49	9	23137.89	2885.86	12			(781.2:59)
		2	1361.51	418.55	7.7	1385.02	373.05	8.9	1317.69	81	119.3
		3	218.29	65.97	6.1	216.25	34.68	6.6	246.15	1.14	24.7
		4	47.2	0	5.1	34.22	0	5.1	34.22	0	6
		5	0	0	4.9	Same		4.9	0	0	5
11	200	1	16474.79	5064.4	16.9	16865.47	4843.9	21.5	14152.40	2204.73	134.3
		2	1655.53	493.03	14.4	1654.3	484.1	17.1	1587.39	109.06	177.5
		3	347.37	0	10.5	333.53	0	11	333.53	0	485.6
		4	69.66	0	9.3	Same		9.5	69.66	0	31.4
		5	0	0	8.8	Same	8.8	0	0	8.9	
12	250	1	25547.94	4842.58	27.2	25750.13	3922.92	39.9			(631.5:38)
		2	1934.68	778.28	21.8	1921.38	790.78	26			(833.4:37)
		3	265.24	44.1	15.2	Same		15.6	252.52	44.1	632.2
		4	2.86	0	14	Same		14	2.86	0	15.6
		5	0	0	13.7	Same		13.7	0	0	13.9
13	500	1	55360.02	15668.19	102.9	54268.76	13940.70	133			(923.6:279)
		2	29683.09	2647.33	75.6	5440.55	855.13	101.3	4505.96	442.69	1290.9
		3	938.38	202.74	68	904.84	202.74	72.9	821.82	30.62	531.6
		4	152.5	49.01	57.2	120.65	17.16	57.6	122.49	3.81	228.7
		5	0	0	67.6	Same		67.6	0	0	67.6

Note: 'Same' means that the solution values for both Z_{sol} and Z_{disp} for DALP-H2 were identical to those for DALP-H1.

For DALP-OPT, a time limit of 10 h for the solution of any displacement problem was imposed, figures in brackets indicate the total time taken: the number of aircraft that had landed, when this time limit was reached.

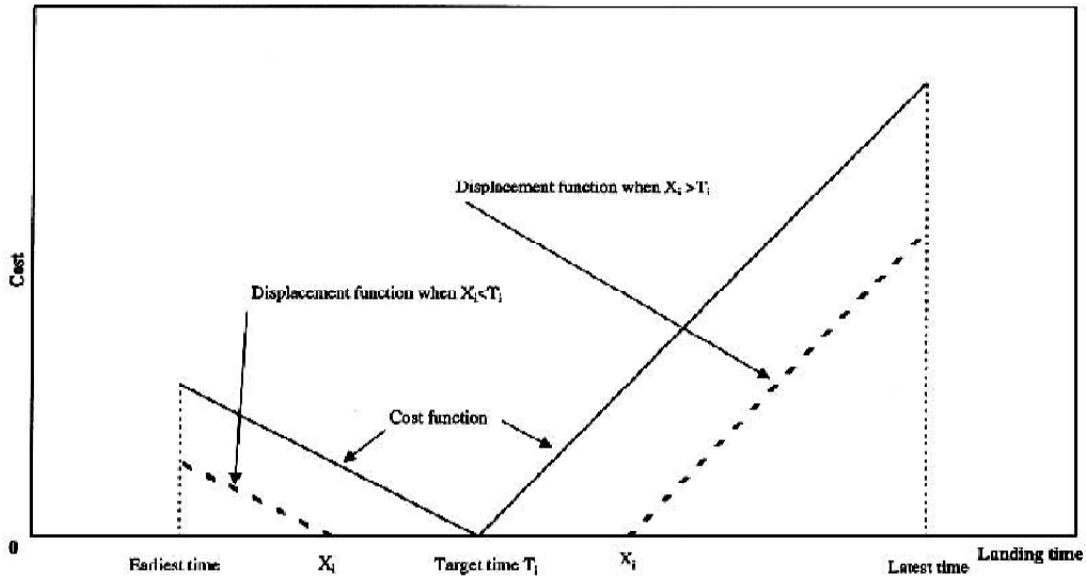

Figure 1 : Cost function and displacement function.

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RESEARCH ARTICLE

Keywords Search in Relational Databases

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ABSTRACT

Relational Database Management System provides users with a query language SQL to query information maintained in large RDBs. It requires users to understand how the information is stored in an RDB on a relational schema and know how to specify their requests using SQL Precisely. Due to rapid information growth in the information era, many real applications require integrating both DB and IR technological in one system. The purpose of this paper is to present the application of RDBMs for rapid searching of keywords.

Keywords :- Relational ,structured query language, schema, integrating, growth

INTRODUCTION

The sophisticated DB techniques provide users with effective and efficient ways to access structured data managed by RDBMSS, and the advanced IR techniques allow users to use keywords to access unstructured data with scoring and ranking. Chaudhuri et al. discussed the issues on integrating DB and IR technologies in [6]. In supporting IR-styled search, commercial RDBMSS (such as *DB2, ORACLE,* SQL-SERVER) support full-text keyword search using a new SQL predicate of *contain (A,* k) where A is an attribute name and k is a user-given keyword. With the new predicate, a built-in full-text search engine in the RDBMSS builds full-text indexes over text attributes in relations, and is used to retrieve the tuples that contain keywords in text attributes in relations efficiently. In addition to full-text keyword search, another type of keyword search is to find how tuples that contain keywords in an *RDB* are interconnected [1, 16, 14, 23, 24, 4, 17, 19, 9, 11, 13, 26]. We call it structural keyword search. Consider a bibliography database maintains publication records in several relations in an *RDB.* It is highly desirable to find out how certain research topics and/or authors are interrelated via sequences of co-authorship/citations. For example, given three keywords, "Keyword", "DB", and "Yannis", the structural keyword search may find that "Yannis" writes a paper cited by two papers whose titles contain "Keyword" and "DB" respectively. Here, "Yannis" possibly appears in a tuple in

an author relation, the three papers are three tuples in a paper relation, all are connected by foreign key references among tuples in other author- paper relation and paper-citation relation. The structural keyword search is completely different from full-text search. The former focuses on the interconnected tuple structures, whereas the latter focuses on the tuple content. Here, we concentrate ourselves on structural keyword search, and simply call it keyword search.

In the literature, the existing work are categorized into schema- based approaches and schema-free approaches for (structural) keyword search. The schema-based approaches [1, 16, 14, 23, 24] process a keyword query in two steps, namely, candidate network *(CN)* generation and *CN* evaluation. In the *CN* generation step, it generates all needed *CNs* (relational algebra expressions) up to a size, because it does not make sense if two tuples are far away in an interconnected tuple structure. In the *CN* evaluation step, it evaluates all *CNs* using SQL. The schema-free approaches [4, 17, 19, 9, 11, 13, 26] support keyword search using graph-based in-memory algorithms by materializing an RDB as a graph. Almost all the existing work take a middleware approach [14, 23, 24, 4, 17, 19, 9, 11, 13, 26] except for two early work [1, 16] that evaluate *CNs* using SQL on an RDBMS directly. The middleware approach does not fully utilize the functionality of RDBMSs, and only uses SQL to retrieve data. In terms of the interconnected tuple structures, the majority of the work focus on connected trees [1, 16, 14, 23, 24, 4, 17, 19, 9, 11]. Recently [13] studies finding sets of interconnected tuples which can be uniquely identified by a root within a user- given radius, and [26] studies finding sets of multi-center communities within a radius. All the three interconnected tuple structures are needed for different applications. But all are dealt in different ways and are not unified in the same framework. A key issue we are studying in this work is how to support the three interconnected tuple structures (all connected trees up to certain size, all sets of tuples that are reachable from a root tuple within a radius, and all sets of multi-center subgraphs within a radius) in the same framework on RDBMSs without middleware. The main contributions of this work are summarized below. We propose a middleware free approach, to support three types of keyword queries to find the three different interconnected tuple structures. We take a tuple reduction approach using SQL without additional new indexing to be built and maintained and without any pre computing required. To compute all connected trees, we propose a new approach to prune tuples that do not participate in any resulting connected trees followed by query processing over the reduced relations. To compute all multi-center subgraphs, we propose a new three-phase reduction approach to effectively prune tuples from relations followed by query processing over the reduced relations. We use the similar mechanism for computing all multi- center subgraphs to process sets of tuples that are reachable from a root tuple within a radius. We conducted extensive performance studies using two commercial RDBMSs and two large real datasets to confirm the efficiency of our proposed approaches.

Keyword Search Semantics

A n m-keyword query is given as a set of keywords of size m, {fc$_1$, k_2, ... ,k_m}, and is to search interconnected tuples that contain the given keywords, where a tuple contains a keyword if a text attribute of the tuple contains the keyword. To select all tuples from a relation *R* that contain a keyword k$_1$, a predicate *contain (A, k$_1$)* is supported in SQL in IBM *DB2, ORACLE,* and Microsoft SQL SERVER, where *A* is a text attribute in *R*. With the following SQL,

***Select *from** R **where** contain (A$_1$, k$_1$) **or** contain (A2, k$_1$)*

it finds all tuples in R containing k$_1$ provided that the attributes A$_1$ and A_2 are all and the only text attributes in relation R. Below, for simplicity, we use $ff_{contai„}(k_1)R$ to indicate the selection of all tuples in *R* that contains a keyword *k*1 in any possible text attributes. We say a tuple contains a keyword, for example *k*1 , if the tuple is included in the result of such selection. In the literature, there are three types of semantics, which we call *connected tree semantics, distinct root semantics,* and *distinct core semantics*. We introduce them below in brief.

Connected Tree Semantics

An m-keyword query finds connected tuple trees [16, 4, 17, 9, 24, 23, 19]. A result of such a query is a minimal total joining network of tuples, denoted as *MTJNT.* First, a joining network of tuples *(JNT)* is a connected tree of tuples where every two adjacent tuples, t_i € $r(R_i)$ and tj € $r(Rj)$ can be joined based on the foreign key reference defined on relational schemas R_i and Rj in G_s (either R_i ^ Rj or Rj ^ R_i). Second, a joining network of tuples must contain all the *m* keywords (by total). Third, a joining network of tuples is not total if any tuple is removed (by minimal). The size of an *MTJNT* is the total number of nodes in the tree. Because it is not meaningful if an *MTJNT* is too large in size, a user-given parameter Tmax specifies the maximum number of nodes allowed in *MTJNTs.* Consider the *DBLP* database in Example 2.1 with a 2-keyword query *K = {Michelle, XML}* and Tmax = 5. There are 7 *MTJNTs* shown in Fig. 3(a). For example, the first connected tree means that paper p_1 is cited by paper p_2 as specified by tuple c_1. Here p_1 contains *Michelle* and p_2 contains *XML.*

Distinct Root Semantics

An *m*-keyword query finds a collection of tuples, that contain all the keywords, reachable from a root tuple (center) within a user-given distance (Dmax). The distinct root semantics implies that the same root tuple determines the tuples uniquely [13, 21, 15, 8]. In brief, suppose that there is a result rooted at tuple t_r. For any of the m-keyword, say *ki,* there is a tuple *t* in the result that satisfies the following conditions. (1) *t* contains the keyword k_l. (2) Among all tuples that contain k_i, the distance between *t* and t_r is minimum. (3) The minimum distance between *t* and t_r must be less than or equal to a user given parameter Dmax. Reconsider the *DBLP* database in Example 2.1 with the same 2-keyword query *K = {Michelle, XML}* (Dmax = 2). The 10 results are shown in Fig. 3(b). The root nodes are the nodes shown in the top, and all root nodes are distinct. For example, the rightmost result in Fig. 3(b) shows that two nodes, a_3 (containing *Michelle)* and p_2 (containing *XML),* are reachable from the root node p_4 within Dmax = 2. Under the distinct root semantics, the rightmost result can be output as a set (p_4, a_3, p_2), where the connections from the root node (p_4) to the two nodes can be ignored as discussed in *BLINKS* [13].

Distinct Core Semantics

An *m*-keyword query finds multi-center sub graphs, called communities [26]. A community, $C_i(V,E)$, is specified as follows. *V* is a union of three subsets of tuples, $V = V_c$ U V_k U V_p. Here, V_k represents a set of keyword-tuples where a keyword-tuple $v_k \in V_k$ contains at least a keyword and all *m* keywords in the given *m*-keyword query must appear in at least one keyword-tuple in V_k, V_c represents a set of center-tuples where there exists at least a sequence of connections between $v_c \in V_c$ and every $v_k \in V_k$ such that $dis(v_c,v_k) \leq$ Dmax, and V_p represents a set of path-tuples which appear on a shortest sequence of connections from a center-tuple $v_c \in V_c$ to a keyword-tuple $v_k \in V_k$ if $dis(v_c,v_k)$ < Dmax. Note that a tuple may serve several roles as keyword/center/path tuples in a community. *E* is a set of connections for every pair of tuples in *V* if they are connected over shortest paths from nodes in V_c to nodes in V_k. A community, C_i, is uniquely determined by the set of keyword tuples, V_k, which is called the core of the community, and denoted as core(C_i) in [26]. Reconsider the *DBLP* database in Example 2.1 with the same 2-keyword query *K = {Michelle, XML}* and Dmax = 2. The 4 communities are shown in Fig. 3(c), and the 4 unique cores are (a_3,p_2), (a_3,p_3), (p_1,p_2), and (p_1,p_3), for the 4 communities from left to right, respectively. The multi-centers for each of the communities are shown in the top. For example, for the rightmost community, the two centers are *p*2 and *c*2 . It is important to note that the parameter Dmax used in the distinct core/root semantics is different from the parameter Tmax used in the connected tree semantics. Dmax specifies a range from a center (root tuple) in which a tuple containing a keyword can be possibly included in a result, and Tmax specifies the maximum number of nodes to be included in a result.

CONCLUSION

Here, we studied three different semantics of *m*-keyword queries, namely, connect-tree semantics, distinct core semantics, and distinct root semantics. We proposed a middleware free approach to compute such m-keyword

queries on RDBMSS using SQL only. The efficiency is achieved by new tuple reduction approaches that prune unnecessary tuples in relations effectively followed by processing the final results over the reduced relations. Our middleware free approach makes it possible to fully utilize the functionality of RDBMSS to support keyword queries in the same framework of RDBMS.

REFERENCES

1) S. Agrawal, S. Chaudhuri, and G. Das. DBXplorer: A system for keyword-based search over relational databases. In *Proc. of ICDE'02,* 2002.
2) Balmin, V. Hristidis, and Y. Papakonstantinou. Object Rank: Authority-based keyword search in databases. In *Proc. ofVLDB'04,* 2004.
3) P. A. Bernstein and D.-M. W. Chiu. Using semi-joins to solve relational queries. *J. ACM,* 28(1), 1981.
4) G. Bhalotia, A. Hulgeri, C. Nakhe, S. Chakrabarti, and S. Sudarshan. Keyword searching and browsing in databases using BANKS. In *Proc. of ICDE'02,* 2002.
5) S. Chaudhuri. An overview of query optimization in relational systems. In *Proc. of PODS'98,* 1998.
6) S. Chaudhuri, R. Ramakrishnan, and G. Weikum. Integrating db and ir technologies: What is the sound of one hand clapping? In *Proc. of CIDR,* 2005.
7) S. Chaudhuri and K. Shim. Including group-by in query optimization. In *Proc. of VLDB'94,* 1994.
8) B. Dalvi, M. Kshirsagar, and S. Sudarshan. Keyword search on external memory data graphs. *PVLDB,* 1(1), 2008.
9) B. Ding, J. X. Yu, S. Wang, L. Qin, X. Zhang, and X. Lin. Finding top-k min-cost connected trees in databases. In *Proc. of ICDE'07,* 2007.
10) S. E. Dreyfus and R. A. Wagner. The steiner problem in graphs. In *Networks,* 1972.
11) K. Golenberg, B. Kimelfeld, and Y. Sagiv. Keyword proximity search in complex data graphs. In *Proc. of SIGMOD'08,* 2008.
12) Graefe. Query evaluation techniques for large databases. *ACM Comput. Surv.,* 25(2), 1993.
13) He, H. Wang, J. Yang, and P. S. Yu. BLINKS: ranked keyword searches on graphs. In *Proc. ofSIGMOD'07,* 2 2007.
14) V. Hristidis, L. Gravano, and Y. Papakonstantinou. Efficient IR-Style keyword search over relational databases. In *Proc. ofVLDB'03,* 2003.
15) V. Hristidis, H. Hwang, and Y. Papakonstantinou. Authority-based keyword search in databases. *ACM Trans. Database Syst.,* 33(1), 2008.
16) V. Hristidis and Y. Papakonstantinou. DISCOVER: Keyword search in relational databases. In *Proc. ofVLDB'02,* 2002.
17) V. Kacholia, S. Pandit, S. Chakrabarti, S. Sudarshan, R. Desai, and H. Karambelkar. Bidirectional expansion for keyword search on graph databases. In Proc. of VLDB'05, 2005.

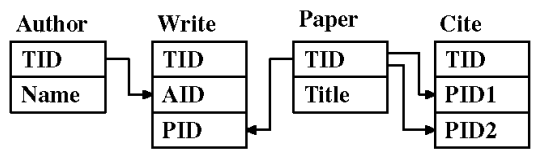

Figure 1: *DBLP* Database Schema

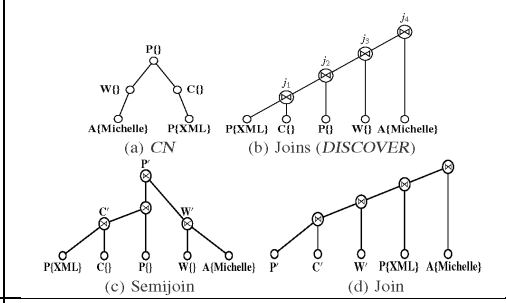

Figure 2: Join vs Semijoin /Join

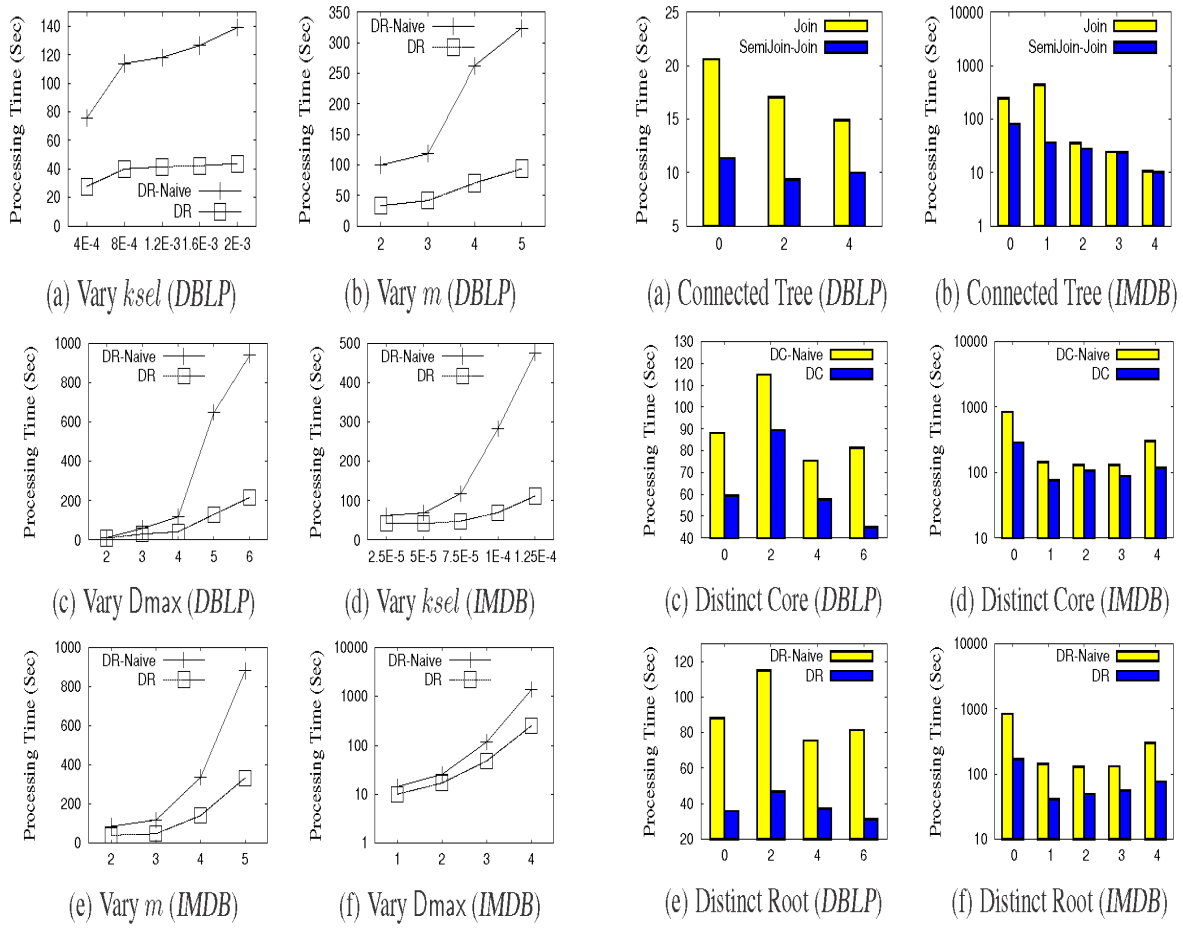

Figure 3a,b,c,d,e,f: Distinct root (DBLP and IMDB) and Query Compactness

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RESEARCH ARTICLE

Performances of Practice Teachers' with "Filipino" as Their Field of Expertise

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ABSTRACT

This study intends to showcase the significance of Philippine languages on technical, personal, and management using the T-test as a means of analyzing the data. This study confirms that practice teachers were more active and efficient in their field of teaching once using "Filipino" or the Philippines language on their teaching hence they were more convenient and has their expertise. Moreover, this study has emphasized to present the data on the Philippines version to exclusively provide precise understanding to teachers on Filipino subject. It observed that there is such a big difference if practice teachers' in Filipino use their vernacular language or the "Filipino" dialect during their classes in discussing topics hence, based on facts their performances increase from average to excellent performers. Their teaching practices make them more valuable and able in teaching actually they have the potentials already even during their baccalaureate studies and much when they are on their field in teaching it was revealed during their practice teaching

PHILIPPINES VERSION

Layonngpag-aaralnatayainangperformansngmgagurong-mag-aaralsakursong BSED-4 medyorsa Filipino para sakanilangpagtuturongkailanganin. Ito'ynapabilangsaparaang Deskriptivnadesinyo, gamitangpormularyosapag-eebalweytngtatlongelemento: panteknikal, personal at pamamahalasaklase. Animnalinggoangeksposyurnilasapaaralan. Dalawangbesesnaisagawaangpag-ebalweyt at sinurisapamamagitanng T-test at *multivariate analysis of variance.*

Natuklasanna may kaunlarangipinakitasaperformansngpagtuturongmgagurong-mag-aaralmulasaunangtangkana Very satisfactory ay nagingoutstanding angperformansnitosalahatngelementongisinalang-alangsaikalawangtangkangpagtataya. Napag-alamangtaglaynanilaangkakayahanpangguromulasakolehiyongnapasukanngkanilangkurso at dahilsasanayang-pagtuturo mas napatindi pa nitoangkakayahangkanilangnasimulan. Hindi silanahihirapansapagsasatupadnggawaindahilakmaitosakanil angmedyor at natutunan. Malaki angpakinabangngnasabingpagsasanay o praktikumsaaktwalnatagpo para sapag-unladngkakayahangpagtuturongmgagurong-mag-aaral.

Keywords: Filipino Practice Teachers'Performances; Descriptive; Outstanding; Practice Teaching

INTRODUCTION

Isang karangalan ng institusyon ang makakabuo ng mga mahuhusay Na mga gurong mag-aaral SA alinmang espesyalisasyon Nile. Nagkindlingmegaperformance ay teakansalamiasperformancenag kolehiyong kanilang pinanggalingan. Lalo na sa mga panahong ito na patuloy ang pag-inog ng pagbago-bago para sa reporma ng pagtuturo sa ilalim ng K-12 kurikulum na kung saan siyang naging hamon sa lahat ng guro baguhan man o bihasa na sa larangan ng pagtuturo. It is perceived that curricular improvement depends largely on the teachers who deliver the reform in their classrooms (Tatto, 2006). Nasa kamay ng mga guro ang tagumpay, pag-asa at kalidad ng karunungan sa bawat mag-aaral. Gayun na lamang na bigyan ng halaga ang pakikibakang mahubog nang maayos ang mga gurong-mag-aaral sa kanilang patapos na gawain upang makasiguro na ginagampanan nila ang kanilang papel sa propesyong pangguro Sa pag-aaral nina Tabacbnick at Zeichner (2016), nabigyang kabuluhan nila ang pagsasanay ng mga gurong mag-aaral sa pagtuturo sa loob ng anim na linggo dahil batay sa resulta, napansin nila ang kalinangan pansosyal na pakikitungo ng gurong mag-aaral sa bawat mag-aaral nila habang kasa-kasama ito sa klasrum. Dagdag pa nila, "*that student teaching does have a significant impact on the development of teachers".* Talagang may makabuluhang epekto ang praktikum para sa pag-unlad ng kakayahang pagtuturo ng mga gurong-mag-aaral.
Mula kay Gonong (2014), isa sa *performance indicators* ng *NCBTS pre-service* ay ang pagpapaunlad ng kakayahang pagtuturo batay sa fidbak ng mga mentor, mag-aaral, kasamahan at ng superbisor. Masusukat dito ang kaunlaran kung hanggang saan ang pag-unlad nila sa unang-katlong linggo na pagsasagawa hanggang sa panlima't anim na linggo ng kanilang kahantaran sa pagsasanay-turo. Ilan sa mga napapansing fidbak ng mananaliksik na ang mga gurong-mag-aaral medyor sa Filipino ay may kahinaan dahil sa mababang marka sa kanilang praktikum gamit ang nasabing pangkalahatang *evaluation instrument* ng STASS ng kolehiyo. Gayunma'y sinubukang pag-aralan ng mananaliksik ang tungkol sa tunay na kaunlaran at performans gamit mismo ang pormularyong naayon sa Filipino para sa ebalwasyon ng kanilang pagtuturo. Masuri ang impak o pakinabang ng gawaing praktikum na kanilang inaabala sa loob ng isang semester ng panahong laan.Ang nasabing pag-aaral ay tumugon din kung paano inililipat ang natutunan sa aktwal na buhay ng bawat gurong mag-aaral ng Surigao State College of Technology, kaalinsabay na rin ang pangangailangang pang-akreditasyon ng nasabing kolehiyo[(Agcaoili & Oshihara, 2014); Armour (2016); Badayos (2012); Deguito (2013); CHED (2014); Oluwatayo and Adebule (2012); *Villafuerte at Bernades (2015)*.

Theoritical Concept (BALANGKAS KONSEPTWAL)

Nailahad sa figyur 1 ang paradima ng pag-aaral, ang unang kahon bilang kumakatawan sa profayl ng mag-aaral na inuugnay sa ikalawang katapat na kahion nakumakatawan sa gurong tagpamatnubay o *supervising teacher* nila na siyang sumuri sa kakayahang ipinakikita ng mga gurong-mag-aaral habang nasa isang klase ng talakayan. Sila ay may kanya-kanyang hawak na tungkulin na masisilip sa bilog ng paradima. Ang mag-aaral ay siyang tayain sa kanilang performans sa pagtuturo at ang gurong tagapamatnubay ay ang siyang kumilatis sa kaniang performans gamit ang pormularyo o rubriks ng Filipino batay sa kanyang naobserbahan sa klase. Ang desinyong ginagamit sa pag-aaral ay *Deskriptiv Design.* Ang mga tagatugon ay ang mga mag-aaral at ebalweytor *supervising teacher* mula sa pampublikong mga matataas na paaralan na silang mag-eebalweyt ng mga gurong mag-aaral ng SSCT sa taong 2016 para lang sa medyor ng Filipino, sekundarya. May pormularyo sa pag-eebalweyt na ginagamit sa pagtataya. May tatlong elementolamang ang hahanapin dito; panteknikal, personal/karakter at pamamahala sa klase. Ang mga ito ay *pattern* sa K-12 na siyang pinakaimportanting tingnan sa panahon ng pagtuturo**.** Ang bawat gurong mag-aaral ay inatasan na magpapaebalweyt sa kanilang *supervising teache*r gamit ang nasabing pormularyo. Ito ay para sa ikalawang semestre ng taong 2016. Mayroon silang anim na linggo na manatili sa paaralan, magkaroon lang ng dalawang beses na pag-eebalweyt sa kanila. Sa ikatlo at ikalimang linggo ang laang panahon para dito. Dito makita ang kaunlaran nila hanggang sa sila ay matapos. Ang mga kagamitng istadistikal na ginagamit ay ang mga sumusunod; Frequency count and percent, T-testat Multiviriate analysis of variance.

MGA PAGTALAKAY AT KINALABASAN NG PAG-AARAL

Talahanayan 1. Propayl ng Tagatugon Ipinakita sa talahanayan 1, ang profayl ng gurong-mag-aaral bilang tagatugon sa unang bahagi ng talatanungan. Karamihan ay mga babae, lahat nagkaroon ng ebalweytor na Filipino medyor at ang karaniwang iniatas na hawakan nila ay nagmumula sa baitang 9 at 10.

Antas Ng Performans Sa Pagtuturo Bilang Panggurong Pagsasanay Na Gawain Sa Unang Tangka

Sa talahanayan 2 hanggang 4 naipakita ang antas ng performans sa pagtuturo bilang panggurong pagsasanay na gawain sa unang tangka ng pagtataya ng mga gurong mag-aaral. Batay sa gawaing panteknikal., personalidad at pamamahalas sa klase. Ang talahanayan 2 ay naglalahad tungkol sa resulta ng Antas ng Performans sa Pagtuturo Batay sa Panteknikal na aspeto sa pagtataya. Makikita sa resulta na sa Gawain "A8. *Nalilinang ang kasanayang interaktibo sa pamamagitan ng pangkatan*" ay nagkaroon ng pinakamalaking nakuhang mean ng performans panteknikal ang mga gurong mag-aaral na kung saan ay 3.51. Ito ay nangangahulugang lubos na kasiya-siya o outstanding ang performans na ipinakita nila dito. Samantala, sa gawain "A4. *Mapanghamon at reflektibo ang follow-up na tanong*" nakuha ang pinakamaliit na antas ng performans panteknikal ng mga gurong mag-aaral na kung saan 3.22 lamang tala. Ito ay nasa deskripsyong higit na kasiya-siya o very satisfactory na performans sa unang tangka ng pagsasanay.

Antas ng Performans sa Pagtuturo Batay sa Personalidad

Sa Talahanayan 3 naman naipakita ang antas ng performans sa pagtuturo ng mga gurong mag-aaral batay sa personalidad Makikita sa talahanayan na ang may pinakamalaking mean ay nasa Gawain " B2. *Sapat ang lakas ng boses upang marinig ang lahat*" sa 3.83 samantalang sa Gawain "B7. *Madaling makapagbigay ng desisyon at pasya" naman ang pinakamaliit* at ito ay 3.56.

Talahanayan 3: Antas ng Performans sa Pagtuturo Batay sa Personalidad . Gayunman, sa lahat ng indikeytors, ang performans ng mga gurong mag-aaral ay nasa antas na *outstanding*. Dahil dito ang pangkalahatang performans ng mga gurong mag-aaral sa pagtuturo batay sa personalidad ay outstanding din na ipinahayag ng overall mean na 3.70.

Talahanayan 4: Antas ng Performans sa Pagtuturo batay sa Pamamahala Batay sa baryabol na pamamahala sa klase naman, ang resulta ng antas ng performans sa pagtuturo ay nailahad sa Talahanayan 4. Ipinakita dito na sa mga gawaing aytem " C1. *Sinisimulan ang klase sa takdang oras;* C5. *Maaliwalas ang klasrum para sa kaalaman;* at C7.*Maingat na pinapasyahan ang mga ideya ng mga mag-aaral sa panahon ng interaksyon*" naipakita ng mga gurong mag-aaral ang pinakamalaking mean na tugon sa 3.53 at naglalarawang outstanding na performans sa mga nasabing gawain. Samantalang sa gawain " C2. *Pinanatili ang disiplina sa klase* " ay nagtamo ng pinakamaliit na mean na tugon sa 3.33 na kung saan naglalarawang higit na kasiya-siya o *very satisfactory* ang performans.Sa kabuuan, may nakuhang mean na 3.52 na naglalarawang *very satisfactory* ang kabuuang performans ng mga gurong mag-aaral kung tungkol sa kakayahan ng kanilang pamamahala sa klase.

Antas Ng Performans Sa Pagtuturo Bilang Panggurong Pagsasanay Na Gawain Sa Ikalawang Tangka

Sa Talahanayan 5 hanggang 7 naipakita nag antas ng performans sa pagtuturo bilang panggurong pagsasanay na gawain sa ikalawang tangka ng pagtataya ng mga gurong mag-aaral, panteknikal. Personalidad at pamamahalas sa klase.

Talahanayan 5: Antas ng Performans sa Pagtuturo batay sa Panteknikal sa Ikalawang Tangka. Makikita sa talahanayan 5 ang datos tungkol sa antas ng performans ng mga gurong-mag-aaral. Ayon sa resulta, natuklasan na sa ikalawang tangka ng pagtataya ng mga gurong mag-aaral ay nasa antas na na outstanding o sa deskripsyong lubos na kasiy-siya sa lahat ng mga panteknikal na gawain. Masuri na sa baryabol na mas mataas na ang antas ng

kanilang performans na kung saan may mean na 3.75 at nasa outstanding lahat ng aytem kung ihambing sa unang tangka nila sa gawaing panteknikal. Dahil dito nakitaan ng kaunlaran sa performans ng mga gurong mag-aaral. Kung mapansin, ang very satisfactory na antas ng performans ng mga gurong mag-aaral sa gawaing aytem A3, A4, A7, at A9 na nagsabing ang : "*A3. Nagpakita ng masteri sa wika at panitikan; A4. Mapanghamon o reflektibo ang mga follow-up na tanong; A5. Ginagamit ang kagamitang pantulong mula sa simula hanggang sa pagtapos ng aralin; A7. Naintegreyt ang liksyon sa pamraang lokalisasyon at kontektwalisasyon;at A9. Makabuluhan ang mga gawain sa pamamagitan pangkatan*". Ang mga ito sa unang tangka ay nagpakita ng performans na VS samantala sa iklawang tangka ay umunlad na sa antas na outstanding.

Talahanayan 6: Antas ng Performans sa Pagtuturo batay sa Personalidad sa Ikalawang Tangka.Talahanayan 6 naman inilahad ang antas ng performans sa pagtuturo ng mga gurong mag-aaral batay sa personalidad sa ikalawang tangka ng pagtataya. Makikita ang antas ayon sa personalidad lahat ay nagtala ng pinakamataas na performans sa deskripsyon lubos na kasiya-siya o outstanding parin katulad ng sa unang tangka. Kapansin-pansin rin na tumaas pa ang mga mean ng bawat performans indikeytor sa nakuhang antas ng mga gurong mag-aaral. Tumaas sa 3.83 mula sa 3.70 ang kabuuang mean ng antas ng performans sa pagtuturo batay sa personalidad.

AntasngPerformanssa Pagtuturo batay sa Pamamahala sa Ikalawang Tangka Sa talahanayan 7, nailahad ang baryabol tungkol sa pamamahala ng klase. Makikita sa datos na ang mga gurong-mag-aaral ay nagtala ng lubos na kasiya-siya o outstanding na performans sa lahat ng gawaing pamamahala sa ikalawang tangka ng pagtataya.

Talahanayan 7: Antas ng Performans sa Pagtuturo batay sa Pamamahala sa Iaklawang Tangka Mapapansin na nagkaroon lamang ng VS (very satisfactory) o higit na kasiya-siya ang antas ng performans sa aytem "*C2. Pinapanatili ang disiplina sa klase; C4. May tiwala sa sarili sa pagtalakay ng liksyon;, C8. Nasunod ang nakatakdang oras sa klase*" sa unang tangka ng pagtataya ng mga gurong mag-aaral na kung saan napaunlad sa ikalawang tangka sa antas na outstanding lahat ng aytem. Itoy nagpapahiwaitg lamang na may kaunlarang natamo ng mga gurong mag-aaralna kung saan masasabing na may malaking bagay ang kanilang aktwal na karansan sa pagtuturo sa aspetong pamamahala sa klase lalo na sa pagdisiplina sa sarili, mga mag-aaral at ang tamang oras sa trabaho.

Talahanayan 8. Makabuluhang Kaugnayan ng Profayl ng mga gurong mag-aaral at ng antas ng kanilang performans sa pagtuturo bilang panggurong pagsasanay na Gawain (Pangkalahatan). Nasa talahanayan 8 ang pagtuos ng ugnayan sa profayl at antas ng performan sa pagtuturo ng gurong-mag-aaral. Ayon sa natuklasan, sa kadahilanang ang natamong Wilks' Lambda value at p-value sa kasarian na 0.867 at 0.651, ay walang makitang ugnayan ng kasarian ng mga mag-aaral sa antas ng kanilang performans sa pagtuturo bilang panggurong pagsasanay. Wala ring nakitang kaugnayan ang dami ng baitang na nahawakan ng mga gurong mag-aaral sa antas ng performans nila sa pagtuturo. Ito ay ayon na rin sa natamong Wilks' Lambda value na 0.723 at p-value na 0.293. Mapapansin na walang makitang p-values sa medyor at asignaturang ipinaturo sa kadahilanang ang medyor ng mga gurong-ebalweytor ay Filipino rin sang-ayon sa asignaturang ipinaturo.

Makabuluhang Ugnayan ng Profayl ng mga gurong mag-aaral at ng antas ng kanilang performans sa pagtuturo bilang panggurong pagsasay na Gawain (bawat Baryabol)

sa Talahanayan 9 naman makikita ang resulta kung may ugnayan sa pagitan ng profayl ng mga gurong mag-aaral at antas ng performans sa pagtuturo bilang panggurong pagsasanay sa bawat aspetong panteknikal, personalidad at pamamahala. Katulad ng nauna nang natuklasan, kahit isa-isahin, wala paring makitang ugnayan ang kasarian at nahawakang baitang sa antas ng performans panteknikal, personalidad at pamamahala ng mga gurong mag-aaral. Sa medyor at asignaturang ipinaturo naman ay ganun din.

Talahanayan 9 : Makabuluhang Ugnayan ng Profayl ng mga gurong mag-aaral at ng antas ng kanilang performans sa pagtuturo bilang panggurong pagsasay na Gawain (bawat Baryabol). Ang mga kalabasan sa pasyang not

significant at invalid ay nagpapatunay na ang mga mag-aaral ay itinalaga talaga sa kanilang gawain sa mga gurong ebalweytor na Filipino medyor na ayon sa kanilang kurso at nasa tamang mag-aaral pansekondarya.

Talahanayan 10.Pagkakaiba ng Performans ng mga gurong mag-aaral sa Pagtuturong nagawa sa una at ikalawang tangka ng pagtataya Sa Talahanayan 10 ipinakita kung may makabuluhan ba ang pagkakaiba ng antas ng performans ng mga gurong mag-aaral sa pagtuturong nagawa sa una at ikalawang tangka ng pagtatayang panteknikal, personalidad at pamamahalas sa klase. Sa kinalabasan, ang nakuhang t- value at p-value na -3.31 at 0.004 sa panteknikal ay nagpapatunay na may makabuluhang pagkakaiba sa performans ng mga gurong mag-aaral sa pagtuturo bilang panggurong pagsasanay sa una at ikalawang tangka ng pagtataya. Ang mean difference na -0.34(una-ikalawa) ay nangangahulugang mas mataas ang antas ng performans batay sa panteknikal ang mga respondents sa ikalawang tangka ng pagtataya. Batay sa personalidad naman, ang natamong p-value ay 0.129 na mas malaki sa level of significance na 0.05. Ito'y nangangahulugan lamang na walang makabuluhang pagkakaiba ang perforamans ng mga gurong mag-aaralsa pagtuturo bilang panggurong pagsasanay batay sa personalidad, sa una at sa ikalawang tangka ng pagtataya. Sa makatuwid, pareho lang ang antas ng performans ng mga tagatugon sa una at ikalawang tangka ng pagtataya. Batay sa pamamahala naman, ang natamong t-value na -2.94 at p-value na 0.009. Ito ay nangangahulugang may makabuluhang pagkakaiba ang antas ng performans ng mga gurong mag-aaral sa pagtuturo batay sa pamamahala bilang panggurong pagsasanay sa una at ikalawang tangka ng pagtataya. Dahil dito, nagbadya na ang mean difference na -0.35 (una-ikalawa) ay nagsasabing tunay na umunlad ang performans ng mga tagatugon sa ikalawang tangka ng pagtataya. Samakatuwid, mayroon makabuluhang kaunlarang makikita sa performans ng mga gurong mag-aaral sa ikalawang tangka ng pagtataya batay sa pamamahala ng klase.

Talahanayan 11. Pagkakaiba ng antas ng Kabuluhang impak dulot ng panggurong pagsasanay na gawain batay sa performans-baryabol. Sa talahanayan 11, ay makikita ang datos bilang kinalabasan sa pagkakaiba ng antas ng kabuluhang impak dulot ng panggurong pagsasanay na Gawain batay sa performans panteknikal, personalidad at pamamahala. Sa nakitang resulta sa lahat ng mga baryabol, ang p-values ay lahat mas malaki sa level of significance na 0.05. Ito ay nangangahulugan lamang na walang makabuluhang pagkakaiba ang antas ng kabuluhang impak ng panggurong pagsasanay na Gawain batay sa panteknikal na performans, personalidad at pamamahala

INTERPRETASYON SA MGA KINALABASAN

Dito masilip ang pagpapakahulugan sa mga kinalabasan ng datos tungkol sa performans ng mga gurong-mag-aaral sa anim na linggo na pagsasanay. Sa unang tangka ng pagtataya mapapansin ang kataasan ng antas ng performans sa tatlong aspetong lalo na sa personalidad na naglalarawang outstanding o lubos na kasiya-siya sa naipakitang kakayahan sa pagtuturo, maliban sa panteknikal na bahagyang mababa sa verysatisfactory ang antas o higit na kasiya-siya ang kakayahannito. Batay sa profayl na nasilip, ang mga araling hawak ng mga gurong mag-aaral ay nasa mataas na lebel nang mga nilalaman dahil ang mga ito ay nagtatalakay ng mga panitikang Asyano at Pandaigdigan ang lawak sa greyd 9 at 10. Lahat ng asignaturang itinalaga sa mga gurong-mag-aaral ay mga Filipino. Mangyari na maaring magawa talaga ng mga gurong-mag-aaral ang pagtuturo na may kahusayan dahil espesyalisasyon nila ang nahawakang asignatura.

Kapansin-pansin ang outstanding na performans sa katangian personal ng mga gurong-mag-aaral, ibig sabihin taglay nila ang naiturong pakikibagay at pag-unawa sa bata bilang ikalawang magulang sa paaralan. Dama nila ang mga pangangailangan at naintindihan nila ang kanilang tungkulin bilang isang guro. Napanatili nila ang kaayusan sa kapaligiran at naipakita nila ang paggalang sa bawat opinyon sa klase. Pinahalagahan nila ang mga payo at natutunan nila sa panahon ng pakitang-turo na pagsasanay bilang kailanganin sa kanilang kurso. Napakarealistiko ang kinalabasan sa unang tangka ng naipakitang performans sa aspetong panteknikal sa antas na VS o *Higit na kasiya-siya*bahagya lang ang kababaan talaga kahit papaano'y ang karaniwang gawi ng mga mag-aaral sa hayskul na alam nang mahirap isipin paano mapanatili ang katiwasayan sa klase ngunit nagawa pa rin nilang naging maayos ang kanilang klase.May masteri sa mga aralin, angkop ang gamit ng estrtehiya o pamamaraan sa pagtuturo at ang paggamit ng kagamitang panturo at iba pang gawaing proseso sa pakatuto sa klase. Nagsabing hindi masyadong

nahihirapan ang mga gurong-mag-aaral sa kanilang paggurong pagsasanay dahil angkop sa kanilang natutunan ang ipinagawa sa kanila. May lubos na kakayahan na rin sila sa aspetong pamamahala sa klase . Naisagawa ng gurong-mag-aaral ang interaktibong pangkatan, kaso di-gaano pang nagawa niya ang kakayahan sa bisa ng pagtatanong bilang follow-up sa mga ideya ng bata, at ang paglolokalays at kaangkupan ng gamit sa grapiko sa ipinagawang pangkatan ayon sa unang tangka.

Hindi man nagpakita ng Outstanding lahat sa unang tangka ngunit sa ikalawang tangka ay nasigurong nagawa lahat ng aspeto sa pagtuturo ng nasa antas Outstanding. Ang puntos ng bawat isa ay nakitaang umunlad ang mga ito sa lahat ng nailahad na dapat gawin sa isang talakayan. Naipakita angpagkamasigasig, haba ng pasensya,tiwala sa sarili, kahandaan, masteri, malohika, integratibong partispasyon at ibapa ay lubos na ganapang naitaguyod ng gurong-mag-aaral sa panahon ng pagtuturo sa ikalawang tangka. Sakatuwid, malinaw na may kaunlarang natamo ng mga gurong-mag-aaral sa karanasang pagsasanay nila sa pagtuturo. Mas pinatindi panga nila sa ikalawang tangka kung anumang naipakita nila sa unang tangka ng pagtataya.Mayroon talagang nakitang kahalagahan o impak ang karanasan o kahantaran nila sa pagsasanay. Hindi sila nahirapan dito dahil umalinsunod sa medyor at natutunan nila ang lahat ng ipinasatupad na gawain.Patuloy ang pag-unlad nila maliban sa nakaukit na sa kanila ang pagiging efectiv na guro bago paman naisalang sa labas na pagsasanay mas lalong naragdagan pa ang kahusayang ito dahil sa kanilang karanasansa aktwal na pagtuturo.Nagbabadya lamang na ang mga gurong ito ay mga mabubutinggurosahinaharap.

NATUKLASAN

1. Saunangtangkang pagtataya, ang antas ng performans ng mga gurong-mag-aaral ay nasa *very satisfactory*(VS) sa aspetong panteknikal at pamamahala samantalang *outstanding* (O) sa aspetong personalidad.
2. Sa ikalawang tangka ng pagtataya, ang antas ng performans ng mga gurong mag-aaral ay outstanding (O) na sa lahat ng aspetong panteknikal, personalidad at pamamahala.
3. Walang makabuluhang ugnayan ang kasarian at nahawakang baitang ng mga gurong mag-aaral sa antas ng kanilang performans sa pagtuturo bilang panggurong pagsasanay batay sa pangteknikal man, personalidad o pamamahala.
4. Walang makabuluhang pagkakaiba ang antas ng performans ng mga gurong mag-aaral sa pagtuturo batay sa personalidad sa una at ikalawang tangka ng pagtataya subalit mayroong makabukuhang pagkakaiba batay sa panteknikal at pamamahala.
5. Walang makabuluhang pagkakaiba ang kabuluhang impak dulot ng pagtuturo bilang panggruong pagsasanay ng mga gurong mag-aaral batay sa panteknikal, personalidad at pamamahala.

KONGKLUSYON

1. 1.Linang na linang ang kahusayan ng mga Gurong mag-aaral sa kakayahang pagtuturo dahil sa naipakitang performans at pag-unlad nito habang sa kanilang eksposyur ng pagsasanay.
2. Malaki ang impak o pakinabangng gawaing panggurong-pagsasanay sa pagpapayaman ng kakayahang pagtuturo sa aktwal o tunay na tagpo.
3. Ang angkop na pamantayan sa pag-eebalweyt ay kawastuan sa performans ang makakamit.

REKOMENDASYON

Batay sa natuklasan at nagabuong kongklusyon, inirekomenda;

1. Supervising teacher.Kung maaari nasa medyor ng Filipino ang siyang ebalweytors sa mga gurong mag-aaral na medyor din sa Filipino.
2. STASS Coordinators. Subukang gumamit ng angkop na Criteria sa pag-ebalweyt ng gurong nagsasanay na katumbas sa medyor nang kanilang kinabibilangan dahil bawat uri o medyor na asignaturang hawak nila ay magkanya-kanya competensis na linangin at akmang paraan o estartehiyang taglayin.

TALASANGGUNIAN

1. Tatto, M. T. (2006). Education reform and the global regulation of teachers' education, development and work: A cross-cultural analysis. *International Journal of Educational Research*, *45*(4), 231–241. https://doi.org/10.1016/j.ijer.2007.02.003;
2. Tabacbnick at Zeichmer (2016). The Impact of the Student Teaching Experience on the Development of Teacher Perspectives. SaGE journal: Journl of teacher educationCopyright © 2016 by American Association of Colleges for Teacher Education;
3. Gonong (2014). PATEF Seminar. Philippine National Research Center for Teacher Quality Philippine Normal University. Slides;
4. Agcaoili, C., & Oshihara, S. (2014). Teachers' pedagogy and conceptions of history: Decolonizing and Transforming History in Elementary. *The SIJ Transaction on Industrial, Financial and Business Management (IFBM)*, *2*(3), 87-94.
5. Armour (2016). The Application of Teacher Cognition in the Classroom: A new teaching competency. Journal of Research & Development in Education, Vol 22(3), 1989, 29-37. ©2016 American Psychological Association | PDF documents;
6. Badayos (2012). Metodolohiya sa Pagtuturo... PNU. Mutya Publishing House INC.;
7. Deguito (2013). Kakayahan ng mga Guro sa Epektibong Pagtuturo ng Wika at Panitikan sa Ingles at Filipino ng mga Paaralang Sekondarya, Distrito ng Tubod, surigao del Norte
8. CHED (2014). Handbook on typology, outcomes-based education, and institutional sustainability assessment. QC: CHED;
9. Oluwatayo and Adebule (2012). Assessment of Teaching Performance of Student-Teachers on Teaching Practice. International Education Studies Vol. 5, No. 5, October 2012; and
10. *Villafuerte at Bernades (2015), Pagtuturo sa Filipino: MgaTeorya at Praktica, Mutya Publishing Home Inc:Valenzuela City.*

Talahanayan 1. Propayl ng Tagatugon

Propayl	Frequency	Percent	Mode
Kasarian			
Lalaki	4	22.2	
Babae	14	77.8	Babae
Medyor			
Filipino	18	100	
Nahawakang Baitang			
Baitang 7	5	27.8	
Baitanag 8	6	33.3	
Baitang 9	8	44.4	Baitang 9 at 10

Talahanayan 2. Antas ng Performans sa Pagtuturo Batay sa Panteknikal

Panteknikal	Mean	SD	Deskripsyon
A1	3.46	0.51	Outstanding
A2	3.48	0.51	Outstanding
A3	3.38	0.62	Very Satisfactory
A4	3.22	0.73	Very Satisfactory
A5	3.39	0.70	Very Satisfactory
A6	3.46	0.62	Outstanding
A7	3.33	0.77	Very Satisfactory
A8	3.51	0.50	Outstanding
A9	3.31	0.78	Very Satisfactory
A10	3.51	0.61	Outstanding
Overall	**3.41**	**0.46**	**Very Satisfactory**

Talahanayan 3. Antas ng Performans sa Pagtuturo Batay sa Personalidad

Personalidad	Mean	SD	Deskripsyon
B1	3.78	0.43	Outstanding
B2	3.83	0.38	Outstanding
B3	3.72	0.57	Outstanding
B4	3.67	0.59	Outstanding
B5	3.67	0.49	Outstanding
B6	3.72	0.46	Outstanding
B7	3.56	0.70	Outstanding
B8	3.61	0.61	Outstanding
B9	3.72	0.46	Outstanding
B10	3.72	0.57	Outstanding
Overall	3.70	0.41	Outstanding

Talahanayan 4. Antas ng Performans sa Pagtuturo batay sa Pamamahala

Pamamahala	Mean	SD	Deskripsyon
C1	3.53	0.61	Outstanding
C2	3.33	0.69	Very Satisfactory
C3	3.51	0.51	Outstanding
C4	3.34	0.62	Very Satisfactory
C5	3.53	0.70	Outstanding
C6	3.46	0.62	Outstanding
C7	3.53	0.50	Outstanding

C8	3.34	0.78	Very Satisfactory
C9	3.46	0.51	Outstanding
C10	3.46	0.51	Outstanding
Overall	**3.44**	**0.48**	**Very Satisfactory**

Talahanayan 5. Antas ng Performans sa Pagtuturo batay sa Panteknikal sa Ikalawang Tangka

Panteknikal (after)	Mean	SD	Deskripsyon
A1	3.78	0.43	Outstanding
A2	3.89	0.32	Outstanding
A3	3.83	0.38	Outstanding
A4	3.61	0.61	Outstanding
A5	3.67	0.59	Outstanding
A6	3.67	0.49	Outstanding
A7	3.83	0.38	Outstanding
A8	3.72	0.46	Outstanding
A9	3.61	0.61	Outstanding
A10	3.89	0.32	Outstanding
Overall	3.75	0.31	Outstanding

Talahanayan 6.Antas ng Performans sa Pagtuturo batay sa Personalidad sa Ikalawang Tangka

Personalidad(after)	Mean	SD	Deskripsyon
B1	4	0	Outstanding
B2	3.83	0.38	Outstanding
B3	3.89	0.32	Outstanding
B4	3.89	0.32	Outstanding
B5	3.94	0.24	Outstanding
B6	3.72	0.46	Outstanding
B7	3.72	0.46	Outstanding
B8	3.67	0.49	Outstanding
B9	3.89	0.32	Outstanding
B10	3.78	0.43	Outstanding
Overall	**3.83**	**0.24**	**Outstanding**

Talahanayan 7. Antas ng Performans sa Pagtuturo batay sa Pamamahala sa Iaklawang Tangka

Pamamahala	Mean	SD	Deskripsyon
C1	3.89	0.32	Outstanding
C2	3.72	0.46	Outstanding
C3	3.83	0.38	Outstanding
C4	3.78	0.43	Outstanding
C5	3.83	0.38	Outstanding
C6	3.72	0.46	Outstanding
C7	3.78	0.43	Outstanding
C8	3.72	0.57	Outstanding
C9	3.89	0.32	Outstanding
C10	3.72	0.57	Outstanding
Overall	**3.79**	**0.31**	**Outstanding**

Talahanayan 8. Makabuluhang Kaugnayan ng Profayl ng mga gurong mag-aaral at ng antas ng kanilang performans sa pagtuturo bilang panggurong pagsasanay na Gawain (Pangkalahatan).

Factors	Wilks' Lambda Value	Error df	p-value	Decision on Ho	Iterpretation
Kasarian	0.867	11	0.651	Not Rejected	Not Significant
Medyor	1	12	------	Result Not Valid	
Nahawakang Baitang	0.723	11	0.293	Not Rejected	Not Significant
Asignaturang Ipinaturo	1	12	------	Result Not Valid	

Talahanayan 9. Makabuluhang Ugnayan ng Profayl ng mga gurong mag-aaral at ng antas ng kanilang performans sa pagtuturo bilang panggurong pagsasay na Gawain (bawat Baryabol)

Factors	Dependent Variable	df	F	p-value	Decision on Ho	Interpretation
Kasarian	Pangteknikal	1	0.017	0.899	Not Rejected	Not Significant
	Personalidad	1	0.332	0.574	Not Rejected	Not Significant
	Pamamahala	1	0	1	Not Rejected	Not Significant
Medyor	Pangteknikal	0	.	-----	Result Not Valid	
	Personalidad	0	.	-----	Result Not Valid	
	Pamamahala	0	.	-----	Result Not Valid	
Dami ng Nahawakang Baitang	Pangteknikal	1	0.017	0.899	Not Rejected	Not Significant
	Personalidad	1	0.148	0.707	Not Rejected	Not Significant
	Pamamahala	1	0.249	0.626	Not Rejected	Not Significant

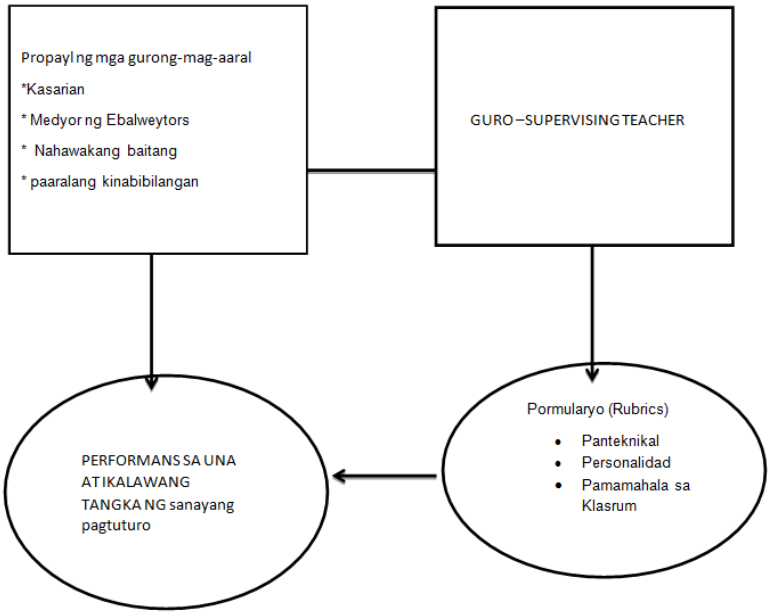
Dami ng Asignaturang ipinaturo	Pangteknikal	0	.	-----	Result Not Valid
	Personalidad	0	.	-----	Result Not Valid
	Pamamahala	0	.	-----	Result Not Valid

Talahanayan 10. Pagkakaiba ng Performans ng mga gurong mag-aaral sa Pagtuturong nagawa sa una at ikalawang tangka ng pagtataya

Baryabol(Una-Ikalawa)	Mean	t	df	p-value	Decision on Ho	Interpretation	Effect Size	Interpretation
Pangteknikal	-0.43	-3.31	17	0.004	Rejected	Significant	0.39	Moderate
Personalidad	-0.13	-1.59	17	0.129	Not Rejected	Not Significant		
Pamamahala	-0.35	-2.94	17	0.009	Rejected	Significant	0.34	Moderate

Talahanayan 11. Pagkakaiba ng antas ng Kabuluhang impak dulot ng panggurong pagsasanay na gawain batay sa performans-baryabol

Performans		Mean	t	df	p	Decision	Interpretation
Pangteknikal	Personalidad	-0.08	-1.74	17	0.101	Not Rejected	Not Significant
	Pamamahala	-0.04	-0.72	17	0.484	Not Rejected	Not Significant
Personalidad	Pamamahala	0.04	0.90	17	0.38	Not Rejected	Not Significant



Figyur 1. Paradima ng Pag-aaral

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RESEARCH ARTICLE

Corporate Social Responsibility : A Business Necessity in the Present Era

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ABSTRACT

Corporate Social Responsibility (CSR) and Sustainable development are interrelated. Indian Companies are implementing Corporate Social Responsibility (CSR) for generation of significant returns to their businesses. Reputed Companies have proved that they can make differentiate in Brand and reputation if they take responsibility for the well being of society and environment in their operational area for their operation. Corporate Social Responsibility is one of the most important factors for sustainable development. According to the Companies Act, 2013, private sector can contribute for the sustainable development and overall economic objective. India is the first country in the world to make corporate social responsibility mandatory. Companies should try to invest in CSR activities and to do their responsibility towards society, instead of only focusing on profit. This paper is focusing on the importance of CSR activities and the necessity of business entity to spend for corporate social responsibility.

Keywords: Corporate Social Responsibility, Economic objective, Sustainable development.

INTRODUCTION

Corporate social responsibility is very much essential for the sustainable development of any country. "Corporate Social Responsibility is the continuing commitment by business to behave ethically and contribute to economic development while improving the quality of life of the workforce and their families as well as of the local community and society at large"(world Business Council For Sustainable Development). A very famous quote is "Saving your wallet is not just the world". Companies have to think not only about their profit but also about the society. According to companies act a company has to spend 2% of its average net profit of the preceding 3 years on

Corporate social Responsibility if it had in any of those years net worth of Rs 500 crore or more, or turnover of Rs 1000 crore. Companies should do CSR activities for the sustainable development. It is now compulsory that if in any year the company is not used 2% of the average profit of previous 3 years that money should go to the escrow account which should be used only for CSR activities. And these funds should be used in next 3 years. If again there will be some remaining fund, it will go the specific government fund. If any company is not following these norms which are coming under CSR range then there can be a fine of Rs.50,000 to Rs 25 lakhs. Apart from financial penalties, there can be also 3 years imprisonment.

Objectives of the study

Against this backdrop, the present study focuses on the following objectives which are as follows:

- To understand how CSR is important for the development of the society
- To understand the necessity of business entity to spend for corporate social responsibility

Literature Review

Andrew et al (1989) have done their analysis to find the corporate social disclosure by using descriptive statistical method. They found that medium and large companies are making more social disclosure than small companies. Douglas and Christopher (1999) studied on environmental reporting standards. The reports issued by the companies and what they show in the website were very different. Belal (1999) done his research in Bangladesh. He found that most of the companies are making disclosure about the employees. Very few companies are only disclosing about environmental and ethical issues. Purushotahman, et al (2000)done their analysis in Singapore by taking different factors like environment, human resources, energy. They tried to find out the relationship between size of the company and CSR. They found that the companies doing economically good are good in corporate social reporting. Most of the companies disclose the human resources. Profit making award winning corporates were following most CSR practices. Porwal and Sharma (1991) found that private sector companies were disclosing more on environment and human resources. They also found that small companies are disclosing less than the larger companies. Agarwal (1992) studied on different social disclosure practice by taking 20 private and public sector companies in India. He has used content analysis and weights for the study. He found that most of the social information is in the director report as notes. And most of these reports are in non-quantitative description. Chander (1994) had done their analysis for a period of 1981 to 1985. He found that quality of CSR activities is better in public sector companies than private sector companies. Gupta (2007) studied on trends of corporate social responsibility in India. He found that CSR activities in India is increasing and also it is very important for India.

Research methodology

The study was conducted using secondary data and published reports from various sources. Secondary data were collected from related articles from refereed journals and blogs on CSR. It mostly applies a descriptive research analysis.

CSR: Sustainability aspects

Some of the sustainability aspects are

a. Governance and management,
b. Stakeholder engagement,
c. Environmental process improvement,
d. Environmental products and services,
e. Local economic development,
f. Community development, and
g. Human resource management

New CSR mandate is a platform through which companies can show their work and hence, can strategize and implement their jobs in a well-organized manner which will be a real time opportunity for the corporate bodies as well as the NGO's to work much harder. According to Chanda Kochhar, MD & CEO of ICICI Bank Limited Corporate Governance can be formed in to 3 R i.e., 'Robust, 'Responsible' and 'Relevant.' It is about the overall response to the society, the consumers, micro and macro environment, internal employees, regulators, government and stakeholders. It should create a culture within the organization to meet those responsibilities.

CSR in the times of recession

Most organizations today understand themselves as an important business and as an integral part of a bankruptcy strategy that, despite the slowdown and tight budgets where one would expect companies to slow down on such tasks and activities, many organizations have continued to drive their CSR projects with the same focus. And when the budget couldn't be increased accordingly, new alternatives helped. Every organization has the highest intelligence that when used properly it will produce results not only for its beneficiaries but also for the value addition of the business itself.

Green business is good business

India Inc has joined hands to do well with all its activities that fall under the CSR. In this regard, it has launched a global platform to showcase all the work done by Indian firms. The Confederation of India Industry (CII) and TVS Group have joined forces to form the CII-TVS Center of Excellence for Responsive Corporate Citizenship. It will provide consulting services and technical assistance to community development and CSR.

- Reliance Industries and two Tata Group firms - Tata Motors and Tata Steel - are the country's most respected companies for their social participation initiatives, according to a Nielsen study.
- The Indian paint industry makes its products environmentally friendly by choosing water-based paint and making it free of carcinogen.
- The heating, ventilation, air conditioning and refrigeration (HVAC) industry works to remove their 'global warming' shame by over-utilizing gases with zero ozone depletion possible (zero ODP).
- Sustainable Technologies and Environmental Projects Ltd (STEPS) plans to start a project to convert plastic, organic and electronic waste into petroleum without the usual hazardous wastes.

Rural Development

- ITC's e-Chaupal has been a positive developmental step and has added value to its agricultural products. It includes improving the lives of farmers and citizens.
- HDFC has embarked on a 'village adoption process' to improve investment status in Indian cities.
- Mahindra Shubhlabh, a division of the Mahindra & Mahindra agricultural business, intends to use selected seed mainly to produce contract farming products.

Today, companies place an emphasis on caring for and displaying empathy as a core asset and encouraging employees to demonstrate these qualities not only, in work situations but also in making a positive impact on society. CSR goes beyond just respecting the allegations and plays a very important role in the development of the organization as a whole. CSR efforts for trusted businesses can vary from lifestyle development, education, health and hygiene, environment, women empowerment, rural development to more. Most of the projects are done as internal projects while others are done in partnership with Government agencies or NGOs by providing direct financial assistance. Corporates also establish separate divisions dedicated to developing, directing and promoting the lives of net neutrals through various economic, educational and health sectors.

Business Capability to deliver

Friedman's argument that "there is one and only one social responsibility of business, that is to use its resources and engage in activities designed to increase its profits so long as it stays within the rules of the game, which is to say, engages in open and free competition, without deception or fraud.", was based on premises that: (1) the competitiveness will erode; (2) business has the fiduciary responsibility towards the shareholders; (3) managers may not be competent to engage in social issues; and (4) there is a possibility of usurpation of governments role. However, there are organizational differences between corporate and voluntary organizations. Voluntary organizations forms have evolved with specific societal objectives. From the objectives, antecedent conditions, structure & processes, it is evident that for-the profit and NGO organizations differ. The relationship of structural appropriateness for specific objective conditions could be a matter of evolution.

CSR and SME

Literature indicated that entrepreneurship create values. Entrepreneurship has an economic dimension as well as ethical dimension. SME sector success depends on factors like integrity, founder-entrepreneur's acumen and benevolent character. One study links entrepreneurship with social and environmental responsibility and higher degree of sustainability-orientation. The ethical values and CSR orientation becomes an integral part of entrepreneurship. The myriad of social issues could become innovation bed for entrepreneurs, thereby bridging the need-innovation gap. With respect to SMEs and its finding, it was indicated that; SMEs are motivated to be socially responsible by having learning for the staff, improved culture, reputation, productivity improvements, personal satisfaction and expansion of customer base. The conclave report, mentioned elsewhere in this article, indicated that the small firms have individuals' awareness about the business ethics, but when the firm grows it needs stringent control. The larger companies pay less attention to transparency of their Boards of Directors than the smaller companies. SMEs have in general low revenue and profitability in the initial few years, their ability to survive depends on factors above and beyond financial ones. Entrepreneurs come with altruistic motives as well. They attract a talent pool, which are similarly oriented. The employees of such organization have values and attitudes, as of a 'family'. Also, since they are small in size, the issues they address are mostly local. The intent and socio-economic context makes them an instrument of change in society. SMEs with less revenue and profitability may not be able to contribute financially for CSR, but they embody ethical business principles, values, care and concern for local issues which help them opportunity discovery, ensuing subsequent growth with a broad base.

Discussion on new firm formation, business model and contribution as offshoot from CSR

The CSR guideline and recent changes to companies act, will prod the companies to look for ways and means to be on the right side of the law, at the same time take advantage of the social marketing offered by CSR. Firms have gone to a level of core-competencies in their own business areas and have divested other areas as the part of strategy, it is a way traversed, and difficult to comeback. In the process of handling seemingly mismatched expectation from business from their core objective and structure, business houses would actively look for support. The support base would be for the ideas, execution, monitoring and reporting of CSR activities. Such support base would open up new vistas for new ventures and be a base for them. These processes in term will try to bring out efficiency in the service delivery processes of the social sectors. The networked service delivery process will build forward and backward linkage with different sectors of the economy.

CONCLUSION

Despite being pushed by different guidelines, law and public in general, the level of CSR spending by different companies have been much below a fair level of expectation. Possible arguments for such a discrepancy could be lack of intent, profit orientation, lack of clarity, or mismatch of the organizational structure to meet demands of new objectives. The main street and Wall Street can't be separated. If the captains of those financial companies, now in trouble or at the bank, had done well with the proper Social Responsibility plan, their ships would have been sunk

and not in the founding stages. Responsible business will be the new mantra. The contribution of CSR to sustainable development will be greatly reduced for those companies that remain committed to CSR values during the economic crisis will face a small degree of elimination of their impact of CSR activities on sustainable growth.

REFERENCES

1. Andrew, B.H., Gul, F.A., Guthrie, J.E. and Teoh, H.Y. (1989), "A note on corporate social disclosure practices in developing countries: the case of Malaysia and Singapore", British Accounting Review, Vol. 21, pp. 371-76.
2. Douglas B. and Christopher. C. S. (1999), "Corporate environmental reports: The need for standards and an environmental assurance service", Accounting horizons, Vol. 13, No. 2, pp. 129-145.
3. Belal, A.R., (1999), "Corporate Social Reporting in Bangladesh" Social and Environmental Accounting, Vol. 19, No. 1, pp. 8-12.
4. Belal, A.R., (2001), "Study of Corporate Social Disclosures in Bangladesh", Managerial Auditing Journal, Vol.16, No.5, pp. 274-289.
5. Carol A., and Zutshi A., (2004), "Corporate Social Responsibility" Australian Accounting Review, Vol 14, No. 3, pp. 31-39.
6. Porwal, L., and Sharma, N. (1991). "Social Responsibilty Disclosures by Indian Companies". The Chartered Accountants, Vol. XXXIX, No.8, pp.630-635.
7. Pratten, J. D., and Mashat, A. A. (2009) "Corporate social disclosure in Libya", Social Responsibility Journal, Vol. 5 No. 3, pp.311 – 327
8. Purushotahman, M., Phil, H. and Ross T., (2000), "Determinants of Corporate Social Reporting Practices of Listed Singapore Companies" An Accounting Review, pp. 101.
9. Porwal, L., and Sharma, N. (1991). "Social Responsibilty Disclosures by Indian Companies". The Chartered Accountants, Vol. XXXIX, No.8, pp.630-635.
10. Agarwal, R., (1992), "Corporate Social Information Disclosure- A Comparative Study" Effective management, pp. 76-85.
11. Chander, S., (1994), "A Study of Perceived Significance of Social Responsibility Information (SRI)" Journal of Accounting and Finance, Vol. VIII, No.1, pp. 67-77.
1. 12. Vasal, V., (1995), "A Spatio- Temporal Analysis on Social Reporting by Companies- Evidence from Indian public sector", Journal of Accounting and Finance, Vol. IX, No. 2, pp. 256-69
12. Carol-Ann, Sirsly, T. and Kai lamertz. (2008), "When does a Corporate Social Responsibility initiative provide a first mover advantage"? Business and society, pp. 343-369.
13. Carroll AB, Shabana KM (2010). The business case for corporate social responsibility: a review of concepts, research and practice. International Journal of Management Reviews; Vol. 12, Issue 1:85–105.
14. Batra, G.S., (1996), "Dynamics of social auditing in corporate enterprises: A study of the Indian corporate sector" Managerial Auditing Journal-Bradford, Vol. 11, No.2, pp.36-45.
15. Milne, Markus J., and Chan, C.C. Christian., (1999), "Narrative Corporate Social Disclosures: How Much of a Difference does They Make to Investment Decision Making"? Review, Volume, 1999, pp. 439-457.
16. Hegde, P., and Bloom, (1997), "Social financial reporting in India: A Case" The International Journal of Accounting, Vol. 32, No.2, pp. 155-172.
17. Gupta A. D. (2007), "Social Responsibility in India towards Global Compact Approach" International Journal of Social Economics, Vol. 34, No.9, pp. 637-663.
18. Chowdhary, V., and Wang, J., (2007), "Corporate Social Responsibility on Internet- a Case study of top 100 Information Companies In India" Management Quarterly Journal, Vol. 21 No.2, pp. 232-247.

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RESEARCH ARTICLE

Instrumentation Training of Students in Surigao State College of Technology and the Needs of Industries

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ABSTRACT

The knowledge and skills in the instrumentation of the students in AIT, BTTE, BSIT, and Engineering specializing electronics and electrical and their teachers teaching in electronics and electrical were investigated, using descriptive-inferential design, and researcher-made survey instrument in gathering data. The frequency count, percent, mean or mode, ordinal rank, one-way analysis of variance, and correlation coefficient were the statistical tools used to answer the problems. Whereby, null hypothesis was tested at a 5% margin of error. Findings showcase that the students has different levels of knowledge and skills in instrumentation by the factors of curriculum and specialization, of which they rated as having poorly trained in instrumentation. The instructors also claimed that they were less knowledgeable and skilled in the instrumentation. The industrial workers also claimed that the skills training on the aspects under study was highly needed in the instrumentation departments of the industries. By the factors of their highest educational attainment, departments, years of experience in the industry, and geographic location of the industrial worker they rated high in knowledge and skills in instrumentation. The results of the study suggest that school authorities may broaden their awareness on the relevance of the instrumentation related training in providing greater employment opportunities for the students; and to provide laboratory equipment, training, and seminars to the students and teachers. Exposure to industries on instrumentation processes is also desired to form part of the student training.

Keywords: Instrumentation, electronics, electrical, teaching-electronics, and technological industries

INTRODUCTION

Along with these eventualities in industries, the present industrialization comprises vast knowledge in technology especially in the field of instrumentation and control [(Cruz, Pillas, Castillo & Hernandez, 2012); (Leonardo, 2005); (Raufaste, 1977); (Fellenius, Altaee, Kulesza & Hayes, 1999); (Puga, 1982); (Marciano Jr, et.al, 2011); Bell, D. A. (2011);

(Parr, et.al, 1991); (Bankoff, 2007)]. Instrumentation works play a vital role in the industry; they maintain the whole system processing and monitor the health of the process, repair the system process of industry and innovation of the technology for more productive output and expand the life span of the industry [(Luk et.al, 2005); (Havskov & Alguacil, 2004); (Cotrel, Dubousset & Guillaumat, 1988); (Morris, 2001); Romani, Williamson & Kaufman, 1982); (Cantrill, Shapiro & Leventhal, 2004); (Fritschen & Gay, 2012); (Bos, Forbes & Veldman, 1997); (Braun, et.al, 2000)]. As observed this era needs more skilled work force to maneuver instrumentation and control to some industrial plants and manufacturing establishment both in local and abroad. However, noticed that only few has the knowledge and skills. Thus, schools and training centers should offers courses mainly in the field of instrumentation and control. For these reasons, the researcher was challenged to conduct this kind of investigation as to how the students are trained along with instrumentation and whether this training fit, to the industrial market, and the demand requirements.

METHODOLOGY

Research Design

The descriptive-inferential design was adopted in the study. The descriptive was employed to determine the profile of the respondents concerning the profiled factors. It used the inferential to draw general conclusions about the instrumentation training and needs from the selected samples of respondents. As to method, it used the survey through the research instruments distributed to the respondents for the needed data. It also involved the collection and analysis of data to test the hypothesis and answer questions on the presence or absence of a significant difference in the ratings of the respondents [(Abt, 1987); (Al-Aufi, & Al-Azri, 2013); (Vîslă, Grosse Holtforth & David, 2015)].

Population and Sample of Respondents

The respondents of this study were the 69 out of 80 Engineers/Technicians of Pacific Cement Corporation and 20 out 30 Instructors/ Guest Lecturers of Surigao State College of Technology and 151 of 200 Graduating Students in Associate Major in Electrical, Electronics, Engineering (ECE, EE, CoE), and the BTTE/BSIT Major in Electronics and Electrical. The Engineers and Technicians participants were those who are inclined with the Instrumentation and Control in the manufacturing industry like the Electrical Engineering Department, Mechanical Engineering Department, Production Department, Quality Assurance Department Safety Department, and Instrumentation Department. The Instructors and Guest Lecturers participants were those who conduct classes and training in Electronics Technology, Mechanical Technology, Electrical Technology, Electronics Engineering, Computer Engineering, and Electrical Engineering of Surigao State College of Technology. The minimum sample size will be determined using the 50% + 1 of the population targeted for the study. The distributions of participants are shown in Table 1.

Research Instrument

The researcher made use of the three sets of the researcher-made questionnaire to ensure the validity of the data gathered. The survey instruments for the Instrumentation Technicians, Instructor/Guest Lecturer, and Students contained two parts. Part 1 solicited information on the curriculum and specialization. Part 2 delved into the extent of the students learning and understanding of instrumentation and control in terms of their knowledge and skills. The reliability of this instrument was established using the run-rerun method and the application of the Spearman Rank correlation coefficient. For the Instructors/Guest Lecturer respondents asked the highest educational attainment, academic rank, and baccalaureate degree. Part 2 delved into the extent of knowledge and skills in the field of instrumentation and control. For the Instrumentation Technician respondents, Part 1 asked information on the highest educational attainment, position, number of years at work, and geographic locations. Part 2 delved into the extent of the knowledge and skills in the field of instrumentation and control training.

Validity

Drafted questionnaire was presented for improvement during the pre-oral examination for their further comments and suggestions of the panel members, revision was made and presented for their approval, test-run was made to the sample of targeted respondents for their comments. The test-run respondents did not give or raise clarification on the items in the questionnaire thus testing for reliability was made.

Reliability

The reliability of the instrument was established using the run-rerun method. The researcher selected a few samples from the population to answer the questionnaires and after the first administration, another set but the same copies were distributed to the same respondents and their answers were analyzed and interpreted. The Pearson Product Moment Correlation coefficients in these tests ranged from 0.685 to 0.821, sufficient to mean that the questionnaires are highly reliable for the study.

Ethics and Data Gathering Procedure

Formal letters were personally given to the College President of Surigao State College of Technology and noted by the Dean of Programs and Standards, to the respective Chairs of the different divisions of the College involved in the data gathering, and to the Head of the Engineering Divisions of Pacific Cement Corporation and to their respective departments down to technicians and control supervisor. These letters were to request permission for the survey. After granted the permission the researcher immediately distributed the survey instruments to the targeted respondents with the help of colleagues and friends. When the answered questionnaires were retrieved, the analyses and interpretation of the data were immediately made using statistical methods.

Data Analysis

The responses to each item were tallied and given equivalent qualitative description as indicated. The data collected were analyzed, and interpreted with the use of the following statistical tools

Frequency Count

This tool was used to determine the profile of the students as to their curriculum and specialization; for the teacher respondents in terms of their highest educational attainment, academic rank, number of years in teaching and baccalaureate degree; and also for instrumentation technician respondents as to their highest educational attainment, position, number of years at work, geographic location.

Weighted Mean

This tool was used to determine the extent of the respondent training in the field of instrumentation and control in terms of knowledge and skills.

One-way Analysis of Variance (ANOVA)

This tool was used to determine the significant difference in the level of knowledge and skills in the field of instrumentation and control between and among the students, instructors, and instrumentation technicians; and between and among their respective factors (Bewick, Cheek & Ball, 2004).

Scheffé Posteriori Test

This was used to specifically determine the existence of the significant difference established
by the ANOVA among 3 or more variables. It was not used in a factor with only 2 variables [(Boik, 1979); (Delph, 2004); (Deloire- Grassin, et.al, 2000).

RESULTS AND DISCUSSION

Curriculum

Of the four (4) different curricula, AIT got the highest number of students with a frequency of 53 or 35.10% which indicated the most numbered graduating students. It was succeeded by the Engineering with a frequency of 38 or 25.17%, then followed by the BSIT with a frequency of 34 or 22.52% and the least was the BTTE with only 26 or 17.22%.

Specialization

Based on findings the Electrical course got the highest number of students with a frequency of 59 or 39.07%, followed by Electronics with only have 53 or 35.10%. The engineering, specifically Computer Engineering, got only 14 or 9.27% followed by Electronics Engineering with 13 or 8.61% and the least was in Electrical Engineers with 12 or 7.95% Electrical Engineering

Profile of the faculty respondents

Highest Educational Attainment

Most of the faculty members are only BS Graduates and full-fledged Masters with equal frequencies of 8 or 40% respectively. They were followed by faculty with units earned in masters with a frequency of 3 or 15% and the lowest was only 1 or 5% for a full-fledged doctorate. The study reveals the concept that most of the instructors who are teaching the fields of Electrical, Electronics, and Engineering EE/CoE/ECE are BS graduates and are also full-fledged masters.

Academic Rank

Analyzing the same Table, the most number of faculty members Electrical, Electronics, Engineering EE/CoE/ECE are Guest Lecturers with a frequency of 11 or 55% followed by Instructors with only 6 or 30%, and the least were those with the rank of Assistant Professor with just 3 or 15% frequency. The data shows that there are more Guest Lecturers than permanent teachers who teach Electrical, Electronics, and Engineering courses on EE/CoE/ECE. This implies that there are more tendencies of inconsistencies in the teaching standards of the engineering program and for turnovers. This is due to no permanency of faculty members to include the inconsistency of instructional standards.

Baccalaureate Degree

Referring to the same Table, the most number of teachers who handled the Electrical, Electronics, Engineering courses of EE/CoE/ECE are 5-year degree holders with a frequency of 11 or 55% and there were only a few faculty with 4-year degree courses with a frequency of 9 or 45%.

Profile of Instrumentation Technicians

Highest Educational Attainment

Most of the instrumentation technicians were BS graduates with a frequency of 66 or 95% followed by a few instrumentation technicians who were BS with units in Masters with a frequency of 2 or 2.90% and only 1 or 1.45% instrumentation technicians with a full-fledged Masters. This marks the idea that a BS graduate is a minimum requirement in working in the industrial instrumentation department. It also suggests that the graduates in Surigao State College of Technology in at least degree programs with sufficient instrumentation training have the advantage for employment in industries.

Department

Of the six(6) identified industrial departments in the study, the Electrical department was the most numbered with a frequency of 50 or 72.46%, followed by the Production department with 6 or 8.70%, then the Mechanical department with 5 or 7.25%, and the Safety department with 4 or 5.80%. The instrumentation department marks as "others" had 3 or 4.35% and the last was the Quality Assurance department with a frequency of 1 or 1.45%. The finding suggests that Electrical knowledge is given the highest importance in the maintenance and monitoring of the whole industry. They play a vital role in industrial processes, especially in instrumentation and control. Hence, instrumentation training is necessary for these electrical and electronics related courses.

Years of Industrial Experience

Most of the instrumentation technicians are working 2 years below in the industry with a frequency of 36 or 52.17%, seconded by instrumentation technicians who rendered service 5 to 6 years with a frequency of 15 or 21.74%, followed by instrumentation technicians who served for 3 to 4 years with a frequency of 12 or 17.39%. Only a few of the instrumentation technicians served the industry for 7 years and above, with a frequency of 6 or 8.70%. This finding suggests that most of the instrumentation technicians are newly hired. It also implies that after their experiences in local industries they opt to venture on working in other bigger industries in the locality and abroad.

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Geographic Location

A significant number of instrumentation technicians are based in the Philippines with a frequency of 68 or 98.55% and only 1 or 1.45% abroad. This indicates that there are also a lot of employment opportunities available in the Philippines where they could apply their knowledge related to instrumentation and control.

Instrumentation Training of Students

Students Ratings

Curriculum

Based on findings that for BTTE students, the highest training was on skills training in instrumentation application with the mean of 2.59 and marked high, followed by the mean of 2.09 on knowledge on control system described as low. The lowest was on training them the knowledge on measuring devices with a mean of 1.95 rated as low. The grand mean of 2.17 suggests that the BTTE students were less trained by their instructors on instrumentation. The students in AIT rated the highest on training them the skills in instrumentation application with the mean of 2.26 which is marked low, followed by the mean of 1.81 on the skills in using the test equipment described as low. The lowest was on knowledge in the control system with a mean of 1.52 rated as low. The grand mean of 1.78 suggests that the AIT students were less trained by their instructors on instrumentation by reason that this topic was not yet included for instruction during the conduct of the study. The students of BSIT rated the highest on skills in instrumentation application with the mean of 3.12 which is marked high, followed by the mean of 2.34 on the skills in using test equipment described as low. The lowest was on knowledge on the control system with the mean of 1.49 rated as not applicable. The grand mean of 2.13 suggests that the BSIT students were less trained by their instructors on instrumentation. The students in Engineering rated the highest on knowledge on measuring devices with the mean of 2.23 which is marked low, followed by the mean of 2.22 on the skills in instrumentation application

described as low. The lowest was on knowledge on the control system with the mean of 2.06 rated as low. The grand mean of 2.17 suggests that the Engineering students were less trained by their instructors on instrumentation. Among the four different curricula, the AIT students rated the lowest in the field of instrumentation. It was found out that during the distribution of questionnaires the students were not aware of the course in the field of instrumentation skills because the course was scheduled late second semester and it was early second semester the survey was conducted thus they rated low in the knowledge and training in instrumentation. Also, only the BTTE and BSIT were highly skilled in instrumentation applications.

Specialization

Findings showcase that the data on every specialization that for students who are majored in Electronics the highest training was on skills in instrumentation application with the mean of 2.61 and mark high, followed by the mean of 1.98 on the skill in using test equipment described as low. The lowest was on the knowledge on the control system with the mean of 1.35 rated as not applicable. The grand mean of 1.85 suggests that the students who are major in Electronics were less trained by their instructors on instrumentation. The data revealed that the students who were specializing in electronics were less trained in instrumentation due to the lack of training facilities and laboratory apparatuses. The students who were majors in Electrical rated the highest training on skills in instrumentation application with the mean of 2.57 and marked high, followed by the mean of 2.07 on the skill in using test equipment described as low. The lowest was on the knowledge on measuring devices with a mean of 1.79 rated as low. The grand mean of 2.07 suggests that the students who are major in Electrical were less trained by their instructors on instrumentation. The students who are major in Electronics Engineering rated the highest training on knowledge on measuring devices with a mean of 2.53 and marked high, followed by the mean of 2.46 on the skill in instrumentation application described as low. The lowest was on the knowledge on the control system with a mean of 1.78 rated as low. The grand mean of 2.29 suggests that the students who are majors in Electronics Engineering were less trained by their instructors on instrumentation. The students who are major in Electrical Engineering rated the highest training on the knowledge on measuring devices with a mean of 2.37 and marked low, followed by the mean of 2.08 on the skill in using test equipment described as low. The lowest was on the skills in instrumentation application with the mean of 2.04 rated as low. The grand mean of 2.14 suggests that the students who are majors in Electrical Engineering were less trained by their instructors on instrumentation. The students who were major in Computer Engineering rated the highest training was on the knowledge on the control system with a mean of 2.36 and marked low, followed by the mean of 2.20 on the skill in instrumentation application described as low. The lowest was on the knowledge on measuring devices with a mean of 1.82 rated as low. The grand mean of 2.11 suggests that the students who are majors in Computer Engineering were less trained by their instructors on instrumentation. In synthesis, the data collected reflected the information that the electronics engineering students were better trained among others, and the electronics were poorly trained by their instructors in instrumentation.

Teachers Ratings in Instrumentation Training

Highest Educational Attainment

Findings shows that the BS Graduates only teachers claimed the highest to teach the skills in instrumentation application with the mean of 2.67 and marked high, followed by the mean of 2.64 on the skills in using test equipment described as high. The lowest was on the knowledge of their teaching the knowledge on measuring devices with the mean of 2.21rated as low. The grand mean of 2.49 and described as less denotes that the teachers who are BS graduates only are insufficient in training their students on instrumentation and control to the students. The teachers/instructors who were BS with units in Master rated the highest to indicate that they are capable to teach on skills using test equipment with a mean of 2.67 and marked high, followed by the mean of 2.50 on the skills in instrumentation application described as high. The lowest was on the knowledge on the control system with the mean of 2.11 rated as low. The grand mean of 2.45 suggests that the teachers/instructors who were BS with units in Master were less knowledgeable in teaching instrumentation and control to the students. The teachers who were full-fledged Masters rated the highest being capable to teach on the skills in instrumentation application with the mean of

2.31, marked low, and followed by the mean of 2.05 on the skills in using test equipment described as low. The lowest was on the knowledge on measuring devices with a mean of 1.80 rated as low. The grand mean of 2.03 suggests that the teachers who were full-fledged Masters were less knowledgeable in teaching instrumentation and control. The teachers who were full-fledged Doctorate rated the highest being capable to teach the skills using the test equipment with the mean of 3.14 marked high, followed by the mean of 3.00 on the knowledge on measuring devices and described as high. The lowest was on the knowledge on the control system with a mean of 2.67, rated as high. The grand mean of 2.91 shows that the teachers who are full-fledged Doctors are extending much of their knowledge in teaching instrumentation and control to the students.

Academic Rank

Based on results the academic rank of a teacher in terms of their academic ranks. The Assistant Professors rated the highest on skills in instrumentation application with the mean of 2.39 and marked low, followed by the mean of 2.05 on skill in using test equipment described as low. The lowest was on their teaching their students on the knowledge of measuring devices with a mean of 1.43 rated as not applicable. The grand mean of 1.95 suggests that the teachers who are Assistant professors lack the necessary competence in sharing knowledge in the field of instrumentation and control. The teachers with the academic rank of Instructor rated the highest in training the students on skills in instrumentation application with the mean of 2.08 though marked low and followed by the mean of 2.05 on the skill in using test equipment described as low. The lowest was the training of their students the knowledge on control system with the mean of 1.78 rated as low. The grand mean of 1.95 suggests that the teachers with the academic rank of Instructors need to improve their focus of teaching their students the knowledge on instrumentation and control. The teachers who are only lecturers rated the highest they are knowledgeable was on skills in instrumentation application with the mean of 2.77 which is marked high, followed by the mean of 2.75 on the skill in using test equipment described as high. The lowest was their less understanding of the knowledge on measuring devices with a mean of 2.47 rated as low. The grand mean of 2.62 shows that the teachers who are lecturers were more knowledgeable in the field of instrumentation and control. Briefly, the data shows that the academic ranks of the teacher, the lecturers are more updated in instrumentation training thus they were effective in teaching instrumentation. It shows that the teacher with the academic rank of assistant professor and instructor were less knowledgeable in instrumentation training.

Baccalaureate Degree

Results revealed that for teachers/instructors who graduated with five years BS, the highest instrumentation training they undergo was on skill in using test equipment and marked low, followed by the mean of 2.32 on skills in instrumentation application described as low. The lowest was on training them the knowledge on measuring devices with a mean of 1.96 rated as low. The grand mean of 2.17 suggests that the teachers/instructors who graduated with five years BS were less trained in the field of instrumentation and control. The teachers/instructors who graduated with four years BS, the highest instrumentation training they undergo was on skills in instrumentation application and marked high, followed by the mean of 2.56 on skill in using test equipment described as high. The lowest was on training them the knowledge on measuring devices with a mean of 2.35 rated as low. The grand mean of 2.50 suggests that the teachers/instructors who graduated with only four years BS were less trained in the field of instrumentation and control. In the analysis, the four (4) year baccalaureate degrees of the teacher are more skilled and knowledgeable in the instrumentation and control system.

Industrial Needs of Instrumentation Skills

Highest Educational Attainment

Those with BS only rated the highest need on skills in instrumentation application with a mean of 3.76 and marked very high, followed by the mean of 3.59 on the skill in using test equipment described as very high. The item which they were more likely knowledgeable and competent was the knowledge on the control system with the mean of 2.60, rated as high. The grand mean of 3.35 suggests that the instrumentation technicians who are BS only were more

Knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians who are BS with units in Masters rated the highest to indicate that they are knowledgeable and competent was on skills in instrumentation application with the mean of 3.67 and marked very high, followed by the mean of 3.36 on the skill in using test equipment described as high. The lowest item to entail that they are knowledgeable and competent was knowledge on measuring devices with the mean of 3.00 rated as high. The grand mean of 3.28 suggests that the instrumentation technicians who are BS with units in Masters were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians who are full-fledged Master degree holders rated the highest need on the knowledge on the control system with a mean of 4.00 and marked very high. The lowest was on the knowledge on measuring devices, skills in using test equipment, and skills in instrumentation application with equal means of 3.00 respectively, rated as high. The grand mean of 3.25 suggests that the industrial workers who are fullfledged Master holders were more knowledgeable and competent to evaluate the needed knowledge and skills in the field of instrumentation and control systems. Concisely, the data shows that the BS only instrumentation technicians were more active and skilled in instrumentation training and shows that the BS was the minimum requirement in the industry. It also shows that most of the full-fledged master instrumentation technicians were less knowledgeable in instrumentation.

By Department

The data showed that different department in the industry and to what extent are their knowledge and competence in the field of instrumentation and control, the instrumentation technicians who belong to the Electrical department rated the highest to indicate that they were knowledgeable and competent was on skills in instrumentation application with the mean of 3.88 and marked very high, followed by the mean 3.75 on skill in using test equipment rated as very high. The lowest that they are knowledgeable and competent was the knowledge on the control system with the mean of 2.53 described as high. The grand mean of 3.44 suggests that the industrial workers who belong to the Electrical department were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians in the Mechanical department claimed the highest need for skills in instrumentation application with a mean of 3.23 and marked high. The lowest that they were knowledgeable and competent was knowledge on measuring devices, knowledge on the control system, and skill in using test equipment with the mean of 2.97 respectively rated as high. The grand mean of 3.03 suggests that the instrumentation technicians who belong to the mechanical department were more knowledgeable and competent in the field of instrumentation and control.

The instrumentation technicians who belonged to the Production department rated the highest need on skills in instrumentation application with a mean of 3.47 and marked high, followed by the mean of 3.05 on skill in using test equipment described as high. The lowest that they were knowledgeable and competent was knowledge on the control system with the mean of 2.61 rated as high. The grand mean of 3.02 suggests that the instrumentation technicians who belong to the Production department were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians who belonged to the Quality Assurance department rated the highest to entail that they were knowledgeable and competent was on skills in instrumentation application with the mean of 3.17 and marked high, followed by the mean of 2.67 on knowledge on control system described as high. The lowest that they were knowledgeable and competent was on skill in using test equipment with the mean of 2.00 rated as low. The grand mean of 2.58 suggests that the instrumentation technicians who belonged to the Quality Assurance department were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians who belonged to the Safety department rated the highest to indicate that they were knowledgeable and competent was on skills in instrumentation application with the mean of 3.50 and marked very high, followed by the mean of 3.46 on knowledge in measuring devices describe as high. The lowest that they were knowledgeable and competent was knowledge on the control system with the mean of 3.04 rated as high. The grand mean of 3.35 suggests that the instrumentation technicians who belong to the Safety department were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians who belonged to other departments rated the highest they were knowledgeable and competent was on skills in instrumentat ion application with the mean of 3.44 and marked high, followed by the mean of 3.39 on knowledge in control system described as high. The lowest that they were knowledgeable and competent was knowledge on

measuring devices with a mean of 2.94 rated as high. The grand mean of 3.28 suggests that the instrumentation technicians who belonged to other departments were more knowledgeable and competent in the field of instrumentation and control. Briefly, the data revealed that among different departments in the industry, the Electrical departments were more concerned in the instrumentation training. The Quality Assurance department rated less aware of instrumentation.

Years of Industrial Experience

It is revealed that for instrumentation technicians with 2 years and below claimed the highest training needs knowledge and competence in instrumentation and control was on skills in instrumentation application with the mean of 3.88 and marked very high, followed by the mean of 3.73 on skill in using test equipment describe as very high. The lowest that they were knowledgeable and competent was knowledge on the control system with the mean of 2.21 rated as low. The grand mean of 3.39 suggests that the instrumentation technicians who are 2 years below experience were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians with 3 to 4 years of experience rated the highest in training the students on skills in instrumentation application with a mean of 3.72 and marked very high, followed by the mean of 3.33 on skills using test equipment described as high. The lowest that they were knowledgeable and competent was knowledge on the control system with the mean of 2.94 rated as high. The grand mean of 3.26 suggests that the instrumentation technicians with 3-4 years' experience were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians with 5 to 6 years' experience rated the highest they were knowledgeable and competent was on skills in instrumentation application with the mean of 3.56 and marked very high, followed by the mean of 3.49 on skills using test equipment describe as high. The lowest that they were knowledgeable and competent was knowledge on the control system with the mean of 3.14 rated as high. The grand mean of 3.36 suggests that the instrumentation technicians with 5-6 years' experience were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians with or experience of 7 years above rated the highest that they were knowledgeable and competent was on skills in instrumentation application with the mean of 3.72 and marked high, followed by the mean of 3.31 on knowledge in control system described as high. The lowest that they were knowledgeable and competent was the knowledge on measuring devices with a mean of 3.08 rated as high. The grand mean of 3.29 suggests that the instrumentation technicians with 7 years above experience were more knowledgeable and competent in the field of instrumentation and control. In a concise statement, the data prove that the 2 years and below experience in the industry of instrumentation technicians are actively trained in instrumentation training, also the instrumentation technicians with 3 to 4 years of industrial experience-rated poorly trained in instrumentation.

Geographic Location

Based on the ratings of instrumentation technicians on the extent these training aspects are needed in the instrumentation departments of industries. The data showed that those who worked in the Philippines, the highest knowledge and competence in instrumentation and control was on skills in instrumentation application with a mean of 3.75 and marked very high, followed by the mean of 3.58 on skill in using test equipment described as very high. The lowest that they were knowledgeable and competent was the knowledge on the control system with the mean of 2.64 rated as high. The grand mean of 3.35 suggests that the instrumentation technicians who worked in the Philippines were more knowledgeable and competent in the field of instrumentation and control. The instrumentation technicians who worked abroad rated the highest that they were knowledgeable and competent was the knowledge on measuring devices with the mean of 3.50 and marked very high, followed by the mean of 3.33 on skills in instrumentation application described as high. The lowest that they were knowledgeable and competent was the knowledge on the control system with the mean of 2.50 rated as high. The grand mean of 3.12 suggests that the instrumentation technicians who worked abroad were more knowledgeable and competent in the field of instrumentation and control. Precisely, the data shows that there were many opportunities in the Philippines in instrumentation compared to working abroad.

The difference in the Ratings of the Respondents

The difference in Student Ratings

The statistical data shows that the bases for analyzing the data to test the null hypothesis that there is no significant difference in the ratings of the student-respondents in the instrumentation and control specific to the knowledge on measuring devices, knowledge in the control system, skills in using test equipment and skills in instrumentation application by the factors of curriculum and specialization. It shows that the bases for analyses on determining the presence of significant differences in the ratings of the students concerning factors included in the study. The data showed that the students training on the knowledge on measuring devices, knowledge on the control system, skills in using test equipment, and skill in instrumentation application were significantly affected by the factors of curriculum and specialization because each of the computed F-values exceeded each required critical value.

Knowledge in Measuring Devices

The Scheffé data showed the reasons that there is a significant difference in the knowledge on measuring devices of the students by the factors of curriculum and specialization. The computed F-values under the curriculum between AIT students and BSIT students exceeded the expected critical F-value of 8.01 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. Referring to Table 3, BSIT students rated their skills training in the knowledge on measuring devices with the mean of 1.58 was higher than AIT students with only 1.54 mean value, meaning BSIT students were significantly knowledgeable and well trained in the knowledge on measuring devices than to those AIT students.Also, the computed F-values under the curriculum between BSIT students and Engineering students exceeded the expected critical F-value of 8.01 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring back to Table 3, the Engineering students rated their knowledge on measuring devices with a mean of 2.23 which was higher than BSIT students with only 1.58 mean value, meaning Engineering students were significantly knowledgeable and well trained in knowledge on measuring devices than the BSIT students. Precisely, by the curriculum, the AIT and BSIT were significantly different in the knowledge in measuring devices in the sense that the BSIT offers programs related to the instrumentation but not in the AIT. Also, the BSIT and Engineering students significantly differed in their knowledge of measuring devices such that the engineering was insufficient instrumentation equipment than the BSIT. The computed F-values under the specialization between students who were majors in Electronics and students who were major in Electrical exceeded the expected critical F-value of 9.72 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring to Table 4, students who are major in Electrical rated their knowledge on measuring devices with the mean value of 1.79 were higher than students who are major in Electronics withonly 1.47 mean value, meaning students who were major in Electrical were significantly knowledgeable and well trained in knowledge on measuring devices than those students who are major in Electronics.

Moreover, the computed F-values under the specialization between students who are major in Electronics and the major in Electronics Engineering exceeded the expected critical F-value of 9.72 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Students who are majors in Electronics Engineering rated their knowledge on measuring devices with the mean value of 2.53 were higher than students who are majors in Electronics with only 1.47 mean values. This means that students who are major in Electronics Engineering were significantly knowledgeable and well trained in knowledge on measuring devices than those students who are major in Electronics. The computed F-values under the specialization between students who are major in Electronics and students who are major in Electrical Engineering exceeded the expected critical F-value of 9.72 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Students who are major in Electrical Engineering rated their knowledge on measuring devices with the mean value of 2.37 were higher than students who are majors in Electronics with only 1.47 mean value, meaning students who are majors in Electrical Engineering were significantly knowledgeable and well-trained in knowledge on measuring devices than to those students who are major in Electronics. Concisely, the data revealed that in specialization, Electronics were different among the

Electrical, Electronics Engineering, and Electrical Engineering in the knowledge on measuring devices in the sense that based on the prospectus they differ in subjects.

Knowledge in Control System

The Scheffé data has the bases for the existence of significant differences along with the knowledge in the control system of the students by the factors of curriculum and specialization. The computed F-values under the curriculum between BTTE students and AIT students exceeded the expected critical F-value of 8.01 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring back to Table 3, BTTE students rated their skills training in the knowledge in control system with the mean of 2.09 was higher than AIT students with only 1.52 mean value, meaning BTTEstudents were significantly knowledgeable and well trained in the knowledge in control system than to those AIT students. The computed F-values under the curriculum between AIT students and BSIT students exceeded the expected critical F-value of 8.01 at a 5% margin of error and thus led to the rejection of the respective null hypotheses. A review of Table 3, AIT students rated their knowledge in the control system with the mean of 1.52 were higher than BSIT students with only 1.52 mean value, meaning AIT students were significantly knowledgeable and well trained on the knowledge in the control system than to those BSIT students. By curriculum, the AIT and BSIT were significantly different on the knowledge in the control system in the sense that the BSIT offers a program in related to instrumentation while the AIT was none, also the BTTE and AIT differ their knowledge control system such that the AIT was insufficient instrumentation equipment than the BTTE.

The computed F-values under the specialization between students who are major in Electronics and the major in Electrical exceeded the expected critical F-value of 9.72 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. Students who are major in Electrical rated their knowledge on control system with the mean value of 1.85 were higher than students who are major in Electronics with only 1.35 mean value, meaning students who are major in Electrical were significantly knowledgeable and well trained in knowledge on control system than to those students who are major in Electronics. Also, the computed F-values under the specialization between students who are major in Electronics and the major in Electronics Engineering exceeded the expected critical F-value of 9.72 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. Referring to Students who are major in Electronics Engineering rated their knowledge on control system with the mean value of 1.78 were higher than students who are major in Electronics with only 1.35 mean value, meaning students who are major in Electronics Engineering were significantly knowledgeable and well trained in knowledge on control system than to those students who are major in Electronics. Also, the computed F-values under the specialization between students who are major in Electronics and Computer Engineeringexceeded the expected critical F-value of 9.72 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring to Table 4, students who are major in Computer Engineering rated their knowledge on control system with the mean value of 2.37 were higher than students who are major in Electronics with only 1.35 mean value, meaning students who are major in Computer Engineering were significantly knowledgeable and well trained in knowledge on control system than to those students who are major in Electronics. Briefly, the data revealed that in specialization, the Electronics were different among the Electrical,Computer Engineering, and Electrical Engineering in the knowledge on control system in the sense that based on the prospectus they differ in subjects.

Skill in Using Test Equipment

The Scheffé data has the reasons that there is a significant difference in skills in using test equipment of the students by the factors of curriculum and specialization. The computed F-values under the curriculum between BSIT students and AIT students exceeded the expected critical F-value of 8.01 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring to Table 3, BSIT students rated their skills training on skill in using test equipment with a mean of 2.34 was higher than AIT students with only 1.81 mean values. This indicates that the BSIT students were significantly knowledgeable and well trained in skills in using test equipment than to those AIT students. From a concise point of view, by the curriculum, the AIT and BSIT were significantly different in the skill in using test equipment in the sense that the BSIT off ers program related to instrumentation while in AIT the

instrumentation and control were embedded only in the curriculum after theconduct of this study. The computed F-values under the specialization between students who are major in Electronics and Electricalexceeded the expected critical F-value of 9.72 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring to Table 4, students who are major in Electrical rated their skills in using test equipment with the mean value of 2.07 were higher than students who are major in Electronics with only 1.98 mean value, meaning students who are major in Electrical were significantly knowledgeable and well trained in skills in using test equipment than to those students who are major in Electronics. Also, the computed F-values under the specialization between students who are major in Electronics and students who are major in Electronics Engineering exceeded the expected critical F-value of 9.72 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. Students who are major in Electronics Engineering rated their skills in using test equipment with the mean value of 2.40 were higher than students who are major in Electronics with only 1.98 mean values. This means that the students who are major in Electronics Engineering were significantly knowledgeable and well trained in skill in using test equipment than to those students who are major in Electronics. In short, the data revealed that in specialization, the Electronics were different among the Electrical and Electronics Engineering in terms of their skills in using test equipment in the sense that based on the prospectus they differ in subjects.

Skill in Implementation Application

The Scheffé data presents the reasons that there is a significant difference in the skills in instrumentation application of the students by the factors of curriculum and specialization. The computed F-values under the curriculum between BTTE students and Engineering students exceeded the expected critical F-value of 8.01 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring to Table 3, BTTE students rated their skills in instrumentation application with the mean of 2.59 were higher than Engineering students with only 2.22 mean value, meaning BTTE students were significantly knowledgeable and well trained on skill in instrumentation application than the Engineering students. Also, the computed F-values under the curriculum between BSIT students and Engineering students exceeded the expected critical F-value of 8.01 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring to Table 3, BSIT students rated their skills in instrumentation application with the mean of 3.12 were higher than Engineering students with only 2.22 mean value, meaning BSIT students were significantly knowledgeable and well trained on skills ininstrumentation application than to those BSIT students. Precisely, by the curriculum, the BTTE and Engineering were significantly different in the skill in instrumentation application in the sense that the BTTE were more skilled than Engineering because they aremore hands-on compared to engineering students.

The computed F-values under the specialization between students who are major in Electronics and Electrical exceeded the expected critical F-value of 9.72 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Referring to Table 4, students who are major in Electronics rated their skills in instrumentation application with the mean value of 2.61 were higher than students who are major in Electrical with only 2.57 mean value, meaning students who are major in Electronics were significantly knowledgeable and well trained in skills in instrumentation application than the electrical students. Concisely, the data revealed that in specialization, Electronics was different compared to Electrical in the skills in the sense that instrumentation application based on the prospectus they differ in subjects. In synthesis, it shows that the AIT differs in other curriculum and for specialization, engineering is different in other specialization.

The difference in Teachers Rating

The ANOVA data showed the bases for testing the null hypothesis that there is no significant difference in the ratings of the teacher's respondents along each of the indicators under study concerning their highest educational attainment, academic rank, and years of baccalaureate. The ANOVA data shows that the teachers training in the field of instrumentation & control specifically in the knowledge on measuring devices, knowledge on the control system, skills in using test equipment, and skill in instrumentation application do not significantly influence the factors on

the highest educational attainment, academic rank and years of baccalaureate. In synthesis, the teachers' level in knowledge and skills in instrumentation was not different in contrary to their highest educational attainment, academic rank, and baccalaureate degree.

The difference in Instrumentation Technician Ratings

The statistical data shows that the bases for analyzing the data to test the null hypothesis that there is no significant difference in the ratings of the instrumentation technician-respondents on the need for the instrumentation training in industries along the aspects included for study an account of their highest educational attainment, department, years of experience in working to the industry, and geographic location. The ANOVA data shows that the instrumentation technician training in the field of instrumentation and control specifically in the knowledge on measuring devices, knowledge on the control system, skills in using test equipment, and skill in instrumentation application were significantly affected with the factors on highest educational attainment, department and years of experience of an industrial worker. Concisely, the data shows that each of the factors on the highest educational attainment, department, and years of service and geographic location of the instrumentation technicians has the corresponding extend of need requirements on skills training in instrumentation.

Knowledge in Measuring Device

The Scheffé data presents the reasons that there is a significant difference in the knowledge in measuring devices of the instrumentation technicians by the factors of department and years of industrial experience. The computed F-values under the department between the Electrical department and Production department instrumentation technicians exceeded the expected critical F-value of 11.80 at a 5% margin of error and thus led to the rejection of the respective null hypothesis. The Electrical department instrumentation technicians rated their knowledge on measuring devices with a mean of 3.61, higher than Production department instrumentation technicians with only 2.94 mean value. This means that the Electrical department instrumentation technicians were significantly better in assessing the need for the knowledge and skills training on the knowledge of measuring devices than those in the Production department instrumentation technicians. The computed F-values under the years of industrial experience between instrumentation technicians who are 2 years & below of experience and instrumentation technicians who are 3-4 years of the experience exceeded the expected critical F-value of 8.25 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis.

Reviewing the data in the instrumentation technicians who were 2 years and below of experience-rated their knowledge in measuring device with the mean value of 3.37 were higher than instrumentation technicians who were 3 to 4 years of experience with only 3.06 mean value. This means that the instrumentation technicians who are 2 years & below of experience were significantly knowledgeable and well-trained on knowledge in measuring device than to those instrumentation technicians who were 3 to 4 years of experience. Also, the computed F-values under the years of industrial experience between instrumentation technicians who are 2 years and below of experience and instrumentation technicians who were 5 to 6 years of the experience exceeded the expected critical F-value of 8.25 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. Instrumentation technicians who were 2 years and below of experiencerated their knowledge in measuring device with the mean value of 3.37 were higher than instrumentation technicians who were 5 to 6 years of experience with only 3.26 mean value, meaning instrumentation technicians who are 2 years and below of experience were significantly knowledgeable and well trained on knowledge in measuring device than to those instrumentation technicians who were 5 to 6 years of experience.

Knowledge in Control System

The Scheffé data showcase the reasons that there is a significant difference in the knowledge in the control system of the instrumentation technicians by the factors of the highest educational attainment and years of industrial experience. The computed F-values under the highest educational attainment between the BS graduate only

instrumentation technicians and full-fledged Master Instrumentation technicians exceeded the expected critical F-value of 6.28 at a 5% margin of error and thus; led to the rejection of the respective null hypothesis. Full-fledged Master instrumentation technicians rated their knowledge on a control system with a mean of 4.00, higher than BS graduate instrumentation technicians with only 2.60 mean values. This predicates that the full-fledged Master Instrumentation technicians were significantly more knowledgeable and well-trained in setting standards on the needed skills on the knowledge in control system than those BS graduate only instrumentation technicians. The computed F-values under the years of instrumentation technicians between instrumentation technicians who are 2 years and below of experience and instrumentation technicians who are 3-4 years of the experience exceeded the expected critical F-value of 8.25 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. The instrumentation technicians who are 3-4 years of experience rated their knowledge on control system with the mean value of 2.94 were higher than instrumentation technicians who are 2 years and below of experience with only 2.21 mean value, meaning instrumentation technicians who are 3-4 years of experience were significantly knowledgeable and well trained on knowledge in control system than those instrumentation technicians who are 2 years and below years of experience. Also, the computed F-values under the years of industrial experience between instrumentation technicians who are 2 years and below of experience and instrumentation technicians who are 5-6 years of the experience exceeded the expected critical F-value of 8.25 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. Iinstrumentation technicians who were 5 to 6 years of experience rated their knowledge in a control system with the mean value of 3.14 were higher than industrial workers who are 2 years and below of experience with only 2.21 mean value.

This means that the instrumentation technicians who were 5 to 6 years of experience were significantly setting the different criteria on assessing the industrial needs in terms of the knowledge in control system than those industrial workers who were 2 years and below of experience. Moreover, the computed F-values under the years of industrial experience between instrumentation technicians who were 2 years and below of experience and instrumentation technicians who were 7 years and above of experience exceeded the expected critical F-value of 8.25 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. The instrumentation technicians who were 7 years and above experiencerated their knowledge in the control system higher with the mean value of 3.31 than the instrumentation technicians who were 2 years and below of experience with only 2.21 mean value. This implies that the instrumentation technicians who were 7 years and above of experience we're having different criteria set the industrial need for the knowledge in control system than to those instrumentation technicians who were 2 years and below of experience. Precisely, the instrumentation technicians in terms of their highest educational attainment and years of service were at different levels of understanding in instrumentation training in terms of knowledge on the control system.

Skill in Using Test Equipment

The Scheffé data has the reasons that there is a significant difference in the skills in using test equipment of the industrial workers by the factor of the department. The computed F-values under the department between Electrical department instrumentation technicians and Mechanical department instrumentation technicians exceeded the expected critical F-value of 11.80 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. The Electrical department instrumentation technicians rated their skills in using test equipment with the mean of 3.75 were higher than Mechanical department instrumentation technicians with only 2.97 mean value, meaning Electrical department instrumentation technicians were significantly knowledgeable and well trained on the skills in using test equipment than to those Mechanical department instrumentation technicians. Also, the computed F-values under the department between Electrical department instrumentation technicians and Production department instrumentation technicians exceeded the expected critical F-value of 11.80 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. The Electrical department instrumentation technicians rated their skills in using test equipment with a higher mean of 3.75 than Production department instrumentation technicians with only 3.05 mean value. It indicates that the Electrical department instrumentation technicians were significantlydifferent in valuing the needed knowledge and skills in using test equipment for the

industry than to those Mechanical department instrumentation technicians. Also, the computed F-values under the department between Electrical department instrumentation technicians and Quality Assurance department instrumentation technicians exceeded the expected critical F-value of 11.80 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. The Electrical department instrumentation techniciansrated their skills in using test equipment with a mean of 3.75 were higher than Quality Assurance department instrumentation technicians with only 2.00 mean values. This means that Electrical department industrial workers were significantly knowledgeable and well trained on the skills in using test equipment than to those Quality Assurance department instrumentation technicians. Briefly, the instrumentation technicians, especially in the Electrical department, were in the different level of appreciating the needed instrumentation skills training in terms of using test equipment as compared with those in the mechanical, production, and quality assurance departments.

Skill in Instrumentation Application

The Scheffé data showcase the reasons that there is a significant difference in the skills in instrumentation application of the instrumentation technicians by the factors of department and years of industrial experience. The computed F-values under the department between Electrical department instrumentation technicians and Mechanical department instrumentation technicians exceeded the expected critical F-value of 11.80 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. The Electrical department instrumentation technicians rated their skills in instrumentation applications with a mean of 3.88 were higher than Mechanical department instrumentation technicians with only 3.23 mean values. This goes to show that Electrical department instrumentation technicians were significantly knowledgeable and well trained on the skills in instrumentation application than to those in Mechanical department instrumentation technicians. The computed F-values under the years of industrial experience between instrumentation technicians who are 2 years and below of experience and instrumentation technicians who were 5 to 6 years of the experience exceeded the expected critical F-value of 8.25 at a 5% margin of error, and thus led to the rejection of the respective null hypothesis. The instrumentation technicians who were 2 years and below experience-rated their skills in instrumentation application with a higher mean value of 3.88 than the instrumentation technicians who were 5 to 6 years of experience with only 3.56 mean value. This indicates that the instrumentation technicians who were 2 years and below of experience were having a significantly different base in setting standards on the needed skills in instrumentation application than to those instrumentation technicians who were 5 to 6 years of experience. In short, the instrumentation technicians, their department, and years of service were in different levels of understanding in instrumentation skills training that the industries need.

CONCLUSIONS

Based on findings the study conclude that: the AIT has a kind of academic requirements suited to the interests of its enrollees and the same can be easily achieved in a shorter period, thus, many are attracted to be in this curriculum; the AIT students are interested to specialize electrical in the sense that it has a broad working opportunity in the Philippines and abroad; that there were no uniform instructional standards set by the teachers on the instrumentation training of students; with an increasing number of students, only a few teachers have a permanent status. Thus, the majority of the teachers who teach electrical, electronics, and engineering subjects were only guest lecturers; in working to the industry, the minimum requirement is BS graduate only possessed with highly intellectual and skilled in instrumentation; and the instrumentation skills training in the Surigao State College of Technology, Surigao is given less emphasis on technological instruction. It also leads to the conclusion that the teachers lack sufficient training and the classroom or laboratory lacks the facilities needed for instrumentation related instruction.

REFERENCES

1. Cruz, R. V. O., Pillas, M., Castillo, H. C., & Hernandez, E. C. (2012). Pagsanjan-Lumban catchment, Philippines: Summary of
2. biophysical characteristics of the catchment, background to site selection and instrumentation. *Agricultural water*
3. *management*, *106*, 3-7;
4. Leonardo, L. R., Rivera, P. T., Crisostomo, B. A., Sarol, J. N., Bantayan, N. C., Tiu, W. U., & Bergquist, N. R. (2005). A study of
5. the environmental determinants of malaria and schistosomiasis in the Philippines using Remote Sensing and Geographic
6. Information Systems. *Parassitologia*, *47*(1), 105;
7. Raufaste, N. J. (1977). High Wind Study in the Philippines. *WIND AND SEISMIC EFFECTS*;
8. Fellenius, B. H., Altaee, A., Kulesza, R., & Hayes, J. (1999). O-cell testing and FE analysis of 28-m-deep barrette in Manila,
9. Philippines. *Journal of Geotechnical and Geoenvironmental Engineering*, *125*(7), 566-575;
10. Puga, G. S. (1982). A study of the maintenance problems of nuclear medicine instrumentation in the Philippines. *Nucleus (Diliman,*
11. *Quezon City)*, *22*(1), 20-27;
12. Marciano Jr, J. S., Zarco, M. A. H., Talampas, M. C. R., Catane, S. G., Hilario, C. G., Zabanal, M. A. B., ... & Cordero, C. N.
13. (2011, October). Real-world deployment of a locally-developed tilt and moisture sensor for landslide monitoring in the
14. Philippines. In *2011 IEEE Global Humanitarian Technology Conference* (pp. 344-349). IEEE;
15. Bell, D. A. (2011). *Electronic instrumentation and measurements*. Englewood Cliffs, NJ: Regents/Prentice Hall;
16. Parr, R. M., DeMaeyer, E. M., Iyengar, V. G., Byrne, A. R., Kirkbright, G. F., Schöch, G., ... & Omololu, A. (1991). Minor and
17. trace elements in human milk from Guatemala, Hungary, Nigeria, Philippines, Sweden, and Zaire. *Biological Trace Element*
18. *Research*, *29*(1), 51-75;
19. Bankoff, G. (2007). One island too many: reappraising the extent of deforestation in the Philippines prior to 1946. *Journal of*
20. *Historical Geography*, *33*(2), 314-334;
21. Luk, C. K., Cohn, R., Muth, R., Patil, H., Klauser, A., Lowney, G. & Hazelwood, K. (2005). Pin: building customized program
22. analysis tools with dynamic instrumentation. *Acm sigplan notices*, *40*(6), 190-200;
23. Havskov, J., & Alguacil, G. (2004). *Instrumentation in earthquake seismology* (Vol. 358). Dordrecht, The Netherlands: Springer.
24. Cotrel, Y., Dubousset, J., & Guillaumat, M. (1988). New universal instrumentation in spinal surgery. *Clinical orthopaedics and*
25. *related research*, *227*, 10-23;
26. Romani, G. L., Williamson, S. J., & Kaufman, L. (1982). Biomagnetic instrumentation. *Review of Scientific Instruments*, *53*(12),
27. 1815-1845.
28. Cantrill, B., Shapiro, M. W., & Leventhal, A. H. (2004, June). Dynamic Instrumentation of Production Systems. In *USENIX Annual*
29. *Technical Conference, General Track* (pp. 15-28);
30. Fritschen, L. J., & Gay, L. W. (2012). *Environmental instrumentation*. Springer Science & Business Media;

31. Bos, B. J., Forbes, S. J., & Veldman, R. L. (1997). *U.S. Patent No. 5,671,996*. Washington, DC: U.S. Patent and Trademark Office;
32. Braun, J. C., Jacobus, C. J., Booth, S., Suarez, M., Smith, D., Hartnagle, J., & Leprell, G. (2000). *U.S. Patent No. 6,050,940*.
33. Washington, DC: U.S. Patent and Trademark Office;
34. Abt, K. (1987). Descriptive data analysis: a concept between confirmatory and exploratory data analysis. *Methods of information*
35. *in medicine*, *26*(02), 77-88;
36. Al-Aufi, A., & Al-Azri, H. (2013). Information literacy in Oman's higher education: A descriptive-inferential approach. *Journal*
37. *of Librarianship and Information Science*, *45*(4), 335-346;
38. Vîslă, A., Grosse Holtforth, M., & David, D. (2015). Descriptive/inferential cognitive processes and evaluative cognitive processes:
39. Relationships among each other and with emotional distress. *Journal of Rational-Emotive & Cognitive-Behavior*
40. *Therapy*, *33*(2), 148-159;
41. Bewick, V., Cheek, L., & Ball, J. (2004). Statistics review 9: one-way analysis of variance. *Critical care*, *8*(2), 130;
42. Boik, R. J. (1979). The Rationale of Scheffé's Method and the Simultaneous Test Procedure. *Educational and Psychological*
43. *Measurement*, *39*(1), 49-56;
44. Delph, L. F. (2004). Testing for sex differences in biparental inbreeding and its consequences in a gynodioecious species. *American*
45. *Journal of Botany*, *91*(1), 45-51;
46. Deloire-Grassin, M. S. A., Brochet, B., Quesson, B., Delalande, C., Dousset, V., Canioni, P., & Petry, K. G. (2000). In vivo
47. evaluation of remyelination in rat brain by magnetization transfer imaging. *Journal of the neurological sciences*, *178*(1), 10-

Table 1. Distribution of Respondents

Respondents	Population	Sample Size	Per cent
Students	200	151	75.5%
Teachers	30	20	66.67%
Instrumentation Technicians	80	69	86.25%
Total	310	240	77.42%

Table 2. Data Analysis

Scale	Parameters/Level	Interpretation
4	3.50-4.00	Very High (VH)
3	2.50-3.49	High (H)
2	1.50-2.49	Low (L)
1	1.00-1.49	Not at All (NA)

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RESEARCH ARTICLE

Operations Research and Queueing Model

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ABSTRACT

This Paper is devoted to a common situation occurring in everyday life is that of queuing or waiting in a line. Queues form at bus stops, ticket booths, doctors clinics, bark counters, traffic lights and so on. Thus the theory of Queue is concerned with the development of mathematical models to predict the behaviour of system that provide services for randomly arising demands. Since the demands (customers) for service are supported to be governed by some probability law. The theory of queues has been developed within the frame work of the theory of stochastic process (Brockmeyer et. el (1948), and Kleinrock, (1975) A.K. Erlang, a Denish telephone engineer, did original work on queueing theory. Erlang started his work in 1905 in an attempt to determine the effects of fluctuating service demand (arrivals) on the utilization of automatic dialing equipment. In studying this problem, Erlang derived what we now call the equilibrium form of kolomorov or equations for Morkov process with a denumerable number of states. Moreover, queueing theory has been applied to a large number of areas as some mentioned above due to the existence of many types of systems in our daily life that provide device for randomly arising demands. It is also a standard tool in various areas of operations research and the range of its applications has widened as operations research has extended its coverage.

Keywords: Operations research, Waiting line, Poisson distribution.

INTRODUCTION

In recent years, attention has been focused on queueing systems which allow variation in the strategy of the servers such as employing multiple servers, service rate variations, etc. But there is very little work reported on the effects of different strategies open to the customer. One of the important customer strategies is called "jockeying". In the literature of Queueing Theory, "jockeying" refers to the movements of customers who have the option of switching from one line to another when several servers, each having it separate and distinct waiting line, are available. Jockeying can only occur when the customer can have more than one waiting line. Jockeying is quite common in

many queueing systems. Most of us have been jockeying for years - switching lines in auto license and supermarkets, changing routes in rush hour traffic and changing suppliers (servers) when confronted by long queues. We shall be concerned here with a rather realistic model which one finds quite frequently. Consider a queuing system consisting of two parallel servers with different service rates. Customers arrive according to a Poisson stream and generate an exponentially distributed workload. On arrival a customer joins the shortest queue, in the case both queues have equal lengths, he joins either queue with probability 1/2. This model is known as the shortest queue model and has been addressed by many authors.

Formulation of the Model and its Transient Equations

Consider a queuing system consisting of two parallel servers with different rates μ_1 and μ_2 respectively. Customers arrive according to a Poisson stream with rate A. Service is provided by independent servers with exponential service at each counter. It will be assumed that the system is in the transient state. The capacity of each queue is finite and equal to N, i.e. the maximum number of customers in the system is restricted to 2N including the ones being served. The system state is a random couplet (ξ, η) of non-negative integers and we write

$$P_{ij}(t) = Pr\{\xi(t) = i, \eta(t) = j\}, \quad i,j = 0,1,2,..,N \tag{1.2.1}$$

for the transient state joint probability.

The rule for an incoming customer is always to join the shorter queue and if both are equal then join either of them with probability 1/2. The moment the server becomes idle and there are customers waiting in the other queue, the customer immediately following the customer who is receiving service at that counter is transferred to the idle server's queue. Clearly, the above condition gives that $P_{jo}(t)$ and $P_{oj}(t)$ are equal to zero for all $j = 2,3,\cdots,N$.

Let $P = \lambda/(\mu_1 + \mu_2)$ be the traffic intensity and $\alpha_1 = \mu_1/(\mu_1 + \mu_2)$ and $\alpha_1 = \mu_2/(\mu_1 + \mu_2)$. The system is taken to be empty at time t = 0.

The differential-difference equations satisfied by $P_{ij}(t)$ are easily obtained by familiar means, with ρ, α_1 and α_2 are defined as above, we obtain

$$P'_{00}(\tau) = -\rho P_{00}(\tau) + \alpha_1 P_{10}(\tau) + \alpha_2 P_{01}(\tau) \tag{1.2.2}$$

$$P'_{01}(\tau) = -(\rho + \alpha_2)P_{01}(\tau) + \frac{\rho}{2} P_{00}(\tau) + \alpha_1 P_{11}(\tau) \tag{1.2.3}$$

$$P'_{10}(\tau) = -(\rho + \alpha_1)P_{10}(\tau) + \frac{\rho}{2} P_{00}(\tau) + \alpha_2 P_{11}(\tau) \tag{1.2.4}$$

$$P'_{11}(\tau) = -(1 + \rho)P_{11}(\tau) + \rho\big(P_{01}(\tau) + P_{10}(\tau)\big) + P_{12}(\tau) + P_{21}(\tau) \tag{1.2.5}$$

$$P'_{12}(\tau) = -(1 + \rho)P_{12}(\tau) + \frac{\rho}{2} P_{11}(\tau) + \alpha_1 P_{22}(\tau) + P_{13}(\tau) \tag{1.2.6}$$

$$P'_{21}(\tau) = -(1 + \rho)P_{21}(\tau) + \frac{\rho}{2} P_{11}(\tau) + \alpha_2 P_{22}(\tau) + P_{31}(\tau) \tag{1.2.7}$$

$$P'_{22}(\tau) = -(1 + \rho)P_{22}(\tau) + \rho\big(P_{12}(\tau) + P_{21}(\tau)\big) + \alpha_1 P_{32}(\tau) + \alpha_2 P_{23}(\tau) \tag{1.2.8}$$

For 2 < n < N – 1

$$P'_{1n}(\tau) = -(1 + \rho)P_{1n}(\tau) + P_{1\,n+1}(\tau) + \alpha_1 P_{2n}(\tau) \tag{1.2.9}$$

$$P'_{n1}(\tau) = -(1 + \rho)P_{n1}(\tau) + P_{n+1\,1}(\tau) + \alpha_2 P_{n2}(\tau) \tag{1.2.10}$$

For $2 \leq k \leq -2$

$$P'_{kn}(\tau) = -(1+\rho)P_{kn}(\tau) + \rho P_{k-1\,n}(\tau) + \alpha_1 P_{k+1\,n}(\tau) + \alpha_2 P_{k\,n+1}(\tau) \quad (1.2.11)$$

$$P'_{nk}(\tau) = -(1+\rho)P_{nk}(\tau) + \rho P_{n\,k-1}(\tau) + \alpha_1 \quad {}_{n+1\,k}(\tau) + \alpha_2 P_{n\,k+1}(\tau) \quad (1.2.12)$$

$$P'_{n-1\,n}(\tau) = -(1+\rho)P_{n-1\,n}(\tau) + \rho P_{n-2\,n}(\tau) + \frac{\rho}{2} P_{n-1\,n-1}(\tau) + \alpha_1 P_{n+1\,n-1}(\tau) + \alpha_2 P_{n\,n}(\tau) \quad (1.2.13)$$

$$P'_{nn-1}(\tau) = -(1+\rho)P_{nn-1}(\tau) + \rho P_{nn-2}(\tau) + \frac{\rho}{2} P_{n-1\,n-1}(\tau) + \alpha_1 P_{n+1n-1}(\tau) + \alpha_2 P_{nn}(\tau) \quad (1.2.14)$$

$$P'_{nn}(\tau) = -(1+\rho)P_{nn}(\tau) + \rho(P_{nn-1}(\tau) + P_{n-1\,n-1}(\tau) + \alpha_1 P_{n+1n}(\tau) + \alpha_2 P_{nn+1}(\tau) \quad (1.2.15)$$

$$P'_{1N}(\tau) = -(1+\rho)P_{1N}(\tau) + \alpha_1 P_{2N}(\tau) \quad (1.2.16)$$

$$P'_{N1}(\tau) = -(1+\rho)P_{N1}(\tau) + \alpha_2 P_{N2}(\tau) \quad (1.2.17)$$

For $2 \leq k \leq N-2$

$$P'_{kn}(\tau) = -(1+\rho)P_{kN}(\tau) + \rho P_{k-1\,N}(\tau)\alpha_1 P_{k+1\,N}(\tau) \quad (1.2.18)$$

$$P'_{Nk}(\tau) = -(1+\rho)P_{N\,k}(\tau) + \rho P_{N\,k-1}(\tau)\alpha_2 P_{N\,k+1}(\tau) \quad (1.2.19)$$

$$P'_{N-1\,N}(\tau) = -(1+\rho)P_{N-1\,N}(\tau) + \rho P_{N-2\,N}(\tau) + \tfrac{\rho}{2} P_{N-1\,N-1}(\tau) + \alpha_1 P_{N\,N}(\tau) \quad (1.2.20)$$

$$P'_{NN-1}(\tau) = -(1+\rho)P_{N\,N-1}(\tau) + \rho P_{N\,N-2}(\tau) + \frac{\rho}{2} P_{N-1\,N-1}(\tau) + \alpha_2 P_{NN}(\tau) \quad (1.2.21)$$

$$P'_{N\,N}(\tau) = -P_{NN}(\tau) + \rho\big(P_{N-1\,N}(\tau) + P_{N\,N-1}(\tau)\big) \quad (1.2.22)$$

where $P'_{ij}(\tau) = \frac{d_{pij}(\tau)}{dr}$ and $P_{ij}(0) = 1$ for $i = 0$ and $j = 0$ and $P_{ij}(0) = 0$ otherwise, and the time has been scaled such that $1/(\mu_1 + \mu_2)$ is taken as the time unit.

Solution of the Equilibrium Equations

In this case P(t) is independent of time i.e. $P'_{ij}(\tau) = 0$ and the corresponding equations can be obtained from the set (1.2.2) - (1.2.22) by taking L.H.S. as zero and writing P_{ij} for $P_{ij}(\tau)$ in each of these equations and we denoted them as (1.2.2)' - (1.2.22)'. Now ignoring equations (1.2.2)' - (1.2.5)', the set (1.2.6)' - (1.2.22)' of difference equations can be written in the matrix form as

$$\begin{bmatrix} A_1 & B_1 & C_3 & 0 & \cdots & \cdot\cdot & 0 \\ 0 & A_2 & B_3 & C_4 & 0 & \cdots & 0 \\ \vdots & & \vdots & \vdots & & \ddots & \vdots \\ 0 & \cdots & 0 & \cdots & 0 & \cdots & 0 \\ 0 & \cdots & & 0 & A_{N-2} & B_{N-1} & C_N \\ 0 & \cdots & & 0 & 0 & A_{N-1} & B_N \end{bmatrix} \begin{bmatrix} P_1 \\ P_2 \\ \vdots \\ \cdot \\ \vdots \\ P_N \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \vdots \\ \cdot \\ \vdots \\ 0 \end{bmatrix}$$

where

$$A_k = (a_{ij})_{(2k+1)\times(2k-1)}, k = 1,2,\dots,N-1$$

with $a_{2k-1\ 2k-1} = a_{2k\ 2k-1} = \rho$

$a_{ij} = 0,$ otherwise.

$$B_k = (b_{ij})_{(2k+1)\times(2k-1)}, k = 2,3,\cdots,N$$

with

$b_{ij} = -2(1+\rho)$, i = 1, 2, …, 2k – 2.

$b_{i+2i} = 2\rho$, i = 1, 2, …, 2k – 4.

$b_{2i-1\ 2i+1} = 2\alpha_1$,

$b_{2i\ 2i+2} = 2\alpha_2$, i = 1, 2, …, 2k – 2.

$b_{2k-3\ 2k-1} = 2\alpha_1$,

$b_{2k-2\ 2k-1} = 2\alpha_2$, k = 2, 3, …, N

$b_{2k-1\ 2k-2} = b_{2k-1\ 2k-3} = \rho$, k = 2, 3, …, N

$b_{2k-1\ 2k-1} = -(1+\rho)$, $k \neq N$

$b_{2N-1\ 2N-1} = -1$ and $b_{ij} = 0$, otherwise.

$C_k = (b_{ij})_{(2k-3)\times(2k-1)}$, k = 3, 4, …, N

with

$c_{11} = {}_{22} = 2$,

$c_{2i-1\ 2i-1} = 2\alpha_2,\ c_{2i\ 2i} = 2\alpha_1$, i = 2,3,…, k – 2

$c_{2k-3\ 2k-2} = \alpha_1,\ c_{2k-3\ 2k-3} = \alpha_2$, k = 3, 4,…, N

and $c_{ij} = 0$, otherwise.

$\boldsymbol{p_k}$ is a column vector of 2k - 1 elements and can be written as

$$\boldsymbol{p_k} = [P_{1k}P_{k1}\ P_{2k}\ P_{k2}\ \dots P_{k-1\ k}P_{k\ k-1}\ P_{kk}]\ ,\ k = 1, 2,\dots,N$$

Where $P_{ij} = \lim_{\tau\to\infty} P_{ij}(\tau)$

According to equation (1.3.1), we obtain

$$A_{i-1}\boldsymbol{p}_{i-1} + B_i\,\boldsymbol{p}_{i+1} + C_{i+1}\,\boldsymbol{p}_{i+1} = 0, i = 2,3,\dots,N-1$$

$$A_{N-1}\boldsymbol{p}_{N-1} + B_N\boldsymbol{p}_N = 0$$

which implies that

$$\boldsymbol{p}_{i+1} = -Q_i\,A_{i-1}\boldsymbol{p}_{i-1},\ \ i = 2,3,\dots,N-1$$

$$\boldsymbol{p}_N = -B_N^{-1}A_{N-1}\boldsymbol{p}_{N-1}, i = N$$

where $Q_i = [B_i - C_{i+1}\,Q_{i+1}\,A_i]^{-1}, i = N-1, N-2,\dots,2$ with $Q_N = B_N^{-1}$

Theorem 1.3.1 : For any integer *i*, *i* = 1,2,3,…, N we have

$$\boldsymbol{p_i} = (-1)^{i+1}\frac{\lambda^2}{2\mu_1\mu_2}Q_i\,A_{i-1}Q_{i-1}\,A_{i-2}\dots Q_2A_1\mathrm{P}_{00}\ \ ,i = 2,3,\dots,N \qquad (1.3.2)$$

$$P_{01} = \frac{\lambda}{2\mu_2}\mathrm{P}_{00} \qquad (1.3.3)$$

$$P_{10} = \frac{\lambda}{2\mu_1}\mathrm{P}_{00} \qquad (1.3.4)$$

with

$$P_{00} = \begin{cases} \dfrac{2\mu_1\mu_2(1-\rho)}{2\mu_1\mu_2(1-\rho) + (\mu_1+\mu_2)^2\rho(1-\rho) + \lambda^2(1-\rho^{2N-1})} & ,\rho \neq 1 \\ \dfrac{2\mu_1\mu_2}{2\mu_1\mu_2 + 2N(\mu_1+\mu_2)^2} & ,\rho = 1 \end{cases} \quad (1.3.5)$$

and $Q_1 = A_0 = 1, Q_N = B_N^{-1}$ *and* $Q_i = [B_i - C_{i+1}Q_{i+1}A_i]^{-1},\ i = N-1, N-2, \ldots, 2.$

Proof : The equations (1.2.2) (1.2.4)' can be written as

$$\alpha_1 P_{10} + \alpha_2 P_{01} = \rho P_{00}$$

$$2(\alpha_1 + \rho)P_{01} - 2\alpha P_{11} = \rho P_{00}$$

$$2(\alpha_2 + \rho)P_{01} - 2\alpha_1 P_{11} = \rho P_{00}$$

The determinant of coefficients P_{11}, P_{10}, P_{01} and P_{00} can be seen to be zero and consequently three of the unknowns P_{11}, P_{10}, P_{01} and P_{00} must be expressed in terms of the fourth. Thus we can write

$$P_{10} = \frac{\lambda}{2\mu_1} P_{00}, P_{01} = \frac{\lambda}{2\mu_2} P_{00} \text{ and } P_{11} = \frac{\lambda^2}{2\mu_1\mu_2} P_{00}$$

Let us define the global system as $\xi + \eta$ and

$$q_k = Pr(\xi + \eta = k), k = 0,1,2,\ldots,2 \quad (1.3.6)$$

and using the boundary conditions $P_{i\,N+i} = 0 = P_{N+i\,i},\ i = 0,1,2,\ldots,N,$ for even k (say k = 2r), we obtain easily

$$q_{2r} = \sum_{m=1}^{r-1} P_{m\,2r-m} + \sum_{m=1}^{r-1} P_{2r-m\,m} + P_{rr} \quad (1.3.7)$$

and for odd $k(say\ 2r+1), we\ get$

$$q_{2r+1} = \sum_{m=1}^{r} P_{m\,2r+1-m} + \sum_{m=1}^{r} P_{2r+1-m\,m} \quad (1.3.8)$$

Clearly,

$$q_0 = \Pr(\xi + \eta = 0) = P_{00} \tag{1.3.9}$$

$$q_1 = Pr(\xi + \eta = 1) = P_{01} + P_{10}$$

$$= \frac{\lambda}{2\mu_1\mu_2}(\mu_1 + \mu_2)P_{00} \tag{1.3.10}$$

$$q_1 = Pr(\xi + \eta = 2) = P_{01} + P_{11}$$

$$= \frac{\lambda^2}{2\mu_1\mu_2}P_{00} \tag{1.3.11}$$

Using the values of P_{01}, P_{10} and P_{11} in the equation (1.2.5)', we can easily obtain

$$\rho P_{11} = P_{12} + P_{21}$$

or $q_1 = \rho q_2$.

Similarly, working on equations (1.2.6)' and (1.2.7)', we get

$$2(1+p)(P_{12} + P_{21}) = 2P_{11} + 2(P_{22} + P_{31} + P_{13})$$

i.e. $q_4 = (1 + \rho)q_3 - \rho q_2$

$$q_4 = \rho^2 q_2.$$

Now put $n = 3$ in equations (1.2.9)' and (1.2.10)' and adding to equation (1.2.8), we get

$$(1+p)(p_{22} + p_{13} + p_{31}) = \rho(p_{12} + p_{21}) - (\alpha_1 + \alpha_2)(p_{32} + p_{23})$$

$$q_5 = (1 + \rho)q_4 - \rho q_3$$

which implies that

$$q_4 = \rho^3 q_2.$$

We now, show that in general $q_k = \rho^{k-2} q_2, k = 2,3,\ldots,2N.$ We consider two cases depending on whether k is even or odd.

Case 1 $k = 2r, 3 \leq r \leq N-1.$

Replacing *n,* by $2r-1, 2r-2, 2r-3$,...,r in the equations (1.2.9)' - (1.2.14)' respectively, we obtain

$$(1+\rho)P_{1\,2r-1} = P_{1\,2r} + \alpha_1 P_{2\,2r-1}$$
$$(1+\rho)P_{2r-1\,1} = P_{2r\,1} + \alpha_2 P_{2r-1\,2}$$
$$(1+\rho)P_{2\,2r-2} = \rho P_{1\,2r-2} + \alpha_1 P_{3\,2r-2} + \alpha_2 p P_{2\,2r-1}$$
$$(1+\rho)P_{2r-2\,2} = \rho P_{2r-1\,1} + \alpha_1 P_{2r-2\,2} + \alpha_2 P_{2r-2\,3}$$
$$\vdots \quad \vdots \quad \vdots$$
$$(1+\rho)P_{r-1\,r+1} = \rho P_{r-2\,r+1} + \alpha_1 P_{r\,r+1} + \alpha_2 P_{r-1\,r+1}$$
$$(1+\rho)P_{r+1\,r-1} = \rho P_{r+1\,r-2} + \alpha_1 P_{r+2\,r-1} + \alpha_2 P_{r+1\,r}$$
$$(1+\rho)P_{rr} = \rho(P_{r-1\,r} + P_{r\,r-1}) + \alpha_1 P_{r+1\,r} + \alpha_2 P_{r\,r+1}$$

Adding all these equations and using the equations (1.3.7) and (1.3.8) we obtain

$$(1+\rho)\left[\sum_{m=1}^{r-1} P_{m\,2r-m} + \sum_{m=1}^{r-1} P_{2r-m\,m} + P_{r\,r}\right] =$$
$$(\alpha_1+\alpha_2)\sum_{m=2}^{r} P_{m\,2r+1-m} + (\alpha_1+\alpha_2)\sum_{m=2}^{r} P_{2r+1-m\,m}$$
$$+\rho\left[\sum_{m=1}^{r} P_{m\,2r-1-m} + \sum_{m=1}^{r} P_{2r-1-m\,m}\right] + P_{1\,2r} + P_{2r\,1}$$

or $$(1+\rho)q_{2r} = q_{2r+1} + \rho q_{2r-1}$$

$$q_{2r+1} = (1+\rho)q_{2r} - \rho q_{2r-1}, \; r = 3,4,\ldots, N-1 \qquad (1.3.12)$$

Case 2 : $k = 2r+1, 2 \leq n \leq N-1$

Similarly, taking $n = 2r, 2r-1, 2r-2, \ldots, r+1$ in the equation (1.2.9)' – (1.2.15)' respectively, we

$$(1+\rho)P_{1\,2r} = P_{1\,2r+1} + \alpha_1 P_{2\,2r}$$
$$(1+\rho)p_{2r-1} = P_{2r+1\,1} + \alpha_2 P_{2r\,2}$$
$$(1+\rho)P_{2\,2r-1} = \rho P_{1\,2r-1} + \alpha_1 P_{3\,2r-1} + \alpha_2 P_{2\,2r}$$

$$(1+\rho)P_{2r-1\,2} = \rho P_{2r-1\,1} + \alpha_1 P_{2r\,2} + \alpha_2 P_{2r-1\,3}$$

$$\vdots \quad \vdots \quad \vdots$$

$$(1+\rho)P_{r-1\,r+2} = \rho P_{r-2\,r+2} + \alpha_1 P_{r\,r+2} + \alpha_2 P_{r-1\,r+3}$$

$$(1+\rho)P_{r+2\,r-1} = \rho P_{r+2\,r-2} + \alpha_1 P_{r+3\,r-1} + \alpha_2 P_{r+2\,r}$$

$$2(1+\rho)P_{r\,r+1} = \rho P_{r-1\,r+1} + \rho P_{rr} + 2\alpha_1 P_{r+1\,r+1} + 2\alpha_2 P_{r\,r+2}$$

$$2(1+\rho)P_{r+1\,r} = 2\rho P_{r+1\,r-1} + \rho P_{rr} + 2\alpha_1 P_{r+2\,r} + 2\alpha_2 P_{r+1\,r+1}$$

Adding these equations and using equations (1.3.7) and (1.3.8), we get,

$$(1+\rho)q_{2r+1} = \rho q_{2r} + q_{2r+2}$$

$$q_{2r+2} = (1+\rho)q_{2r+1} - \rho q_{2r}, \qquad r = 3,4,\ldots,N-1 \tag{1.3.13}$$

Consequently, we obtain

$$q_k = (1+\rho)q_{k-1} - \rho q_{k-2},\ k = 2,3,\ldots,2N. \tag{1.3.14}$$

and the result for $k = 2N$ comes directly from equations (1.2.21)' and (1.2.20)'. Now, assume the relation $q_k = \rho^{k-2}q_2$ is true for some $m \leq k$, then from (1.3.14) we get

$$q_{m+1} = (1+\rho)q_m - \rho q_{m-1}$$

$$= [(1+\rho)\rho^{m-2} - \rho\rho^{m-3}]q_2$$

$$= \rho^{m-2}q_2$$

Hence the result holds for $k = 2,3,\ldots,2N$,

$$\text{Since } \sum_{k=0}^{2N} q_k = 1$$

Using $q_k = \rho^{k-2}q_2, k = 2,3,\ldots,2N$, we obtain

$$q_0 + q_1 + q_2\left(\frac{1-\rho^{2N-1}}{1-\rho}\right) = 1$$

Substituting from (6.3.9)' (6.3.10) and (6.3.11) we easily get

$$q_0 = P_{00} = \frac{2\mu_1\ {}_2(1-\rho)}{2\mu_1\mu_2(1-\rho) + (\mu_1+\mu_2)^2\rho(1-\rho) + \lambda^2(1-\rho^{2N-1})}$$

which establishes the theorem.

Solution for the Transient Case

As discussed in the previous chapters we assume that the probability $P_{ij}(\tau)$ is of the form as

$$P_{ij}(\tau) = e^{-(1+\rho)\tau}\rho^{i+j}\sum_{m=0}^{\infty}\alpha(m,i,j)\frac{\tau^m}{m!}, \rho = \lambda/(\mu_1+\mu_2) \tag{1.4.1}$$

where $a(m,i,j)$ are constants to be determined, we then have

$$P'_{ij}(\tau) = e^{-(1+\rho)\tau}\rho^{i+j}\sum_{m=0}^{\infty}[\alpha(m+1,i,j) - (1+\rho)\alpha(m,i,j)]\frac{\tau^m}{m!} \quad (1.4.2)$$

Substituting from (6.4.1) and (6.4.2) into equations (6.2.2) - (6.2.22) we can easily get

$$a(m+1,0,0) = a(m,0,0) + P\left(\alpha_1\alpha(m,1,0) + \alpha_2\alpha(m,0,1)\right) \quad (1.4.3)$$

$$a(m+1,0,1) = \frac{1}{2}a(m,0,0) + (1-\alpha_2)\alpha(m,0,1) + \alpha_1\rho\alpha(m,1,1) \quad (1.4.4)$$

$$a(m+1,0,1) = \frac{1}{2}a(m,0,0) + (1-\alpha_2)\alpha(m,0,1) + \alpha_2\rho\alpha(m,1,1) \quad (1.4.5)$$

$$a(m+1,1,1) = a(m,0,1) + a(m,1,0) + \rho\left(a(m,1,2) + a(m,2,1)\right) \quad (1.4.6)$$

$$a(m+1,1,2) = \frac{1}{2}a(m,1,1) + \rho(\alpha_1 a(m,2,2) + a(m,1,3)) \quad (1.4.7)$$

$$a(m+1,2,1) = \frac{1}{2}a(m,1,1) + \rho\left(\alpha_2 a(m,2,2) + a(m,3,1)\right) \quad (1.4.8)$$

$$a(m+1,2,2) = \alpha_1\rho a(m,3,2) + \rho\alpha_2 a(m,2,3) + a(m,2,1) + a(m,1,2) \quad (6.4.9)$$

For $2 < n < N-1$

$$a(m+1,1,n) = \rho(a(m,1,n+1) + \alpha_1 a(m,2,n)) \quad (1.4.10)$$

$$a(m+1,n,1) = \rho\left(a(m,n+1,1) + \alpha_2 a(m,n,2)\right) \quad (1.4.11)$$

For $2 \le k \le n-2$

$$a(m+1,k,n) = a(m,k-1,n) + \rho\left(\alpha_1 a(m,k+1,n) + \alpha_2 a(m,k,n+1)\right) \quad (1.4.12)$$

$$a(m+1,n,k) = a(m,n,k-1) + \rho\left(\alpha_1 a(m,n+1,k) + \alpha_2 a(m,n,k+1)\right) \quad (1.4.13)$$

$$a(m+1,n-1,n) = a(m,n-2,n) + \frac{1}{2}a(m,n-1,n-1) + \rho\left(\alpha_1 a(m,n,n) + \alpha_2 a(m,n-1,n+1)\right) \quad (1.4.14)$$

$$a(m+1,n,n-1) = a(m,n,n-2) + \frac{1}{2}a(m,n-1,n-1) + \rho\left(\alpha_1 a(m,n+1,n-1) + \alpha_2 a(m,n,n)\right) \quad (1.4.15)$$

$$a(m+1,n,n) = a(m,n-1,n) + a(m,n,n-1) + \rho\left(\alpha_1 a(m,n+1,n) + \alpha_2 a(m,n,n+1)\right) \quad (1.4.16)$$

$$a(m+1,1,N) = \rho\alpha_1 a(m,2,N) \quad (1.4.17)$$

$$a(m+1,N,1) = \rho\alpha_2 a(m,N,2) \quad (1.4.1)$$

For $2 \leq k \leq N-2$

$$a(m+1,k,N) = a(m,k-1,N) + \alpha_1 \rho a(m,k+1,N) \quad (1.4.19)$$

$$a(m+1,N,k) = a(m,N,k-1) + \alpha_2 \rho a(m,N,k+1) \quad (1.4.20)$$

$$a(m+1,N-1,N) = a(m,N-2,N) + \frac{1}{2}a(m,N-1,N-1) + \alpha_1 \rho a(m,N,N) \quad (1.4.21)$$

$$a(m+1,N,N-1) = a(m,N,N-2) + \frac{1}{2}a(m,N-1,N-1) + \alpha_2 \rho a(m,N,N) \quad (1.4.22)$$

$$a(m+1,N,N) = \rho a(m,N,N) + a(m,N-1,N) + a(m,N,N-1) \quad (1.4.23)$$

with initial condition

$$a(0,0,0) = 1, \quad a(0,i,j) = 0, \ \forall i,j, i+\neq 0 \quad (1.4.24)$$

By working on these recurrence relations iteratively we can easily determine the coefficients $a(m,i,j)$ of τ^m in equation (1.4.1) computationally.

REFERENCES

1. Abate, J. and Whitt, W. (1988) - Approximations for the $M|M|1$ busy-period distribution, *Queueing Theory and Appl*., 149 - 191, North Holland, New York.
2. _(1987) – Transient behaviour of the $M|M|1$ queue: starting at the origin, *Queueing Systems*, 2, 41 - 65.
3. __(1989) – Calculating time -dependent performance measures for the $M|M|1$ queue, *IEEE Trans. Comm*., 37, No. 10, 1102 - 1104.
4. Adan, I.J.B.F., van de Waaresenburg Houtum, G.J., Wessels, J. and Zijm, W.H.M. (1993) - A compensation procedure for multiprogramming queues, *O.R. - Spektrum*, 15, 95 - 106.
5. Adan, I.J.B.F. and Wessels, J. (1993a) - Analysing shortest expected delay routing for erlang servers, Memorandum COSOR 93-38, Department of Mathematics and Computer Science, Eindhoven University of Technology.
6. Adan, I.J.B.F., Wessels, J. and Zijm, W.H.A. (1990a) - Analysis of the symmetric shortest queue problem, *Stochastic Models*, 6, 691 - 713.
7. __ (1990b) An asymmetric shortest queue problem, in : *Operations Research Proceeding,* Berlin, 434-441.

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RESEARCH ARTICLE

Modulation of Rapid Cell Death in *Bordetella bronchiseptica*

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ABSTRACT

Previous studies showed that *Bordetella bronchiseptica* was found to exhibit a nutrition stress-related, caspase dependent, post-exponential rapid cell death (RCD). In the present study addition of certain amino acids, glucose, caffeine (a known inhibitor of a phosphodiesterase that breaks down cAMP), and forskolin (from the herb *Coleus forskholii*, known to activate the enzyme adenylate cyclase that forms cAMP) to the rapid cell death (RCD)-favoring medium prevented RCD. These inhibitors inhibited the caspase enzyme activity in vivo and consequently the RCD process. Similar to XCG, the RCD in *Bordetella* is accompanied by rapid depletion of intracellular NAD^+ levels. A Psi blast search with yeast metacaspase picked up a caspase-like protein in the *Bordetella* protein database having more than 60% similarity at catalytic "cysteine-histidine" dyad characteristic of all metazoan caspases.

Keywords: glucose, nutrition, protein, enzyme, *Bordetella bronchiseptica,*

INTRODUCTION

In eukaryotes, programmed cell death (PCD) is a genetically regulated self destruction process for the elimination of damaged or unwanted cells. It plays an important role in the development and maintenance of the integrity of organisms [1-3]. Cells undergoing PCD exhibit a number of biochemical, physiological, and morphological features. Similarly to eukaryotes, PCD in bacteria is a complex and regulated process that is essential for bacterial communities' survival, differentiation, and spreading [4]. Other advantages of multicellular organization in bacteria are stress response, development, genetic transformation, and biofilm formation [5-6]. The similarities observed between cell death systems of animals, plants, and bacteria suggests endosymbiotic acquisition of bacteria by

eukaryotes. PCD in a cell is induced by a certain signal(s). The end point of the signaling activity is the induction and activation of caspases (cysteinyl aspartate-specific proteases), the proteases that finally execute PCD. Several investigators have reported the occurrence of PCD in bacteria regulated by chromosomal and extrachromosomal toxin-antitoxin pairs of molecules. In *Escherichia coli*, such chromosomal toxin-antitoxin systems include *mazEF*, *chpBIK*, *relBE*, *yefM-yoeB,* PezAT and *dinJ-yafQ* [7]. In *S. aureus* cidA/lrgA holin-antiholin modules mediate cell death. The bacteriocin CipB is required for altruistic lysis in *Streptococcus mutans* biofilms [5]. PCD, originally viewed as a domain of multicellular state, is a genetically regulated phenomenon that results in post-exponential stationary phase cell death in bacteria such as *Xanthomonas campestris* pv. *Glycines* (Xcg), *Bacillus subtilis* and *Bordetella bronchiseptica* [8-10]. PCD in bacteria is characterized by certain molecular features akin to eukaryotic PCD such as externalization of phosphatidyl serine, increased cellular reactive oxygen species levels, Biosynthesis of catalytically active caspase-like protein in the mid-log phase cultures. The amino acids glycine and L-alanine as well as the metabolites such as pyruvate and citrate were found to induce the synthesis of an active caspase-3-like protein that was associated with the onset of RCD[8]. Computational analysis of the already sequenced genomes revealed that the apoptosis-related domains in bacteria typically form complex multi-domain architectures. These multi-domain proteins contain fusions between apoptosis-related domains, such as apoptotic ATPases fused with a meta caspase or a toll interleukin-receptor (TIR) domain [11-12]. Xcg caspase was found to be inherently associated with poly(ADP-ribose) like protein (PARP) like protein in the modulation of RCD [13]. The affinity purified Purified caspases from Xcg and *bacillus subtilis* was found to migrate at 80 Kda on SDS-PAGE [9-10]. *Bordetella bronchiseptica* is a small, Gram-negative, rod-shaped bacterium known to cause infectious bronchitis in dogs and other animals, but rarely infects humans[14-15]. Results of previous studies showed that *Bordetella* was found to exhibit a nutrition stress-related, caspase dependent, postexponential rapid cell death (RCD) [9]. The present study was carried out to understand whether the RCD process in *Bordetella* mimicks the cell death phenomenon in Xcg.

MATERIALS AND METHODS

Cell viability studies, caspase protein assay and western analysis were performed as described previously [8, 9. 10, 13].

Intracellular NAD^+ Assay

Intracellular NAD^+ levels were assayed by means of enzymatic cycling procedure as described previously [13]. The absorbance (A_{570}) was recorded in a spectrophotometer. The results were calibrated with NAD standards.

RESULTS AND DISCUSSION

Inhibition of RCD by cAMP and its modulators

Glucose (2%), cyclic AMP (1 mM), forskolin (30 µM) and caffeine (1 mM) were found to significantly inhibit the RCD process without inhibiting caspase biosynthesis (Fig.1). Approximately 75% inhibition of *in vivo* caspase activity was observed in the presence of RCD inhibitors such as glucose, cAMP, forskolin and caffeine (Table 1).

Amino acids as inhibitors of RCD

Of the twenty standard amino acids tested, ten were found to inhibit the RCD in LB growing *Bordetella* culture (Table-2). All basic amino acids (arginine, lysine, and histidine) and acidic amino acids glutamic acid and aspartic acid completely inhibited RCD in LB growing *Bordetella* cultures at 100 mM concentration (Table-2 and Table-3). The viable cell count at 96 h of incubation was maintained at ~8 $\log_{10}$ cfu/ml in the presence of the three basic amino acids. In addition proline, leucine, isoleucine, and glutamine also showed inhibition of RCD at 100 mM in LB grown culture. In case of L-Cys RCD was inhibited at a very low concentration of 7.5 mM concentration (Table-2 and Table-3). All the above repressing amino acids were found to inhibit RCD immediately after addition to the culture during

exponential phase and as late as 24 h (Table-2). These results indicated that the repression was not at the level of caspase biosynthesis, but at some other levels of regulation of RCD after caspase-3 biosynthesis

NAD^+ depletion in RCD promoting media

Nicotinamide adenine dinucleotide (NAD^+) is an important cofactor in all living cells that is involved in fundamental cellular processes such as metabolism, cell signalling, gene expression, DNA repair etc. NAD^+ levels were found to be depleted during aging and in certain conditions such as cancer, neurodegenerative diseases and various metabolic disorders [16]. Boosting NAD^+ levels helps in overcoming age related disorders. *Bordetella* cultures displayed rapid depletion of NAD^+ in RCD promoting media (LB + 100 mM alanine). In LB medium alone without RCD inducer alanine, the depletion of NAD^+ levels were gradual, implying conservation of NAD^+ in non-RCD promoting medium (Fig. 2). These observations were consistent with previously reported observations in Xcg wherein the cells undergoing RCD showed rapid depletion of cellular NAD^+ in the post exponential phase [13].

In Xcg fortification of caffeine, forskolin and glucose to LB medium enhanced intracellular cAMP levels at the onset of stationary phase, while RCD inducers contributed to depletion of intracellular cAMP [8]. In certain eukaryotes, such as yeasts, higher glucose levels have been reported to result in higher cAMP levels [17]. However, contrary to expectations, we observed higher cellular cAMP levels were observed in the presence of inhibitors of RCD including glucose and lower cAMP levels in the presence of inducers of RCD. It appears that *Bordetella* has a system similar to Xcg. Similar to Xcg rapid depletion of cellular NAD^+ was observed in the RCD of *Bordetella*. Psi BLAST search with yeast caspase showed the presence of metacaspases in the members of *Xanthomonadaceae*, *Anabaena*, and the metacaspases of fungi and possessed a conserved catalytic “cysteine-histidine” dyad of human caspases. A caspase family protein from Bordetella bronchiseptica (NCBI Reference Sequence: WP_033457779.1) exhibited >60% similarity at the “cysteine-histidine” dyad with Putative caspase gene of *Xanthomonas campestris* pv. *glycines* (Reference ID: DQ394570.1). The signal transducing mechanism as well as the biological characteristics of this bacterial caspase remains to be elucidated.

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REFERENCES

1. Zmasek CM, Godzik A. Evolution of the animal apoptosis network. Cold Spring Harb Perspect Biol 2013;5:1-12.
2. Shalini S, Dorstyn L, Dawar S, kumar S. Old, new and emerging functions of caspases. Cell Death Differ 2015; 22:526–539.
3. Engelberg-Kulka H, Amitai S, Kolodkin-Gal I, Hazan R. Bacterial Programmed Cell Death and Multicellular Behavior in Bacteria. PLoS Genet 2006;2:e135.
4. Bayles K. Bacterial programmed cell death: making sense of a paradox. Nat Rev Microbiol 2014;12:63–69.
5. Stijn HP, Marien IdJ. For the greater good: Programmed cell death in bacterial communities Microbiol Research 2018;207:161-169.
6. Allocati N, Masulli M, Di Ilio C, De. Laurenzi V. Die for the community: an overview of programmed cell death in bacteria. Cell Death Dis 2015;6:e1609.
7. Fraikin N, Goormaghtigh F, Melderen LV. Type II toxin-antitoxin systems: evolution and revolutions. J Bacteriol 2020;202:1-14.
8. Raju KK, Gautam S, Sharma A. Molecules involved in the modulation of rapid cell death in *Xanthomonas.* Journal of Bacteriol 2006;188:5408-16.

9. Kalidindi KR. Caspase Dependent Rapid Cell Death in *Bordetella bronchiseptica*. Indian J Natural Sci 2020;10:24251-256.
10. Kalidindi KR. Caspase Dependent Rapid Cell Death in *Bacillus subtilis*. Indian J Natural Sci 2020;10:24727-32.
11. Leopold E, Claudia B, Marcela H, John LV, Wolfgang S, Aumaid U et al., Identification of Novel Mammalian Caspases Reveals an Important Role of Gene Loss in Shaping the Human Caspase Repertoire. *Mol Biol Evol 2008;*25:831–841.
12. Koonin E, Aravind L. Origin and evolution of eukaryotic apoptosis: the bacterial connection. Cell Death Differ 2002;9:394-404.
13. Raju KK, Misra HS, Sharma A. Xanthomonas caspase displays an inherent PARP-like activity. FEMS Microbiology Letters; 2007;272:259-68.
14. Galeziok M, Roberts I, Passalacqua J. Bordetella bronchiseptica pneumonia in a man with acquired immunodeficiency syndrome: a case report. J Med Case Reports 3 2009;76:1-9.
15. Woolfrey BF, Moody JA. Human Infections Associated with Bordetella bronchiseptica. Clinical Microbiol Reviews 1991;*4*:243-255.
16. Yahyah A, Yumin Q, Jun T, Evandro FF. Therapeutic potential of boosting NAD^+ in aging and age-related diseases. Translational Medicine of Aging 2018;2:30-37.
17. Sonia CP, Ma L, Cauwenberg J, Winderickx M, Crauwels A, Teunissen D et al., Involvement of distinct G-proteins, Gpa2 and Ras, in glucose- and intracellular acidification- induced cAMP signaling in the yeast *Saccharomyces cerevisiae*. EMBO J *1998;*17:3326-3341

Table 1. *In vivo* Caspase activity of *Bordetella* cells when grown in LB fortified with different RCD inhibitors. Approx. 20 μg of the total protein was used for each assay with a specific colorimetric caspase-3 substrate (Ac-DEVD-pNA) and absorbance (A_{405}) was recorded after 30 min

RCD Inhibitors	*In vivo* caspase activity
LB	0.165±0.005
LB + Glucose (2%)	0.063±0.002
LB + cAMP (1 mM)	0.065±0.005
LB + Caffeine (2.5 mM)	0.060±0.003
LB + Forskolin (30 μM)	0.061±0.005

Table 2. Viable count of *Bordetella* cells (cfu/ml) at 96 h of incubation when grown in LB medium having RCD repressors added at different time intervals.

Molecules repressing RCD	**Conc. (mM)**	**Time (h) of addition of inducer**			
		0	6	15	24
L-Arg	100	$2x10^8 \pm 1x10^7$	$3x10^7 \pm 2x10^6$	$2x10^8 \pm 1x10^7$	$1x10^8 \pm 2x10^7$
L-Lys	100	$2x10^8 \pm 8x10^6$	$3x10^8 \pm 1x10^7$	$2x10^8 \pm 4x10^7$	$3x10^8 \pm 8x10^6$
L-His	100	$2x10^8 \pm 1x10^7$	$2x10^8 \pm 1x10^7$	$1x10^8 \pm 4x10^7$	$2x10^8 \pm 8x10^6$
DL-ASP	100	$2x10^7 \pm 8x10^6$	$2x10^7 \pm 7x10^5$	$2x10^{67} \pm 1x10^7$	$2x10^7 \pm 2x10^7$
L-Glu	100	$2x10^7 \pm 4x10^5$	$3x10^7 \pm 2x10^4$	$1x10^6 \pm 9x10^7$	$3x10^7 \pm 1x10^7$
L-Gln	100	$2x10^9 \pm 2x10^8$	$2x10^8 \pm 7x10^7$	$2x10^8 \pm 8x10^7$	$3x10^8 \pm 1x10^8$
L-Pro	100	$4x10^8 \pm 9x10^7$	$8x10^7 \pm 9x10^7$	$2x10^8 \pm 2x10^7$	$2x10^8 \pm 1x10^7$
L-Cys	7.5	$3x10^8 \pm 2x10^7$	$9x10^7 \pm 6x10^6$	$2x10^8 \pm 5x10^7$	$2x10^8 \pm 7x10^7$
L-Leu	100	$7x10^7 \pm 7x10^6$	$7x10^7 \pm 7x10^6$	$2x10^8 \pm 6x10^7$	$2x10^8 \pm 4x10^7$
L-Ile	100	$7x10^8 \pm 5x10^8$	$7x10^7 \pm 8x10^6$	$3x10^8 \pm 1x10^8$	$4x10^7 \pm 8x10^6$
LB alone	0	$1x10^5 \pm 2x10^5$	$1x10^5 \pm 1x10^5$	$4x10^5 \pm 1x10^5$	$2x10^5 \pm 1x10^5$

Figures rounded to nearest whole number.
Cfu: colony forming units
Numbers after (±) symbol denote standard deviations from three replicates

Table 3. *In vivo* caspase-3 enzyme activity of *Bordetella* cells grown in LB medium with different RCD repressors. Caspase-3 activity was determined using Ac-DEVD-PNA (p- nitroanilide) as substrate and cell lysate as enzyme source.

Molecules repressing RCD	Conc. (mM)	Absorbency at 405 nm
LB (Control)		0.144 ± 0.04
L-Arg	100	0.060 ± 0.0007
L-Lys	100	0.060 ± 0.002
L-His	100	0.057 ± 0.003
DL-ASP	100	0.056 ± 0.001
L-Glu	100	0.069 ± 0.007
L-Gln	100	0.056 ± 0.007
L-Pro	100	0.060 ± 0.003
L-Cys	7.5	0.060 ± 0.003
L-Leu	100	0.052 ± 0.005
L-Ile	100	0.049 ± 0.01

Numbers after (±) symbol denote standard deviations from three replicates.

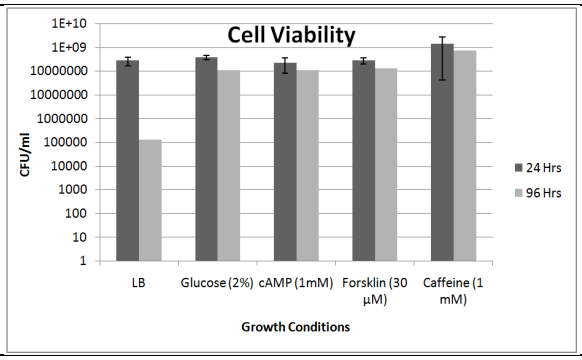

Fig. 1. Viable cell count of Xcg (cfu/ml) at the onset of stationary phase (24 h) and during RCD phase (96 h), showing inhibition of RCD in cells grown in LB medium with glucose, cAMP, caffene, and forskolin. The mean and SD of at least three replicates were plotted as cfu/ml.

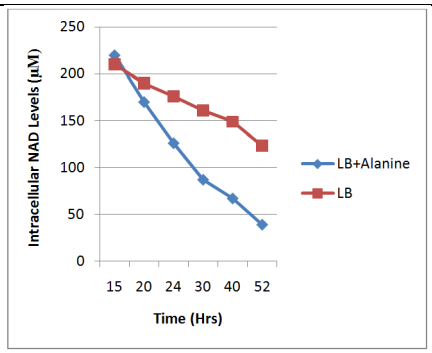

Fig.2. Intracellular NAD+ levels measured at different time intervals (15, 20, 24, 30, 40 and 52 h) in *Bordetella* cells grown under different growth conditions (LB and LB+100 mM alanine). NAD+ levels were represented in µM and each point on the graph is the mean of three independent determinants.

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RESEARCH ARTICLE

Removal of Heavy Metals from Aqueous Solution by using Agricultural and Industrial Wastes as Adsorbents

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ABSTRACT

Fresh water accounts for 3% of water resources on the Earth. Human and industrial activities produce and discharge wastes containing heavy metals into the water resources making them unavailable and threatening human health and the ecosystem. . Metal ion contamination of drinking water and waste water is a serious ongoing problem especially with high toxic metals such as lead, cadmium, copper, arsenic and zinc. The heavy metals pollution among various types of contaminations is a serious hazard for environment and human health. Different methods of removing heavy metals have different advantages and disadvantages, among them biological techniques of absorption or adsorption have been considered. In this study, Arsenic is a toxic metal, which is carcinogenic in nature as reported earlier. The *Prunus armeniaca* is the family of apricot pit shell (*Prunus armeniaca*) which is used as an adsorbent in this study. The removal efficiency of arsenic by the apricot pit shell (APS) was determined by means of adsorption parameters pH, contact time, initial concentration and adsorbent dosage. Therefore especially the use of these materials is attractive from the economic point of view as the most affordable and cheap.

Keywords: Adsorption parameters, Environmental sludge, Heavy metals, Initial concentration.

INTRODUCTION

Adsorption

A separation where in certain fluid elements are transferred to solid surface of the adsorbents is known as adsorption. Transfer of molecules from bulk solution to solid surface occurs based on concentration gradient. Here when a solid surface is exposed to a fluid phase, the molecules from the fluid phase accumulate or concentrate at the surface of a solid. All adsorption processes depend on mass transfer rates and solid-liquid equilibria [1]. The process is referred to as "desorption" if the mass transfer takes place in opposite direction. Highly porous materials are chosen as adsorbents, and adsorption occurs mostly on the pore walls are at particular sites within the particle. Difference in shape, molecular weight or polarity makes the molecule stronger on the surface of other materials which makes separation easier. Solute diffusion rate in the capillary pores of adsorbent determines the overall adsorption rate. Rate of adsorption is equal to the square root of contact time with adsorbent.

Types of Adsorption Processes

Adsorption can be carried out as batch, semi batch and continuous processes. When little quantities are to be treated, batch processes are generally carried out and the equilibrium distribution depends on the contact time in batch process [2]. Heavy metals in waste water include Cd, Cu, Zn, Cr, and As and most of the companies fail to solve the problems caused due to these discharge, as they lack proper technical knowledge and economic capabilities. The concentration of various heavy metals in waste water ranges from 10ppm to 100 ppm [3]. Adsorbate and adsorbent experience certain attractive forces which bind them and these forces can be due to Vander Waals forces which are weak in nature or they may be due to chemical bonds which are strong in nature. On the basis of attraction and the strength of force prevailing between adsorbate and adsorbent, adsorption can be categorized into two.

Physical Adsorption

Also known as physisorption, it occurs when the attractive forces present between adsorbate and adsorbent are weak like Van der Waals forces as in the low enthalpy of adsorption(i.e. Δ adsorption = 20 to 40KJ/mol) and occurs with development of multilayer of adsorbate on adsorbent. This phenomenon decreases with an increase in temperature and usually takes place at a lower temperature which is generally much below the boiling point of the adsorbate [4].

Chemical Adsorption

Also known as chemisorption, it occurs when the attractive forces between the adsorbate and adsorbent are chemical forces of attraction or via chemical bond. Here only a single layer formation of the adsorbate on adsorbent takes place and it has a high enthalpy of adsorption (i.e., ΔHadsorption = 200 to 400KJ/mol). This phenomenon first increases and then decreases with a rise in temperature [5].

Biosorption

The removal of metals or nonmetals and tiny particulates from a solution by means of any biological component is known as biosorption [6]. Cellular products and living and nonliving biomass can be used for effective adsorption [7], but their cost-effectiveness and reusability factor still remains under question. There are various physical, chemical and biological methods to remove metal ions from aqueous solutions. Some of the conventional techniques like filtration, membrane technology and ion exchange are very expensive and chemical precipitation and electrochemical treatment are prove to be ineffective especially when the concentration of metal ion is 1–100mg/L. It also results in large sludge production [8]. Many biological materials have high eradication rate in decreasing the concentration of heavy metals from ppm to ppb level [9]. Few types of biosorbents bind onto heavy metals with no specific priority, whereas others are specific for certain types of metals [10, 11]. This is one of the major reasons that research and studies on biosorption have become one of the most active work areas. In particular the low cost biosorbents obtained from agricultural and animal wastes are of major interest [12]. But the selection of biosorbent

for a specific metal is a challenge and merely a hit and trial method, resulting from a series of experiments and in-depth research. We have attempted to carry out relevant researches on biosorption phenomena for the effective removal of metal ions using various agricultural wastes and to provide a summary of available information none a wide range of biosorbents through this paper [13].

Heavy metals

Heavy metals play an important role in water pollution. The heavy metals are continuously released into the aquatic eco system from industrial process like mining, ore processing, metal processing, metal polishing, cleaning, paint manufacturing and battery manufacturing industries. These industries are producing large amounts of effluents, which are leading to detrimental effects on human life and environment, when it is discharged into water bodies. Moreover the heavy metals are not metabolized and they are bioaccumulated into our body through the biological chain [14]. The major pollutants in effluents are mercury, chromium, arsenic, lead, zinc, copper, and cadmium. Among them arsenic is one of the most toxic metal which causes serious health hazards to the environment. Arsenic is the primarily most common inorganic contaminant in the ground water. Arsenic is the 19th most abundant element in Earth's crust with an average concentration of 1.5-5 mg/kg. Some important alloys contain arsenic as the basic element. Arsenic and arsenic compounds are used in the manufacture of pigments, sheep-dips, leather preservatives and poisonous baits. They are also used in catalysts, pyrotechnics, antifouling agents in paints, pharmaceutical substances, dyes and soaps, ceramics, alloys (automotive solder and radiators), and electrophotography. Generally arsenic exists in two oxidation state they are As (III) and As (V) [15]. Although trivalent arsenic (As^{3+}) is required in trace amounts for sugar and lipid metabolism [16], few cases have been reported where its complete removal from the diet has caused arsenic deficiency. Arsenic is one such metal, which is a potent carcinogenic and mutagenic [17]. Also Long-term exposure to arsenic from drinking-water and food can cause cancer and skin lesions. It has also been associated with cardiovascular disease and diabetes. In utero and early childhood exposure has been linked to negative impacts on cognitive development and increased deaths in young adults. Arsenic is becoming more toxic form of the metal due to its association with methyl group as mono methyl arsenic (MMA). It is more rapidly, in acidic environment.

However, at high concentration, Arsenic may overcome the reducing capacity of environment and thus, persists as a pollutant. Its concentration in industrial waste water ranges from 1.5 mg/L to 2.3 micro gram/L [18]. According to that of Environment protection agency (EPA) the tolerance limit for the discharge of as into inland surface water is 0.01 mg/L and in potable water is 0.05 mg/L. The As is considered as a pollutant by Environment protection agency (EPA) because of its toxicity, water soluble and carcinogenic nature [19].The permissible limit for arsenic based on World Health Organization (WHO) value is 0.01 mg/L and it is also referred as carcinogenic and genotoxic [20]. The Bureau Indian Standard (BIS) given that the no relaxation beyond 0.01 mg/l for portable water above this limit may cause carcinogenic [8]. According to the ministry of environment and forest, India suggests that the minimal national standard (MINAS) has a limit to discharge the effluent in surface water as 2 mg/L [21]. The LD 50 values for arsenic ranged between 50 and 150 mg/kg [22]. So it is necessary to remove such a toxic metal from our environment. In practice there are various conventional methods available for the removal of toxic metals such as reverse osmosis, precipitation, chemical reduction etc., but these methods are required high experimental set-up, more expensive and also less effective. Of these methods biosorption is the most promising method for the removal of toxic metals which is low cost, produced less secondary sludge, more effective and eco-friendly. Biosorption is important from two points that the elimination of poisonous metals and the recovery of precious elements. Generally biosorption is considered to be fast physico-chemical method and it may possible when the dissolved species present in sorbent and sorbate to be sorbed with aid of the higher affinity of biosorbent species for the sorbate species [23]. In recent years, many researchers used an agricultural waste such as fruit peels [12, 13], plant leaves [24, 25] vegetable shells [26, 27, 28, 29], rice husks [30] and sawdust [31, 32] etc. for the adsorption process because of their high removal efficiency and low cost. In this study, Apricot pit shell (*Prunus armeniaca*) was taken as an adsorbent for the removal of the arsenic. The present study investigates the removal efficiency of an Apricot pit shell (*Prunus armeniaca*) against trivalent arsenic, analyzes the adsorption parameter and the experimental results.

LITERATURE REVIEW

Nisha gaur et al, 2018

Biosorption is a promising approach for removal of heavy metals. It is not only cost-effective but also shows selectivity and high efficiency toward the removal of heavy metals. Moreover, it does not produce any toxic sludge. These observations postulated for the first time that soya bean adsorbent at the dose of 3 g/100 ml was effective in ameliorating Pb and As-induced contamination from wastewater. However, better efficacy was shown by the same at optimum temperature (37 °C), pH (4.0 for Pb and 2.0 for As) and contact time (60 min). Additionally, the isotherm study indicates that the Langmuir and Freundlich isotherm models can adequately model sorption data. As the temperature of the solution increased, the equilibrium removal of metal ions deceased. It was found that the adsorption by soya bean adsorbent is an exothermic process. The thermal degradation analysis suggested that the degradation occurs in two steps and the soya waste is thermally stable. All the adsorbents mentioned in Table 2 were effective in the removal of Pb and As from wastewater. In the current study, soya waste adsorbent removed 80% of Pb and 40% of As from wastewater. The results are comparable with other mentioned adsorbent in Table 3. Some of the adsorbent are showing more than 95% removal and 100% removal as well. These adsorbents were modified with different chemicals to enhance its adsorption capacity. But in the present study adsorbent was used without prior chemical treatment or modification. Therefore, in the future studies its efficiency can be enhanced and evaluated by preparing adsorbent through chemical treatment.

Khai Ngyen et al, 2019

Iron-ore sludge (SBC) shows potential in the adsorption of As and heavy metals from water. The adsorption performance can be described by both the pseudo-first-order and the pseudo-second-order kinetic models, with a slightly better fit of the data to the latter, indicating that chemical adsorption occurred. The Langmuir maximum adsorption capacities of Pb, As, Cd, Zn, and Mn in the single-metal experiments were 1.305, 1.113, 0.771, 0.745, and 0.710 mg/g, respectively, and in the mixed-metal experiments for Pb, Cd, Zn, and Mn were 1.059, 0.484, 0.447 and 0.370 mg/g, respectively. The results show that iron-ore sludge is a promising adsorbent to remove potentially toxic pollutants from water.

MATERIALS AND METHODS

Apricot (*Prunus armeniaca*) fruit has been recommended for human consumption due to its numerous health benefits, including fiber, minerals and a variety of vitamins, such as Vitamin A, Vitamin C, Vitamin K, thiamine, riboflavin, niacin, and panthotenic acid. Apricot fruit also possesses a relatively high antioxidizing capacity attributed to phenolic and carotenoid compounds [33–37]. The fruits can be used fresh, dried, or processed as fruit juice, jam, and jelly. Apricots may also be consumed canned 16% of US production [38].

Adsorbent

In the present study Apricot pit shell (*Prunus armeniaca*) were taken as adsorbent for this experimental work. They were washed with distilled water several times to remove dirt particles and kept under shade for some time, dried for three hours in an oven at 150ºC and then allowed to cool at room temperature, the dried components were roasted and converted to charcoal (Bio adsorbent) with the help of China dish, subsequently they were crushed and the ground charcoal were stored in an air –tight container, without adding chemicals.

Adsorbate

The stock solution (100 mg/L) was prepared by dissolving 0.139 g of H_2AsO_4 (AR grade, Merck chemicals) in distilled water. The working solution was obtained by diluting stock solution. Once again the concentration of stock and working solutions were confirmed by calorimeter.

Batch adsorption studies

This is a way expressing very dilute concentrations of substances. Just as per cent means out of hundred, so parts per million or ppm means out of a million. Usually describes the concentration of something in water or soil. One ppm is equivalent to 1 milligram of something per liter of water (mg/L) or 1 milligram of something per kilogram soil (mg/kg). The metal solution used in this study were prepared as the stock solution containing 1000 mg/L of each metal. 100 ml of adsorbate solution with known concentration was taken in 250 ml conical flask and 1g of each adsorbent was added separately and then reactant was stirred by magnetic stirrer without any PH modification at room temperature. For a wide range contact time 30-180 mints. After that the solution was filtered by Whatman 42 filter paper and concentration of the filtered solution was determined by atomic absorption spectrophotometer [40] The percentage removal was determined by the following expression.
The amount of adsorption efficiency was calculated by,

$$\text{Adsorption percentage} = \frac{Co-Ce}{Co} \times 100$$

Where
Co is the Initial concentration of metal ion in the solution (mg/lit)
Ce is the final concentration of metal ion in the solution (mg/lit).

RESULTS AND DISCUSSION

Bioremediation is one of the new cleanup concepts, which involves the use of plant charcoal to clean contaminated environments. In the present study pit shell of apricot fruits were used for the phytoremediation. Arsenic is a serious cumulative body poison. Natural water usually contains up to 0.01mg/L of arsenic, maximum concentration of arsenic in drinking water is 0.10 mg/L prescribed by (WHO). That is why very small concentration i.e. 8ppm of arsenic solution was prepared for the present investigation. It was found that the carbon dose played an important role in the adsorption of heavy metal arsenic (As) from waste water. Phytoremediation is compensated by bio adsorbent. Materials such as (potato peels, tea dust, egg shell, seed shell, rice husk, fly ash, almond seed shell etc.,) have been widely investigated as potential bio adsorbents of heavy metals [41]. In the present study with apricot pit shell (*Prunus armeniaca*) it was found that the observed concentration with percentage of arsenic (table2, fig-1) and the adsorption percentage of arsenic in ppm by using batch adsorption technique (table-3). Were maximum the presence of apricot pit cell (*Prunus armeniaca*) which were 99.142% and 0.007 respectively. The particle size and dose of carbon in different parts of the plants. These adsorbents appears to be technically feasible, user friendly and ecofriendly process. This work suggests that various such potential adsorbents are to be screened and used as good adsorbent material for to remove heavy metals from the environment including arsenic. The effect of the amount of adsorbent on the removal of As by apricot pit shell is depicted in (table-3)for varied adsorbent doses of 30, 40, 50, 60 and 70 mg/L. As removal using apricot pit shell increased from 59.68% to 99.142% i.e. with the increase of the amount of absorbent concentration.

CONCLUSION

In this study the Apricot pit shell was found to be effective adsorbent for the removal of trivalent arsenic 100 % removal is carried out by using 0.007g of adsorbent for all initial concentration and maximum removal of

arsenic is done at pH 3.8. From the isotherm studies, the adsorption capacity. This strongly suggests that the favorable adsorption take place on the surface of the adsorbent. Thus Apricot pit shell was suitable adsorbent for the removal of trivalent arsenic.

REFERENCES

1. Campbell, O.E.; Merwin, I.A.; Padilla-Zakour, O.I. Characterization and the effect of maturity at Harvest on the Phenolic and Carotenoid Content of Northeast USA Apricot (Prunus armeniaca) Varieties. J. Agric. Food Chem. 2013, 61, 12700–12710.
2. Campbell, O.E.; Padilla-Zakour, O.I. Phenolic and carotenoid composition of canned peaches (Prunus persica) and apricots (Prunus armeniaca) as affected by variety and peeling. Food Res. Int. 2013, 54, 448–455.
3. B.-C.Pan, H.Qiu, L.V.Lu, Q.-J.Zhang, Q.-X.Zhang, andW.-M. Zhang, "Critical review in adsorption kinetic models," Journal of Zhejiang University Science A, vol. 10, pp. 716–724, 2009.
4. A. Mishra and B. D. Tripathi, "Utilization of fly ash in adsorption of heavy metals from wastewater," Toxicological and Environmental Chemistry, vol. 90, no. 6, pp. 1091–1097, 2008.
5. M.F.DeBoodt, "Application of the sorption theory to eliminate heavy metals from waste waters and contamined soils. In interaction at the soil colloid- soil solutions interface," in Interactions at the Soil Colloid—Soil Solution Interface, G. H. Bolt, M. F. De Boodt, M. H. B. Hayes, and M. B. McBride, Eds., vol. 190 of NATO ASI Series E: Applied Sciences, pp. 293–320, Springer, Berlin, Germany, 1991.
6. J. P. Fraissard, Physical Adsorption: Experiment, Theory, and Applications, vol. 491, Springer Science & Business Media, Berlin, Germany, 1997.
7. B. M. W. Trapnell and D. O. Hayward, Chemisorption, Butter- worths, Oxford, UK, 1964.
8. J. Wang and C. Chen, "Biosorption of heavy metals by Saccha- romycescerevisiae: areview, "BiotechnologyAdvances, vol.24, no. 5, pp. 427–451, 2006.
9. G. M. Gadd, "Interactions of fungi with toxic metals," New Phytologist, vol. 124, no. 1, pp. 25–60, 1993.
10. B. Volesky, "Detoxification of metal-bearing effluents: biosorption for the next century," Hydrometallurgy, vol. 59, no. 2-3, pp. 203–216, 2001.
11. B. Volesky and Z. R. Holan, "Biosorption of heavy metals," Biotechnology Progress, vol. 11, no. 3, pp. 235–250, 1995.
12. M. Jaishankar, B. B. Mathew, M. S. Shah, T. P. Krishnamurthy, and S. K. R. Gowda, "Biosorption of few heavy metal ions using agricultural wastes, "Journal of Environment pollution and Human Health, vol. 2, no. 1, pp. 1–6, 2014.
13. S. E. Bailey, T. J. Olin, R. M. Bricka, and D. D. Adrian, "A review of potentially low-costs adsorbents for heavy metals," Water Research, vol. 33, no. 11, pp. 2469–2479, 1999.
14. N. Gaur, G. Flora, M. Yadav, and A. Tiwari, "A review with recent advancements on bioremediation-based abolition of heavy
15. Zavvar Mousavi, H.; Seyedi, S. R, Int. J. Environ. Sci. Tech, 2011, 8 (1), 195.
16. Khai M. Nguyen , Bien Q. Nguyen , and Ha T.H. Nguyen, J. of. Applied Science, 2007.
17. Kirkley A. G., Carmean C. M., Ruiz D., et al. Arsenic exposure induces glucose intolerance and alters global energy metabolism. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 2018; 314(2):R294–R303. Doi: 10.1152/ajpregu.00522.2016.
18. Singh R., Singh S., Parihar P., Singh V. P., Prasad S. M. Arsenic contamination, consequences and remediation techniques: a review. *Ecotoxicology and Environmental Safety*. 2015; 112:247–270. Doi: 10.1016/j.ecoenv.2014.10.009.
19. Panel JieGeBiswarupGuhab et al, science direct, volume 725, July 2020.
20. Nisha Gaur1 · Aayush Kukreja1 · Mahavir Yadav1 · Archana Tiwari1, Applied Water Science (2018) 8:98, 18 June 2018.
21. Belete Geremew, A Review on Elimination of Heavy Metals from Wastewater Using Agricultural Wastes as Adsorbents. Science Journal of Analytical Chemistry. Vol. 5, No. 5, 2017, pp. 72-75. Doi: 10.11648/j.sjac.20170505.12

22. Mohamed CHIBAN1, Mohamed ZERBET, Gabriela CARJA and Fouad SINAN1, Application of low-cost adsorbents for arsenic removal: A review, Journal of Environmental Chemistry and Ecotoxicology Vol. 4(5), pp. 91-102, 2 March, 2012
23. Thomas M. Missimer, Christopher M. Teaf, William T. Beeson, Robert G. Maliva, John Woolschlager, and Douglas J. CovertNatural Background and Anthropogenic Arsenic Enrichment in Florida Soils, Surface Water, and Groundwater: A Review with a Discussion on Public Health Risk,Int J Environ Res Public Health. 2018 Oct; 15(10): 2278.
24. J. Sirajudeen, J. Naveen, S. Arul Manikandan and M. M. Mohamed Mubashir, Removal of chromium (VI) from aqueous solution by using Citrus limetta peel as an adsorbent, Pelagia Research Library, Der Chemica Sinica, 2013, 4(2):133-143, ISSN: 0976-8505 Coden (USA) cshia5 .133.
25. Ashraf. M. A, Maah, M. J, Yusoff. I, Int. J. Environ. Sci. Tech, 2010, 7 (3), 581.
26. El-Ashtoukhya E.-S.Z, Amina. N.K, Abdel wahabb.O, Desalination, 2008,223, 162.
27. Gurusamy Annadurai, Ruey-Shin Juang, Duu-Jong Lee, J. Hazard. Materials, 2002, 92, 263.
28. Jafar Ahmed.A, Suganthana Balasubramanian, Der Chemica Sinica, 2010, 1 (2): 35.
29. Ratna S. Shelke, Jagdish V. Bharada, Balaji R. Madjea and Milind B. Ubale, Der Chemica Sinica , 2011 , 2 (4):6.
30. Onundi, Y. B.; Mamun, A. A.; Al Khatib, M. F.; Ahmed, Y. M, Int. J. Environ. Sci. Tech, 2010, 7 (4), 751.
31. Okoye, A. I.; Ejikeme, P. M.; Onukwuli, O. D, Int. J. Environ. Sci. Tech, 2010, 7 (4), 793.
32. Gabriela Huama´n Pino a, Luciana Maria Souza de Mesquita a, Mauricio Leonardo Torem a, Gustavo Adolfo Saavedra Pinto b, Minerals Engineering, 2006, 19, 380.
33. Renugadevi N, Anitha. G and Lalitha, Advances in Applied Science Research, 2010, 1 (2): 102.
34. Zulkali M M D, Ahmed A L, Norulakmal N H, Biores Technol , 2006 , 97, 21.
35. Mehmet Emin Argun, Sukru Dursun, Celalettin Ozdemir, Mustafa Karatas, J.Hazard. Mater, 2007, 141, 77. [22] Bulut Yasemin Tez Zek, Journal of Environmental Sciences, 2007, 19, 160.
36. Bulut Yasemin Tez Zek, Journal of Environmental Sciences, 2007, 19, 160.
37. Yiğit, D.; Yiğit, N.; Mavi, A. Antioxidant and antimicrobial activities of bitter and sweet apricot (Prunus armeniaca L.) kernels. Braz. J. Med. Biol. Res. 2009, 42, 346–352.
38. Ali, S.; Masud, T.; Abbasi, K.S. Physico-chemical characteristics of apricot (Prunus armeniaca L.) grown in Northern Areas of Pakistan. Sci. Hortic. 2011, 130, 386–392.
39. Campbell, O.E.; Merwin, I.A.; Padilla-Zakour, O.I. Characterization and the effect of maturity at Harvest on the Phenolic and Carotenoid Content of Northeast USA Apricot (Prunus armeniaca) Varieties. J. Agric. Food Chem. 2013, 61, 12700–12710.

Table-1 Low cost adsorbent data

Low cost adsorbents	Main consistent	Primary source	Physical structure	Chemical characterization (%)	Primary use
Apricot pit shell	Its collected from the apricot fruits	Fruit	First, in the fruit pit shells are agitated mechanically and then shell becomes granular structure, solubility in water, chemical stability and its local availability at almost no cost	Cellulose - 21.3 Hemi cellulose – 12.4 Lignin – 13.5 Carbon – 63 Hydrogen – 19 Oxygen – 7 Nitrogen -3.4 Calcium – 6 Sodium – 1 Potassium – 25 Iron – 20	Wastewater treatment

Table – 2 experimental work program

Low cost adsorption	Run	Metals	pH	Mixing speed (rpm)	Contact time (min)	Adsorbent dose (g/l)
Apricot pit shell	1	As	4.21	250	30	20
	2		6	60:250	30	20
	3		4.5	250	30:150	5:30
	4		3.8	250	120	20
	5		6	250	30	30

Table -3 As removal efficiency for different absorbent doses

Heavy metal	Adsorbent dose	In As mg/l	Apricot pit shell Outlet – As mg/l	Removal ratio %
As	30	9.67	4.5	59.68
	40	9.67	3.2	71.28
	50	9.67	2.3	83.67
	60	9.67	0.08	96.345
	70	9.67	0.007	99.142

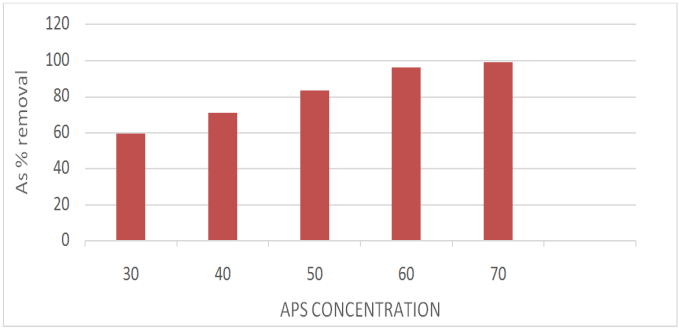

Fig.1 removal efficiency of As heavymetal using apricot pit cell

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SHORT COMMUNICATION ARTICLE

A Woman is a Shining Star in the Dark Sky a Study of Sashi Deshpande's *'That Long Silence'*

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ABSTRACT

A woman is considered as an epitome of kindness, love, care and sacrifices. She is the perfect emblem of patience. She holds her horses for the welfare of the family. Even in this modern society, male domination is prevalent in most of the families. A male is chiseled as a decision maker and a chieftain and a woman is meant for silent sacrifices and she sacrifices all her dreams, wishes and serves as a hidden camera that operates and captures the beautiful smiles and happiness of the family members. Certainly, she is the main reason for all the memorable records of memories that would never fade from the minds and hearts of the family members. This article highlights the world of woman through the protagonist Jaya in the novel 'That Long Silence'. The novelist, Sashi Deshpande's in her novel, *That Long Silence* vividly portrays a woman in a middle class family who suffers a lot to come out of the hard shell bound by conventions and culture enforced by the family and emerges out as a new woman breaking the fetters with the tools of individuality.

Keywords: emblem, chieftain, conventions, fetters, individuality

> "No act is to be done according to (her) own will by a young girl, a young woman, or even by an old woman, though in (their own) houses." (The laws of Manu 5.148)

A Woman is always under the control of a man. Woman is expected to obey the orders of man and elders and she is denied the power of expressing her wishes or decisions. She fills the bill to paint the lively smiles in the faces of

the family members with the brush of sacrifices hiding the pains. Sashi Deshpande presents the realistic women searching for her identity. She vividly portrays the struggles that women face between the two borders, tradition and modernity. The novelist depict revolt of her protagonist against the marginalization of women by men through the character Jaya in the novel *That Long Silence.* The novelist is an expert in capturing the woman's psyche and showcasing the feelings, emotions through the incidents. In the novel, *That Long Silence* the protagonist, Jaya is born into a middle-class, conventional family. She is clever, curious, and bright and she is a strong individual and the qualities are strongly condemned by her grandmother who expects her to be conventional and blindly follow the paths of women whose job is to excel at household chores. In the perspective of men and in laws, skills at doing the household chores and merely obeying the orders of men and in laws of the family are categorized under the folders of civilized and cultured women. In their perspective, the polite and unquestioned obedience make the family go a long run.

Jaya learns to play the part of a subservient woman, while retaining a sense of individuality. She learns the fact that people never likes the women who shine with the glitters of individuality or uniqueness. Therefore, she learns and excels in the art of long silence for the years to roll on. She writes in her free time, though she has failed to become successful as an author. Jaya marries Mohan, a successful businessman who is merely an epitome of authoritarian. He is like other men who never understands the feelings of woman, desires of woman and expects to do her household chores and their relationship is not intimate or happy. She is expected to execute the orders of her husband and never allowed to express her views.

When the days pass on, unexpected, unfortunate incidents come in their lives. Life becomes miserable when Mohan is suspended from his job due to misconduct. Jaya and Mohan have been down on their luck ever since Mohan's suspension. Jaya and Mohan face economic turmoil and the distance of separation becomes wide. Jaya begins writing to supplement the family income. Mohan dislikes it and moreover the articles are the reflection of her life exhibiting her dissatisfaction and unhappiness in the family. This aggravates the degree of anger and dislike on Jaya. Though he dislikes it, he is compelled to remain quiet due to the financial crisis. The miserable incidents lay Jaya a path to move towards self realization and self exploration. The downhearted events, dispirited married life, lot of bitter pills and loneliness have motivated to travel in search of her true self challenging gender oriented tradition. In the early married life, she was merely an executor of her husband's orders and later she rebuilds her life with her skills of writing. Her passion of writing becomes an outlet for her dissatisfaction.

It is vivid that Mohan and Jaya are in the position to support each other. They understand but they don't express their feelings and emotions to each other and art of the long silence has led to furthermore complications in their life. Their son leaves home and followed by Mohan. At this juncture, Jaya analyses and realizes that she was also a part of all the problems. Her long silence never let him know her intentions to supplement the family. She failed to render her moral support when her husband was in his trying period. The author colorfully weaves the threads of inner thoughts of a woman to make a festoon of Woman's psyche. The festoon looks beautiful and colorful and similarly a woman looks beautiful and pretty with smiles hiding all the sorrows and pains. The incapability of a woman to revolt against her husband makes her more submissive and silent. Silence is the best defensive tool that she holds to prolong the married life. The desires, dreams, passion and goals of a woman soon after marriage vanish into the air.

Ultimately, she evaluates and analyses her whole life and she tries to emerge as a new woman with great strength and courage. Jaya is one of the Shashi Deshpande's victorious strong women protagonists who is trampled by the male dominance in the early married life and later fights with vigor to prove her identity and individuality. The author makes the readers clearly visualize the inner conflicts of Jaya who suffers and craves for the quest of the self and identity. When Jaya goes for self examination she understands and realizes her mistakes and decides to drive away her long silence in order to build good relationship with Mohan. At this juncture, she receives a telegram from Mohan that he would come home soon. Jaya decides to accept Mohan and decides to paint the entire family with

colors of happiness and love. Thus, the novel ends with the renewal of faith. Jaya decides to live a balanced contented life. Self-actualization is possible if a woman decides to be herself, to reveal the genuine value of her free and inborn individuality in its entirety.

Works Cited

1. Figes, Eva. *Patriarchal Attitudes: Women in Society* (London : Macmillan, 1986) P.125
2. Sandhu, Sarabjit. "The Images of Woman in *That Long Silence." Indian Women Novelists*, Ed.
3. R.K.Dhawan. New Delhi: Prestige, 1991.
4. R.S. Pathak (ed), *The fictions of Shashi Deshpande* (Creative Books 1988) P.202.
5. Deshpande, Shashi. *That Long Silence*. Noida: Penguin Books India. Ltd., 1989.

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RESEARCH ARTICLE

Prospective Study of Antibiotics Utilization in Multi Speciality Hospitals in Narasaraopet at Guntur District, Andhrapradesh

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ABSTRACT

Drug use is a complex process uncertainties in diagnosis, treatment and medication adherence contribute to wide variations in the way drugs are used for any given conditions. In any country, a large number of sociocultural factors also contribute to the way drugs are used. In India, this include national drug policy, illiteracy, poverty, use of multiple health care systems, drug advertising and promotion, same of prescription drugs with out prescription, competition in the medical and pharmaceutical marketplace and limited availability of and unbiased drug information. The complexity of drug use means that optimal benefits of drug therapy in patient care may not be achieved because of under use, over use or misuse of drugs. One method to evaluate and improved drug use is conducting drug use evaluation studies. This study was prospective observational study in multi speciality hospitals in Narasaraopet at Guntur district Andhra Pradesh.The study was conducted from August 2018 to Dec 2019 in various multi speciality hospitals in Narasaraopet at Guntur district Andhra Pradesh. Total three departments we collected data Pediatrics , orthopaedic , gynaecology A total of 400 patients were participated in the current study out of 140(35%)were males and 260 (65%)were females. In this study most common group antibiotics is cephalosporins 152 (34.9%) out of 395 of which mostly cefitriaxone are most commonly prescribed 60 (46%). Study provides the information about the prospective study of antibiotics utilization in multi speciality hospital. It has helped to identify irrational prescribing patterns of drugs in various departments like pediatrics, gynaecology orthopaedic.

Keywords: Antimicrobial resistance, Drug information, Diagnosis, treatment.

INTRODUCTION

Drug use is a complex process uncertainties in diagnosis, treatment and medication adherence contribute to wide variations in the way drugs are used for any given conditions. In any country, a large number of socio cultural factors also contribute to the way drugs are used. In India, this include national drug policy, illiteracy, poverty, use of multiple health care systems, drug advertising and promotion, same of prescription drugs with out prescription, competition in the medical and pharmaceutical marketplace and limited availability of and unbiased drug information. The complexity of drug use means that optimal benefits of drug therapy in patient care may not be achieved because of under use, over use or misuse of drugs. Inappropriate drug use may also lead to increased cost of medical care, antimicrobial resistance, adverse and patient mortality. One method to evaluate and improved drug use is conducting drug use evaluation studies. Drug use/usage/utilization evaluation (DUE) was originally known as drug utilization review (DUR) in the 1970s and early 80s the terms drug utilization review and use drug evaluation are inter changeable. Medication use evaluation is another term that is used in place of due by some authors since 1994. According to the world health organization (WHO), MUE is similar to DUE in all respects except that it is patient outcome oriented and places emphasis on assessing clinical outcomes. MUE mainly aims at assessing and improving patient outcomes and there by improving the individual patients health related quality of life (HRQOL). Regardless of the terminology the main of DUE studies is to promote rational drug use. DUE is discipline that aims to understand how and why drugs are used as they are, so that drug use healthy outcomes can be improved DUE can play a key role in helping the health care system understand, interpret and improve the prescribing, administration and use of medications. DUE information may assist healthcare system and hospitals to design educational programmes that may improve prescribing and drug use. Some DUE programmes may provide physicians with feedback on their performance and prescribing patterns compared to predetermined criteria or treatment protocols. DUE information may also allow physicians to compare their approach to treating certain diseases with their peers. The peer pressure generated by these comparisons may be useful in motivating physicians to change their prescribing habits in an effort to improve care.

ANTIBIOTICS

History

Although potent antibiotic compounds for treatment of human disease caused by bacteria such as tuberculosis, plague or leprosy were not isolaeted and identified until the twentieth century,the first known use of antibiotics was by the ancient Chinese over 2,500 years ago. The antibiotic properties of penicillium spp. Were first described in France by Ernest duchense in 1897.However, his work went by without much notice from the scientific community until Alexander Fleming's discovery of pencillins. Modern research on antibiotic therapy began in Germany with the development of the narrow- spectrum antibiotic salvarsan by Paul Ehrilich in 1909, for the first time allowing an efficient treatment of the then - widespread problem of syphilis. The drug which was also effective against other spirichaetal infections, is no longer in use modern medicine. Antibiotics were further developed in Britain following the re - discovery of pencillin in 1928 by Alexander Fleming. More than ten years later, Ernst Chain and Howard Floret became interested in his work and came up with the purified form of penicillin. The three shared the 1945 Nobel prize in medicine."Antibiotic" was originally used to refer only to substances extracted from a fungus or other microorganisms, but has come to include also the many synthetic and semisynthetic drugs that have antibacterial effects. Based on chemical structure Aim and objectives: The main aim of the present study was Drug utilization of the various hospitals and also main objectives shows that improving the rationality of the drugs, improving the Socioeconomic status of patients.

METHODOLOGY

This study was prospective observational study, its shows that Patients with age group of 5-70 years are inclusive criteria and above 70 years and ICU patients were excluded.

RESULTS AND DISCUSSION

A total number of 400 peoples were involved in the study. Out of 140 were males and 260 were females. The gender distribution of patients enrolled for the study was presented in Table -1, Figure -1. A total of 400 prescriptions were collected randomly and analyzed. A total of 2030 drugs were prescribed, Average number of drugs per encounter were 5.1. Drugs prescribed from essential drugs list (WHO) were 740(33.21%). Total number of antibiotics prescribed were 395(19.5%) mostly CEFTRIAXONE were prescribed 60 (16%)

CONCLUSION

Study provides the information about the prospective study of antibiotics utilization in multi speciality hospital. It has helped to identify irrational prescribing patterns of drugs in various departments like pediatrics, gynaecology orthopaedic. Hence, the clinical pharmacist must be considered to be an integral part. They should be involved in collection and presentation of prescribing data as a part of clinical audit and also counselling of patients/ care takers. Pharmaceutical care is needed in the correct management of drugs which is even more important in various departments. The WHO core indicators helped to improvise the prescribing pattern, identify significant problems involved in the knowledge gap of patients or caretakers understanding of instructions provided by consultants and even to minimize the cost burden on patient.

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REFERENCES

1. G.Parthasarathi,kiran nyfort –hansen,milap c nahata, clinical pharmacy practice page 447-460
2. Prescription writing. British National Formulary 1998; No. 35 (March, 1998): 4-6.
3. WHO. Model list of essential drugs Geneva: World Health organization (1988)
4. Krishnaswamy K, Dinesh Kumar B, Radhaiah G. A drug use survey – precepts and practice. Eur J clin Pharmacology 1985:29.363- 370.
5. Pradhan SC, she wade DG, Bapna JS. Drug utilization studies. National Med J India (1988); 1:185-189.
6. Srishyla MV, Krishnamurthy M, Naga Rani MA, ClareM, Andare C, Venkataraman BV. Prescription audit in an Indian hospital setting using the DDD concept. Indian J Pharmacol 1994(26) 23-28.
7. HisMajestys Government, Department of drug Administration. National list of essential drugs Nepal (Third revision) 2002
8. Bhantnagar T, Mishra CP, Mishra RN. Drug prescription practices: a house hold study in rural Varanasi. Indian J PrevSoc Med (2003) ;34(1&2):33-39.
9. Abdullah D, Ibrahim N, Ibrahim M. Medication errors among geriatrics at the out patientpharmacy in a teaching hospital in keltan. Malaysian J Med sci. (2004) ; 11(2) : 11-17.s

10. Pramil T, Rajiv A, Gaurav G. Pattern of Prescribing at a paediatric outpatient setting in northern india. Indian J Pharm Pract 2012;5(1):4-8.

Table 1: Gender Distribution

	Number	Percentage
Males	140	35%
Females	260	65%
total	400	

Table -2 Based on age group total prescriptions - 400 Males were 140 Females were 260

S.No	Age group	No.of male patients	No.of female patients
1	0-20	80	120
2	21-40	20	100
3	41-60	20	25
4	61-70	20	15

Table 3: Total 400 Patients undergone the various kind of departments study was presented.

Type of Ward	No. of patients	%
Orthopedics	140	35%
Gynecology	120	33%
Pediatric	140	32%

Table. 4: Total 2030 Number of dosages forms used in this three departments

S.NO	NAME OF THE DEPARTMENT	DROPS	SYRUP	INJECTIONS	TABLETS	CAPSULES	POWDERS	CREAMS
1	ORTHOPETIC	NILL	70	215	310	190	45	50
2	GYNECOLOGY	NILL	130	125	330	202	50	NILL
3	PEDIATRIC	50	100	75	60	8	5	15
4	TOTAL	50	300	415	700	400	100	65

Table -5: Total NUMBER OF PRESCRIPTIONS 400 BASED ON CATEGORY OF DRUGS is 2030

S.NO	CATEGORY OF DRUG	Pediatric	ORTHOPEATIC	GYNOCOLOGY	TOTAL
1	ANTI-HISTAMIN	100	0	32	132
2	ANTI-BIOTIC	180	160	55	395
3	ANTIPYRETIC	60	50	43	153
4	MULTIVITAMINS	95	60	60	215
5	BRONCHODIALATOR	75	0	0	75
6	APLHA AGONIST	50	0	0	50
7	ANTIEMETIC	10	0	34	44
8	ANTISEPTIC	15	35	0	50
9	ANTIFUNGAL	10	0	0	10
10	ANTIACID	5	72	42	119

11	ANTI HELMINTICS	7	0	0	7
12	ANTI EPILEPTIC	2	45	0	47
13	NSAIDS	2	0	0	2
14	CALCIUM	0	0	80	80
15	IRON SUPPLEMENTS	10	25	47	82
16	HORMON	0	0	80	80
17	LAXATIVES	0	0	20	20
18	ANTI HYPERTENSIVE	0	40	0	40
19	ANTICOAGULANT	0	40	10	50
20	URINARY ALKANIZES	0	0	18	18
21	ANTI DIABETIS	0	40	20	60
22	CORTICOSTEROIDA	0	0	30	30
23	EXPECTORANT	0	12	12	24
24	H2 BLOCKERS	0	0	14	14
25	ANTITHYROID	0	0	10	10
26	VACCINS	0	0	16	16
27	ANTICHOLINERGIC	0	35	0	35
28	ANTIOXIDANT	0	33	0	33
29	DIURETIC	0	15	15	30
30	ANGIOTENSION	0	35	0	35
31	ANTI DEPRESANTS	0	30	0	30
32	ANTIARRHYTHMICS	0	40	0	40

Table-6 : Total number Antibiotics used in three departments 395

S.NO	NAME OF THE ANTIBIOTICS	NUMBER
1	CEFTRIOXONE+SULBACCTUM	30
2	PIPERACILLIN+TAZOBACTAM	30
3	AMINOGLYCOSIDE ANTIBIOTIC	20
4	LINEZOLID	15
5	AMPICILLIN + SULBACCTUM	25
6	CEFUROXIME	38
7	CEFTRIOXONE	30
8	AMOXICILLIN	20
9	AZITHROMYCIN	15
10	AMOXICILLIN+ CLAVULANATE	30
11	PREDNISOLONE SODIUM PHOSPHATE	15
12	MOTELUKAST SODIUM	25
13	AMIKACIN SULATE	25
14	CEFIXIME	39
15	CIPROFLOXACIN	12
16	OFLOXACIN	6
17	GENTAMICIN	10
18	METRONIDAZOLE	10

Table 7: analysis of prescriptions in the light of w. H. O prescribing indicators

Parameters	Observed value
Total number of prescriptions analyzed	400
Total number of drugs prescribed	2030
Total number of drugs prescribed from essential drug list	740
Average number of drugs per encounter	5.1
Total number of antibiotics prescribed	395
Percentage of encounters with an antibiotic prescribed	82.42%
Percentage of encounters with injections prescribed	20.8%
Percentage of drugs prescribed from essential drug list	33.21%

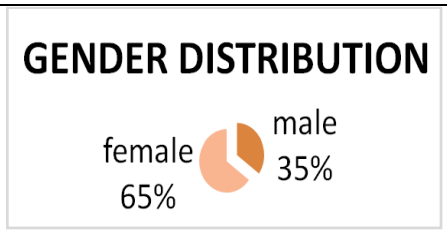

Figure 1. Gender Distribution.

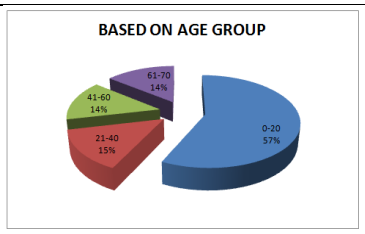

Figure 2. Based on age group total prescriptions - 400 Males were 140 Females were 260.

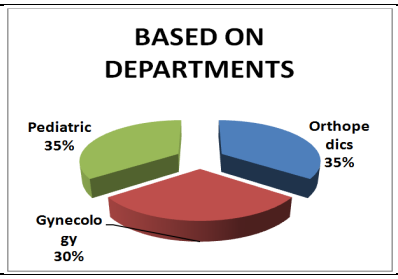

Figure 3. Total 400 Patients undergone the various kind of departments study was presented

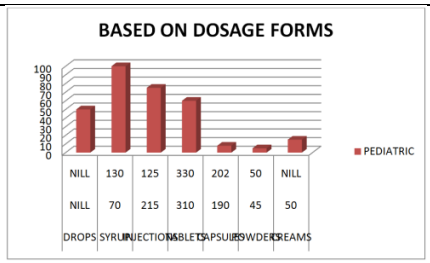

Figure 4. Total 2030 Number of dosages forms used in this three departments.

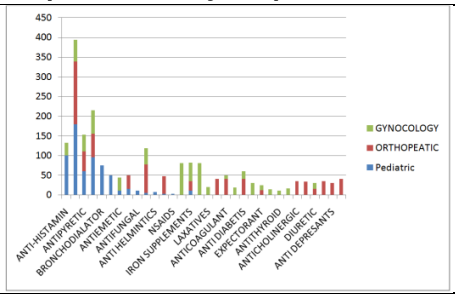

Figure 5. Total Number of Prescriptions 400 Based on Category of Drugs is 2030

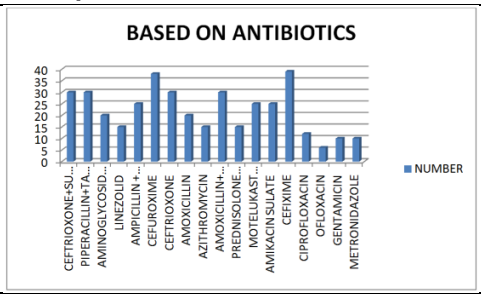

Figure 6. Total number Antibiotics used in three departments 395

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RESEARCH ARTICLE

Growth and Characterization of a Semiorganic L-Histidinium Methyl Benzoate NLO Single Crystal

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ABSTRACT

A new semi-organic crystal of L-Histidinium Methyl Benzoate (LHMB) has been successfully synthesized by taking L-histidine and methyl benzoic acid and single crystals have been grown by solvent evaporation method for the first time. The grown single crystals have been analyzed with XRD, FTIR, TG/DTA measurements. Its mechanical behavior has been assessed by Vickers microhardness measurements. Its nonlinear optical property has been tested by Kurtz powder technique and found better SHG efficienc that potassium dihydrogen phosphate single crystal. Its optical behavior was examined by UV-Vis., and found that the crystal is transparent in the region between 240-1200 nm. Hence it may be very much useful for the Second Harmonic Generation (SHG) applications.

Key words: Nonlinear optical crystal solution growth technique, Powder XRD, FTIR, TG/DTA, UV-Vis, Hardness.

INTRODUCTION

Nonlinear optical (NLO) crystals play a major role in modern technology involving lasers, sensors, interferometers, memory chips detectors, electrical devices and optical components. Of late, lots of efforts are being taken to form and study new nonlinear optical materials with interesting properties such as large nonlinearity, high resistance to laser damage, low UV cut off, moderate birefringence and good mechanical strength [1, 2]. NLO crystals with high conversion efficiencies for second harmonic generation and transparent in the visible and ultraviolet ranges are required for various devices in the field of optoelectronics and photonics. L-Histidinium family crystals have been subjected to extensive researchby several researchers [3-4] for their efficient nonlinear optical properties. The

title compound of L-HistidiniumMethyl Benzoate (LHMB) has already been grown by gel and slow cooling method [5-7]. But there is no report is available for the growth of L-Histidinium Methyl Benzoate (LHMB) by solvent evaporation method using methyl benzoic acid. To the best of our knowledge this is the first report to the literature. In the present article we have reported the detailed thermal, optical, mechanical and spectral studies ofLHMB.

EXPERIMENTAL

Synthesis and growth

The commercially available raw materials were purified by repeated recrystallization process and the recrystallized salt was used for the present synthesis process. L-histidineand methyl benzoic acid were mixed in the ratio of 3:1 in deionized water.The solution was stirred continuously for 24 hours and subsequently heated in order to complete the reaction process. Then the saturated solution was allowed to cool to room temperature and kept in a vibration free area with a tightly closed plastic cover [8]. Good quality single crystals of L-Histidinium Methyl Benzoate (LHMB) have been collected from the mother solution in a time span of 25 days. The grown single crystal is shown in Fig.1.

Characterization analyses

The harvested single crystal has been analyzed by different instrumentation methods in order to check its suitability for device fabrication. Powder XRD analysis has been carried out for the as grown specimen of LHMB. The presences of L-Histidinium Methyl Benzoate (LHMB) group have beeni dentified from the FTIR analysis. Its optical behavior has been analyzed by UV-Vis., analysis and found that there is no absorption in the entire visible region [9]. Thermal stability of the sample was tested using differential scanning calorimetry and thermo analysis respectively. The relative second harmonic generation has been carried out by Kurtz technique in order to confirm its second harmonic generation efficiency.

Powder X-ray diffraction analysis

Finely crushed powder of LHMB was subjected to powder X-ray diffraction analysis using a Rich Seifert diffractometer with CuKα (χ = 1.5417) radiation. The sample was scanned over the range of 10-70 degrees at a scan rate of 1 degree per minute. The recorded spectrum is shown in the Fig.2. The differences in the peak amplitude can be attributed to the different sizes and orientation of the powdered grains. Using the value of d, the hkl values of allthe reflections were obtained. The powder XRD experiment shows that the synthesized material and the grown crystals are the single phase of LHMB. The unit cell parameters have been calculated using the TREOR programme. The observed values are good in agreement with the reported literature values [10].

Fourier Transform Infra-red (FTIR) analysis

The recorded FTIR spectra were compared with the standard spectra of the functional groups. All the absorption frequencies and their tentative assignments are listed in Table 1. The IR band at 3138 cm^{-1} in the medium envelop region of 3000-3300 cm^{-1} is assigned to the $[NH_3]^+$ stretching vibration mode. The deprotonated carboxylic group (COO^-) has two important characteristic absorption bands around 1600 and 1420cm^{-1}, which are the asymmetric and symmetric stretching modes, respectively. In LHMB, these bands occur at 1639 and 1421cm^{-1}. The broad bands at 2970 and 2818cm^{-1} in the IR spectrum are assigned to the CH_2 symmetric stretching [11-12]. The functional group NO_2 has been represented with the asymmetric and symmetric stretching modes in the expected region of aromatic nitro compounds (1370 - 1330 cm^{-1}). The wagging and rocking modes of vibration of NO group are also observed. b:broad, s: strong, vs: very strong, sh: shoulder, m: medium, w: weak, vw: very weak, sym: symmetrical, asym: asymmetrical, str: stretching.

TG/DTA analyses

The thermal stability of the LHMB crystal was carried out by thermo gravimetric (TG) and differential thermal analysis (DTA) studies using NETZSCH STA 409 C analyzer in the nitrogen atmosphere at the heating rate of 10 ºC / min in the temperature range between from 25 to 400 ºC and the resultant thermogram is shown in the Figure. 4. The TGA curve shows that there is a loss of weight in the range between 96 ºC and 306 ºC in association with a sharp endothermic peak in DTA, which can be ascribed to the absorption of energy for breaking of bonds at the initial stage of decomposition [13]. The TGA illustrates that there is no loss below 197.2 ºC, thus assigned as the melting point of the crystal. From the results of DTA, this is observed that there is no transformation inside the structure was observed before melting point of197.2 ºC. Thus from the thermal studies, the crystal can retain its textureup to 197.2º C, which proves its suitability for the fabrication of nonlinear optical devices.

Second Harmonic GenerationTest

NLO property of the little compound was tested by Kurtz powder technique using Nd:YAG laser as the source. The generation of second harmonic generation was confirmed by emission of green radiation from the respective crystal. The details of the experimental setup used in the present study for measuring the powder SHG efficiency is reported elsewhere [14]. The observed results indicate that the relative SHG efficiency in LHMB crystal is better than the standard inorganic potassium dihydrogen phosphate (KDP) crystal.

Optical examination

The absorption spectra of LHMB crystal were recorded in the range 200-1200 nm using SHIMADZU UV_1061 UV-Visible spectrophotometer. The recoded spectrum is shown in the Fig.5. It is observed that the cut off wavelength of LHMB crystal is at 300 nm and the crystal is found to be transparent in the region of 240-1200 nm. Absence of absorption in the region between 250 to 1200 nm is the key requirement for the materials having NLO properties [15]. The less absorbance behavior in the entire visible region also conforms to the colorless nature of the crystal. Hence the title compound may be used for the nonlinear optical applications in the above mentioned wavelength range.

Vickers microhardness measurements

Hardness of the crystal carries information about the strength, molecular bindings, yield strength and elastic constants of the material [16]. In the present study, microhardness measurements were carried out on L-Histidinium Methyl Benzoate (LHMB) single crystals. Smooth surface of LHMB was subjected to the Vickers static indentation test at room temperature (303K) using a Leitz Wetzler hardness tester fitted with a Vickers diamond pyramidal indenter and attachedto a Leitz incident light microscope. Loads of different magnitude (5,10,15, 20 and 35 gm) were applied over a fixed interval of time. The indentation time was kept as 5s for all the loads. The hardness was calculated using the relation $Hv = (1.8544*P)/d^2$ kg/mm^2 (where p is the applied load in kg and d is the diagonal length of the indentation impression in micrometer). The load above 35g develops multiple cracks on the crystal surface due to the release of internal stresses generated locally by indentation [17]. The hardness decreases with increase in load. So, it may suggest for the NLO applications below 35gm of applied load.

CONCLUSIONS

The title compound of L-Histidinium Methyl Benzoate (LHMB) was successfully synthesized and the single crystals have been grown by solution growth technique. Its lattice dimensions have been determined from the powder X-ray diffraction analysis. The presence functional groups in L-Histidinium Methyl Benzoate (LHMB) have been identified from the FTIR analysis. Fromthe thermal measurements we found that the compound is stable up to 265^{0}C and hence it may be useful for SHG applications below its melting point. Optical analysis shows that there is no absorption in the entire visible region.Its second harmonic generation behavior have been tested by using Nd:YAG laser as a source.

REFERENCES

1. K.Selvaraju, R.Valluvan and S.Kumararaman, Materials Letters 60 (2006), p.2848.
2. V. Bisker-Leib, M.F. Doherty, Cryst. Growth Des. 3 (2003) 221 – 237.
3. V.G. Dmitriev, C.G. Gurzadyan, D.N. Nikoyosyon, Han Book of Nonlinear Optical Crystals, third ed., Springer, Berlin, 1999.
4. K.Ambujam, K.Rajarajan, S.Selvakumar, J.Madhavan, Gulam Mohamed and P.Sagayaraj, Optical Materials 29(2007), p.657.
5. Ra.Shanmugavadivu, G.Ravi and A.NixonAzariah, Journal of Physics and Chemistry of Solids 67(2006), p.1858.
6. K.Ambujam, K.Rajarajan, S.Selvakumar, I.VethaPotheher, Ginson P.Joseph and P.Sagayaraj, Journal of Crystal Growth 286(2006), p.440.
7. S.K. Kurtz, T.T. Perry, J. Appl. Phys. 39 (1968) 3798 – 3814.
8. K.Ambujam, S.Selvakumar, D.PremAnand, G.Mohamed and P.Sagayaraj, Crystal Research Technology 41(2006), p.671.
9. T.Balakrishnan, R.RameshBabu and K.Ramamurthi, Spectrochemica Acta: Part A 2007, in press.
10. M.NarayanBhat and S.M.Dharmaprakash, Journal of Crystal Growth 242 (2002), p.245.
11. R.F. Belt, G. Goshurov, Y.S. Lin, Laser Focus, 10 (1985) 110 – 124.
12. R.S. Calark, Photonics Spectra, 22 (1988) 135 – 136.
13. R.Rajasekaran, R.Mohan Kumar, R.Jayavel and P.Ramasamy, Journal of Crystal Growth 252(2003), p.317.
14. N.Vijayan, R.Rameshbabu, M.Gunasekaran, R.Gopalakrishnan and P.Ramasamy, Journal of Crystal Growth 256(2003), p. 174.
15. B.Ducourant, R.Fourcade and G.Mascherpa, Reviews in Chemical Minerals 20(1983), p.314.
16. R.J. Gambino, Bull. Mater. Res. Soc. 15 (1990) 20 – 22.
17. D.S. Chemla, J. Zyss (Eds.), Nonlinear Optical Properties of Organic Molecules and Crystals, Vols. 1 and 2, Academic Press, New York, 1987.

Table 1. FTIR Spectral Data for LHMB Crystal

Wave number (cm^{-1})	Tentative assignments
3138^{m}	NH_3^+ str.
2970^{b}, 2818^{b}	CH_2 sym.str.
2560^{b}, 2363^{m}	C-H combinational overtone
1639^{s}	COO^--asym.str.
1533^{s}	N=C-N str.
1491^{m}	Ring deformation
1421^{m}	COO^- sym. str.
1377^{sh}	CH_2 deformation
1348^{vs}	NO_2sym.str + C-C str.
1288^{m}	C-C str. + C=O str.
1136^{vw}	C-H in plane bending
1067^{vw}	Ring breathing + C-H in plane bending
1001^{vw}, 904^{m}	N-H bending
831^{s}	C-C str.

754[m]	CCC in plane bending
694[s]	NO_2 wagging
667[vw]	NO_2 rocking
652[vw]	COO^- wagging
575[vw]	C-NO_2[str.]
422[w]	CCC out of plane bending

b:broad, s: strong, vs: very strong, sh: shoulder, m: medium, w: weak, vw: very weak, sym: symmetrical, asym: asymmetrical, str: stretching.

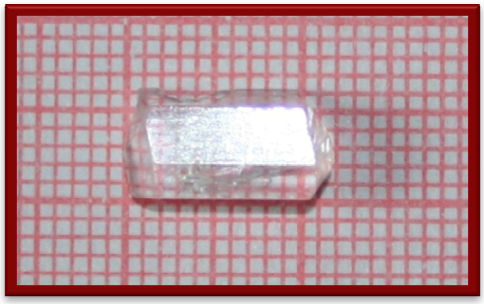

Fig.1. As grown single crystal of LHMB

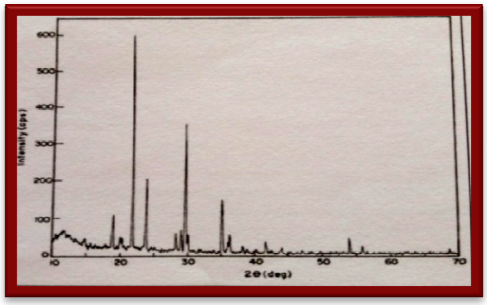

Fig.2. Powder X-ray diffraction pattern of LHMB

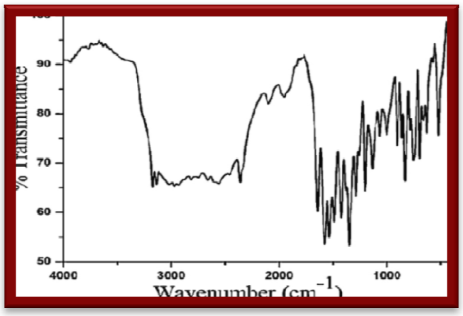

Fig.3. FTIR spectral pattern of LHMB

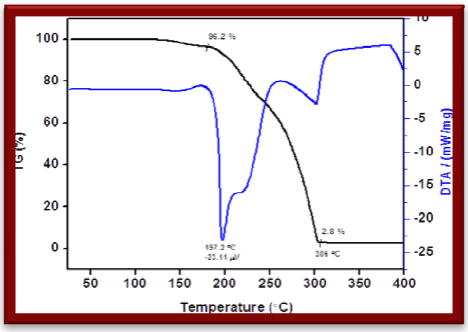

Fig.4. TG/DTA spectrum of LHMB

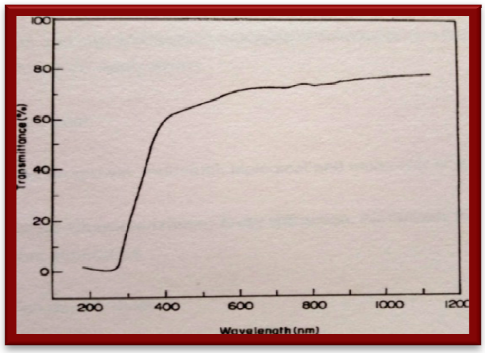

Fig.5. UV-Vis., absorption spectrum of LHMB

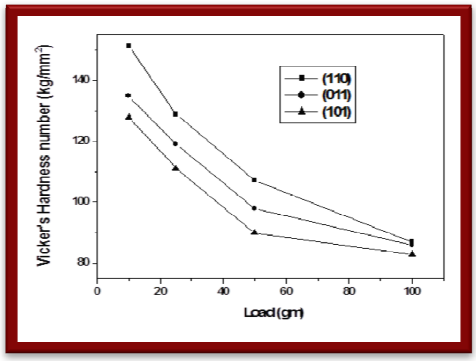

Fig.6. Vickers microhardness studies of LHMB

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RESEARCH ARTICLE

Collaborative and Hybrid Recommendation Framework for CBFRS

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ABSTRACT

Different Options accessible on the web, there is necessity to filter, rank and expertly give pertinent material. Numerous Internet clients have the issue of data over-burden. To decrease this issue, there is necessity of one arrangement. Recommendation systems settle this issue by looking at through immense limit of powerfully created information to convey researchers with customized content and administrations. A large portion of exploration has been finished on the Collaborative and Hybrid Recommendation Framework, Content-Based Framework has not been that widely investigated. This paper presents a writing audit of certain papers on Content-Based Recommendation Framework. Usage of a content-based recommendation contains contrasting the highlights of a Client Profile, with the qualities of a content thing, to foresee to the client novel applicable things. This exploration conveys data about improvements in content-based recommendation systems and offers specialists with understanding and future degree on Content - Based Recommendation Systems.

Keywords: Collaborative and Hybrid Recommendation System, Content-Based recommendation systems, Personalized Recommendation systems.

INTRODUCTION

In Present days, E-commerce technology is very well known for data explosion. Most studies annoyed to develop the self-governing system which identifies the user's desires [1]. Most mainstream instrument that helps users to recommend as per their interests is Recommendation System (RS). The primary objective of recommendation systems is to help users to deal with the data burden problem by delivering personalized recommendations, content and service. Recommendation systems are progressively being used in E-commerce for recommending books, music, movies, TV shows or different types of objects. Recommendation systems are essential instruments that overcome

the data overload by examining through the large set of information and recommending data relevant to the user. Content based methodology proposes items that are matches to the ones the active user has indicated a favorite for in the past rather than on the favorites of other users. CBF methods are developed for data retrieval and data filtering study. In the CBF method, each user can work independently and will be recommended the most closely data of the objects as indicated by their request [4]. This paper focuses on completely and systematic learning of content based recommendation approach. The fundamental objective is:

1) An outline of this methodology is to concentrate on the effective techniques and application fields that realized these techniques;
2) Developments and guidelines for future work are useful for next level of content-based recommendation approach.

Approximately all the examination has been done on collaborative or hybrid recommender system however very less work is done on content based recommendation system [2]. This paper delivers an outline of content-based recommendation approach, by keeping the objective to show multiple perspectives in design and commonsense scenario. Introductory section related to the paper represents the fundamental aspects and terms of content based recommendation approach, a significant level structure, and key benefits and disadvantages. Following section in the paper presents a survey of current systems used in numerous application fields, by comprehensively describing both conventional and innovative methods for presenting objects and researcher profiles. The most extensively accepted methods for learning researcher profiles are likewise explored. The last section of the paper argues developments and future work. An earlier style framework for giving content-based recommendations is described, so as to understand the primary components of the architecture, the process for creating recommendations and the advantages and downsides of utilizing this sort of recommendation technique.

RELATED WORK

Dima S. Mahmoud in [11] researched on however the content based filtering will recommend a listing of things to the users from big quantity of data. They increased the content based mostly filtering algorithmic rule by victimization artificial bee colony optimization so as to seem over a large knowledge set and suggest a listing of things to the users. Y. F. Zhao in [10] used the content based mostly technology and k-nearest neighbor in recommendation systems for effective traffic light management in urban traffic. For this they 1st found the similar traffic conditions so a matching degree has been analyzed between the present traffic conditions, so numerous temporal arrangement plans are being predicted. Prem Melville in [14] has given a content boosted cooperative filtering approach during which it used a content based predictor for inflating the user knowledge and delivered customized suggestion victimization collaborative filtering. It differs from the pure content based mostly and cooperative filtering approach. One of the classical and advantageous algorithms in recommender systems for customized suggestions is collaborative filtering. But the most important demerit of this form of filtering technique is that they go through from sparse user rating record matrix problem. So Jiaqi Fan in [9] proposed an algorithm which built-in content-based recommendation algorithm and consumer activity level. Pasquale Lops in [12] introduced a content based totally recommender system which built-in user- generated content with semantic analysis. It used to be named as FIRSt system. By making use of machine learning techniques, FIRSt enables the content-based recommender to infer user interests.

Discovering data on an enormous site can be a troublesome and tedious cycle. So Robin van Meteren in [8] depicted a recommender system PRES (Personalized Recommender System) that pre-owned substance based separating procedures to recommend little articles about home upgrades. A space, for example, this ensnares the client model must be extremely powerful and gained from positive criticism as it were. Recommender systems apply knowledge discovery (Figure 1: Recommendation System) procedures to help individuals find what they truly need. Chen Jian

in [13] proposed a straightforward effective ordering structure and a heuristic data recovery method algorithm for looking through converse k closest neighbor in the high dimensional dataset.

CONTENT BASED FILTERING

The content-based filtering approach is based on the reason that the client might want to consider like be regarding those recently observed by him (Balabanovic e Shoham 1997). With data on a particular content and information about a particular client that can be identified with this data, it is conceivable to characterize the connection among client and content. This methodology utilizes content-based filtering procedures, for instance, filtering by catchphrase and inactive semantic investigation. Content-based recommendation system (for example Last.fm6 and Amazon7) investigate thing highlights to discover things which are like top choices of the client. Content based proposal approach filter enormous storehouses of articles (for example: Television resources, articles, news, pages, books, music follows) thinking about items recently positioned by a researcher and developing an examine model of researcher top picks, expressed as researcher profile, fabricated upon the qualities of the items positioned by the researcher. Content based recommendation system investigates particularly rankings conveyed by the dynamic researcher to develop their profile. Else, collaborative filtering approaches require rankings from various clients to distinguish "nearest neighbors" of the current researcher. In collaborative recommendation system, new thing can be suggested when it is positioned by any client, else it can't be suggested. Content based recommendation doesn't have this virus start issue. It has capacity of suggesting objects not as yet positioned by any client. But still some drawbacks exist in CBRS, as like adequate highlights must be accumulated before content based recommendation approach can really know client likings and convey right recommendations. Thus, if there are barely any rankings accessible for a novel client, the approach can not to convey guaranteed recommendations.

Components of CBRS

The recommendation cycle is acted in three stages [3], (Figure: 2 Content Based Recommender System) every one of which is taken care of by different components, they are:

CONTENT ANALYZER: At the point when data has no structure (for example text), a few sort of pre-preparing step is expected to remove organized applicable data. Information things are investigated by highlight extraction strategies so as to move thing portrayal from the first data space to the objective one (e.g. Web pages spoke to as watchword vectors). This portrayal is the contribution to the Profile Learner and then, Filtering Component.

PROFILE LEARNER: This component gathers information illustrative of the client inclinations furthermore, attempts to sum up this information, so as to build the client profile. For example, the Profile Learner of a Web page recommender can actualize an importance input strategy [5] in which the learning strategy joins vectors of positive and negative models into a model vector speaking to the client profile. Preparing models are Web pages on which a positive or negative input has been given by the client;

FILTERING COMPONENT: This module misuses the client profile to propose important things by coordinating the profile portrayal against that of things to be suggested. The outcome is a double or nonstop pertinence judgment (figured utilizing some closeness measurements [6]), the last case bringing about a positioned list of conceivably intriguing things. In the previously mentioned model, the coordinating

Content Based Recommender System Models

Keyword-Based Vector-Space Model: The researcher utilized this model with fundamental TF-IDF gauging method to speak to a movie as a vector of loads, where each weight shows the level of relationship between a movie and a term or keyword [15].

Item Representation: The items (movies) are spoken to by a lot of highlights (additionally called characteristics or properties). These traits are: name of the movie, storyline, keywords, movie category, and the associates. The theoretical speaks to the movie when the recurrence of a term in the paper is being resolved.

TF-IDF and Cosine Similarity: The researcher utilized TF-IDF and cosine comparability to decide how applicable a movie is to a client's advantage [7]. The significance expands relatively to the occasions a term (in the client's inquiry) shows up in the movie name. TF-IDF is given by:

Term frequency, evaluates how as frequently as conceivable a term presents in a document

$$TF = \frac{\text{No. of times term t Present in a document}}{\text{Total no. of terms in the document}}$$

IDF, Inverse document frequency which checks how critical the terms that present in the document

$$IDF(X) = \log\left(\frac{\text{Total No of Documents}}{\text{No of documents with term x in it}}\right)$$

In Text based TF/IDF technique, a model utilizing the MovieLense data sets. In initial step pre-processing and cleaning of data is performed, after that feature extraction is finished utilizing TF/IDF vectorizer which brings about feature thing grid. Cosine closeness work is used to compute comparative thing from feature-thing lattice. Figure 3 shows the working model of Text-based TF/IDF.

EXPERIMENTS AND RESULTS

Dataset

The dataset utilized in the analysis is MovieLens. The MovieLens dataset is gathered through site movielens.umn.edu during the seven-month time span. The dataset comprises of 943 users, 1664 movies, and 99392 ratings (with estimations of 1-5) putting away the criticisms of users to movies. Figure 4 shows the sample dataset.

Experimental Results

The implementation was done in python using Google's Co-Laboratory (COLAB). First collect all the tags of each movie by all users and generate the genere keyword for each movie to build the item-content filtering. This metadata is then transformed into vector of features. This paper implements the combination of TF-IDF and Cosine Similarity to find the similarities among the user and the item for the recommendation system. Singular value decomposition is used to reduce the dimensionality for the features developed by the TF-IDF. From figure 6 it shows that the cumulative Variance is increased according to the SVD value.

CONCLUSION

Data over-burden is a significant issue as the web is promptly rising. The proficiency of the data sifting calculations is of essential significance for giving better customized suggestions to the client. The work here examined various strategies to improve the presentation of the substance based and collective separating strategies in Recommender Systems. All the techniques introduced above have their own benefits and negative marks. So as a future upgrade all

the holes of these techniques are viewed as together to propose another calculation for a superior proposal framework.

REFERENCES

1. Deepa Mandave, Govind S. Pole, "A Review on Content Based Recommendation System", IJIRCCE.2016
2. Parul, Kavita khanna ,"Literature Survey: Recommender Systems ",*IJETMAS*, March 2015, Volume 3 Special Issue, ISSN 2349-4476
3. Pasquale Lops, Marco de Gemmis and Giovanni Semeraro, "Content-based Recommender Systems: State of the Art and Trends", Book Reference.
4. Pasquale Lops, "Semantics-aware Content-based Recommender Systems".
5. Swathi S R, Sreeja Devi P, Dr.Shelbi Joseph3, SeethaParameswaran, "Various Methods of Using Content-Based Filtering
   Algorithm for Recommender Systems", IJIRSET.2017
6. Herlocker, L., Konstan, J.A., Terveen, L.G., Riedl, J.T.: "Evaluating Collaborative Filtering Recommender Systems". ACM Transactions on Information Systems 22(1), 5–53 (2004)
7. Rocchio, J.: "Relevance Feedback Information Retrieval". In: G. Salton (ed.) The SMART retrieval system - experiments in automated document processing, pp. 313–323. Prentice- Hall, Englewood Cliffs, NJ (1971)
8. Robin van Meteren. a. M. V. Someren."Using Content-Based Filtering For Recommendation", IEEE, 2006.
9. Jiaqi Fan, Weimin Pan, Lisi Jiang, "An Improved Collaborative Filtering Algorithm Combining Content Based Algorithm And User Activity", IEEE, 2014.
10. Y. F. Zhao, F. Y. Wang, H. Gao, F. H. Zhu, Y. S. Lv, "Content-based Recommendation for Traffic Signal Control", 18th International Conference on Intelligent Transportation Systems, IEEE, 2015.
11. Dima S. Mahmoud, Robert I. John , "Enhanced Content Based Filtering Algorithm Using Arificial Bee Colony Optimization", SAI Intelligent Systems Conference, IEEE, 2015.
12. Pasquale Lops, Marco de Gemmis, Giovanni Semeraro, Paolo Gissi, CataldoMusto, FedelucioNarducci, "Content-based Filtering with Tags: the FIRSt System", Ninthe International Conference on Intelligent Systems Design and Applications, IEEE, 2009.
13. Chen Jian, Yin Jian, Huang Jin, "Automatic Content-Based Recommendation in e-Commerce", IEEE, 2003
14. Prem Melville, Raymond J. Mooney, Ramadass Nagarajan, "Content-Boosted Collaborative Filtering For Improved Recommendations", IEEE, 2002.
15. Simon Philip, P.B. Shola (PhD) , Abari Ovye John, "Application of Content-Based Approach in Research Paper Recommendation System for a Digital Library", IJACSA, Vol. 5, No. 10, 2014

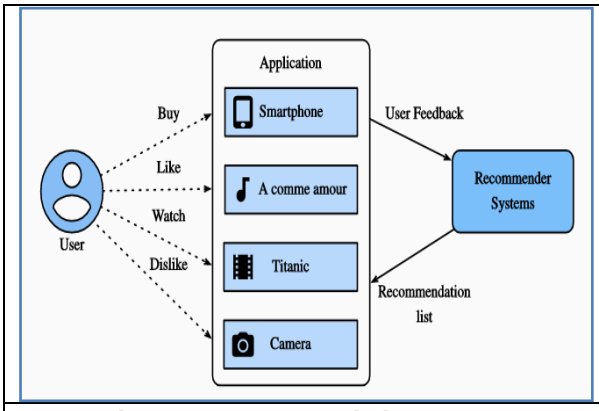

Figure 1: Recommendation System

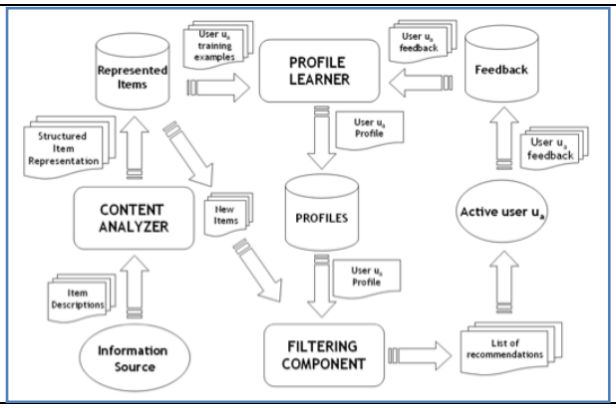

Figure 2: Content Based Recommender System

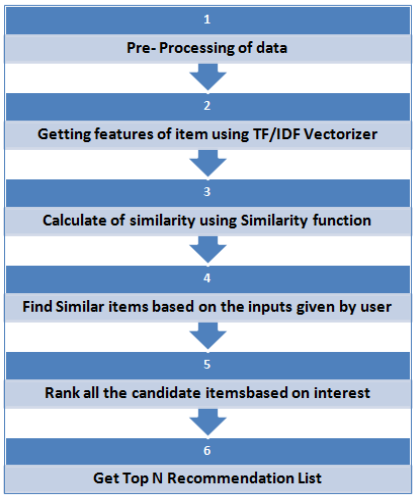

Figure 3: Text based TF/IDF Model

	movieId	title	genres	userId	tag
0	1	Toy Story (1995)	Adventure Animation Children Comedy Fantasy	1644.0	Watched
1	1	Toy Story (1995)	Adventure Animation Children Comedy Fantasy	1741.0	computer animation
2	1	Toy Story (1995)	Adventure Animation Children Comedy Fantasy	1741.0	Disney animated feature

Figure 4 : Sample Dataset

userId	1	2	3	5	7	8	11	13	14	16	...	138474	138475	138477	138483	138484	138486	138487	138490	138492	138493
movieId																					
1	0.0	0.0	4.0	0.0	0.0	4.0	4.5	4.0	4.5	3.0	...	5.0	0.0	3.0	4.0	0.0	5.0	0.0	0.0	0.0	3.5
2	3.5	0.0	0.0	3.0	0.0	0.0	0.0	3.0	0.0	0.0	...	4.0	0.0	0.0	3.0	3.0	0.0	0.0	0.0	0.0	4.0
3	0.0	4.0	0.0	0.0	3.0	5.0	0.0	0.0	0.0	0.0	...	0.0	0.0	0.0	0.0	4.0	0.0	0.0	0.0	0.0	0.0

3 rows × 80046 columns

Figure 5: Similarity based on User ID and Movie ID

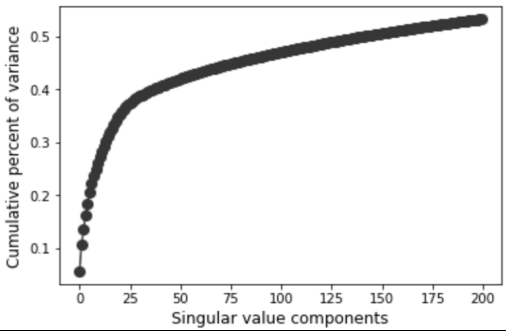

Figure 6: Comparison of Cumulative Variance and Singular Value components

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REVIEW ARTICLE

Comparison of LDA and NMF Topic Modeling Techniques for Restaurant Reviews

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ABSTRACT

To manage the rapid explosion of digital document archives, there is a need for a techniques to categorize the text documents automatically based on the content. Topic modeling is a technique comes with group of algorithms that reveal, discover and annotate thematic structure in collection of documents. Thus Topic Modeling is as major revolution in text mining, which identifies the hidden topics present in the data. This paper adopts Restaurant Reviews for topic Modeling. Most of the Hotel Booking websites like Trip Advisor, Golbibo, Yatra, etc.... will use the online ratings and customer feedbacks for analyzing the facility, Quality and service of the Restaurants, which is useful for the traveller who is searching for suitable restaurant. But most of the travellers felt difficult in reading all the reviews and then come to a conclusion. Thus Topic modeling can help in this perspective to find the correct aspect found in the Restaurant reviews. Based on that aspect the traveller can select a restaurant. Latent Dirichlet Allocation (LDA) and Non-Negative Matrix Factorization method (NMF) which are the techniques of Topic Modeling are explored in the current research article. Here the customer reviews for Restaurants were taken from Trip Advisor website using web crawlers for two restaurants each in four metropolitan cities. Performance metrics such as Coherence Score and Execution Time were used to evaluate the topic modeling techniques, which produce quality topics for Restaurant Reviews. Based on the experimental results NMF method identifies the hidden information with greater Mean Coherence Value as well as very less execution time while comparing with LDA.

Keywords: Topic Modeling, Latent Dirichlet Allocation, Non-Negative Matrix Factorization, Mean Coherence Value.

INTRODUCTION

The Internet connects billions of people in the world and it is a core pillar of modern society. Now a day's internet is used as the most democratic communication medium. It allows users to express their opinions about any topic, product, etc. But, it is very difficult to read all the interested documents by an individual. So we need techniques for analyzing the collection of documents. Topic modeling is one such unsupervised learning technique that helps users to discover and understand the aspect inside the unlabelled text documents. Topic modeling approaches extract aspects from documents and categorize them in to similar classes. The Topic modeling is a statistical method, and it discovers hidden semantic patterns from the collection of the unstructured document. These techniques render an in depth Knowledge of the latent semantic structure of a huge amount of texts. Large collection of documents is represented in terms of topics, and topics are represented in terms of words. The topic modeling discovers word-use patterns and how to connect and share similar patterns among the documents (Alghamdi & Alfalqi, 2015). Latent Dirichlet allocation and NMF are highly accepted Techniques which are used in the field of Topic modeling (Saqib et al., 2019). LDA is one of the widely used Probabilistic models whereas NMF, a matrix factorization technique is used for multivariate analysis. Both the NMF and LDA generate output depending on the allotted input. These methods are used to extract aspect and keywords then group the aspects into different categories, it also used for spam detection (Gao & Li H, 2011). It should be noted that previous trainings are not needed in the LDA model. This model assumes that each document is a collection of the topic and each topic is collection of words. LDA produces the desired number of topics and list of words with each topic with their probability distributions. This method helps to identify the similarity between documents, by analyzing the probability distribution of the topics of these documents. Thus, Data mining applications widely use LAD topic modeling. LDA requires pre-defined number of topics, if it is too small, then the topics are more general in nature and it is too large then there is a chance for the topic overlapping. For learning descriptive topics LDA are better (Raya et al, 2019).

Factorizing from more multi furious vectors to less dimensional portrayals takes place in NMF, a linear algebraic model. The topic modeling vectorizes the given corpus. In NMF vectors are nonnegative (Belford et al., 2018).To reduce the dimension of the feature vectors of the text data NMF is more effective. It is also a simple and adaptive algorithm for document clustering. NMF is more feasible when the area of the data is absolutely positive and when the divisions are constructed desirably. This section showcases the glimpses of Topic Modeling techniques and its two popular methodologies LDA and NMF. The section 2 discusses about the research work carried out by the researchers. In section 3, Sentiment Analysis, taxonomy of sentiment analysis, topic Modeling methods and its Applications were explained. Section 4, explains the architecture of the methodology the carried out in this paper and also explained the topic modeling techniques such as LDA and NMF. The fifth section deals with the result that is derived from the experiments of the research work. The last section brings out the best efficient Topic modeling techniques which are NMF.

RELATED WORKS

This section discusses some of the research work that uses Topic modeling techniques to extract aspect in Aspect based sentiment analysis. For extraction of aspects and their categorization, topic modeling has been widely used in these recent years (Qiannan, et al., 2019). **(**Brody, Elhadad, 2010) Proposed an unsupervised topic model technique for feature extraction. This method applies standard LDA on each sentence. Here each sentence is treated as document and this method focused in small number of topics. The aspect from each sentence is the output of this model. They also presented a method with the help of polarity propagation that automatically identify positive and negative opinion words. In (Tribhuvan, Bhirud, 2017), they propose architecture for feature based opinion mining that is based on Topic Modeling. They design an algorithm that automatically annotates features extracted through LDA topic model. LDA topic model is applied to extract product features from product reviews and the annotation algorithm is applied on these extracted features**.** In (Anoop, Asharaf, 2018), the aspect-specific sentiment analysis is proposed with the help of latent Dirichlet allocation (LDA). To perform the aspect-specific sentiment analysis, they

extracted the topic (hidden themes also) word and mapped with various aspects of an entity. For each aspect, this method shows accuracy ranges from 74 % to 81 %. In (Stevens, et al., 2012) they provide an evaluation of three distinct Topic Modeling techniques, Latent Dirichlet Allocation (LDA), Latent Semantic Analysis (LSA) and Non-Negative Matrix Factorization (NMF).Their experiments show that different Topic Modeling has different strengths. LSA is best at creating a compact semantic representation of documents and words in a corpus, while LDA best for descriptive topics. NMF learns more incoherent topics than LDA and LSA. They suggest if the application which has a human end-user interaction with learned topics then LDA is the best choice**.** In (Qiannan et al., 2019) Authors proposed a novel approach for implicit aspect identification based on non-negative matrix factorization (NMF). Based on inter-relations between aspect and opinion words these approach clusters the aspects, which enhanced the performance of aspect clustering. This method represents review sentences by word vectors. To identify and predict target implicit aspects a classifier is constructed. This approach is evaluated on CR and ABSA15 dataset. Two-stage Non-negative Matrix Factorization (NMF) is proposed in (Barman et al., 2006). The first stage extract uncorrelated basis probabilistic document feature vectors and in the second stage clustering or classification is done. The clustering produces more than 98.5% accuracy.

Topic Modeling

Topic Modeling is one of the significant unsupervised techniques which segregate text in order to group them according to their information provided. It removes stop words and highlights the distinct words in all the documents, so as to identify the topics easily as depicted in figure 1. It also sets the value of each word based on their frequency in the particular document. The unstructured and unlabelled text corpus has to be converted into a Vector Space Model (VSM). Commonly used methods like Bag of Words (BoW) and Count Vectorizer have limitations of generating a high dimensional VSM. This is due to the total number of occurrences of each word in a text document and the model fails to appropriately map these words to the chosen topics which would ultimately misrepresent the feature vector. Topic Modeling can be used for several applications as mentioned below.

Application of Topic Modeling

- **Recommendation Systems**: In many real-time systems, for example, job recommendation by mapping the right job for interested candidates based on their information, history, sociology, location, media theory, and other contexts.
- **Financial Analysis:** In many commercial activities like structuring of the stock market exchange, using stock value information to induce subjects over diverse trades on a market organization, and other activities.
- **Bioinformatics:** To identify the knowledge structure of the field, e.g., study patient-related texts constructed from their clinical records.
- **Manufacturing Applications:** It is used in numerous search engines, online advertising systems, and social media blogs.
- **Computer Science:** Extracting valuable information from data, image processing, and annotating images with words.
- **Social Network Analysis (SNA):** Mining information about the real world in social web platforms such as inferring significant aspects about the users and services.
- **Software Engineering:** A mining unstructured repository in the software industry such as source code, test, and bugs to support many engineering tasks like program comprehension and location.
- **Uncovering Themes in Texts:** Useful for detecting trends in online publications for example, Headlines in news and Highlights in forums.
- **Document Summaries:** Use topic models to understand and summarize scientific articles enabling faster research and development. The same applies to historical documents, newspapers, blogs, and event fiction.

RESEARCH METHODOLOGY

Topic Modeling, an application of Natural Language Processing generates the topics on its own as if people select topics from humpty amount of text. The instances of huge documents can be generated from feedback of the users from hotels, movies, user feedbacks, news stories and emails of customer complaints and so on. Knowing what people are talking about and understanding their problems and opinions is highly valuable to businesses, administrators, political campaigns. It should be noted that it is very difficult to study through entire documents manually and group the headings separately. Thus is required an automated algorithm that can read through the text documents and automatically output the topics discussed.

Corpus Creation

In this paper, topic Modeling is done for the Restaurant Reviews domain. Here the customer reviews for Restaurants were taken from Trip Advisor website using web crawlers for two restaurants each in four metropolitan cities mentioned in the Table 1. The architectural overview for the proposed model is shown in figure 2. The following section gives a detailed view of the proposed work. The proposed system uses customer reviews data as input and extracts aspect set for Restaurant Reviews. This Aspect Extraction model contains two phases, Pre-processing and Feature Extraction phase. Sentence Segmentation, Stop Word Removal, Stemming, Formatting Removal, Word Lemmatisation, Tokenization and POS Tagging are the processes adopted for Data Pre-processing phase.

Sentence Segmentation

Identification of sentence closings in particular reviews takes place in the procedure of sentence segmentation. Every text input review is dividing into separate sentences. Actually the entire review statements extracted by the web crawler were given as input to data pre-processing phase.

Stop Word Removal:

Most frequently used words in English are not useful in text mining. Such words are called stop words.Stop words generally do not carry any particular sense and they are used only for the constructing structured sentences. It consists of the following significant classifications viz: conjunctions, pronouns and preposition. Stop word removal is used to remove unwanted words in each review sentence. Words like is, are, was etc. Initially feedback or reviews saved in the document are given as input in order to remove the stop words. It should be noticed that the list of stop words would already be gathered and saved as text documents.

Formatting Removal

Formatting Removal is the process of removing unwanted formats that available in the dataset. It removes the Email address of the user given in the comment by identifying the '@' symbol and '.' symbol present in the data. It also removes the new line character and the distracting single quotes that present in the data.

Tokenization

Tokenization is yet another process in which the word limitations are identified with the help of which the series of character in a document are broken as separate words ie the point in which one finishes and other word begins. In the field of computational linguistics, the selected words are considered as tokens where as there are no word limitations in the written language system. In this system the words are manually marked. Tokenization is otherwise called as word segmentation.

POS Tagging

The Part-Of-Speech of a word is a linguistic category that is defined by its syntactic or morphological behavior. Common POS categories in English grammar are: Noun, Verb, Adjective, Adverb, Pronoun, Preposition, Conjunction, and Interjection.POS is an important step in which all the words in a sentence are named according to

their part of speech. POS which is a significant procedure in opinion mining is crucial in deciding salient features and feedbacks from the given input. POS tagging can be done either manually or with the help of POS tagger tool. POS tagging of the reviews by human is time consuming. POS tagger is used to tag all the words of reviews. Stanford tagger is used to tag each word in an online review sentences. Every one sentence in customer reviews are tagged and stored in text file.

TF - IDF

TF-IDF is a numerical statistic measure used to score the importance of a word (term) in any content from a collection of documents based on the occurrences of all word, and also analyses the level of relevance of keywords which are used in the given text. Term Frequency not only considers the frequency but also induces discriminative information for each term. As mentioned in equation 1 Term Frequency refers to the number of frequency of particular word occurs in a document is divided by the whole sum of words in the selected document.

$$TF = \frac{No.of Occurrences of a Word in the Document}{No.of Words in all Documents} \quad \text{..... Equ (1)}$$

Topic Modeling

Topic Modeling is a methodology for processing the massive volume of data generated in corpus and extracting the hidden and interesting concepts, useful features, and latent variables from data that depend on the context of the application. There are several Topic Modeling algorithms are available, in this paper, we focused on two frequently used Topic Modeling methods that are built using a Probabilistic model and Non-probabilistic model, such as LDA and NMF respectively.

- **LDA** – Latent Dirichlet Allocation – Based on Probabilistic Graphical Models.
- **NMF** – Non-Negative Matrix Factorization – Based on Linear Algebra.

Latent Dirichlet Allocation

The relationships among topics, terms and text documents are studied in LDA, a Probabilistic Model. It is an unsupervised technique, and is based on bag of words assumption. The documents exhibit multiple topics and topic has a probability distribution over words. Each word from given set of words is segmented according to the list of titles that are given in the document. Each topic title is designed with an infinity set of fixed rules. The Topics can generally be designed or developed as varieties of topics from the cluster of probable topics. In the arena of topic modeling, this probability of topics renders an accurate presentation of a given text. LDA is a three level Hierarchical Bayesian Model, in which each document in the corpus is modelled as a finite mixture over an underlying set of topics. Each topic is in turn, modelled as a infinite mixture over an underlying set of topic probabilities. Finally, the topic probabilities provide an explicit representation of a document. This algorithm defined generative process as a joint probability distribution over both observed and hidden variables. The process of learning the topic distribution is described through plate notation given in figure 3. The equation 2, determine the Joint probability distribution to generate both observed and hidden variables.

$$P(\theta, z, W|\alpha, \beta) = P(\theta|\alpha)\prod_{n=1}^{N} P(z_n|\theta)P(W_n|z_n, \beta) \quad \text{.....Equ (2)}$$

Where 'α' & 'β' are the smoothing parameters, 'θ' is a joint distribution of a topic mixture, 'W' is the vocabulary set composed by as set of 'N' words. Z_n is as topic presented in a document.

Non-negative Matrix Factorization

Non-negative matrix factorization is an unsupervised Topic Modeling technique. It can able to perform both dimension reduction and clustering simultaneously. Ensemble Method is used for topic modeling via matrix factorization. The more specific topic model for the body of unstructured document can be generated with the help of NMF Techniques [13]. Two parts of matrix factorization including ensemble generation and ensemble integration

combinations of ensemble learning for topic modelling. NMF model can extract relevant information about topics without any previous insight into the original data D. It decomposes original data into two non-negative matrices U and V as denoted in equation 3.

$D \approx UV$ …. *Equ(3)*

where U and V are Non-negative element such as $U \geq 0$, and $V \geq 0$. The Weighted sum of the components in matrix D is

$D_i = \sum_{j=1}^{k} U_{ij} * V_j$ …….*Equ(4)*

The Graphical Representation of the NMF topic modelling is mentioned in the figure 4, For a given text, the entire input corpus is decomposed into two Matrices which are term Topics Matrix 'U' and Topic Document Matrix V, corresponding to K coordinates axes and N points in a new semantic space respectively. Here factor U is a combination of Documents 'M' and topics 'K', on the other hand, factor 'V'is a combination of topics 'K' and terms 'N'. Here N is the No. of terms that present in a Topic cluster.

EXPERIMENTAL RESULTS

To evaluate the effectiveness of the topic modeling techniques that adopted in this paper, experimentation is performed. The proposed Topic Modeling is implemented in Google Co-laboratory (Colab) using python. The extracted Customer Reviews for Restaurant from the Trip advisor were fed into the system as input. In this paper two Topic Modeling Techniques were taken for experiment such as LDA and NMF. LDA is a Probabilistic Model implemented using Gensim package. On the other hand, NMF is a Non-Probabilistic Model implemented using Sklearn package.

Execution Time

Execution time is nothing but the time taken by the system while executing or completing the given task. It is one of the evaluation metrics. Efficiency of the system can be determined or checked by measuring the time a given code might take. The Table 2 shows the execution time results for LDA and NMF Topic modeling techniques from the Restaurant Reviews dataset for 'K' No. of Topics. Based on the Execution Time, it is evident that NMF shows lower execution time than the LDA. Thus NMF is better than LDA.

Coherence Score

Coherence Score is a widely used performance metric to evaluate topic modeling methods. It gives a realistic measure to identify the total number of topics that present in a document. Each generated topic has a list of words such as cluster of words. This measure finds the average of pair wise word similarity scores of the words associated with the topic. The topic model with high Coherence Measure value is considered a good topic model. To compute topic coherence Score of a topic model, first selecting top n frequently occurring words in each topic. Here we assign 'n' as 10. Next calculate the Normalized Point wise Mutual Information (NPMI) scores for each of the words selected in the first step and aggregate all the Normalized Point wise Mutual Information (NPMI) scores to calculate the coherence score for a particular topic. The mean coherence score measured for all topics that are given in the topic model in order to determine the score. NPMI is a measure used to find how often two words co-occurs in a given document. It is calculated by dividing the probability that both words occur by the probability for occurrence of each word separately. $P(\omega_i)$, is the Probability of single word present in the document 'd'. 'i' and 'j' are the words that taken as a top words that present in the topic 't', $\Theta_{\omega_j,d}$ is the word that present in the document.

$P(\omega_i) = \sum_d \Theta_{\omega_i,d}$ …….*Equ(5)*

$P(\omega_i, \omega_j) = \sum_d \Theta_{\omega_i,d} * \Theta_{\omega_j,d}$ …….*Equ(6)*

$NPMI(\omega_i, \omega_j) = \frac{\ln P(\omega_i) + \ln P(\omega_j)}{\ln P(\omega_i, \omega_j)} - 1$ …….*Equ(7)*

$$Coherence(t) = \frac{\sum_{i=1}^{n-1}\sum_{j=i+1}^{n} NPMI(\omega_i,\omega_j) * P(\omega_i|\, t) * P(\omega_j|\, t)}{\sum_{i=1}^{n-1}\sum_{j=i+1}^{n} P(\omega_i|\, t) * P(\omega_j|\, t)} \quad \text{.....Equ(8)}$$

Table 3 shows the Mean Coherence Score comparison for LDA and NMF Topic modeling techniques from the Restaurant Reviews dataset for the k values from 1 to 20. In that, LDA has the Mean Coherence Score range from '0.170' to '0.469'. Thus the highest Mean Coherence Score obtained by the LDA is '0.469'. On the other hand, NMF has the Mean Coherence Score range from '0.577' to '0.729'. Thus the highest Mean Coherence Score obtained by the NMF is '0.729'. Based on the Mean Coherence Score it is evident that NMF scores better than LDA. Figure 5 shows the best coherence score comes from 15th number of topics using LDA Topic modeling method. Thus the topics produced after 15th were declined. Topic coherence measure is a good decision making process, which shows the apt words for the topics. In this experimental study, 15 topics were extracted for analysis and discussion, because this much number of topics produced highest Mean Coherence Score value such as 0.469 while compared with various 'k' topic values. Figure 6 shows the best coherence score comes from 17th number of topics using NMF Topic modeling method. Thus the topics produced after 17th were declined. Topic coherence measure is a good decision making process, which shows the apt words for the topics. In this experimental study, 17 topics were extracted for analysis and discussion, because this much number of topics produced highest Mean Coherence Score value such as 0.729 while compared with various 'k' topic values.

CONCLUSION

The hotel reviews analysis provided hidden topics, relevant and useful words. This information would help the researchers to work upon a more customized and personalized Hotel Recommender System for customers to choose good hotels based on their preferences. In this paper, Topic Modelling was done from the Feature Extraction process using LDA algorithm and NMF algorithm. In the first step, an efficient Vector Space Model was created using TF-IDF calculations. In the second step, Topic Modeling methods such as LDA and NMF would help to find the words belonging to a topic appeared in the review documents. It is in dense to present each input document in the form of various topics and topics as different words. The Topic Modeling methods LDA and NMF were compared based on the performance metrics such as Mean Coherence Score and execution time. In that, NMF secured more Coherence score as 0.729 while comparing with LDA Coherence Score as 0.469 and also NMF has less execution time when compared to LDA. Hence NMF is better while comparing with LDA. In future, the research work is planned to extract the Aspects from the Topics obtained using NMF. Based on that, sentimental analysis for Hotel Reviews were planned to generate.

REFERENCES

1. Alghamdi R., Alfalqi K., (2015), "A Survey of Topic Modeling in Text Mining", (IJACSA) International journal of Advanced Computer Science and Applications, 6(1).
2. Anoop, V.S., Asharaf S., (2018), "Aspect-Oriented Sentiment Analysis: A Topic Modeling-Powered Approach", https://doi.org/10.1515/jisys-2018-0299.
3. Barman P.C., Nadeem Iqbal, and Soo-Young Lee, (2006), "Non-negative Matrix Factorization Based Text Mining: Feature Extraction and Classification", © Springer-Verlag Berlin Heidelberg, 703 – 712.
4. Belford, M., Namee, Mb., and Greene, D., (January 2018), "Stability of Topic Modeling via Matrix Factorization', Expert Systems with Applications, .https://doi.org/10.1016/j.eswa.2017.08.047.
5. Brody, S. & Elhadad, N., (June 2010), "An Unsupervised Aspect-Sentiment Model for Online Reviews", in Human Language Technologies: in Proceedings of the 11th Annual Conference of the North American Chapter of the Association for Computational Linguistics (NAACL-HLT-10), Los Angeles, USA, 804-812.

6. Gao S and Li H, (2011), "A Cross-Domain Adaptation method for Sentiment Classification using Probabilistic Latent Analysis", In the 20th ACM International Conference on Information and Knowledge Management, ACM, Glasgow, Scotland: 1047-1052.
7. https://www.statista.com/statistics/617136/digital-population-worldwide/
8. Qiannan Xu, Li Zhu, Tao Dai, Lei Guo, Sisi Cao., (2019), "Non-negative matrix factorization for implicit aspect identification", Received: 18 October 2018 / Accepted: 18 May 2019 © Springer-Verlag GmbH Germany, part of Springer Nature.
9. Raya KS., Ahmadb, A. ,and Aswani Kumar C, (2019), "Review and Implementation of Topic Modeling in Hindi", International Journal of Applied Artificial Intelligence, ISSN: 0883-9514 (Print) 1087-6545 (Online) , Taylor & Francis.
10. Saqib MS., Ahmad, S., Syed, HA, Naeem, T, and Alotaibi, MF., (2019), "Analysis of Latent Dirichlet Allocation and Non-negative Matrix Factorization using Latent Semantic Indexing", International Journal of Advanced and Applied Sciences, 6(10), 94-102.
11. Stevens K, Kegelmeyer P, Andrzejewski D, and Buttler D. (2012), "Exploring topic coherence over many models and many topics". In the 2012 Joint Conference on Empirical Methods in Natural Language Processing and Computational Natural Language Learning, Association for Computational Linguistics, Jeju Island, South Korea, 952-961.
12. Tribhuvan, P &Bhirud, S., (2017), "Annotating features extracted through Latent Dirichlet Allocation for feature based opinion mining", International Journal of Advanced Research in Computer Science, 8(6).
13. Zhang, L. & Liu, B., (2014), "Aspect and Entity Extraction for Opinion Mining", Data Mining and Knowledge Discovery for Big Data, Springer Berlin Heidelberg, 1-40.

Table 1: Customer Reviews from Trip Advisor for Restaurant

Metropolitan City	Top Restaurant	Reviews
Delhi	Anna Maya	1,530
	Tamra	1,580
Kolkata	Mocambo	1,110
	Ballygunge Place	1,230
Chennai	Saravana Bhavan	1,280
	Murugan Idli Shop	1,179
Mumbai	Trishna	1,110
	Lake view Café	1,070
Total No. of Reviews		**10,089**
Total No. of Sentences		**26,059**

Table 2: Comparison of Execution Time for LDA and NMF for 'k' No. of Topics

Topics	Execution Time	
K	**LDA**	**NMF**
Topic #01	10.234	0.102
Topic #02	26.786	0.350
Topic #03	42.528	0.597
Topic #04	59.064	0.875
Topic #05	76.467	1.231
Topic #06	93.728	2.057

Topic #07	111.830	2.629
Topic #08	130.542	3.291
Topic #09	149.961	3.950
Topic #10	170.363	4.666
Topic #11	191.325	5.647
Topic #12	213.072	6.744
Topic #13	235.231	7.606
Topic #14	258.373	9.286
Topic #15	281.830	10.968
Topic #16	306.927	13.182
Topic #17	333.001	15.765
Topic #18	360.671	18.179
Topic #19	387.641	21.075
Topic #20	415.522	24.086

Table 3: Comparison of Mean Coherence Score using LDA and NMF for 'k' No. of Topics

Topics	**Mean Coherence Score**	
K	**LDA**	**NMF**
Topic #01	0.170	0.577
Topic #02	0.206	0.621
Topic #03	0.245	0.610
Topic #04	0.253	0.640
Topic #05	0.370	0.658
Topic #06	0.334	0.674
Topic #07	0.370	0.689
Topic #08	0.412	0.694
Topic #09	0.417	0.690
Topic #10	0.442	0.682
Topic #11	0.457	0.697
Topic #12	0.463	0.696
Topic #13	0.449	0.696
Topic #14	0.461	0.714
Topic #15	0.469	0.722
Topic #16	0.440	0.712
Topic #17	0.371	0.729
Topic #18	0.339	0.713
Topic #19	0.316	0.728
Topic #20	0.345	0.705

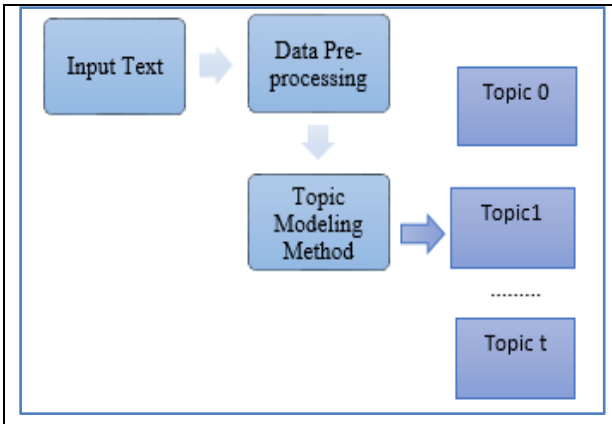

Figure 1: Topic modeling method steps to extract Topics

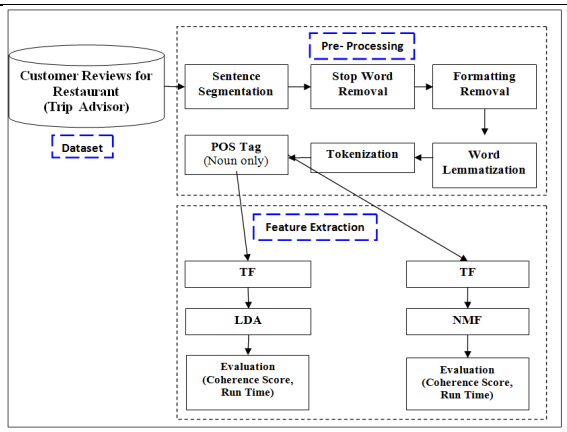

Figure 2: Architecture of the Proposed Aspect Extraction Process

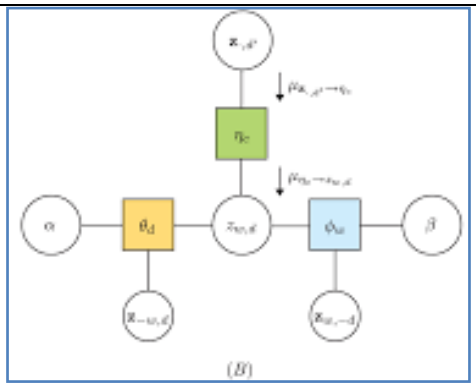

Figure 3: Graphical Representation of the LDA Topic Modeling Algorithm

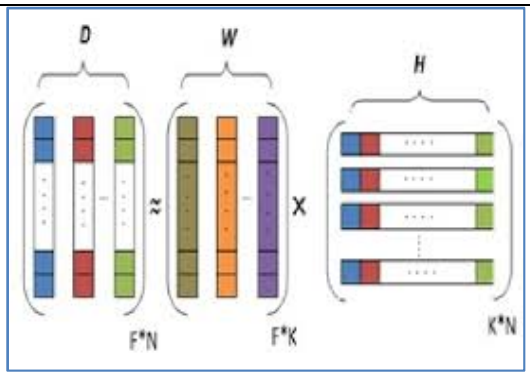

Figure 4: Graphical Representation of the NMF Topic Modelling Algorithm

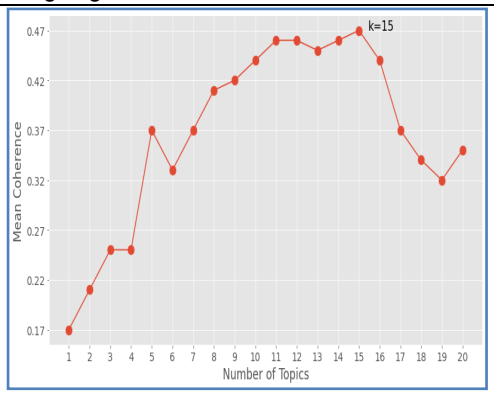

Figure 5: Mean Coherence Score for 'k' number of Topics using LDA

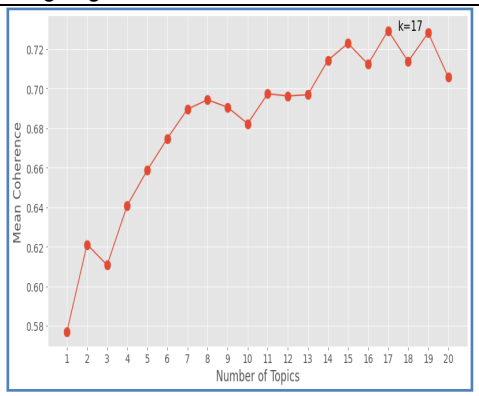

Figure 6: Mean Coherence Score for 'k' number of Topics using NMF

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RESEARCH ARTICLE

Larvicidal Activity of Seagrass *Syringodium isoetifolium* (Aschers.) against Dengue Vector *Aedes aegypti* (L.) and Filarial Mosquito *Culex quinquefasciatus* (Say)

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ABSTRACT

Mosquitoes are major public health pests due to their role as biological vectors of many pathogens which cause deadly diseases like malaria, filariasis, encephalitis, dengue, chikungunya, zika and yellow fever. Mosquito management is the important requirement to prevent the disease transmission. Naturally available pesticidal molecules are generally target specific and possess no or less side effects. In the present study mosquito larvicidal activity of hexane, dichloromethane (DCM) and ethanolic extracts of seagrass *Syringodium isoetifolium* (Aschers.) (*S.isoetifolium*),was tested against third instar larvae of *Aedes aegypti* and *Culex quinquefasciatus* after 24 and 48 hours of treatment. The result shows that hexane extract was the most toxic to *Ae.aegypti* larvae.

Keywords: *Syringodium isoetifolium, Aedes aegypti, Culex quinquefasciatus,* FTIR, GCMS, Larvicidal activity

INTRODUCTION

Mosquitoes are potential vector insects cause public health problems. Worldwide, they play a major role in causing dreadful diseases to the human beings since they carry pathogenic viruses and parasites (Hafeez et al.,2011; Samidurai, et al., 2009; Elumalai et al.,2013). According to the recent reports of WHO (2017), more than 80% of the world's population is at risk of vector-borne diseases such as dengue, chikungunya and lymphatic filariasis.17% of

communicable diseases affect more than 700,000 peoples annually. To control the issue, various applications of commercially available chemicals such as temephos, fenthion and growth regulators like diflubenzuron, methoprene and biological insecticides like *Bacillus* formulations are followed worldwide (Lin et al., 2010). The repeated usage of these effective insecticides causes environmental damage, health problems, disruption of natural food chain, resistance development and non-target effects (Suwanbamrung et al., 2010). Therefore, pesticidal compounds from natural resources are evitable because of their biodegradable property, eco-friendly property and economic feasibility (Yusniawati., 2017). In that prospective, many plant extracts and their secondary metabolites were studied and analysed for larvicidal effects against different species of mosquitoes (Girdhar et al., 1988). Several research works have been carried out using bacteria, microalgae and macroalgae against mosquito larvae. But very limited works have been done on screening seagrasses against mosquito larvae where, it is advantageous because of its lifecycle (Ravikumar *et al*., 2005). They are marine flowering plants (angiosperms) grow in tidal and subtidal regions than in coastal regions. According to Ameer et al 2011, there are about 60 species reported across the world. They help in the production of energy, supplies nutrition to the other marine organisms and also helps in the shore stabilisation by absorbing toxic elements (Malea et al., 1995; Caccia et al., 2003; Ferrat et al., 2003). They are used as food in coastal regions (Hemminga & Duarte, 2000). They have medicinal properties such as antimicrobial, anti-mosquito, antioxidant, antipyretic and antitumour due to the existence of secondary metabolites (Subhashini et al., 2013; Papenbrock., 2012; Puglisi 2007).

In particular, seagrass *S.isoetifolium* has a property of heavy metal absorption (Sudharsan et al., 2012) and also exhibited antibacterial activity against seventeen human pathogens and five fish pathogens (Chitra et al., 2015). The compound called Chicoric acid was isolated from *S.filiforme* (Nuissier et al., 2009) and also screened against mosquito larvae of *Ae.aegypti* and *C.quinquefasciatus* (Syed Ali *et al*., 2012., Devi *et al.,* 1997). From the available literature, it is understood that very few works were carried out towards mosquito larvicidal activity of *S.isoetifolium*. Hence, the main objective of the present work is to screen mosquito larvicidal activity of *S.isoetifolium* against third instar larvae of *Aedes aegypti* and *Culex quinquefasciatus*.

MATERIALS AND METHODS

Collection, Processing and authentication

Sea grass *S.isoetifolium* (Aschers.) as shown in Fig.1 was collected from the deep bottom of the sea, southeast coastal region of Asia, Mandabam, Rameswaram. The samples were collected, brought to lab, washed thoroughly to remove all the sand particles, debris and microorganisms. They were cut into small pieces and allowed to dry under shade for more than a week. A single specimen was pressed in herbarium and was authenticated by Taxonomist, Dr. G. Gnanasekaran, Madras Christian College, Tamil Nadu, India. The herbarium samples are maintained in Pachaiyappa's College with the voucher number SGSIPC03.

Extract preparation

The dried seagrass was blended in an electronic machine and made into coarse powder. The powder was sequentially soaked in three different solvents namely hexane, dichloromethane (DCM) (Rankem, India) and Ethanol (Thermo Fisher Scientific Company, India). Initially, one part of powder was soaked in three litres of hexane (w/v) at room temperature for 48 hours. The extract was filtered and concentrated at 50ºC in a rotatory evaporator (Equitron model, cat#: 8925.REG.760. Vacuum Regulator- Analogue, The science House, Chennai, India). Then the junk was soaked in dichloromethane and ethanol. Thus the powder was sequentially extracted using solvents in the increasing order of polarity (Hexane<DCM<Ethanol) and the procedure was repeated twice to get a better yield. The concentrated extracts were stored in a glass vials for further studies.

Preliminary Phytochemicals Screening

The phytochemical constituents of *S.isoetifolium* were qualitatively analysed in all the three different solvent extracts following the methods of (Senthil Kumar and Reetha, 2009; Naser et al., 2009).15mg of crude extract of *S.isoetifolium* was dissolved in 15ml of DMSO (Dimethosulphoxide) and qualitative tests were done for proteins, tannins, saponins, flavonoids, alkaloids, quinones, glycosides, triterpenoids, phenol, steroid and coumarin

Gas Chromatography - Mass Spectrometry (GCMS)

The phyto compounds present in hexane extracts of *S.isoetifolium* was subjected to GCMS analysis using Clarus 680 GC model. This is made up of gas chromatogram integrated with the mass spectrometer connected to the fused silica column, packed with Elite-5MS (5% biphenyl 95% dimethylpolysiloxane, 30 m × 0.25 mm ID × 250 μm df) and mass detector operated at 230 °C and ionization energy of 70 eV was utilised. The components were separated using Helium gas (as a carrier) at a constant flow of 1 ml/min. The extract sample of 1 μL was injected into the instrument at the oven temperature of 60 °C for 2 min and then increased to 300 °C at the rate of 10 °C/min and the injector temperature was set at 260°C during the chromatographic run. The spectral data were compared with the database of known components which were stored in the GCMS NIST library from the software turbo Mass version.

Fourier Transmission Infrared analysis (FTIR)

About 0.2 mg of dried crude extracts of *S.isoetifolium* was dissolved in 1ml of chloroform and studied the various frequencies of different functional groups using FTIR analysis. The analysis was carried out using the instrument IRAffinity-1S, Japan using ATR mode and the wave number ranges between 2900 cm^{-1} to 720 cm^{-1}.

Mosquito larvae culture

The larvae of *C.quinquefasciatus* and *Ae. Aegypti* were obtained from Entomology Research Institute, Loyola college, Chennai. The larvae were maintained at laboratory conditions 27±1ºC; 65-70% rh with 11±1 hour photoperiod. Third instar larvae (Fig 2.1; Fig 2.2) were used for conducting experiments (Rahuman et al., 2000; Mayoub et al., 2016)

Bioassay for Larvicidal activity of seagrass

Four different concentrations 62.5, 125, 250 and 500ppm were prepared from each solvent extract. First the required quantity of extract was mixed with 400µl of DMSO and then mixed with 100ml tap water. Untreated water control and DMSO control were maintained separately. Twenty third instar larvae of *C.quinquefasciatus* were taken in 100ml treated water, each concentration and control was replicated five times. Larvicidal activity against *Ae.aegypti* was also tested following the same procedure. Dead larvae were counted and recorded after 24 and 48hours of exposure. The corrected mortality was calculated using abbott's formula (Abbott's, 1925).

Statistical analysis

The statistical analysis was carried out using SPSS (Statistical Package for Social Sciences software) version 21.0. The LC_{50} (Concentration of sample that kills 50 % organisms) and LC_{90} (Concentration of sample that kills 90 % organisms), Slope concept, Correlation coefficient (r), Chi square test (x^2) and level of significance 'p' value was calculated using Probit analysis (Finney,1971).

Molecular docking analysis

The major compound tetrapentacontane,1,54-Dibromo was found in GC-MS analysis used as ligand. 2D structure of the same was retrieved from Pubchem database converted to 3D structure using ChemSketch and saved as Mol2 format (Fig.5B). The ace1 receptor (enzyme responsible for neurotransmission). The FASTA sequence was retrieved from uniprot database were modelled using SWISS MODELLOR, stored in PDB format (Fig 5A). Molecular docking was performed using SWISSDOCK and the interaction between receptor–ligand complex was viewed in Chimera visualizer (Grosdidier et. al., Proteins. 2007)

RESULTS AND DISCUSSION

The extractive value of hexane, dichloromethane and ethanolic extracts of *S.isoetifolium* (whole part) was summarised in (Table.1). Except ethanolic extract, other extracts were obtained in the form of gels. The phytocompounds were absent in hexane extracts of *S.isoetifolium* where as flavonoids, triterpenoids and phenols were present in DCM; saponins, alkaloids and glycosides were present in ethanolic extracts (Table.2). The potent hexane extract of *S.isoetifolium* was also analysed using Gas Chromatography and Mass Spectrometry analysis. From the analysis three bioactive compounds were found to be present as shown in the (Table 3). They are as follows; 2-octadecyl-Propane-1,3-Diol (alcoholic groups), 1-Hexyl-2-Nitocyclohexane ($C_{12}H_{23}O_2N$) with peak area and retention time 0.50% and 31.50 minutes With reference to Sengodan et al., 2020 the compound was reported from *Avicennia marina* (Forssk.) with the area percentage 3.22% which was already found to be effective against third instar larvae of three different mosquito vectors *C.quinquefasciatus*, *Ae. Aegypti* and *An. stephensi*. Third compound was tetrapentacontane,1,54-Dibromo (C_{54} H_{108} Br_2), which showed the highest peak area percentage and retention time of 96.66 and 27.39 minutes, respectively. Presence of halogenated bromine group was found, as already reported by Orlando et al.,2016, halogenated compound called sesquiterpene was isolated from the marine algae *Laurentia dendroidea* which had the highest toxicity against second instar larvae of *Ae.aegypti*. Hence, it is understood that presence of some halogenic compounds might play a vital role in mosquito larvicidal activity of S.*isoetifolium*. The hexane extract of *S.isoetifolium* was taken to further analysis to find active groups using FTIR analysis (Fig.3). The various peaks of absorption spectra indicate various functional groups. They are as follows; 2954 cm^{-1}(alkanes, C-H stretch), 2851 cm^{-1}(carboxylic acids, O-H stretch), 1459 cm^{-1} (alkanes, C-H bend), 1376 cm^{-1} (Nitro compounds, N-O asymmetrical stretch) and 721 cm^{-1} (alkyl aldehyde, C-Br stretch) with reference to Janakiraman and Johnson et al.,2015.

The crude extracts of *S.isoetifolium* was tested against third instar larvae of *Ae.aegypti*. Hexane extracts exhibited maximum larvicidal activity of 26 and 50% at 500ppm, 24 and 46% at 250ppm, 22 and 28% at 125ppm, 21 and 26% at 62.5ppm at 24 and 48 hours respectively (Fig.4). DCM extracts showed moderate activity of 1-16% from 62.5 to 500ppm concentrations and ethanolic extracts did not exhibit activity. The results on LC_{50} and LC_{90} calculations revealed that hexane extract of *S.isoetifolium* was found to be efficient with the lowest LC_{50} and LC_{90} values of 1.016 and 36.041ppm, respectively at 24 hours exposure and 3.164 and 43.979ppm, respectively at 48 hours exposure and the p value was found to be 0.038, which was significant (Table 4). DCM extracts showed moderate activity with the LC_{50} and LC_{90} values of 0.451 and 16.618ppm, respectively at 24 hours exposure and 32.835 and 701.61ppm, respectively at 48 hours exposure respectively (Table 4).Ali et al., 2012, tested the larvicidal activity of the ethanolic extracts of *S.isoetifolium* root and leaf. The extracts were incubated for 21 days in the dark condition. The leaf extracts were efficient against fourth instar larvae of *Ae.aegypti* with the LC_{50} value of 0.060±0.04 µg/ml and LC_{90} of 0.897 µg/ml at 24 hours. In the present research hexane extracts of *S.isoetifolium* (Whole plant) was incubated for 48 hours which was effective against third instar larvae of *Ae.aegypti* and the LC_{50} and LC_{90} values found to be 1.016 and 36.041 ppm, respectively at 24 hours post treatment and 3.164 and 43.979 ppm, respectively at 48 hours post treatment, which clearly shows that the hexane extract of the seagrass was more effective than ethanolic extract. From the above researches, it reveals that non polar solvent, hexane extract has a greater influence over ethanolic extracts, consumed less incubation period and 'p' value was more significant. From the current research *S.isoetifolium* extracts were ineffective against third instar larvae of *C.quinquefasciatus*. Devi et al, 1997,also reported that larvicidal activity of *S.isoetifolium* against the third instar larvae of *C.quinquefasciatus* was ineffective in Chloroform fractions till 450 mg $L^{-1}$and in petroleum ether at 2000 mg L^{-1}. Hence, it was clear that *S.isoetifolium* did not have much efficacy against *C.quinquefasciatus* when compared to *Ae. Aegypti*. Moreover, molecular docking results reveals that, ligand binds with the active site of receptor with the energy of -12.59Kcal/Mol. Lesser the binding energy indicates that there is a strong interaction between the protein-receptor complex (Fig.5). Hence, this lead compound might be a strong inhibitor of ace1 receptor.

CONCLUSION

In this present research, it is understood that hexane extracts of *S.isoetifolium* was efficient against third instar larvae of *Ae.aegypti* than a polar solvent but, hexane extracts did not exhibited prominent secondary metabolites from qualitative analysis. FTIR analysis reveals that there could be influence of alkane group. The major phytocompound tetrapentacontane, 1,54-Dibromo was identified from GCMS analysis might be responsible for the larvicidal efficacy of *S.isoetifolium*. Moreover, results from the molecular docking studies shown that the same compound also has a strong binding interaction with ace1 receptor. In future, detailed studies such as isolation and purification of active compound are necessary which could serve as an eco-friendly mosquito larvicide.

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REFERENCES

1. Abbott,W.S.A method of computing the effectiveness of an insecticide. J. Econ. Entomol(1925);18, 265–267.
2. Ameer.A, Shaffai A. El, and A. Rouphael, Field Guide to Seagrasses of the Red Sea(IUCN Publication, Courbevoie (2011).
3. Caccia VG, Millero FJ, Palangues A. The distribution of trace metals in Florida Bay sediment. Mar Pollut Bull (2003); 46(11):1420–1433
4. Chithra Roy A.R, Uma maheswari G. Evaluation of antifungal activity of syringodiumisoetifolium against selected fungal pathogens; int journal of Multidisciplinary research paper review (2015) ;1 (9); 246-250
5. Devi P, Solimabi W, D' Souza L,Kamat.S.Y .Toxic effects of coastal and marine extracts on mosquito larvae. Botanica Marina (1997); 40(6).533-535.
6. Elumalai, D., Kaleena, P.K., fathima, Mujeera, Nareshkumar, C. Phytochemical screening and larvicidal activity of *Tridax procumbens* (L) against Anopheles stephensi (Liston), *Aedes aegypti* (L) and *Culex quinquefasciatus* (say). Int. J. Biosci. Res (2013) 2, 1–14.
7. Ferrat L, Pergent-Martinim C, Romeo M. Assessment of the use of biomarkers in aquatic plants for the evaluation of environmental quality: application to seagrasses. AquatToxicol (2003); 65(2):187–204.
8. Finney, D.J. In: Probit Analysis. Cambridge University Press, London.(1971). 68–72.
9. Girdhar G, Deval K, Mittal PK and Vasudevan P, Mosquito control by Calotropis latex, J Pesticides (1988); 26–29.
10. Grosdidier.A., Zoete V., Michielin O. Docking of small molecules into Protein active sites with a multiobjective evolutionary optimisation. (2007);1;67(4):1010-25
11. Hafeez F, Akram W, Abdul E, Shaalan S.Mosquito larvicidal activity of citrus limonoids against Aedesalbopictus. Parasitol Res (2011); 109: 221-229.
12. Hemminga, M. A., & Duarte, C. M. Seagrass ecology. New York (2000); Cambridge University Press (298 pp.).
13. Janakiraman.N, Johnson. M. Functional groups of tree ferns (cyathea) using FTIR: Chemotaxonomic implications. Romanian J Biophys (2015); 25,131-141.
14. Lin AS, Stout EP, Prudhomme J, Le Roch K, Fairchild CR, FranzblauSG. Bioactive bromophycolides R-U from the Fijian red alga Callophycus serratus. J Nat Prod (2010); 73: 275-278.
15. Mahyoub, J.A., Hawas, U.W., Al-Ghamdi, K.M., Aljameeli, M.M.E., Shaher, F.M., Bamakhrama, M.A., Alkenani, N.A., The Biological Effects of Some Marine extracts against *Aedes aegypti* (L.) Mosquito Vector of the Dengue Fever in Jeddah Governorate, Saudi Arabia, J. Pure Appl. Microbiol (2016); 10(3) 1949 – 1956.
16. Malea P, Kevrekidis T, Haritonidis S. The short-term uptake of zinc and cell mortality of the seagrass Halophilastipulacea (Forsk.) Aschers, Israel. J Plant Sci (1995); 43:21–30.

17. Nazar, S., Ravikumar, S., Williams, G. P, Ali, M. S., Suganthi, P. Screening of Indian coastal plant extracts for larvicidal activity of *Culex quinquefasiatus*, Ind. J. Sci and Technol (2009); 2(3), 24-27.
18. Nuissier G, Diaba F, Grignon-Dubois M. Bioactive agents from beach waste: Syringodium flotsam evaluation as a new source of L-chiro-inositol. Innovat Food SciEmerg Tech (2009); 9:396–400
19. Orlando S.N, Simone A G, Angélica R S, Fernanda L S M, Richard I S, Rodrigo N F J S, Jorge L C M, Eldo C F B M and José R S;Larvicidal Potential of the Halogenated Sesquiterpene (+)- Obtusol, Isolated from the Alga Laurenciadendroidea J. Agardh (Ceramiales: Rhodomelaceae), against the Dengue Vector Mosquito *Aedes aegypti* (Linnaeus) Diptera: Culicidae (2016);1-14
20. Papenbrock J (2012), ISRN Botany 10, 103892.
21. Puglisi MP, Engel S, Jensen PR, Fenical W. Antimicrobial activities of extracts from Indo-Pacific marine plants against marine pathogens and saprophytes. *Mar Biol* (2007);150, 531–540.
22. Rahuman. A. A, Geetha Gopalakrishnan, Saleem Ghouse. B, Arumugam. S, B. Himalayan. Effect of *Feronia limonia*on mosquito larvae. Fitoterapia (2000);71; 553-555
23. Ravikumar S, Nazar S, Nural Shiefa A and Abideen S. Antibacterial activity of traditional therapeutic coastal medicinal plants against some pathogen, J Environ Biol, 26 (2005) ;383–386.
24. Samidurai K, Jebanesan A, Saravanakumar A, Govindarajan M, Pushpanathan T. Larvicidal, ovicidal and repellent activities of *Pemphis acidula* Forst. (Lythraceae) against filarial and dengue vector mosquitoes. Aca J Entomol(2009); (2); 62-66.
25. Sengodan K, Manohar V, Uthirarajan K, Venkatesan M, Ramachandran S , Prabhakaran V S, Chinnaperumal K, Muthugounder S S , Surajit De M, Arumugam V , Patcharin K, Sengottayan S-; Biological Effects of Avicennia Marina (Forssk.) Vierh. Extracts on Physiological, Biochemical and Antimicrobial Activities Against Three Challenging Mosquito Vectors and Microbial Pathogens; Environ SciPollut Res Int (2020); 27(13):15174-15187.
26. Senthilkumar, P.K, Reetha, D .Screening of antimicrobial properties of certain Indian medicinal plants. J. Phytol. 1, (2009);193–198.
27. Subhashini.P, Dilipan.E, Thangaradjou.T, and Papenbrock.J. Bioactive natural products from marine angiosperms.Nat. Prod. Bioprospect. (2013); 3, 129-136.
28. Sudharsan. S, Seedevi. P, Ramasamy. P, Subhapradha.N, Vairamani.S and Shanmugam.A Heavy metal accumulation in seaweeds and sea grasses along southeast coast of India; CODEN(USA): JCPRC5ISSN (2012): 0975-7384.
29. Suwanbamrung C, Nukan N, Sripon S, Somrongthong R, Singchagchai P. Community capacity for sustainable community based dengue prevention and control: study of a sub- district in Southern Thailand. Asian Pac J Trop Med (2010); 3: 215-219.
30. Syed Ali M, Ravikumar S, Margaret Beula J. Bioactivity of seagrass against the dengue fever mosquito *Aedes aegypti* larvae Asian Pac J Trop Biomed (2012); 2: 570-573
31. WHO,2017;https://www.who.int/neglected_diseases/news/comprehensive_global_approach_against_vectorborn diseases/en/
32. Yusniawati, Y, Yasman, Y, Handayani, W. Bioactivity of Thalassiahemprichii (hydrocharitaceae) methanolic extract from West Bali National Park as Aedesaegyptilarvacide (2017); *AIP Conference Proceedings*, 2023, art. no. 020130.

Table 1: Extractive value and form of *S.isoetifolium* solvent extracts

S.No	Sea grass	Voucher Number	parts used	Solvent Extracts	Weight of the crude powder sample(g)	Extractive value(g)	Extract form
1	***S. isoetifolium***	**SGSIPCI03**	**whole part**	Hexane	305	3.322	gel
				DCM	301	3.879	gel
				Ethanol	297	4.038	solid

Table 2: Preliminary phytochemical analysis of *S.isoetifolium* solvent extracts

S.No	Phytochemical tests	Hexane	DCM	Ethanol
1	Aminoacid	-	-	-
2	Protein	-	-	-
3	Tannins	-	-	-
4	Saponins	-	-	+
5	Flavonoids	-	+	-
6	Alkaloids	-	-	+
7	Quinones	-	-	-
8	Glycosides	-	-	+
9	Triperpenoids	-	+	-
10	Phenol Test	-	+	-
11	Steroids	-	-	-
12	Coumarin	-	-	-

+Presence –Absence

Table 3: Identification of phytocompounds from hexane extracts of *S.isoetifolium*

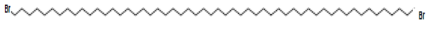
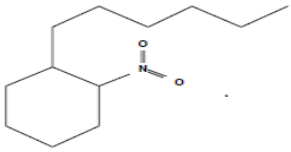
S.No	RT (min)	Area %	Molecular weight (Dalton)	Compound Name	Compound structure
1	25.437	2.327	328	2-Octadecyl-Propane-1,3-Diol	 $C_{21}H_{44}O_2$
2	27.393	96.658	914	Tetrapentacone,1,54-Dibromo-	 $C_{54}H_{108}Br_2$
3	31.500	0.508	214	1-Hexyl-2-Nitrocyclohexane	 $C_{12}H_{23}O_2N$

Table 4: Lethal concentrations of *S.isoetifolium* solvent extracts against *Ae.aegypti* larvae at 24 and 48 hours Post Treatment

Sea grass	Extracts	Time of exposure(hours)	LC_{50} (µg/ml)	LC_{90} (µg/ml)	Slope	r	x^2	p value
S.isoetifolium	Hexane	24	1.0163	36.041	0.783±0.23	0.839	6.533	0.038*
	DCM	24	0.4518	16.618	0.818±0.19	0.950	1.851	0.396
	Ethanol	24	**No Mortality**					
	Hexane	48	3.164	43.979	1.213±0.43	0.990	0.179	0.672
	DCM	48	32.835	701.61	0.963±0.69	0.999	0.001	0.966
	Ethanol	48	**No Mortality**					

* Statistically significant, if $P \leq 0.05$

The solvents extracts concentrations from 62.5-500

Systematic Classification:
Kingdom: Plantae
Clade: Angiosperms
Clade: Monocots
Order: Alismatales
Family: Cymodoceacea
Genus: *Syringodium*
Species: *isoetifolium*

Fig 1. *Syringodium isoetifolium* (Asch.) Dandy

Fig. 2.1 Third instar larvae of *Aedes aegypti*

Fig. 2.2 Third instar larvae of *Culex quinquefasciatus*

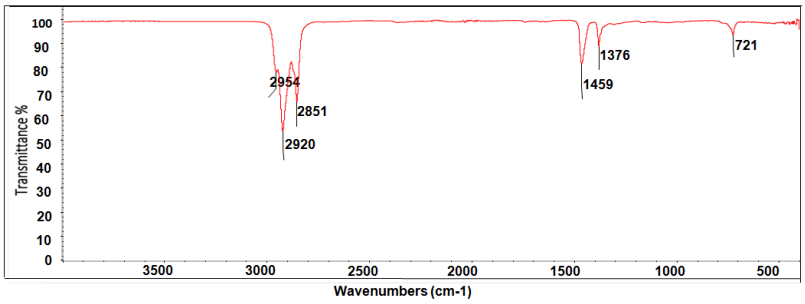
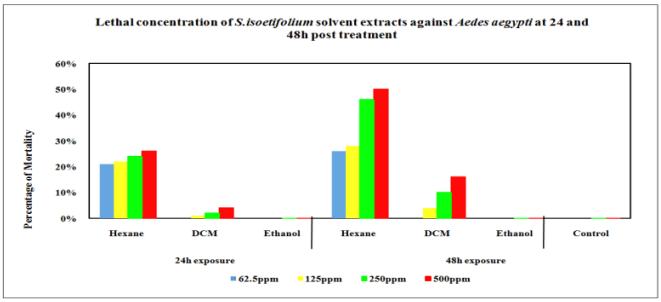


Fig. 3 FTIR spectrum of hexane extracts of *S.isoetifolium*



Contol= Untreated water and DMSO

Fig.4. Lethal concentration of *S.isoetifolium* solvent extracts against *Aedes aegypti* at 24 and 48h post treatment

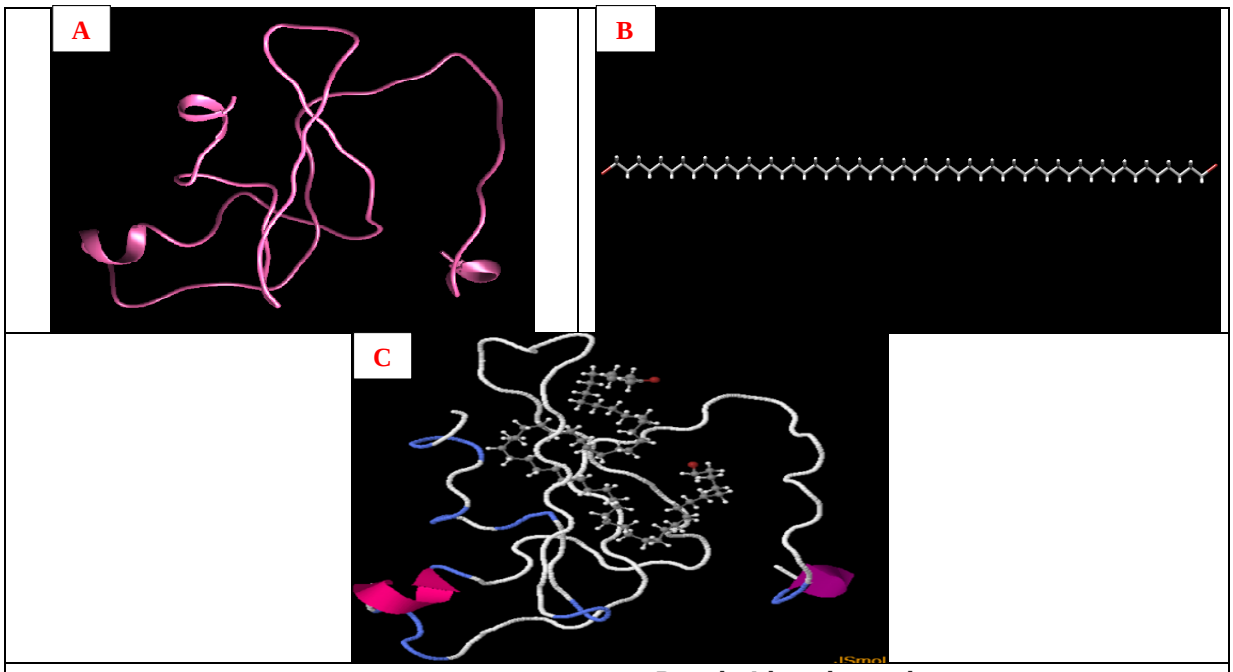


Fig.5. (A) Receptor (B) Ligand (C) Protein-Ligand complex

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RESEARCH ARTICLE

Rereading of Kamala Das as an Eco-Feminist with Special Reference to Her Selective Poems

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ABSTRACT

Eco-feminism, a branch of feminism, denotes environmentalism and the association between women and the earth, as a foundation to its analysis and practice. Eco-feminism is the third wave of the feminist revolution. This term was coined by the French writer Francoise D' Eaubonne in her book *Le Feminisme Ou La Mort*. Feminism is referred to the human entity while eco-feminism is a wider term which focuses the protest against the subjugation of the humans and also the non-human entity. Kamala Das, a stupendous Indian English poet and litterateur, is well-established for her corpus of literary works in English and also in Malayalam. She is bold enough to pen the agony and the longing of women through her writings. Because of her gripe against patriarchy, embracing of matrilineal culture with a romantic fervor, the exploration of female sexuality and sexual desires of women in her compositions, she is complimented as the foremost feminist author of the Indian Poetry in English. Nature takes pivotal role in her works. Das illustrates the natural and instinctive inclination of women towards nature in a comprehensible feminist orientation in her works. Besides, she is the one closer to the soil and life. She vibrantly depicts the images of nature through her verses and connects the realities of life and brings the philosophical thoughts to the readers. In this paper, the authors establish that Kamala Das is an expert in dealing the theme of Eco-feminism through her selective poems.

Keywords: Eco-feminism, environmentalism, agony, longing, non-human entity, revolution, matrilineal culture, feminist orientation, nature

INTRODUCTION

Eco-feminism is a branch of feminism that focuses on environmentalism and the relationship between women and the earth as a basic foundation to its analysis and practice. Eco-feminist thinkers draw on the concept of gender to analyze the relationships between humans and the natural world (Mac Gregor, 286). The term Eco-feminism was coined by the French writer Francoise d' Eaubonne in her book *Le Feminisme ou la Mort* (1974). In the perspective of Francoise d' Eaubonne, eco-feminism relates the oppression and domination of all marginalized groups like women, children, the poor to the oppression and domination of nature (animals, land, water, air, etc.). Her fundamental intention was to call out to women to save the planet. Francoise d' Eaubonne, a founder of the stream of Feminism and Ecology, claims that the root cause of domination of women and nature is patriarchy.

Eco-feminist Theory

Eco-feminist theory asserts that a feminist perspective of ecology does not place women in the dominant position of power, but rather calls for an egalitarian, collaborative society in which there is no one dominant group (Merchant, 193). The analysis of Eco-feminist establishes the connections between women and nature in the perspective of culture, religion, literature and iconography and also addresses the analogous between the oppression of nature and of women. These parallels include but are not limited to seeing women and nature as property, seeing men as the curators of culture and women as the curators of nature, and how men dominate women and humans dominate nature. Eco feminism emphasizes that both women and nature must be respected (Carol, 1).

Kamala Das as a Feminist

Eco-feminism is an effective tool in literary tradition which gives equivalent platform to women activists and ecological concerns. It encompasses a list of writers such as Rabindranath Tagore, A.K. Ramanujan, Nissim Ezekiel, Kamala Markandaya and one among them is Kamala Das. Das is the first Hindu woman writer of Indian English Literature who brings in writing her personal experiences, sexual feelings and also her bodily needs unexpurgated. She expressed her revolt against the deep rooted depression which has been prevalent in the patriarchal society. For this reason, she is a 'woman' in the true sense of the word as defined by Cixous, "the woman in her inevitable struggle against the conventional man and the universal subject who must bring women to their senses and to their meanings in history" (880). Das' restiveness as a sensitive woman in a male-dominated society is replicated in her poems and prose writings. Through her energetic voice against the male dictatorship, she becomes an enthusiastic spokesperson for women's liberation. She also focuses the awareness and the need for the recognition of the claims and also the rights of the Indian women. She is aptly illustrated as a forceful and vehement feminist and plays a very significant role in making the feminist concern and points of views depicted openly in her poetry. She is a pertinent and thought-provoking poet with not only a feminine sensibility, but also a feminist.

Kamala Das as an Eco-Feminist

Eco-feminism is a practical movement for social change that discerns interconnections among all forms of oppression: the exploitation of nature, the oppression of women, class exploitation, racism, colonialism (Gaard on Back cover). Hence, an Eco-feminist is a feminist who has compassion towards the oppressed communities and fights for the equality for all the humans as well as non-human beings. They aim at identifying the relation between the different kinds of dominations also. In addition to that it is an ideology and movement which relates the similarity between the oppression of women and nature by the masculine centered attitudes and practices associated with the patriarchal society. Being an eco-feminist, the portrayal of subjugation of women and the depletion of nature became inseparable in the works of Kamala Das. It is highly evident that she is instigated by the nature because of her rich tradition in her family, the habits of life of the people in her village who had an organic relation with nature, the rituals and customs of village life and also the greatest influence of her grandmother. The analysis of the following poems will prove that Kamala Das is an eco-feminist.

A Hot Noon in Malabar

Kamala Das meticulously deals with the ecological aspects of Eco-feminism in the poem entitled "A Hot Noon in Malabar". She expresses her yearning for happy childhood and family house in Malabar in this poem. The outside world is boring and defiled to the poetess and the summer in the city where she lives now is a torture to her. The following lines depict the climate and illustrate the routine life of Malabar:

This is a noon where beggars with whinning
Voices, a noon for men who come from hills
With parrots in a cage … (SC 1-3)

In cities, during the hot noon, the poet's soul is tortured with intense heat, because it reminds her equally of a hot noon in her family home at Malabar, where she was happy and gay despite the heat. Now everything is odd, dirty and painful, then everything was well-known, innocent and pure. It was hot, strangers were stirring the dust with their wild feet; but they are different, blameless and familiar when they looked at her. She yearns for the innocence and purity of her old family home; because she feels that it is the greatest torture to be there in a strange city on that hot noon. A.N. Dwivedi expresses the basic features of Das' poetry in the following observation which justifies the above description, " Kamala Das's poetry abounds in details of misery and grief, loneliness and helplessness, death and disease coldness and frigidity, frustration and dejection and all these render her vision tragic" (81). When others are annoyed by the heat, dust and noise, the poet longs for the hot noon in Malabar and it is associated with:

wild thoughts, wild love. To
Be here, far away, is torture. Wild feet Stirring up the
dust, this hot noon, at my
Home in Malabar, and I so far away… (SC 21-24)

Everything seemed to be well-known and intimate but now everything is weird and conveys a feeling of alienation and awfulness. She languishes for the bygone time, for a summer noon in her ancestral home in Malabar. This poem contrasts the irresistible past with the miserable present. The natural and the spontaneous life of Malabar is a contrast to the speaker's suppressed lonely life in the city. Malabar comes to symbolize her childhood days and she recaptures it to regain her lost self. Whenever she longs for true love and suffers from alienation and loneliness, she brings the comparison between past and present like this poem and also it could be observed in a few other poems also. Thus, through this poem she vividly portrays both nature and the woman fuses together. She depicts the nature as a character throughout her poem not simply as a background for the poem. Das' new dimension of existence of man in nature is presented here.

The Suicide

In the poem titled "The Suicide", swimming symbolizes such a temporary resolution of tensions. During the innocent childhood, her soul and the body were at home with each other, swimming was a kind of dance and picturized as, "The only movement I know well / Is certainly the swim./ It comes naturally to me" (OP 66-68). E.V.Ram Krishnan insists, "Since the poet cannot disinherit either the body or the soul and live with one of them, the whole climax of the poem saturates into the idea of suicide where the agency which can take away one of them is the sea, an old symbol of timelessness" (204). Then, adulthood intervened and the harmony broke in the form of her grandmother's cry, "Darling, you must stop this bathing now" (OP 79). It is her grandmother who awakens the realization in the poet of the changing contours of her body as she bathes in sunshine in the "pale green pond" (70) near her house in Malabar. After her marriage, the poet feels aloof and no one showers love on her is evident here. The disappointed lady searches for relief in the flawless lap of nature. Thus, Das exhibits her knowledge about the nature. She reveals the nature as a medium to illustrate her pain and loneliness. This is a well-known Eco-feminist artistic practice.

Summer in Calcutta

Das is one of the creative writers who used nature images to draw her feelings of lust, love, frustration and pathos in her sensational poetry of love, sex and agony. She never writes about nature and its beauty but she used it as a medium of expression and also her choice of grotesque and strange metaphors from nature helped her to draw her own life in her writings. The poetess too chooses the nature elements like water, sun, earth and especially sea to express her dual psyche, her sensational emotions and desires. Sun imagery in Das' poems enforces the intense and powerful feelings of lust in which the life of man is destroyed. It represents the hot desires or passionate emotions of the poet and her lovers. But Das is never able to control her sensual feelings and she drinks it again and again, which is expressed in a poem entitled "Summer in Calcutta":

What is this drink but
The April sun, squeezed
Like an orange in
My glass? I sip the
Fire, I drink and drink
Again, I am drunk,
Yes, but on the gold Of suns. (SC 1-8)

The April sun brings the warm, sensuous and exciting feelings of the poet here and she drinks "the juice of the April sun". The poetess adds that her feelings about sex are hot and beyond self-control. The repetition of the words "drink" and "drunk" suggest the repeated emergence of sensual desires. K. R. Ramchandran Nair writes:

The April sun becomes the 'noble venom' that flows through the poet's veins providing a temporary triumph over life's despairs. Just as the sun is transformed into a juice, transformed into laughter, despair is transformed into hopeful desire. (10)

CONCLUSION

It is apparent that the role of nature is inevitable in the works of Kamala Das. She is comforted by the nature and not by the human. Being a feminist poet, Das has nurtured a special bonding with the nature whenever she feels lonely and frustrated. She loves nature as a vivid and life-giving property in all its primitiveness and purity. She presents the innumerable colours, shapes and movements of nature by its entire means throughout her works. Most of the works of Das are 'first person narrative' which is considered as the characteristic of eco-feministic writings. Das is well-known for her creation of peculiar ecosystem in her writing.

WORK CITED

1. Das, Kamala. *Summer in Calcutta*, New Delhi: Everest Press, 1965. Print.
2. Adams, Carol (2007). *Eco feminism and the Sacred*. Continuum. p. 1–8.
3. Cixous, Helene. "The Laugh of the Medusa." *Women in Sexist Society: Studies in\ Power and Powerlessness*. Ed. Vivian Gorrick and Barbara K.Moran. London: Basic Books, 1971. Print.
4. Dwivedi, *A. N. Kamala Das and Her Poetry*. New Delhi: Atlantic Publishers and Distributors, 2000. Print.
5. Gaard, Greta, and Patrick D. Murphy, eds. *Ecofeminist Literary Criticism*: *Theory, Interpretation, Pedagogy*. Urbana: U of Illinois P, 1998. Print.
6. MacGregor, Sherilyn (2006). *Beyond mothering earth: ecological citizenship and the politics of care*. Vancouver: UBC Press. p. 286. ISBN 978-0-7748-1201-6.
7. Merchant, Carolyn (2005). "Eco feminism". *Radical Ecology*. Routledge. pp. 193–221.

8. Nair, Ramchandran K.R. *The Poetry of Kamala Das.* New Delhi: Reliance Publishing House, 1993. Print.
9. Ramkrishnan, E.V. *Crisis and Confession: Studies in Poetry of Theodre Roethke, RobertLowell and Sylvia Plath.* Delhi: Chanakya Publications. 1988. Print.
10. Saluja, Vineeta Kaur. Dr. and Charu Kohli. "Sketches of Feminine Sensibility in the Writings of Kamala Das." *Global Journal of Multidisciplinary Studies* 3.3 (2014): 79. Print.
11. https://en.wikipedia.org/wiki/Eco-feminism

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RESEARCH ARTICLE

Service Sector, Indian Story: An Introduction

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ABSTRACT

In this paper, we discuss the service sector which is based on Indian story. A service is the non-material equivalent of a goods. A service provision is an economic activity that does not result in ownership, and this is what differentiates it from providing physical goods. It is claimed to be a process that creates benefits by facilitating a change in customers, a change in their physical possessions, or a change in their intangible assets. By supplying some level of skill, ingenuity, and experience, providers of a service participate in an economy without the restrictions of carrying stock (inventory) or the need to concern themselves with bulky raw materials. On the other hand, their investment in expertise does require marketing and upgrading in the face of competition which has equally few physical restrictions.

Keywords: Service Sector, Service system, Service specification

INTRODUCTION

SERVICE SECTOR

A service is a set of benefits delivered from the accountable service provider, mostly in close co-action with his service suppliers, generated by the functions of technical systems and/or by distinct activities of individuals, respectively, commissioned according to the needs of his service consumers by the service customer from the accountable service provider, rendered individually to the authorized service consumers on their dedicated request, and, finally, utilized by the requesting service consumers for executing and/or supporting their day-to-day business tasks or private activities. The service sector consists of the "soft" parts of the economy such as insurance, government, tourism, banking, retail, education, and social services. In soft-sector employment, people use time to deploy knowledge assets, collaboration assets, and process-engagement to create productivity (effectiveness), performance improvement potential (potential) and sustainability. The tertiary sector is the most common workplace. Services can be paraphrased in terms of their main attributes. They are intangible and insubstantial; they cannot be handled, smelled, tasted, heard, etc. There is neither potential nor need for storage and they are said to be inseparable and perishable. Because services are difficult to conceptualize, marketing them requires creative

visualization to effectively evoke a concrete image in the customer's mind. From the customer's point of view, this characteristic makes it difficult to evaluate or compare services prior to experiencing the service delivery. They are perishable, unsold service time is a lost economic opportunity. For example a doctor who is booked for only two hours a day cannot later work those hours— she has lost her economic opportunity.

Other service examples are airplane seats (once the plane departs, those empty seats cannot be sold), and theatre seats (sales end at a certain point). There is a lack of transportability as services tend to be consumed at the point of "production" although this does not apply to outsourced business services. There is a lack of homogeneity as services are typically modified for each consumer or each new situation (consumerised). Mass production of services is very difficult. This can be seen as a problem of inconsistent quality. Both inputs and outputs to the processes involved providing services are highly variable, as are the relationships between these processes, making it difficult to maintain consistent quality. There is labor intensity as services usually involve considerable human activity, rather than a precisely determined process. Human resource management is important. The human factor is often the key success factor in service industries. It is difficult to achieve economies of scale or gain dominant market share. There are demand fluctuations and it can be difficult to forecast demand which is also true of many goods. Demand can vary by season, time of day, business cycle, etc. There is buyer involvement as most service provision requires a high degree of interaction between service consumer and service provider. There is a client-based relationship based on creating long-term business relationships. Accountants, attorneys, and financial advisers maintain long-term relationships with their clients for decades. These repeat consumers refer friends and family, helping to create a client-based relationship.

Service system

Service system (or value co-creation system) is a configuration of technology and organizational networks designed to deliver services that satisfy the needs, wants, or aspirations of customers. Marketing, operations, and global environment considerations have significant implications for the design of a service system. Three criteria used to classify service systems include: customer contact, capital intensity, and level of customer involvement. Properly designed service systems employ technology or organizational networks that can allow relatively inexperienced people to perform very sophisticated tasks quickly — vaulting them over normal learning curve delays. Ideally, empowerment of both service provider employees and customers (often via self service) results from well designed service systems. Service systems range from an individual person equipped with tools of the trade (e.g., architect, entrepreneur) to a portion of a government agency or business (e.g., branch office of a post office or bank) to complete multinational corporations and their information systems (e.g., Domino's Pizza, Federal Express). Hospitals, universities, cities, and national governments are designed service systems. The language, norms, attitudes, and beliefs of the people that make up a service system may evolve over time, as people adjust to new circumstances. In this sense, service systems are a type of complex system that is partially designed and partially evolving. Service systems are designed to deliver or *provision* services, but they often consume services as well. Every service system is both a service provider and a customer of multiple types of services. Because service systems are designed both in how they provision and consume services, services systems are often linked into a complex service value chain or value network where each link is a value proposition. Service systems may be nested inside of service systems (e.g., staff and operating room unit inside a hospital that is part of a nationwide healthcare provider network). Service system designers or architects often seek to exploit an economic complementarily or network effect to rapidly grow and scale up the service. For example, credit cards usage is part of a service system in which the more people and businesses that use and accept the credit cards, the more value the credit cards have to the provider and all stakeholders in the service system. Service system innovation often requires integrating technology innovation, business model (or value proposition) innovation, social-organizational innovation, and demand (new customer wants, needs, aspirations) innovation.

For example, a national service system may be designed with policies that enable more citizens (the customers of the nation) to become an entrepreneur, and thereby create more innovation and wealth for the nation. Service systems may include payment mechanisms for selecting a level of service to be provided (upfront or onetime payment) or payment based on downstream value sharing or taxation derived from customers who received the benefit of the service (downstream or ongoing payment). Payments may also be in the form of credit (creative arts) or other types of intangible value "Service system" is a term frequently used in the service management, service operations, services marketing, service engineering, and service design literature. While the term frequently appears, it is rarely defined. Given the growing importance of this term in the literature, this entry begins to organize historical usages, examples, and inferred definitions.

A service system worldview is a system of systems that interact via value propositions. One recent definition is a service system is a value coproduction configuration of people, technology, internal and external service systems connected via value propositions, and shared information (language, laws, measures, etc.). The smallest service system is a single person and the largest service system is the global economy. The external service system of the global economy is considered to be nature's services or ecosystem services. Service systems can be characterized by the value that results from interaction between service systems, whether the interactions are between people, businesses, or nations. Most service system interactions aspire to be win-win, non-coercive, and non-intrusive. However, some service systems may perform coercive service activities. For example, agents of the state may use coercion in accordance with laws of the land. Karni and Kaner in "An engineering tool for the conceptual design of service systems" first provide a general definition of a system, and then specify the distinctive characteristics of a service system: A system is an organized set of objects which process inputs into outputs that achieve an organizational purpose and meet the need of customers through the use of human, physical, and informatics enablers in a sociological and physical environment (adapted from Nadler 1981; Check land 1981).

It is architectured as a set of nine interlinked classes of objects: (1) *customers* - those benefiting from the system (or otherwise affected by it); (2) *goals* - aims, purposes or central meaning of the system and the organizations; (3) *inputs* - physical, human, financial, or information entities to be processed by the system; (4) *outputs* - physical, informational or human entities after processing by the system; (5) *processes* - transformations for obtaining outputs from inputs; (6) *human enablers* - human resources owning and/or operating the system; (7) *physical enablers* - physical resources which aid in operating the system; (8) *informatic enablers* - information and knowledge resources supporting the system; and (9) *environment* - physical, economic, technological, social, ecological or legal factors influencing the system. A service system is nevertheless distinguished from other types of systems by the fact that the customer may be actively involved in all nine classes: (1) *customer* - as initiator and receiver of the service (e.g., the customer is characterized as looking for novelty, reliability - or both); (2) *goals* - as setting the primary objectives for the design and operation of the service (e.g., the service should an Internet shopper to configure the product variant he wishes to purchase); (3) *input* - as a client upon whom the service is to be performed (e.g., a patient coming for treatment); (4) *output* - as a client upon whom a service has been performed (e.g., the patient after treatment); (5) *process* - as a participant in the process (e.g., an Internet sales transaction incorporates a dialogue facility between a customer and a sales agent); (6) *human enabler* - as a resource in the process (e.g., an Internet sales transaction involves the customer as an independent agent); (7) *physical enabler* - as providing a resource to the process (e.g., an Internet shopper uses his own computer to access the vendor site); (8) *informatic enabler* - as applying his own knowledge to the process (e.g., an Internet shopper uses his own know-how regarding the product to configure the model he wishes to buy); and (9) *environment* - as setting constraints or standards for acceptable service levels (e.g., an Internet shopper demands 24-hour availability of a dialogue facility). Richard Normann in "Reframing Business" introduces the notion of a *value-creating system*. *Prime Movers* are the ones who reconfigure value-creating systems. Since the term service is often defined as value coproduction, a service system might well be called a value-coproduction system. Norman writes about the unbundling and re-bundling of value-creating systems as one of the main trends of our time.

Service specification

Any service can be completely, consistently and clearly specified by means of the following 12 standard attributes

- Service Consumer Benefit(s)
- Service-specific Functional Parameter(s)
- Service Delivery Point
- Service Consumer Count
- Service Readiness Time(s)
- Service Support Time(s)
- Service Support Language(s)
- Service Fulfillment Target
- Maximum Impairment Duration per Incident
- Service Delivering Duration
- Service Delivery Unit
- Service Delivering Price
- The meaning and content of these attributes are

Service Consumer Benefits Describe the (set of) benefits which are callable, receivable and effectively utilizable for any authorized service consumer and which are provided to him as soon as he requests the offered service. The description of these benefits must be phrased in the terms and wording of the intended service consumers.

Service-specific Functional Parameters specify the functional parameters which are essential and unique to the respective service and which describe the most important dimension of the service output, e.g. maximum e-mailbox capacity per registered and authorized e-mail service consumer.

Service Delivery Point describes the physical location and/or logical interface where the benefits of the service are made accessible, callable and receivable to the authorized service consumers. At this point and/or interface, the preparedness for service delivery can be assessed as well as the effective delivery of the service itself can be monitored and controlled.

Service Consumer Count specifies the number of intended, identified, named, registered and authorized service consumers which are allowed and enabled to call and utilize the defined service for executing and/or supporting their business tasks or private activities.

Service Readiness Times specify the distinct agreed times of day when the described service consumer benefits are accessible and callable for the authorized service consumers at the defined service delivery point receivable and utilizable for the authorized service consumers at the respective agreed service level

- all service-relevant processes and resources are operative and effective
- all service-relevant technical systems are up and running and attended by the operating team
- The specified service benefits are comprehensively delivered to any authorized requesting service consumer without any delay or friction.

The time data are specified in 24 h format per local working day and local time, referring to the location of the intended service consumers.

Service Support Times specify the determined and agreed times of day when the usage and consumption of the contracted services is supported by the service desk team for all identified, registered and authorized service consumers within the service customer's organizational unit or area. The service desk is the single point of contact for any service consumer inquiry regarding the contracted and delivered services. During the defined service support times, the service desk can be reached by phone, e-mail, web-based entries and/or fax, respectively. The time data are specified in 24 h format per local working day and local time, referring to the location of the intended service consumers.

Service Support Languages specifies the languages which are spoken by the service desk team(s) to the service consumers calling them.

Service Fulfillment Target specifies the service provider's promise of effective and seamless delivery of the defined benefits to any authorized service consumer requesting the service within the defined service times. It is expressed as the promised minimum ratio of the counts of successful individual service deliveries related to the counts of called individual service deliveries. The effective service fulfillment ratio can be measured and calculated per single service consumer or per consumer group and may be referred to different time periods (workday, calendar-week, work-month, etc.)

Maximum Impairment Duration per Incident specifies the allowable maximum elapsing time between

- the first occurrence of a service impairment, i.e. service quality degradation or service delivery disruption, whilst the service consumer consumes and utilizes the delivered service,
- And the full resumption and complete execution of the service delivery to the content of the affected service consumer.

Service Delivering Duration pacifies the promised and agreed maximum period of time for effectively delivering all specified service consumer benefits to the requesting service consumer at the defined service delivery point

Service Delivery Unit specifies the basic portion for delivering the defined service consumer benefits. The service delivery unit is the reference and mapping object for all cost for service generation and delivery as well as for charging and billing the consumed service volume to the service customer who has ordered the service delivery.

Service Delivering Price specifies the amount of money the service customer has to pay for the consumption of distinct service volumes. Normally, the service delivering price comprises two portions

- a fixed basic price portion for basic efforts and resources which provide accessibility and usability of the service delivery functions, i.e. service access price
- a price portion covering the service consumption based on
    - fixed flat rate price per authorized service consumer and delivery period without regard on the consumed service volumes,
    - staged prices depending on consumed service volumes,
    - fixed price per particularly consumed service delivering unit.

Service delivery The delivery of a service typically involves six factors:

- The accountable service provider and his service suppliers (e.g. the people)
- Equipment used to provide the service (e.g. vehicles, cash registers)
- The physical facilities (e.g. buildings, parking, waiting rooms)

- The requesting service consumer
- Other customers at the service delivery location
- Customer contact

The service encounter is defined as all activities involved in the service delivery process. Some service managers use the term "moment of truth" to indicate that defining point in a specific service encounter where interactions are most intense. Many business theorists view service provision as a performance or act (sometimes humorously referred to as dramaturgy, perhaps in reference to dramaturgy). The location of the service delivery is referred to as the stage and the objects that facilitate the service process are called props. A script is a sequence of behaviors followed by all those involved, including the client(s). Some service dramas are tightly scripted, others are more ad lib. Role congruence occurs when each actor follows a script that harmonizes with the roles played by the other actors. In some service industries, especially health care, dispute resolution, and social services, a popular concept is the idea of the caseload, which refers to the total number of patients, clients, litigants, or claimants that a given employee is presently responsible for. On a daily basis, in all those fields, employees must balance the needs of any individual case against the needs of all other current cases as well as their own personal needs. Under English law, if a service provider is induced to deliver services to a dishonest client by a deception, this is an offence under the Theft Act 1978.

The service-goods continuum

The dichotomy between physical goods and intangible services should not be given too much credence. These are not discrete categories. Most business theorists see a continuum with pure service on one terminal point and pure commodity good on the other terminal point. Most products fall between these two extremes. For example, a restaurant provides a physical good (the food), but also provides services in the form of ambience, the setting and clearing of the table, etc. And although some utilities actually deliver physical goods — like water utilities which actually deliver water — utilities are usually treated as services. In a narrower sense, service refers to quality of customer service: the measured appropriateness of assistance and support provided to a customer. This particular usage occurs frequently in retailing.

List of economic services

In 2005, USA was the largest producer of services followed by Japan and Germany, reports the International Monetary Fund. 50% of the U.S. Economy consists of services compared to 20% in 1947.

The following is an exhaustive list of service industries, grouped into rough sectors. Parenthetical notations indicate how specific occupations and organizations can be regarded as service industries to the extent they provide an intangible service, as opposed to a tangible good.

- business functions (that apply to all organizations in general)
  - consulting
  - customer service
  - human resources administrators (providing services like ensuring that employees are paid accurately)
- child care
- cleaning, repair and maintenance services
  - janitors (who provide cleaning services)
  - gardeners
  - mechanics
- construction
  - carpentry
  - electricians (offering the service of making wiring work properly)
  - plumbing

- death care
  - coroners (who provide the service of identifying corpses and determining time and cause of death)
  - funeral homes (who prepare corpses for public display, cremation or burial)
- dispute resolution and prevention services
  - arbitration
  - courts of law (who perform the service of dispute resolution backed by the power of the state)
  - diplomacy
  - incarceration (provides the service of keeping criminals out of society)
  - law enforcement (provides the service of identifying and apprehending criminals)
  - lawyers (who perform the services of advocacy and decision making in many dispute resolution and prevention processes)
  - mediation
  - military (performs the service of protecting states in disputes with other states)
  - negotiation (not really a service unless someone is negotiating on behalf of another)
- education (institutions offering the services of teaching and access to information)
  - library
  - museum
  - school
- entertainment (when provided live or within a highly specialized facility)
  - gambling
  - movie theatres (providing the service of showing a movie on a big screen)
  - performing arts productions
  - sports
  - television
- fabric care
  - dry cleaning
  - Laundromat (offering the service of automated fabric cleaning)
- financial services
  - accounting
  - banks and building societies (offering lending services and safekeeping of money and valuables)
  - real estate
  - stock brokerages
  - tax return preparation
- foodservice industry
- hairdressing
- health care (all health care professions provide services)
- hospitality industry
- information services
  - data processing
  - database services
  - language interpretation
  - language translation
- risk management
  - insurance
  - security
- social services
  - social work
- transport

- utilities
  - electric power
  - natural gas
  - telecommunications
  - waste management
  - water industry

REFERENCES

1. Articles published in the leading newspapers like The Hindu, The Economic Times Financial Express, and Business line.
2. www.wikipedia.org
3. David Friedman, New America Foundation (2002-06-16).
4. Sir Keith Joseph, Center for Policy Studies (1976-04-05).Stockton Lecture, *Monetarism Is Not Enough*
5. Services Sector in the Indian Economy : Macro Dynamics—Sectoral Dynamics—Policy Issues/edited by P. Jegadish Gandhi and P. Ganesan.
6. India's Economic Transition : The Politics of Reforms/edited by Rahul Mukherji.
7. Indian Microfinance: The Challenges of Rapid Growth/PrabhuGhate
8. Services sector in India: recent policy initiatives by A. Vijayakumar
9. Service sector in Indian economy by TalluruSreenivas
10. Consumer rights in service sector Vallanadu Narayanan Viswanathan
11. Studies in Indian economy Ed. K.R. Gupta
12. Outsourcing to India: the offshore advantage by Mark Kobayashi-Hillary
13. Service Sector In India by M.S.Singh
14. Tourism in India and India's economic development by Kartik Chandra Roy, Clement Allan Tisdell
15. India at the crossroads: sustaining growth and reducing poverty by Tim Callen, Patricia Reynolds, Christopher Towe

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REVIEW ARTICLE

Medical Negligence in Oral Surgery- A Review

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ABSTRACT

The doctor/dentist/oral surgeon and patient relationship has been transformed over the last several decades. Health professionals are increasingly viewed as providers of service for consideration at the time of health crisis or when there is a disease. In current day health practice, any single error or malpractice is punishable by law, and the current day jurisdiction is very straightforward pertaining to any medical error or blunder, thus resulting in severe repercussions to the health care provider. And as oral surgeons/dentist are also subjected to procedures which can lead to serious complications and can result in medical malpractice, thus it is important to know about ethical practice and should be aware about these laws against medical malpractice. In various studies conducted to assess the level of awareness among medical and dental professionals it was found that Dentists are often ignorant about the laws governing their profession. Thus it is imperative for health professionals today to be aware of such laws, which will be beneficial to patients and doctors and society as a whole. The aim of this review was to investigate all the medical negligence and errors related to oral surgery practice, and to analyze the different causes of litigation. Inclusion criteria involved all the closed cases that proved malpractice against an oral and maxillofacial surgeon or involved a dentist who performed an oral and maxillofacial surgical procedure.

The most common reason behind medical negligence is lack of proper communication between the patient and the doctor, failure to take proper medical history, poor records based system, and improper informed consent. In the current day scenario, medical error or negligence has posed a huge threat to doctors and surgeons all across the globe and has resulted in several medico-legal cases. The purpose of the review is to evaluate medical malpractice involving various oral surgical procedures performed in oral surgery and primary emphasis is on informed consent and lack of proper medications.Overall the purpose of this article is to educate dental practitioners and oral surgeons about the types of treatment which may result in a greater incidence of legal claims and malpractice, so better awareness and proper training is must among health care professions so that they will be better prepared to avoid these medical mishaps during practice. This article provides general information to a dentist regarding how to go about with safer practice and minimize lawsuits.

Keywords: Medical Negligence, Oral Surgery, Medical Error, Lawsuit, Dental Malpractice, Surgical Error.

Mesh Terms: Errors, Medical Mistake, Medical Practice Management, Medical Legislation, Medical Ethics.

INTRODUCTION

Health profession has long been considered as the noble profession since the beginning of medicine and doctors have been considered as god's apprentice in serving humanity (Ramsey, 2002). The sole purpose of a doctor/dentist is to reduce a patient's pain and distress and provide them a healthy life. For such a noble profession comes with greater responsibilities in the medical and dental professions, the impact of health professionals is improving the standards of health and well-being in society.In recent times doctor-patient relationship has changed drastically, it's no more unanimous belief in what the doctor says and following all the instructions as it is, with the advancement in technology today almost every patient has access to the internet and the knowledge acquired from internet is more dangerous and in today's fast moving world (Gigerenzer et al., 2007), everybody wants quick fixes, with so much high expectations and lack of trust and patience has led to poor quality of practice, in spite of newer technology and advancement in medicine, the law related to the medical malpractice and errors remains the same. And every practitioner must be well aware of these ethical principles and laws, and must have a systematic and ethical practice. There are several ethical guidelines related to medical and dental practice, and every doctor and dentist should be well aware of these ethical principles related to the field.

In the 4th century BC, Hippocrates, a physician-philosopher, directed physicians "to help and do no harm". Similarly, respect for persons and for justice to mankind has been present in the development of societies from the earliest times (Cassell, 2000). However, specifically in regard to ethical decisions in medicine, in 1979 Tom Beauchamp and James Childress published the first edition of Principles of Biomedical Ethics, popularizing the use of principlism in efforts to resolve ethical issues in clinical medicine (Laura Weiss Roberts and Reicherter, 2014) (Rauprich and Vollmann, 2011). Thus, in both clinical medicine and in scientific research it is generally held that these principles can be applied, even in unique circumstances, to provide guidance in discovering our moral duties within that situation. Medical ethics is a system of moral principles that apply values to the practice of clinical medicine and in scientific research. Medical ethics is based on a set of values that professionals can refer to in the case of any confusion or conflict. Ideally, for a medical practice to be considered "ethical", it must respect all four of these principles: autonomy, justice, beneficence, and non-maleficence (Institute of Medicine, Board on Health Sciences Policy and Committee on Conflict of Interest in Medical Research, Education, and Practice, 2009). The ethical principles are as follows,

Autonomy

Any notion of moral decision-making must involve the person who has to make the voluntary decisions. In health care decisions, our respect for the autonomy of the patient is of primary importance without controlling or influencing them in any way so that they can make rational decisions for themselves (McLeod and Sherwin, 2000). This principle is the basis for the practice of "informed consent" in the physician/patient transaction regarding health care. Requires that the patient have autonomy of thought, intention, and action when making decisions regarding health care procedures. Therefore, the decision-making process must be free of coercion or coaxing. In order for a patient to make a fully informed decision, she/he must understand all risks and benefits of the procedure and the likelihood of success (Epstein and Street, 2011).

Justice

The idea that the burdens and benefits of new or experimental treatments must be distributed equally among all groups in society. Justice in health care is usually defined as a form of fairness, or as Aristotle once said, "Giving to each that which is his due." This implies the fair distribution of goods in society and requires that we look at the role of entitlement (Powers et al., 2006). Requires that procedures uphold the spirit of existing laws and are fair to all players involved. The health care provider must consider four main areas when evaluating justice: fair distribution of scarce resources, competing needs, rights and obligations, and potential conflicts with established legislation (Connolly and Ward, 2008).

Beneficence

The ordinary meaning of this principle is that health care providers have a duty to be of a benefit to the patient, as well as to take positive steps to prevent and to remove harm from the patient. These duties are viewed as rational and self-evident and are widely accepted as the proper goals of medicine, it requires that the procedure be provided with the intent of doing good for the patient involved (Beauvais, Richter and Kim, 2019). It demands that health care providers develop and maintain skills and knowledge, continually update training, consider individual circumstances of all patients, and strive for net benefit.

Non-maleficence

The principle of no maleficence states that the health care provider must not intentionally create harm or injury to the patient, either through acts of commission or omission. Requires that a procedure does not harm the patient involved or others in society (Giardina et al., 2020). Few specialists who are new into practice operate under the assumption that they are doing no harm or at least minimizing harm by pursuing the greater good. Negligence can be defined as an act recklessly done by a person resulting in foreseeable damages to the other. Medical Negligence basically is the misconduct by a medical practitioner or doctor by not providing enough care resulting in breach of their duties and causing harm to their patients (Babatunde, 2018).Though the saying says “to err is human”, but in medicine or dental practice where patients consider and look upon the health care providers as god and expect to get cure for their illness, so it's important to provide treatment with no room for errors, as we as health care providers are dealing with life, and any mishap and misconduct can cost immensely.

There are various types of negligence,

1. Doctors negligence
a) Civil negligence
b) Criminal negligence
2. Patient negligence
3. Contributory negligence
4. Composite negligence
5. Corporate negligence (Kelley and Wendt, 2001)

Pertaining to the field of medicine we must emphasize more on civil negligence and criminal negligence, as any mistake on the physicians part, than the patient has all the rights to file a complaint against the physician which can either result in imprisonment and fine or both, The Supreme Court of India has enlisted that the essential component of negligence are 'duty', 'breach', and 'damage', and as a dental practitioner the physician must implement these components into their practice and make sure no breach in practice is conducted so that no law pursuits can be charged against their professional practice(American Dental Association, 2005).This review is done to create more awareness among the medical and the dental practitioners so that any kind of medical negligence can be avoided and prevented in their professional practice.

DISCUSSION

Doctors and surgeons were considered to be god like people few decades ago,[(2)] but in recent days there has been a huge paradigm of shift between the doctor and patient relationship and there are various reasons behind that, one of which is medical negligence and error in one's own practice. Medical negligence is a combination of two words. The second word solely describes the meaning, though the meaning of negligence has not been described in a proper way but it is an act recklessly done by a person resulting in foreseeable damages to the other. Negligence is an offense under tort, IPC, Indian Contracts Act, Consumer Protection Act and many more. Medical Negligence basically is basically misconduct by health care workers towards patients. Medical negligence has caused many deaths as well as adverse results to the patient's health, and thus bringing down the medical practice and increasing several lawsuits. A patient generally approaches a doctor/hospital supported his/its reputation. Expectations of a patient are two-fold: doctors and hospitals are expected to supply medical treatment with all the knowledge and skill. Though a doctor might not be during a position to save lots of his patient's life in the least times, he's expected to use his special knowledge and skill within the most appropriate manner keeping in mind the interest of the patient who has entrusted his life to him.

The primary step to avoid any negligence or error starts off with taking an proper informed consent, a detailed medical history which included any pre-disposing or underlying medical conditions any previous surgeries and any medications or drug allergies so as to rule out any complications or errors while doing any further intervention. Failure of a doctor and hospital to discharge this obligation is actually a tortious liability. A tort is a civil wrong as against a contractual obligation a breach that attracts judicial intervention by way of awarding damages. Thus, a patient's right to receive medical attention from doctors and hospitals is actually a civil rights. The relationship takes the form of a contract to some extent due to consent, payment of fee, and performance of surgery/providing treatment, etc. while retaining essential elements of tort. The doctor-patient relationship relies on mutual trust and conviction[3].

Medical profession is not based on any mathematical calculation or any business strategy but it's a service oriented life-saving job which earns the highest respect among any other professions. The profession of dentistry imparts knowledge and skill that is used for the service of the people. A dental professional has a responsibility toward individual patients and society[4]. This special status that society confers on the dental healthcare professionals requires them to behave in an ethical manner. This responsibility must be at the core of the dental professional's ethical behavior[5]. However, with an increase in commercialization in all spheres of life, this profession has come under public scrutiny. Earlier the role and service provided by the medical and dental professionals was considered noble and charitable. However, today with an increase in medical negligence and malpractices, this profession is looked upon with doubt and contempt[6]. A dental professional may be charged for negligence, if he or she fails to provide the required information to the patient before obtaining proper consent for a particular interventional treatment[7]. Will be subjected to medical lawsuit. Procedures that a maxillofacial surgeon performs are mainly, extractions, impactions, fracture in the head and neck region, pathologies, head and neck oncology, RTA's, cosmetology, and reconstruction procedure, all these procedures are not something that must be treated lightly, one

must have a thorough knowledge and skills to avoid and prevent any medical error in medical practice. The Consumer Protection Act (CPA) may be a comprehensive piece of legislation implemented in 1986 in India, which aims to supply a forum to safeguard the rights of the purchasers and establishes guidelines for the speedy redress of their grievances against unethical medical practices [8]. All services rendered to a patient by a medical or dental practitioner is covered under the CPA, except when the service is provided free of cost, especially in charitable or governmental dispensaries and hospitals and primary health centers [9]. Therefore, it becomes imperative for all healthcare professionals (including dentists) to be aware of such laws, which are valuable for patients, healthcare professionals, and the entire community as a whole.

Author	Research Title	Year	Inference
Layton et al	Informed consent in oral and maxillofacial surgery: a study of the value of written warnings	1994	Written information significantly improves patients recall and recognition of important warnings and dyesthesia of tongue is p<0.001
Hillary Rodham clinton	Making patients safety the centerpiece of medical liability reform	2006	To improve both patient safety and medical liability climate, the tort system must achieve four goals reduce rates of preventable patient injuries; promote open communication between physicians and patients.
Lucian l. leape	Institute of medicine medical error figures are not exaggerated	2000	Errors and excess mortality can be eliminated but only if concern attention is shifted away from individuals
Peter f svider	Craniofacial surgery andadverse outcomes	2015	Of the 88 cases included, 62.5% were decided in the physicians favor, 9.1% were resolved with an out of court settlement, and 28.4% ended in jury awarding damages for malpractice.
Atula.gawande	Risk factors for retained instruments and sponges after surgery	2003	Patients with retained foreign bodies were more likely than controls to have had emergency surgery with an p <0.001

The first MPS (medical practice study) did, in fact, have significant limitations and important methodological weakness. It was not designed primarily to study risk factors for injury, for example, but to assess the extent of injury that could lead to malpractice litigation, hence the exclusion of nondisabling injuries and the focus on negligence [10]. Another serious weakness of the MPS is that it relied on implicit judgments by physicians. While extensive efforts were made to strengthen the accuracy and reproducibility of these judgements through training of physicians' reviewers, use of a highly structured data collection instrument, and duplicate review with review and resolution of disagreements, errors undoubtedly occurred. It is possible that these errors "can celed out" i.e., over interpretation of medical error. The most common cases of medical malpractice include leaving a gauze or instrument at the site of operation following surgery, causing trauma to body parts unrelated to the treatment site, performing on the wrong part of the body, inserting a fixation screw for a metal plate into the root of a tooth during facial bone fracture surgery, and causing severe malocclusion by neglecting normal occlusion during fixation of a reduced facial bone fracture [11].

Complications refer to unexpected events that may occur even after adequate treatment, such as postoperative neurologic injury, infection, hemorrhage, hematoma, and drug-related side effects. Complications can be resolved without any serious problems if the cause is detected early and adequate treatment provided. In this case, it is rare for the medical staff to take legal responsibilities [12]. However, in cases of malpractice, civil and criminal penalties are unavoidable if negligence of the medical staff is evident and results in a fatal outcome. Ozdemir et al. have investigated 1,548 malpractice cases that occurred in Turkey between 1991 and 2000. Of these, 14 cases (0.9%) were

related to surgical, prosthetic, and endodontic dental treatment[13]. The main causes of malpractice were negligence and inadequate treatment. It has been further suggested that standardized diagnostic and therapeutic protocols that both, meet ethical principles and comply with legal rules, are critical for minimizing the incidence of malpractice3. Graskemper4 have reported that malpractice could be significantly reduced by risk management, which facilitates a close cooperation among medical staff, ensures that patients receive a thorough explanation of the treatment process, and helps to minimize negligence during treatment[14]. Proper diagnosis, treatment planning, surgical techniques, and detailed patient information are crucial for minimizing treatment related claims. Moreover, it has been highly recommended that referrals be made to relevant specialists for high-risk treatments. Healthcare professionals are required to faithfully fulfill the duty of care and provide prior explanation, help medical staff and patients maintain close relationships, and promptly deal with any problems that may arise. In the oral and maxillofacial surgical field, various unexpected complications and side effects often occur, and malpractice is a very likely occurrence if careless treatment is performed[15]. All oral and maxillofacial surgeons should take great interest in studying and dealing actively with complications and medical problems. It is documented that a doctor owes a requirement of care to his patient. This duty can either be a contractual duty or a requirement arising out of tort law. In some cases, however, though a doctor-patient relationship isn't established, the courts have imposed a requirement upon the doctor. In the words of the Supreme Court "every doctor, at the governmental hospital or elsewhere, features a professional obligation to increase his services with due expertise for shielding life" (Parmanand Kataria vs. Union of India)[16]. These cases are however, clearly restricted to situations where there is danger to the life of the person. Impliedly, therefore, in other circumstances the doctor doesn't owe a requirement.

Reasonable degree of care and skill means the degree of care and competence that an "ordinary competent member of the profession who professes to possess those skills would exercise within the circumstance in question." At this stage, it's going to be necessary to notice the excellence between the quality of care and therefore the degree of care. The standard of care is a constant and remains the same in all cases. It is the need that the conduct of the doctor is reasonable and wishes not necessarily conform to the very best degree of care or rock bottom degree of care possible. The degree of care may be a variable and depends on the circumstance. It is used to refer to what actually amounts to reasonableness in a given situation [17-19]. Thus, though an equivalent standard of care is predicted from a generalist and a specialist, the degree of care would vary. In other words, both are expected to require due care but what amounts to due care with reference to the specialist differs from what amount of due care is standard for the generalist. In fact, the law expects the specialist to exercise the standard skill of this speciality and not of any ordinary doctor. Though the courts have accepted the necessity to impose a better degree of duty on a specialist, they need refused to lower it within the case of a novice.

It's the duty of the medical professional to avoid and not cause any medical error, from the time of Lord Denning until now it has been held in several judgments that a charge of professional negligence against the medical professional stood on a special footing from a charge of negligence against the driving force of a motor car. What causes all these medical negligence, Failure of an operation and side effects are not negligence. The term negligence is defined because the absence or lack of care that an inexpensive person should have taken within the circumstances of the case. One such scenario where. In the allegation of negligence during a case of wrist drop, the subsequent observations were made. Nothing has been mentioned in the complaint or in the grounds of appeal about the type of care desired from the doctor in whom he failed. It is not said anywhere what sort of negligence was done during the course of the operation. Nerves could also be hampered at the time of operation and mere cutting of a nerve doesn't amount to negligence. It is not said that it has been deliberately done. To the contrary it is also not said that the nerves were cut in the operation and it was not cut at the time of the accident. No expert evidence whatsoever has been produced.

"Allegation of medical negligence may be a serious issue and it's for the one that sets up the case to prove negligence supported material on record or by way of evidence". The complaint of medical negligence was dismissed because the applicant failed to establish and prove any instance of medical negligence[20]. "Merely because the operation did

not succeed, the doctor cannot be said to be negligent" and the appeal of the doctor was allowed[21]. "A mere allegation will not make a case of negligence unless it is proved by reliable evidence and is supported by expert evidence" and the appeal was dismissed[22]. "The commission cannot constitute itself into an expert body and contradict the statement of the doctor unless there is something contrary on the record by way of an expert opinion or there's any medical treatise on which reliance might be based" and therefore the Revision petition of the doctor was allowed[23].

CONCLUSIONS

Finally many articles were taken as reference for this review, the purpose of the review is medical negligence has been a serious problem in today's generation, a lot of practitioners have been loosing there practice license due to these errors, so to avoid these malpractice and errors in practice one must be highly skillful and to increase one's skills it comes with years of practice and to reduce the errors an informed consent prior starting any procedure is highly mandatory and recording of cases followed by thorough and complete medical examination and history taking should be a must in clinical practices. Just because you are happy with your treatment or results does not mean the doctor is liable for medical practice. "To err is human- building a safer and solid health system is the need of the hour".

REFERENCES

1. Singh G, Gambhir RS, Singh S, Talwar PS, Munjal V. Knowledge and awareness of the Consumer Protection Act among dental professionals in India: A systematic review. Indian J Dent 2014;5:146-51
2. Haripriya A, Haripriya V. Knowledge about Medical Law and its Negligence among Doctors: A Cross-Sectional Study. Int J Sci Res Publ 2014;4:1-3.
3. Kennedy I, Grubb A. Medical law: text and materials, London: Buttcrworths, 1988: I71 180.
4. Rolam v. Board of Governors of Friern General IIospital (1957). 2 All ER 118. I WLR 582.
5. Canterbury v. Spence. (1972). 464 F 2d 772 U.S. Court of.+pcdk.
6. Kim YK, Lee YJ, Yun PY, Choi YH, Kim SG. Complication Q & A in dentistry. Seoul: DaehanNarae Publishing; 2015. pp. 1–17
7. Kim YK. Complications and medicolegal problems. J Korean Assoc Oral Maxillofac Surg. 2014;40:259
8. Ozdemir MH, Saracoglu A, Ozdemir AU, Ergonen AT. Dental malpractice cases in Turkey during 1991-2000. J Clin Forensic Med. 2005;12:137–142.
9. Smt. Savitri Singh v. Dr. Ranbir PD. Singh and others. 2004;(1) CPJ 25
10. Dr. Kamta Prasad Singh v. Nagina Prasad. 2000;(III) CPJ 283
11. Ajay Kumar v. Dr. DevendraNath. 2004;(II) CPJ 482.
12. Dr. Akhil Kumar Jain v. Lallan Prasad. 2004;(II) CPJ 504.
13. Amar Singh v. Frances Newton Hospital and Anr. 2001;(I) CPJ 8.
14. Sardool Singh v. Muni Lal Chopra and another. 1999;(I) CPJ 64 (Punjab
15. Dr. Manjit Singh Sandhu v. Uday Kant Thakur and others. 2002;(III) CPJ 242.
16. Director, Rajiv Gandhi Cancer Institute and Research Centre and Ors. 2003;(I) CPJ 305 (Delhi)
17. Marble City Hospital and Research Centre and Ors. v. V.R. Soni. 2004;(II) CPJ 102 (MP)
18. Surinder Kumar (Laddi) and anr. V. Dr. Santosh Menon and Ors. 2000;(III) CPJ 517.
19. Rajinder Singh v. Batra Hospital and Medical Research Centre and Anr. 2000;(III) CPJ 558.
20. Mam Chand v. Dr. GS Mangat of Mangat Hospital. 2004;(I) CPJ 79 (NC)
21. Dr. (Smt) Kumud Garg v. Raja Bhatia. 2004;(I) CPJ 369.
22. Smt. Vimlesh Dixit v. Dr. R.K. Singhal. 2004;(I) CPJ 123 (Uttaranchal)
23. AIR 1989 SC 2039.
24. Dr. Harkanwaljit Singh Saini v. Gurbax Singh and Anr. 2003;(I) CPJ 153 (NC)

25. Kumari M, Kumar G,. Reddy LVK, Sinha P. Negligence in Medical and Dental Professionals: A Review. Int J Oral Health Med Res 2017;4(1):86-90.
26. American Dental Association (2005) Practice Options for the New Dentist. American Dental Association.
27. Babatunde, R. A. (2018) 'BREACH OF DUTY OF CARE IN MEDICAL NEGLIGENCE: SCOPE AND LIMITATION'. Available at: http://www.academia.edu/download/58000235/BREACH_OF_DUTY_OF_CARE.pdf
28. Beauvais, B., Richter, J. P. and Kim, F. S. (2019) 'Doing well by doing good', Health Care Management Review, pp. 2–9. doi: 10.1097/hmr.0000000000000163.
29. Cassell, E. J. (2000) 'The Principles of the Belmont Report Revisited: How Have Respect for Persons, Beneficence, and Justice Been Applied to Clinical Medicine?', The Hastings Center Report, p. 12. doi: 10.2307/3527640.
30. Connolly, M. and Ward, T. (2008) Morals, Rights and Practice in the Human Services: Effective and Fair Decision-making in Health, Social Care and Criminal Justice. Jessica Kingsley Publishers.
31. Epstein, R. M. and Street, R. L. (2011) 'Shared Mind: Communication, Decision Making, and Autonomy in Serious Illness', Annals of family medicine. The Annals of Family Medicine, 9(5), pp. 454–461.
32. Giardina, T. D. et al. (2020) 'Health Care Provider Factors Associated with Patient-Reported Adverse Events and Harm', The Joint Commission Journal on Quality and Patient Safety, pp. 282–290. doi: 10.1016/j.jcjq.2020.02.004.
33. Gigerenzer, G. et al. (2007) 'Helping doctors and patients make sense of health statistics', Psychological science in the public interest: a journal of the American Psychological Society. SAGE Publications Sage CA: Los Angeles, CA, 8(2), pp. 53–96.
34. Institute of Medicine, Board on Health Sciences Policy and Committee on Conflict of Interest in Medical Research, Education, and Practice (2009) Conflict of Interest in Medical Research, Education, and Practice. National Academies Press.
35. Kelley, P. J. and Wendt, L. A. (2001) 'What judges tell juries about negligence: A review of pattern jury instructions', Chi. -Kent L. Rev. HeinOnline, 77, p. 587.
36. Laura Weiss Roberts and Reicherter, D. (2014) Professionalism and Ethics in Medicine: A Study Guide for Physicians and Physicians-in-Training. Springer.
37. McLeod, C. and Sherwin, S. (2000) 'Relational autonomy, self-trust, and health care for patients who are oppressed'. Available at: https://ir.lib.uwo.ca/cgi/viewcontent.cgi?article=1348&context=philosophy epub.
38. Powers, M. et al. (2006) Social Justice: The Moral Foundations of Public Health and Health Policy. Oxford University Press.
39. Ramsey, M. (2002) Professional and Popular Medicine in France 1770-1830: The Social World of Medical Practice.Cambridge University Press.
40. Rauprich, O. and Vollmann, J. (2011) '30 Years Principles of biomedical ethics: introduction to a symposium on the 6th edition of Tom L Beauchamp and James F Childress' seminal work', Journal of Medical Ethics, pp. 582–583. doi: 10.1136/jme.2010.039222rep.

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RESEARCH ARTICLE

Association of Obesity with Postoperative Cardiac Surgery Complications

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ABSTRACT

Excessive body weight has become a major problem in industrialized and developed countries. Obesity is a risk factor of adverse postoperative outcomes after cardiac surgery in patients having cardiovascular disease.The objective of this study wasto compare the postoperative outcomes in different categories of BMI in patients undergoing cardiac surgery. In this single-center study, a total of 130 patients having age between 50-70 years planned for coronary artery bypass grafting were included in this study. Abrief history regarding heart disease, cardiac surgery (CABG), post-operative outcomes, duration, and clinical laboratory findings was recorded on a structured questionnaire.Post-operative complications in patients having different body mass index (BMI) were compared using the Chi-square test. There were 57 (43.85%) patients who were having normal body mass index (BMI), 43 (33.08%) patients were having overweight and only 30 (23.08%) patients were obese. Cardiovascular complications were found in 1 (1.8%) normal weight patients, in 4 (9.3%) overweight patients and in 9 (30.0%) obese patients (p-value <0.001). Infectious complications were found in 5 (11.6%) overweight patients and in 8 (26.7%) obese patients (p-value 0.015). Bleeding complications were found in 7 (23.3%) obese patients (p-value 0.002) and Acute renal failure (ARF) was diagnosed in 6 (20.0%) obese patients (p-value 0.04). Obesity association was found with a considerable increase in the frequency of postoperative complications in terms of cardiovascular and bleeding complications.

Keywords: Body mass index, Coronary artery bypass grafting, Obesity, Postoperative complications.

INTRODUCTION

It is widely known that cardiovascular disease (heart disease and stroke) is the most frequent cause of death, where it causes a staggering 44% of all deaths. This sobering statistic is coupled with the fact that medical advances have been responsible for large reductions in cardiovascular mortality in Japan and the USA[1]. Thus, despite a marked

improvement in treatment, cardiovascular events continue to kill more people than any other cause. The reason for this apparent paradox is not known but might stem from the fact that the bulk of our therapies target symptomatic coronary and cerebrovascular disease, which occurs late in the disease process [2].Almost 50% of sudden cardiac death still occurs in people with no documented previous history of overt cardiac disease [3]. The morbidity and mortality associated with being overweight or obese have been known to the medical profession for more than 2000 years [4]. Excessive body weight has become a major problem in industrialized and developed countries, where it has reached the proportion of an epidemic [5]. Individuals from disadvantaged communities are also not exempted and are at substantial risk of obesity and its complications [7]. Several large epidemiologic studies have proved that mortality increases with obesity [6]. Obese individuals are prone to many cardiovascular risk factorsT2DM is strongly associated with overweight and obesity [11-12]. Increased body weight is a major risk factor for the metabolic syndrome which itself is a cluster of coronary heart disease risk factors [13-17]. This study provides data about the influence of BMI on postoperative complications in patients undergoing heart surgery. Slightly more than half of the patients (50.5%) had no postoperative complications. Post-operative cardiovascular complications were present in 32.1% normal BMI patients, 46.2% in overweight, and 21.8% in obese which shows that overweight patients have an increased risk of cardiovascular complications. 28.4% In normal weighted patients have infectious complications, 48.7% in overweight, and 23% in obese patients. Post-operative bleeding among normal-weight patients 32.4%, 43.2% overweight, and 24.3 obese. 31.5% of patients had acute kidney failure, 47.8% in overweight, and 20.7% obese after heart surgery [18]. Till date several studies have been conductedto observe the effect of BMI in CVD as a risk factor in preoperative patients but very few studies have been carried out to check the effect of BMI on postoperative cardiac surgeries especially in the Pakistani population.

METHODOLOGY

Thisnonprobability consecutive sampling, case series study was conducted between 14-Nov-2018 to 13-May-2019.After obtaining ethicalapproval of the study from the College of Physicians and Surgeons of Pakistan, written informed consent was obtained from all the patients subject qualifying inclusion criteria, presenting at the Department of Cardiac Surgery, Tabba Heart Institute, Karachi. Demographic details of the patient brief history regarding heart disease, cardiac surgery (CABG), post-operative outcomes, duration, and labs (ECG, CBC, urine D/R, C/S, electrolytes, urea creatinine, x-ray, and ultrasound chest) were recorded on a structured questionnaire.While patients undergoing other surgical modalities such as excision of atrial myxoma and Bentall - De Bono surgery or Chronic renal failure patient on peritoneal dialysis or Deranged LFTs (ALT>40IU, AST>40IU) or Patients with hypothyroidism (TSH>5IU) or Patient with deranged coagulation profile [Prothrombin time more than 10.5 and INR more than 1.0] were excluded from the study. Frequency and percentages were calculated for qualitative variables like gender, diabetes mellitus, hypertension, smoking, BMI categories (normal/overweight/obesity), and outcomes Postoperative complications (cardiovascular, infectious, bleeding, and ARF). A chi-square test was used to observe the difference.

RESULTS

A total number of 130 patients planned for coronary artery bypass grafting were included in this study. The mean age of patients was 59.51$\pm$5.17 years. The mean body mass index (BMI) of patients was 26.42$\pm$4.59 Kg/m^2. There were more male patients as compared to the fem female patients 95 (73.08%) male patients and only 35 (29.62%) female patients in this study.

DISCUSSION

Many studies have concluded that obesity is associated with more favorable outcomes in terms of mortality (short-term and long-term) after cardiac surgery, despite its association with higher cardiovascular risk factors and the risk of death in the normal population. The reason for this may be that excessive adipose tissues may confer advantage at times of stress and illness [126-127]. So the improved outcomes in obese patients may be due to high metabolic reserves and body fat which is absent in patients with low BMIs [128-129]. In the present study, cardiovascular complications were found in 1.8% of patients having a normal weight, in 9.3% overweight patients, and in 30.0% obese patients (p-value <0.001). Infectious complications were found in 5.3% normal-weight patients, in 11.6% overweight patients and in 26.7% obese patients (p-value 0.015). Bleeding complications were found in 1 (1.8%) normal weight, 7.0% overweight and in 23.3% obese patients (p-value 0.002). Acute renal failure (ARF) was diagnosed in 3.5%) normal-weight patients, in 11.6% overweight patients and in 20.0% obese patients (p-value 0.04). Terada et al. found infectious complications in 7.9% normal-weight patients, in 8.6% normal-weight patients, and 10.2% obese patients. While the authors found renal complications in 7.1% normal-weight patients, 6.1% overweight patients, and 5.6% obese patients [130]. Devarajan et al. found infectious complications in 6.2% normal-weight patients, in 4.8% overweight patients, and 5.6% obese patients [131]. Hussain et al. found renal complications in 1.4% normal-weight patients, 1.1% overweight patients, and 1.0% obese patients [132].

Another study by Sood et al. found cardiovascular complications in 1.5% normal-weight patients, 1.3% overweight patients, and 1.10% obese patients. While they found infectious complications in 4.10% normal-weight patients, 3.20% overweight patients, and in 3.2% obese patients. Renal failure was found in 1.6% normal-weight patients, 1.10% overweight and in 1.0% obese patients [133]. The task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) in their published '2014 ESC/ EACTS Guidelines on myocardial revascularization' point out that BMI (35 kg/m^2) was an independent predictor of death and MI during a 5-year follow-up of patients who underwent CABG operations [140]. Postoperative permanent lifestyle changes including regular physical activity and a healthy diet are two current guideline recommendations. In previous guidelines, the Task Force recommended more specific long-term lifestyle and risk factor management after myocardial revascularization including diet and weight control. The authors recommend that BMI and/or waist circumference be assessed at each follow-up visit with the goal of a 10% reduction from baseline BMI. Given that, in this investigation, a BMI >30 kg/m^2 was associated with increased pulmonary morbidity after CABG operations, and the ESC/EACTS guidelines above, it is reasonable to ask patients with above-normal BMIs undergoing elective CABG operations to aim to achieve a preoperative BMI of 25–30 kg/m^2[140].

CONCLUSION

Obesity association was found with a considerable increase in the frequency of postoperative complications in terms of cardiovascular and bleeding complications. Prevention of these complications in obese patients following CABG operations can lead to an improved postoperative course and overall outcome.

REFERENCES

1. World Health Organization Program Fact Sheet #310: 2004 Death Rates. WHO international web site 2008 October. Available at: URL: http://www.who.int/mediacentre/factsheets/fs310/en/index.html
2. Kannel WB. Silent myocardial ischemia and infarction: Insights from the Framingham study. CardiolClin. 1986;4(4):583-91.
3. Corrado D, Basso C, Thiene G. Sudden cardiac death in young people with apparently normal heart Cardiovasc Res. 2001;50(2):399-408.

4. Bray GA. Historical frame work for the development of ideasabout obesity. In: Handbook of obesity, Bray, GA, BouchardC, James WPT (eds). New York: Marcel Dekker, Inc; 1997.
5. World Health Organization. Food and health in Europe: a new basis for action. WHO; regional publication European series, No. 96. Compehagen: WHO; 2004.
6. Grundy SM, Banett JP. Metabolic and health complications of obesity. Dis Mon 1990;36(4):641–731.
7. Haslam DW, James WP. Obesity. Lancet 2005;366:1197–209.
8. Freedman DM, Ron E, Ballard-Barbash R, Doody MM, Linet MS. Body mass index and all-cause mortality in a nationwide US cohort. Int J Obes (Lond). 2006;30:822–9.
9. Price GM, Uauy R, Breeze E, Bulpitt CJ, Fletcher AE. Weight, shape and mortality risk in older persons: elevated waist hip ratio, not high body mass index, is associated with greater risk of death. Am J ClinNutr 2006;84:449–60.
10. Pischon T, Boeing H, Hoffmann K, Bergmann M, Schulze MB, Overvad K, et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med 2008;359:2105–20.
11. Golditz GA, Willet WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med 1995;122:481–6.
12. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factor forclinical diabetes in men. Diabetes care 1994;17:961–9.
13. Hanson RL, Imperatore G, Bennett PH, Knowler WC. Components of the "metabolic syndrome" and incidence of type 2 diabetes. Diabetes 2002;51:3120–7
14. Chen Z, Yang G, Offer A, Zhou M, Smith M, Peto R, Ge H, Yang L, Whitlock G. Body mass index and mortality in China: a 15-year prospective study of 220 000 men. Int J Epidemiol. 2012;41(2):472-81
15. Yi SW, Ohrr H, Shin SA, Yi JJ. Sex-age-specific association of body mass index with all-cause mortality among 12.8 million Korean adults: a prospective cohort study.Int J Epidemiol. 2015;44(5):1696-705.
16. Wang YF, Zhe TA, Jin GU, Tao LX, Long LI, Li HB, et al. BMI and BMI Changes to All-cause Mortality among the Elderly in Beijing: a 20-year Cohort Study. Biomed Environ Sci. 2017;30(2):79-87.
17. Tobias DK, Hu FB. Commentary: obesity and mortality in China: the shape of things to come.Int J Epidemiol. 2012;41(2):481-3.
18. Costa VE, Ferolla SM, Reis TO, Rabello RR, Rocha EA, Couto CM, et al. Impact of body mass index on outcome in patients undergoing coronary artery bypass grafting and/or valve replacement surgery. Rev Bras Cir Cardiovasc. 2015;30(3):335-42.

Table 1: Association between Body Mass Index and complications.

		Body Mass Index			
		Normal Weight	**Over weight**	**Obese**	**P-value**
		(N=57)	(N=43)	(N=30)	
Cardiovascular Complications.	Post-Operative Complications	1	4	9	<0.001
	Age 50-60 Years	0	1	3	0.08
	Age 61-70 Years	1	3	6	0
	Male	0	2	5	0.007
	Female	1	0	4	0.01
	Smoking History	1	2	3	0.04
	without Smoking History	0	2	6	0.006
	Hypertension	1	1	4	0.04
	without Hypertension	0	3	4	0.005
	Diabetes Mellitus	0	2	2	0.16
	without Diabetes Mellitus	1	2	7	0.001
	with Family History	0	1	1	0.26
	without Family History	1	3	8	0.001

Infectious Complications	Post-Operative Complications	3	5	8	0.015
	Age 50-60 Years	2	3	4	0.36
	Age 61-70 Years	1	2	4	0.008
	Male	1	4	6	0.008
	Female	2	1	2	0.66
	Smoking History	2	3	5	0.24
	without Smoking History	1	2	3	0.04
	Hypertension	3	2	4	0.32
	without Hypertension	0	3	4	0.02
	Diabetes Mellitus	1	3	2	0.42
	without Diabetes Mellitus	2	2	6	0.06
	with Family History	0	0	1	0.06
	without Family History	3	5	7	0.04
Bleeding Complications	Post-Operative Complications	1	3	7	0.002
	Age 50-60 Years	0	1	5	0.007
	Age 61-70 Years	1	2	2	0.28
	Male	0	2	6	0.001
	Female	1	1	1	0.94
	Smoking History	1	2	1	0.62
	without Smoking History	0	1	6	0.002
	Hypertension	1	2	3	0.21
	without Hypertension	0	1	4	0.004
	Diabetes Mellitus	0	1	2	0.11
	without Diabetes Mellitus	1	2	5	0.02
	with Family History	0	0	1	0.06
	without Family History	1	3	6	0.01
Acute Renal Failure	Post-Operative Complications	2	5	6	0.04
	Age 50-60 Years	1	3	4	0.16
	Age 61-70 Years	1	2	2	0.28
	Male	0	4	6	0.002
	Female	2	1	0	0.49
	Smoking History	1	2	1	0.62
	without Smoking History	1	3	5	0.1
	Hypertension	2	2	2	0.75
	without Hypertension	0	3	4	0.02
	Diabetes Mellitus	1	3	2	0.42
	without Diabetes Mellitus	1	2	4	0.08
	with Family History	0	0	1	0.06
	without Family History	2	5	5	0.11

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RESEARCH ARTICLE

A Study on Anti-Putrefaction Nature of *Sarcostemma acidum* (SA) on Carbon Steel

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ABSTRACT

A novelty based ethanolic extract of the medicinal plant *Sarcostemma acidum* (SA) with and without Zn^{2+} ions were used as anti-corrosion agents to establish its ability against corrosion by weight-loss method . And binary mixture of the inhibitor was used as anti-corrosion agent on carbon steel in river water medium and corrosion resistive efficiency was determined. For the maximum concentration ratio of the inhibitor systems (SA, SA-Zn^{2+}) extends the stability of the protective film and retains the inhibition efficiency. The film formation and the type of inhibitor was determined by electrochemical studies. A layer of resistive film formed on the surface protects the metal and it was confirmed by the spectral analysis like FT-IR. The film formation is confirmed by the surface morphology SEM which also confirms the complexation between the metal cation and SA, SA-Zn^{2+}.

Keywords: anti-corrosion agent; FT-IR; *Sarcostemma acidum*; SEM; impedance

INTRODUCTION

Metals are used almost in all fields of technology, industries and home appliances. Corrosion (putrefaction) is a natural deterioration process which can be controlled but cannot be completely prevented. In past years, chemical inhibitors were used to control corrosion. Later it was found that the chemical inhibitors were hazardous and toxic. So eco-friendly, non–toxic chemical inhibitors were used. In recent days, green inhibitors from natural products have been used as inhibitors which are eco-friendly andnon-toxic [1-3]. *Sarcostemma acidum (SA)*is a plant which belongs to

the family 'Asclepiadaceae'. It is widely distributed in Tropical and subtropical regions of India. The leaves of the plant has antiviral and rejuvenating nature. [4]. The present objective is,

- to evaluate the anti- putrefaction property of *Sarcostemma acidum (SA)*by the inhibition efficiencies of SA, SA-Zn^{2+} systems in resisting the corrosion on carbon steel in river water medium.
- toanalyse the protective film formed on the metal surface by FT-IR spectra and electrochemical methods.
- to study the surface morphology by SEM analysis.

MATERIALS AND METHODS

Metal Specimens

The metal specimens is carbon steel with the composition (wt%) of S-0.026 , P -0.06, Mn- 0.4, C- 0.1 and balance iron. The dimensions of the metal active surface are 1.2 X 4.1 X 0.2 cm which is used for weight loss measurements. The carbon steel specimens were polished, washed in double distilled water and degreased with acetone and used for the weight loss method.

Extraction

The leaves of *Sarcostemma acidum* (SA) were collected from *Pachaimalai* hills near Trichy (Dt). The leaves were washed thoroughly for about 7 times in the running tap water and it was taken and dried under shade. About 100g of the powder was soaked in 500ml of ethanol under cold percolation method. At regular intervals of time the extract was filtered and distillation was carried out to collect the crude extract and then stored in an amper bottle and refrigerated [5]. The crude extract is used for phytochemical screening and for other studies [6].

Weight-Loss Method

Determination of Corrosion Rate

The specimens were immersed in beaker containing 100ml acid solutions without and with different concentration of *Sarcostemma acidum* (SA) leaves extract using hooks. Before it was immersed, the specimens were cleaned and the weight is recorded. After 72 hours, the test specimens were removed and then washed with double distilled water, dried and reweighed. The average mass loss of two parallel carbon steel specimens were obtained [7].
From the change in weight of specimens the corrosion rate was calculated using the following relationship,

$$\text{Corrosion Rate} = \frac{87.6 \times W}{A \times T \times D} \text{ (mpy)}$$

W = Loss in weight in mg
A = Surface area of the specimen (cm^2)
T = Time in hours
D = Density ($7.2 g/cm^3$)
Corrosion Inhibition Efficiency (IE) was then calculated using the equation
$IE = 100[1-(W_2/W_1)]$ %
Where,
W_1 = Corrosion rate in the absence of inhibitor and
W_2 = Corrosion rate in the presence of inhibitor

Infra Red (IR) Spectroscopy

Infrared spectroscopy is a well developed technique to identify chemical compounds. The specimens were suspended by means of hooks in solution having with and without inhibitor for 72 hours. After 72 hours the specimen were taken out. Then the film formed on the metal surface was scratched off and taken for FT-IR spectral study.

SEM Analysis

A Scanning Electron Microscope (SEM) is a type of electron microscope that images a sample by scanning it with a beam of electrons in a raster scan pattern. It contains the information about the sample's surface topography. The specimens were suspended by means of hooks in solution in the presence and in the absence of inhibitor for 72 hours. Then the specimens were taken out and the metal specimen was analyzed.

Potentiodynamic Polarization

Polarization studies were carried out in a CHI-electrochemical work station with impedance model 660A. A three-electrode cell assembly was used. The working electrode was carbon steel. A SCE was the reference electrode. Platinum was the counter electrode. From polarization study, corrosion parameters such as corrosion potential (Ecorr), corrosion current (Icorr), Tafel slopes anodic = ba, and cathodic = bc were calculated and LPR value was also determined. The scan rate (V/S) was 0.01. Hold time at (Efcs) was zero and quiet time (s) was two [8].

AC Impedance Spectra

The instrument used for polarization study was used to record AC impedance spectra also. The cell set up was also the same. The real part (Z') and imaginary part (Z'') of the cell impedance were measured in ohms at various frequencies. The observations of charge transfer resistance (Rf) and the double layer capacitance (Cdl) were determined. AC impedance spectra were recorded with initial E(v) = 0, high frequency (Hz) = 1x105, low frequency (Hz) = 1, amplitude (V) = 0.005, and quiet time (s) = 2.

RESULTS AND DISCUSSION

Qualitative Preliminary phytochemical screening

The active phytochemicals present in *Sarcostemma acidum (SA)* have been determined by qualitative preliminary phytochemical screening. The secondary metabolites such as terpenoids, alkaloids, and flavonoids are present except tannins, protein, glycosides and quinone are tabulated in Table-1. The presence of these active phytochemicals is responsible for the inhibitive property against corrosion.

Gas Chromatography – Mass Spectroscopy (GC – MS)

Gas chromatography – Mass spectroscopy analysis is used to identify the composition percent of phytochemicals of the ethanolic extract of *Sarcostemma acidum (SA)*. The mass spectra of the active phyto constituents were compared with the mass spectral data in the NIST – library. The chromatogram of the ethanolic extract of *Sarcostemma acidum (SA)*and the mass spectrum of the major active phytochemical were depicted in Fig.1 & 2.

Determination of Corrosion rate and inhibition efficiency – Weight loss method. (RP –Zn^{2+} system).

The corrosion rate (CR) and the inhibition efficiency (IE) of the ethanolic extract of *Sarcostemma acidum (SA)* on carbon steel in Cauvery river water were determined using weight loss method. For various concentration of the SA extract along with Zn^{2+} (0, 25 and 50 ppm) systems in which carbon steel specimens were immersed for about one day. The IE and CR values of various concentration of SA and Zn^{2+} (0, 25 and 50 ppm) were tabulated in Table 2 and their plots were depicted in Fig. 3.

As a result, it was found that the ethanolic extract of SA at 500 ppm of concentration is more effective. The inhibition efficiency of the pure ethanolic extract of SA is 68% when 50ppm of Zn^{2+} is added then the IE% has increased to 93%. There is a decrease in corrosion rates. *Sarcostemma acidum*(SA) and Zn^{2+} ion alone doesn't have individual inhibitive nature and efficiency. But, SA - Zn^{2+} (500 : 50ppm) inhibitor complex gives a good inhibition efficiency. Thus the complexation of SA - Zn^{2+} was found to be good inhibition power than that as in individual. This indicates the existence of synergism between SA and Zn^{2+} (500:50ppm) . The increase in IE is due to the formation of SA - Zn^{2+} complex diffused from the bulk of the solution to the metal surface. A thin layer of inhibitive complex SA - Zn^{2+}gets

deposited as Zn $(OH)_2$on the cathodic region of the metal surface. Thus the binary inhibitor mixture controls both the anodic and cathodic reaction.

Effect of pH – (SA - Zn^{2+}) system

The effect of pH for the SA - Zn^{2+} system is determined by three different pH (acidic, neutral, basic) values of 3, 8 and 12. The variation in the pH of the system affects the inhibition property. At pH = 8, the system shows a maximum IE of 93% when the pH values is reduced to pH=3 by the addition of HCl, the IE decreases. Similarly when the pH is increased by the addition of NaOH, (pH=12) IE of the inhibitor system decreases. At high pH value, the transport of Zn^{2+} ions to the metal surface is reduced due to the deposition of Zn^{2+} ion as Zn $(OH)_2$. The results of the SA - Zn^{2+} pH variation are tabulated in table 3.

Effect of pH – (SA - Zn^{2+}) system

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Effect of immersion period – (SA – Zn^{2+}) System

It is indicated clearly in the table 4that the effect of immersion period on the binary inhibitive mixture. When the immersion period is increased, the IE of the system decreases and CR increases. This indicates that the protective layer formed on the metal surface deteriorates and dissolves in the solution by the corrosive environment and enhances corrosion process [9]. The variation of CR and IE of RP – Zn^{2+} system due to the increase in immersion period, is tabulated in table 4 and the plot is depicted in the Fig 4.

Potentio dynamic polarization study

The polarization study is an electro chemical method used to identify the formation of protective film on the metal surface. If there is the formation of protective film, on the metal surface, then the LPR value (linear polarization resistance) increases and corrosion current (I_{corr}) decreases. The polarization curves of carbon steel immersed in the presence and absence of the binary inhibitor mixture are correlated in Fig 5.the corrosion parameters such as corrosion potential (E_{corr}) and LPR values are tabulated in Table 5. Thus the binary inhibitor mixture SA – Zn^{2+} controls both anodic and cathodic reaction. Similar observations were observed by various authors who has reported the inhibitive nature of the plant extract to be a mixed inhibitor.

AC – impedance Spectra

Fig. 6 represents the nyquist plots of the carbon steel immersed in the blank (RW) and RP – Zn^{2+} Systems. If the metal surface is protected by the resistance (Rct) increases and the double layer capacitance (Cdl) decreases. In impedance study, the depressed semicircle suggests that the inhibition process of corrosion is attributed to the charge transfer process. The results obtained from the impedance analysis were tabulated in Table 6. It was found that in the presence of binary inhibitor mixture SA – Zn^{2+} (500: 50 ppm) the charge transfer resistance value increases and the double layer capacitance value decreases. This observed variation depends on the thickness of the protective layer formed on the metal surface. This confirms that the binary inhibitor mixture (SA – Zn^{2+}) has a good inhibitive ability for carbon steel in RW.

Analysis of FT – IR Spectra

FT – IR is a technique used to identify the functional groups present in the inhibitor that is adsorbed on the metal surface. The FT – IR spectrum of the film formed on the surface of the metal immersed in RW in the presence of the

binary inhibitor mixture. The FT-IR Spectra of SA extract and SA – Zn^{2+} (500 : 50ppm) are in Fig.7. A few drops of an ethanolic extract of SA was dried on the watch glass, a solid residue is obtained. Thus the obtained residue of SA extract is taken for FT-IR spectral analysis. For solid extract of SA, a band at 3386 cm^{-1} is observed due to – OH stretching. A band at 1641 cm^{-1} indicates the C=C stretching frequency. The band observed at 1488 $cm^{-1}$is due to C-H bending. The FT – IR spectrum of the protective film that is formed on the metal surface immersed in SA – Zn^{2+} system (500:50ppm) is depicted in Fig. 7. A band appeared at 3336 cm^{-1}indicates – OH stretching frequency. For C = C stretching frequency the band is obtained at 1636 cm^{-1}. For the -CH bending vibration a band is obtained at 1393 cm^{-1}. The variation in the frequencies from higher to lower values indicates the complexation of SA and Fe^{2+}, Zn^{2+} ion. The Zn-O stretching frequency is observed at 705 cm^{-1}. Thus it is concluded that Fe^{2+} - SA protects the anodic region and $Zn(OH)_2$ protects the cathodic region of the metal surface and retards the process of corrosion.[10-12].

Scanning Electron Microscope (SEM) analysis

The texture and pore structure of the inhibited and unhibited metal surface immersed in RW are shown in Fig 8. The SEM analysis is the surface morphology which explains the precipitation of the binary inhibitor mixture on the metal surface. From Fig. 8 a, it is clearly observed that the polished metal specimen was smooth and has no corrosion product on the active sites of the metal surface. From Fig 8.b, it is observed that the metal surface immersed in RW was found to be rough and has corrosion product on the metal surface. The metal surface was also found to have cracks and damages From Fig. 8.c, it is observed that the metal immersed in SA-Zn^{2+} system, the surface was found to be smooth and the damage was reduced on comparing with the metal surface in blank (RW). Thus, the complexation of SA – Zn^{2+} as SA – Fe^{2+} and Zn^{2+} ion as $Zn(OH)_2$ is formed as protective film on the metal surface protects the anodic and cathodic sites of the metal respectively. The precipitate adsorbed on the surface is insoluble and highly protects the carbon steel and retards the process of corrosion.

CONCLUSIONS

Thus the ethanolic extract of the medicinal plant *Sarcostemma acidum* (SA) with and without Zn^{2+} ions were found to posses active phytoconstituents and the GC-MS analysis illustrated the predominant phytochemical present in the plant. These active phytocompounds are responsible for the anti-corrosion ability. And binary mixture of the inhibitor was used as anti-putrefaction agent on carbon steel in river water medium and corrosion resistive efficiency was determined by weight loss method. At a concentration of 500:50 (SA-Zn^{2+}) maximum concentration ratio of the inhibitor systemextends the stability of the protective film and retains the inhibition efficiency. The electrochemical studies confirms the film formation and the type of inhibitor protection. The variation of inhibition efficiency varies with respect to pH and immersion period. A layer of resistive film formed on the surface protects the metal and it was confirmed by the spectral analysislike FT-IR. The film formation is confirmed by the surface morphology SEM which also confirms the complexation between the metal cation and SA, SA-Zn^{2+}.

REFERRENCES

1. Kilbourn BT, Cer. Eng. Sci. Proc. 6 (1985) 1331.
2. Bethencour M., BotanaFJ, Calvino JJ, Marcos M, Corros. Sci. 40 (1998) 1803.
3. Arenas MA, Conde A, de Damborenea J, Corros. Sci. 44 (2002) 511.
4. Asha V, Pushpangadan P, *Ancient Science of Life,* 17, 3 (1998) 235 – 238.
5. Bharath Kumar R, Suryanarayana B Promising antidote plant species from the tribals of Sriharikota Island, Andhra Pradesh. Life Sciences Leaflets 2011;19: 769-779.
6. Alphonsa Juliet HelinaJ K, DayanaJayaleelaG, and Alex RamaniV, "Phytochemical screening and antimicrobial studies on the medicinal plant Flueggealeucopyrus(Willd.), World Journal of Pharmacy and Pharmaceutical Sciences, 4, 717-726.

7. Rajendran S, Apparao B.V and Palanisamy N, *Proc. 8th Europ. Symp. Corros. Inhibitors*, Ferrara, Italy,1(1995) 465.
8. Epshiba R, Peter Pascal Regis A and Rajendran S, *Int. J. Nano. Corr. Sci. Engg. 1(1) (2014).*
9. AppaRao B.V., *International Journal of Materials and Chemistry*, 3, 2 (2013)17-27.
10. Kalaivani, R., Narayanasamy, B., Selvi, J. A., Amalraj, A., Jayasundari, J. and Rajendran, S., *PortugaliaeElectrochimica Acta*. 27(2009), 177.
11. Rajendran, S., Apparao, B. V. and Palanisamy, N., *Proc. 8th Europ. Symp. Corros. Inhibitors*, Ferrara, Italy, 1(1995), 465.
12. Vera, R., Schrebler, R., Cury, P., Del Reo, R. and Romero, H., *J. Appl. Electrochem*., 37(2007), 519-525.

Table 1 Preliminary Phytochemical Screening

S.No	Phytochemical	Reagent used	Inference
1.	Terpenoids	Thionyl chloride	+
2.	Reducing Sugar	Felling 4 x B	-
3.	Anthraquinine	Magnesium Acetate	+
4	Flavonoids	Magnesium HCl	+
5.	Glycoside	Antmono with H_2SO_4	-
6.	Alkaloids	Mayer's Reagent	+
7.	Tamins	Head acetate	-
8.	Saponins	Water	-
9.	Protein	Ninlydrin	-
10.	Quinone	Con.HCl	-

Table 2. Determination of CR and IE of SA - Zn^{2+} system

SA (ppm)	IE%			CR (mmpy)		
	Zn^{2+} (ppm)			Zn^{2+} (ppm)		
	0	25		0	25	
0	-	14	**0**	-	14	**0**
100	47	56	**100**	47	56	**100**
200	50	63	**200**	50	63	**200**
300	55	70	**300**	55	70	**300**
400	61	76	**400**	61	76	**400**
500	68	83	**500**	68	83	**500**

Table 3. Effect of pH – (SA - Zn^{2+}) system

System	pH		
	3	8	12
Blank CR (RW)	0.9485	0.8192	0.9034
SA - Zn^{2+} (500:50) CR	0.2583	0.0573	0.1355
IE%	73	93	85

Table 4. Effect of immersion period - SA – Zn^{2+} system

Immersion period (days)	CR (mmpy)		IE%
	Blank (RW)	SA – Zn^{2+} (500:50)ppm	
1	0.8192	0.0573	93
3	0.8556	0.1540	82
5	0.9209	0.1840	80
7	0.9868	0.2565	74

Table 5 Corrosion parameters of carbon steel in RW by polarization method with and without SA – Zn^{2+} system

System	E_{corr} Mvevs SCE	I_{corr}(A / cm^2)	b_a (mV/dec)	b_c (mV/dec)	LPR ohm cm^2	Type of Protection
Blank (RW)	-316.65	12.533	136.49	132.89	2334	-
SA – Zn^{2+} (500:50)	-365.82	9.960	207.38	226.36	4718	Mixed

Table 6 AC – impedance study (a) Blank – RW, (b) RP– Zn^{2+} system

Concentration		R_{ct} (Ω cm^2)	C_{dl} ($\mu F/cm^2$)
RP (ppm)	Zn^{2+} (ppm)		
0	0	858	3.0931×10^{-7}
500	50	1056	2.0853×10^{-7}

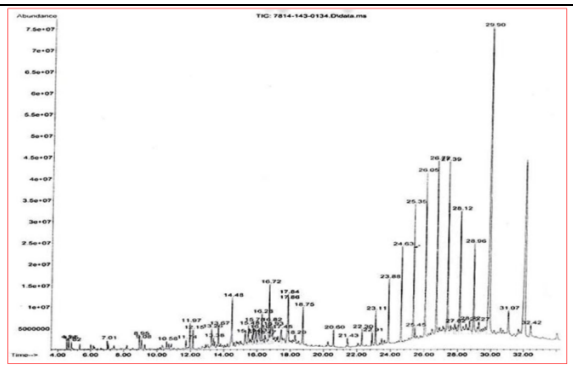

Fig.1.Gas Chromatogram of ethanolic extract of *Sarcostemma acidum (SA)*

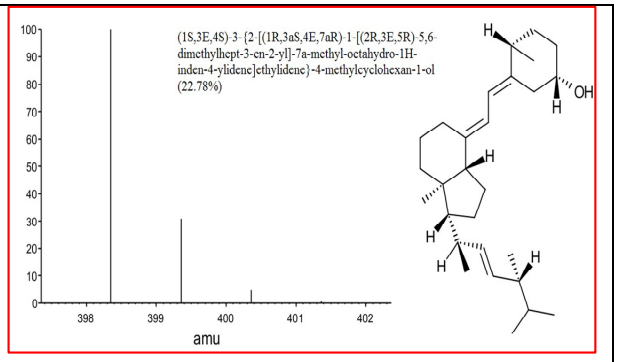

Fig. 2. Mass spectrum of Major active constituent present in the ethanolic extract of *Sarcostemma acidum (SA)*

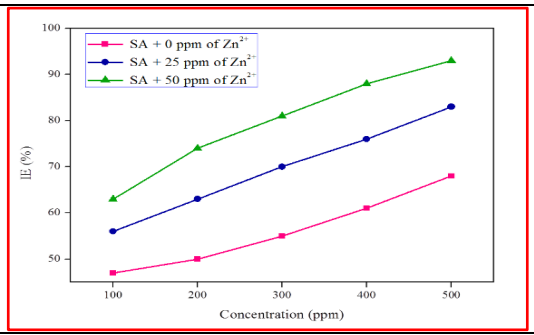

Fig. 3 Graphical representation of Concentration and IE of SA- Zn^{2+} system

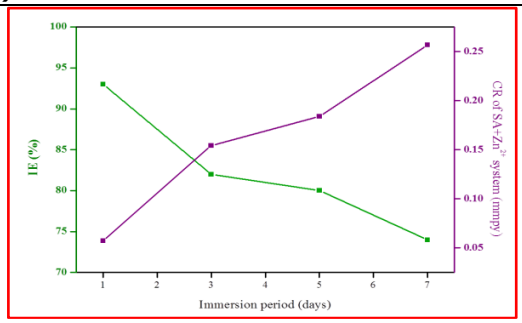

Fig. 4. Graphical representation of effect of immersion period [SA-Zn^{2+}] system

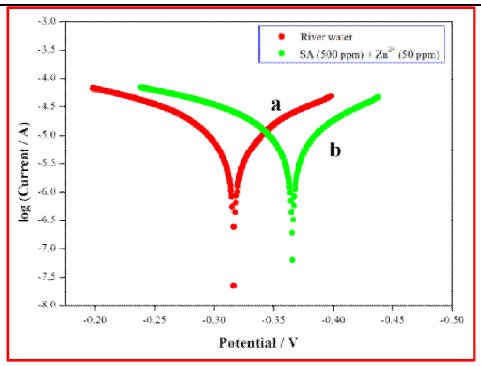

Fig. 5 Polarization curves correlation of carbon steel in RW and SA-Zn^{2+} systems

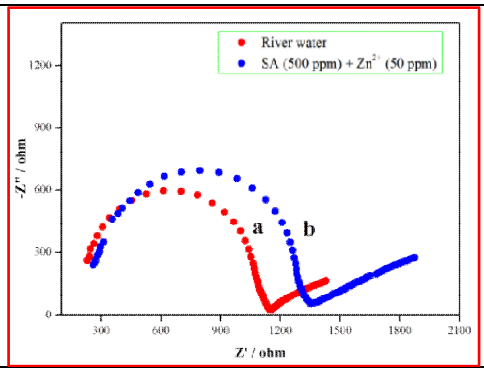

Fig 6. AC – impedance spectra(a) Blank – RW, (b) SA–Zn^{2+} system

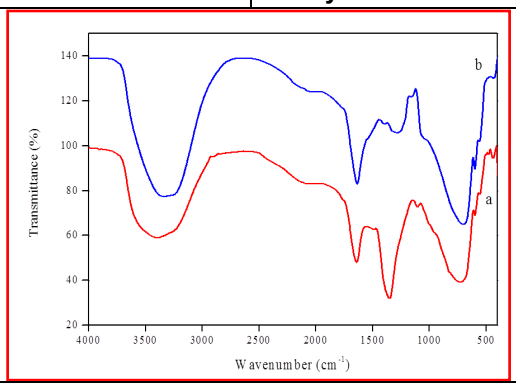

Fig. 7. FT – IR spectra (a) dried SA extract and (b) SA – Zn^{2+} (500: 50ppm)

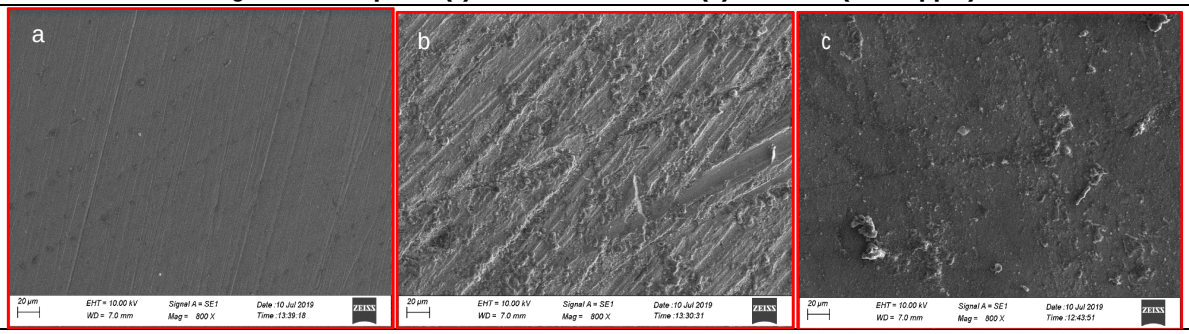

Fig. 8 SEM Images a) Polished Carbon b) Blank c) SA-Zn^{2+}

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RESEARCH ARTICLE

An Investigation on Structural, Optical Properties *In vitro* Antimicrobial, Antioxidant and Cytotoxicity Activities of Thiourea Derived Bioactive Metal Complexes for Pharmaceutical Applications

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ABSTRACT

The good quality biological and optical properties of bisthiourea cadmium chloride Cd $[CS(NH_2)_2]_2Cl_2$; (BTCdCl) and bisthiorea zinc chloride Zn $[CS(NH_2)_2]_2Cl_2$; (BTZnCl) crystals were grown by slow evaporation solution growth technique maintaining the pH at 4. The as-grown BTCdCl and BTZnCl crystals were characterized by FTIR, UV-Vis-NIR, single crystal XRD, antioxidant, cytotoxicity and antimicrobial analysis. The calculated lattice parameters; a = 13.1107(3) Å; b = 5.8145(3) Å; c = 6.4833(6) Å of BTCdCl crystallized at orthorhombic system with the space group $Pmn2_1$ and the measured parameters; a = 12.9995(16) Å; b = 12.7309(16) Å; c = 5.8842(6) Å of BTZnCl crystallized at orthorhombic system with the space group Pmna were recognized as non-centrosymmetric crystals by single crystal X-ray diffraction studies. The required functional groups of Cl-Zn-S, Cl-Cd-S, N-C-N, C-N-H, and H-N-H bonds in BTZnCl and BTCdCl were identified by FTIR analysis. The UV-Vis-NIR spectrum showed the lower cutoff wave length at 262.65 nm and 282.15 nm 335nm of BTZnCl and BTCdCL samples in the ultra-violet region and the 95% of transmittance in the entire visible region showed the good optical conductivity of grown BTCdCl and BTZnCl crystals. The present bioactive materials exhibited good antimicrobial activity against *E. Coli* (G -Ve), *Staphylococcus* (G +Ve) and *Candida albicans* (Fungus) were measured by MIC assay. Further, the calculation of IC_{50} = 40.02 µg / mL and IC_{50} = 44.83 µg/mL values of BTZnCl and BTCdCl crystals showed the higher anticancer activity against human cervical cancer cell line (HeLa) were found using MIT assay. In addition to that the significant antioxidant activities of the

present thiourea derived biomaterials confirmed that they were the potential antioxidant materials in the pharmaceutical applications.

Keywords: UV-Vis-NIR, FTIR, Single crystal XRD, Antioxidant activity, Antimicrobial activity, Cytotoxicity activity.

INTRODUCTION

Naturally an organic thiourea material exists in dipolar nature (NH^{3+} and COO^{-}) and exhibit the non-linear optical and bioactive properties arising from the intramolecular charge transfer between two groups of opposite nature [1]. Complexes enclosing thiourea assemblies engage an important position amongst organic reagents as bioactive ligands for transition metal ions [2]. The large amount of bonding potentials is provided by the O, N, and S atoms of thiourea molecule to its metal complexes [3]. Therefore, the metal complex of thiourea ligands posses a wide range biological properties considering antibacterial, antifungal and cytotoxicity properties [4]. Metal ions like copper, zinc, and ferrous are played a vital role to exhibit good antimicrobial and cytoxicity activities towards human beings have been reported [5]. Owing to the occurrence of the mutual attraction between the oppositely charged metal ions and cell membrane in the structural matrix of metal-ligand complexes, the $metal^{2+}$ penetrates into the cell membrane and reacts with sulfhydryl groups inside the cell membrane. Therefore, the bacterium lipid layer gets battered due to the entrance of metal ions resulting to the enhanced lipophilicity behaviour [6]. The thiourea derived metallic crystallites have been established themselves as potential materials for screening antimicrobial, antioxidant, and anticancer activities in pharmaceutics due to the presence of their carbonyl and carboxyl groups [7].

Recently, the organo metallic complexes of Cu (II) and Zn (II) with their bonding of C-H, M-O- H and the intramolecular charge transfer causing them to be more effective in the non-linear optical and bioactive fields have been reported [8]. Hence, the researchers are focused on the II (B) group metals (Zn, Cd) as these compounds typically have a large transparency in the UV region because of their closed d shell playing a key role in biological chemistry [9]. The thiourea incorporated Ni, Cu and Zn metal complexes exposed to potential pharmaceutical applications have been reported [10]. Furthermore, some metals with d10 configuration, such as zinc and cadmium readily combine with thiourea forming a stable compound with high optical nonlinearity and good physiochemical behavior [11]. As we conclude that, there are precise reports on pharmaceutical applications of thiourea derived metal complex of ligands, we focus our present work to investigate the synthesis, characterization, crystal structure, optical conductivity, anti-oxidant, antimicrobial and cytotoxicity activities of the zinc and cadmium thiourea derivatives for pharmaceutical applications.

MATERIALS AND METHODS

Synthesis and growth of BTCdCl and BTZnCl crystals

The expected purified elements such as cadmium chloride (LOBA Chemie, 99.95 % Assay), thiourea (LOBA Chemie, 99.95 % Assay) and zinc chloride (LOBA Chemie, 99.99 % Assay) by AR grade were utilized as the source materials in the slow evaporation solution growth process. The double distilled deionised water was used as the perfect solvent substance to transmit the soluble state of the requisite reactants, through upholding the pH at 4.0 and varying the temperature range from 28°C to 55°C. Bis (thiourea) cadmium and zinc chloride (BTCdCl) single crystals were formed by dissolving cadmium chloride/zinc chloride and thiourea in the double distilled deionised water maintaining the ratio of 1:2 in an aqueous medium. The present prepared solution was stirred thoroughly using a magnetic stirrer to control the co-precipitation of numerous phases, as thiourea is a good coordinating material, to create different phases of thiourea-metal complexes. When the cadmium chloride/zinc chloride is reacted with thiourea, bisthiourea cadmium chloride/zinc chloride is produced [12] according to the following reactions,

$CdCl_2$+2[CS $(NH_2)_2$]—> Cd [CS $(NH_2)_2$]$_2Cl_2$ ***... (1)***

$ZnCl_2$+2[CS $(NH_2)_2$]—>Zn [CS $(NH_2)_2$]$_2Cl_2$ ***... (2)***

The solution was thoroughly filtered by maintaining the pH at 4.0 to increase the growth rate of the crystals and they were kept in a dust free environment at room temperature for three to four weeks. Finally, the as-grown colourless BTCdCl and BTZnCl crystals were harvested in a period of 24-30 days**.**

RESULTS AND DISCUSSION

Single crystal XRD analysis

Single crystals of BTCdCl and BTZnCl are the divalent cadmium and zinc chloride complex of thiourea. The single crystal X-ray diffraction method with MoKα (k¼ 0:7170 Å) radiation using a CAD-4 diffractometer was used to analyze the structural parameters of the BTCdCl and BTZnCl single crystals. These crystal structures consist of central ions Cd^{2+} and Zn^{2+}, which are associated with S atoms, and $C1^-$ ions to form the distorted tetrahedrons and the structures of BTCdCl and BTZnCl were solved by full-matrix least-squares methods using SHELX-98 program and established that the structures of BTCdCl and BTZnCl complexes belong to orthorhombic with space group $Pmn2_1$ and Pnma were well assigned CCDC numbers 1966383 and 1966384.The structures of these two materials are described by Cd and Zn-centered coordination tetrahedral, with the two sulfur atoms from two thiourea and two chlorine atoms at the apices (cf.Fig 1**.**). The direction of the thiourea ligands is determined by intramolecular N-H---Cl hydrogen-bonding interactions [13]. The same direction of the identical distorted tetrahedrons is an advantage to the superposition of micro effects in the structural matrix of the present samples owing to increase in the optical and biological effects [14]. The coplanar formation of the thiourea molecules within the structural matrix that accounts for the large bioactivity nature of the as- grown BTCdCl and BTZnCl crystals. The calculated (cf.table.1) cell parameters and space groups are found to be constant with the previously reported values [15]. The establishment of the strong single –bond covalent radii of BTCdCl and BTZnCl crystal structures depend upon their Cd-S and Zn-S distances in the range at 2.5070(6) Å and 2.333(7) Å indicating a fairly strong covalent interaction. The same applies to the Cd-Cl [2.5158(9) Å] and Zn-Cl [2.3091(10) Å] distances of the as-grown crystals, which rise linearly with the size of the chlorine atoms concur well with the single-bond covalent radii.

The better optical and biological activities of the as-grown BTCdCl and BTZnCl crystals are mostly done by the presence of the C=S, N=H, N-H---Cl bonds that are donated to the pi electron conjugation scheme and are accountable for the charge transport method in the structural derivatives of thiourea matrix [16]. The bond angles N(2)-C(1)-N(1) (117.75°) of BTCdCl and N(1)-C(1)-N(2) (118.0°) of BTZnCl are surrounded by the angular edge and the contact pathway is linear which specifies the intramolecular charge shift relations leading to the bio active character of the as-grown complexes [17]. Some selected hydrogen bond lengths and bond angles of C-N, C-S, N=H and N-C-N bonds for BTCdCl are superior than the BTZnCl as given in Table 5.5 and they are revealed the strong optical and pharmaceutical actions of the as-grown thiorea derivative complexes A tetrahedral arrangement is formed by the coordination of the two sulfur and chlorine atoms to cadmium and zinc atoms from the two-thiourea molecules. The two coordinated thiourea units are formed as a planar in the crystal structures of BTCdCl and BTZnCl and also similar bond distances and angles are found between the coordinated thiourea and uncoordinated thiourea molecules. Bond lengths of the carbon-nitrogen groups of C(1)–N(1) 1.314(3) Å for BTCdCl and N(1)-C(1) 1.304(3) Å for BTZnCl match the carbon-sulpur groups of C(1)–S(1) 1.718(2) Å for BTCdCl and S(1)-C(1) 1.7111(2) Å for BTZnCl. They lie between the double and single bonds of the present samples and agreed well with the related structures [18]. The related explanations are accurate for the C–N bonds of the BTCdCl and BTZnCl crystals. This is owing to the strong delocalization in the chelate ring. The crystal packing is mostly determined by N-H---X intramolecular hydrogen bonds [19]. The function of the chloride ions is to manage the crystal structure by transporting the wide range of the intramolecular hydrogen bonds connecting the thiourea amino hydrogen and chloride ions, leading to the development of bulky three-dimensional crystals. The range of N-H (cf.table 3) of all

four member water molecules of BTZnCl and BTCdCl (0.86–0.88 Å) crystals and the strong Zn-Cl and Cd-Cl with distances from 2.30-2.54 Å build their 2D structures into 3D structures.

Optical absorption analysis

The UV-Vis absorption spectra of BTZnCl and BTCdCl complexes using PERKIN ELMER LAMDA 35 Spectrometer in the range from 200 nm-800 nm confirm the lower cutoff wavelengths nearly equal to 300 nm are shown in Fig.2 (a) &Fig.2 (b). The UV-Vis Absorption spectra of BTZnCl and BTCdCl complexes show the lower cutoff wavelengths at 262.65 nm and 282.15nm.The band at 262.65 nm would be credited to π-$\pi*$ transition within the thiourea unit, while the second band at 282.15nm can be attributed to n-$\pi*$ transition within -C=H group. The optical conductivity in the semi organic non-centro symmetric thiourea derivatives is owing to the occurrence of asymmetric N-H bond, polar C=N pi bond, Zn-N-H and Cd-N-Cl asymmetric stretching bonds contribute to the well-built π electron charge transformation in the thiourea derivative matrixes [20].Upon the metal coordination compound, the n-$\pi*$ transition of ligand shifts to a longer wavelength. This indicates the coordination of ligand to metal. The pointed absorption peaks seen in both the spectra of the UV region is done by the splitting of transition of energy levels of metal ions in the highest occupied d orbital to the lowest unoccupied d orbital of $Cd^{2+}$and Zn^{2+} ions when the UV light is absorbed. Hence, the amount of splitting of the energy levels depends on the ligand around Cd^{2+} and Zn^{2+} metal ions, which increases the stability, optical conductivity and polarization of the BTCdCl and BTZnCl complexes formed in view of the fact that the difference between the energy levels of the d orbital increase. As a result, these metal complexes of ligand exhibit two excitation bands from 260nm to 290nm of sharp absorption peaks near the UV regions.

Solubility analysis

Solubility is one of the characterizations identifying the better pharmaceutical [21] activities of the as-grown samples using deionized warm water as a solvent. Solubility analysis was studied in the cryostat connection based constant temperature bath (CTB) with a precision of +0.01 K. The solubility of BTCdCl and BTZnCl crystals were calculated in the temperature range of 30 °C to 55 °C. The solution was stirred constantly for one hour to attain saturation. After reaching saturation, the concentration of the solute was calculated gravimetrically at the equilibrium state. A similar method was repeated and the solubility curves of the samples were plotted from 15 mg / 150 ml to 35 g /150 ml at different temperatures (Fig.3 (a) & Fig.3 (b)).It is seen from the curve that the solubility increased linearly with temperatures due to the soluble nature of cadmium chloride, thiourea and zinc chloride in water. These results show that better solubility supports the utility of BTCdCl and BTZnCl crystals for non-linear optical limiting applications.

Antimicrobial analysis

The antibacterial and antifungal activities of the as-grown BTCdCl and BTZnCl compounds are tested by disc diffusion technique as shown in Fig.4. Metal complexes were screened for their antibacterial activities and the results have been given in table 4**.**Results were compared with the standard drug gentamycin at the same concentration level.

The increased bond length in the structural activity relationship between Cl-Zn-S, Cl-Cd-S, N-C-N, C-N-H and H-N-H bonds in BTZnCl and BTCdCl crystals showed that the biological properties of the complexes enhancing the antimicrobial activity.In the concept of cell permeability, the lipid membrane that surrounds the cell favours the passage of only lipid soluble materials since the liposolubility is an important factor that controls the antimicrobial activity [22]. The increasing lipid solubility character of the metal chelate favours its permeation through lipid layer of the microorganism which probably leads to break–down of permeability barrier of the cell process. During this process, increase in the lipophilic nature of the central metal (II) ions favours its permeation more efficiently through the lipid layer of the microorganisms, thus making the thiourea drived cadmium and zinc metal chelate compounds showed more antimicrobial active**.** Metal Complex of antimicrobial active C-H , N=H and C=S part with metal (II) ions reducing the polarity of Zn (II) and Cd (II) ions significantly because of the partial sharing of their positive

charge with donor groups and delocalization of pi electrons over the whole thiourea incorporated metal chelates resulting in high lipid solubility**.** An increase in the concentration of test sample gives rise to more efficient effect against the studied microorganisms. It has also been observed that concentration plays a vital role in increasing the degree of inhibition so that when the concentration is increased, the activity also is enhanced. The MTT quantitative assays gave minimum inhibitory concentration values in the range 25 µl–100 µl confirmed that the results are superior to the previously published [23].

Antioxidant analysis

Free radicals of reactive oxygen groups and nitrogen groups generation by cells are normal physiological movement. Disproportionate formation of these radicals are induced to damage the cells in human body by joining with the bio molecules, such as protein, carbohydrates, lipids, which finally direct to various diseases, such as cancer, coronary heart disease, aging, neurodegenerative disorders, and diabetes. Antioxidants play a significant role to manage such oxidative stress states by neutralizing these reactive radicals. The antioxidant activity of the synthesized bisthiourea cadmium chloride and bisthiourea zinc chloride was studied by 2, 2-diphenyl-1-picrylhydrazil (DPPH) radical scavenging assay and compared with ascorbic acid (AA) as standard (Fig.5). The compound 2, 2-diphenyl-1-picrylhydrazil (DPPH) scavenging activity is directly proportional to increase in the concentration of the bisthiourea cadmium chloride and bisthiourea zinc chloride materials. The DPPH radical scavenging activity will be calculated according to the following expression,

Percentage (%) of the inhibition ratio = [(Absorption by Control – Absorption by sample)/ Absorption by control] x 100 ***... (3)***

The bisthiourea zinc chloride complex showed (cf.Table.5.8) an efficient radical scavenging action of 98 ± 0.12 % by the concentration of 100 µg/mL, whereas the bisthiourea cadmium chloride shows 74 ± 0.14 % of scavenging activity at the same concentration. The similar antioxidant property was also found for thiourea derivatives synthesized from shiff base ligands [24].

Cytotoxicity analysis

The anticancer activity of BTZnCl and BTCdCl against the human cervical cancer cell line (HeLa) are shown in Fig 6(a) and Fig. (b). The cytotoxicity of the present compounds against the cervical cancer cell lines was determined by IC50 values. Molecules which are accomplished by hydrogen bonds contain hydrogen atoms that are combined with covalent bonds to highly electronegative substances (O, N, and S). The existences of hydrogen bonding among molecules of a material specify that they are polar molecules. This means the molecules will be soluble in a polar solvent such as water. The Cd^{2+} and Zn^{2+} metals penetrated into the cell covering and reacted with sulfhydryl groups inside the cell membrane.Therefore, the bacterium lipid layer undergoes to the spoiled state due to cytotoxic behaviour of the metals resulting in the drainage of the cytoplasmic material**.**The chelation increases the lipophilic character of present bisthiourea cadmium chloride and bisthiourea zinc chloride materials favouring their penetration from back and forth to the lipid layer of the bacterial membranes. Hence, the quantity of inhibition is subjected by the nature of the coordinated anion and their absorption. The higher activity of the thiourea zinc complex (cf. Fig.7) is possibly due to the higher solubility than the thiourea cadmium (cf. Fig.8) complex. As a result, low solubility decreases the chances of the thiourea cadmium complex reacting with the cells to enhance in cytotoxicity.The cytotoxicity of the present compounds against the cancer cell lines was determined by IC50 values, the smaller the IC50 value in the same condition is higher the cell growth inhibitory potency is shown in table 6.One of the majority interesting significance of metal coordinated scheme is the strong spatial arrangement of the ligands about the metal ion. The importance of Zn (II) and Cd (II) metal ions under biological analysis is that they present an elevated amount of coordination complexes with deformation [25].

CONCLUSION

The potential as-grown organometallic bisthiourea zinc chloride and bisthiourea cadmium chloride crystals were produced by using the slow evaporation process in the varying temperature range from 28°C to 55°C. The orthorhombic structure and the $Pmn2_1$ and Pnma space system of the as-grown copper sodium tartrate single crystal was identified by the single crystal XRD. From the Ultra Violet optical studies, the observed lower cut-off absorption wave length near 300nm illustrated that the electronic charge transformation from the metal to ligand functional groups of the present chelating material, increases the ionic conductivity. The bisthiourea zinc chloride complex showed superior antimicrobial activity than bisthiourea cadmium chloride compound against *E. coli* (G -Ve), *Staphylococcus* (G +Ve), and *Candida albicans* (Fungus) due to the presence of N-H…N, C-S, C=N and N-H electron transfer bonds, establishing the progressed liposolubility mechanisms of the present chelating materials and find their appropriateness in the pharmaceutical and clinical fields. Further, the remarkable antioxidant actions of grown thiourea derived complexes proved that they are the potential antioxidant materials in the healthcare applications. The anticancer activities of present thiourea derived complexes were analyzed against the human cervical cancer cell line (HeLa). The calculated $IC_{50} = 40.02 \mu g/mL$ and $IC_{50} = 44.83 \mu g/mL$ values of BTZnCl and BTCdCl crystals with higher solubility would result in higher cytotoxicity. Therefore, metal based thiourea derivatives confirmed that they may be anticancer bioactive materials in the pharmaceutical applications.

REFERENCES

1. Wei Quan Tian , John D. Goddard Weiqi Li, Yangyang Hu, Cheng Zhong, Xin Zhou and Qiang Wang, *J.Mater.Chem.C*, 2016; 4: 6054-6062.
2. Khan et al, *Spectrochim. Acta Part A* 2011; 81:199– 208.
3. Suhair M. S. Jambi, International Journal of *ChemTech Research*,2019;12: 177-187.
4. Saeed, S. Rashid, N. Jones, P.G. Hussain, R. Bhatti, M.H, Cent. *Eur. J. Chem*. 2010; 8**:** 550-558.
5. Nurit Beyth, Yael Houri-Haddad, Avi Domb, Wahid Khan, and Ronen Hazan, *Evidence-Based Complementary and Alternative Medicine,*2015;1**:** 1-16.
6. Peter A. Ajibade,Bioinorg *Chem Appl*, 2015;1:1-9
7. Ashraf A. Aly, Alaa A. Hassan Maysa M. Makhlouf **and** Stefan Bräse , *Molecules,* 2020; *25:* 1-54.
8. Morteza Montazerozohori, Sayed Alireza Musavi, A. Masoudiasl, Monika Kučeráková, Journal of Industrial and Engineering Chemistry,2014;20:2463-2470.
9. Liang, Lei, Zheshuai Lin, Yicheng Wu, *Cryst. Growth Des*, 2017; 17**:** 2254–2289.
10. Gün Binzet, Hakan Arslan, *Journal of Chemistry,* 2013:1**;** 1- 9.
11. Liu XT, Wang XQ, Lin XJ et al., *Appl Phys A*, 2012:107**;** 949–957.
12. PrameelaKumari S. *Int. Journal of Engineering Research and Applications*,2014; 4**:**125-144.
13. Deng-Gao Chen, Ssu-Yu Ho, Kew-Yu Chen, Elise Y. Li and Pi-Tai Chou, *J. Am. Chem. Soc,* 2019; 141: 9885–9894.
14. Edgar Alves Araujo Junior, Francisco Xavier Nobre, Giancarlo Silva Sousa, Laecio Santos Cavalcante, Maria Rita de Morais Chaves Santos, Flavio Leandro Souza and Jose Milton Elias de Matos *etal.,RSC Adv.,* 2017; 7**:** 24263-24281.
15. L. Ruby Nirmala, J. Thomas Joseph Prakash, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy,* 2013; 110: 249–254.
16. Alexander D. Volodin Alexander A. Korlyukov and Alexander F. Smol'yakov, *Crystals*, 2020; *10:* 1-22.
17. Solmaz, U., Gumus, I., Binzet, G., Celik, O., Balci, G. K., Dogen, A., & Arslan, H, *Journal of Coordination Chemistry,*2018;71: 200–218.
18. Li M, Li R.K ,*Cryst EngComm* ,2013;15: 4176–4180.
19. Hans-Jörg Schneider, *Chem. Sci.*, 2012; 3:1381-1394.
20. Zhang, L., Zhou, L., Hou, B., et al, *Trans.Tianjin Univ*, 2018; 24**:**532-537.

21. Coltescu A.R, Butnariu M, Sarac I, *Biomed Pharmacol J*, 2020; 13: 577-583.
22. Shrivastava, M., Shrivastava, G. and Shrivastava, G. *PharmaTutor*, 2018;6: 1-5.
23. Ghorab. *Chemistry Central Journal,*2017; 11: 1-14.
24. Reddy MS, Prathima B, Saraswathi M, Babu S, Sarala Y, Reddy AV, *J App Pharm Sci*, 2016; 6: 090- 096.
25. Vikas Kumar, Swapandeep Singh Chimni. *Anti-Cancer Agents in Medicinal Chemistry,* 2015; 15: 163-175.

Single crystal XRD analysis

Table 1: Calculated lattice factors of BTCdCl and BTZnCl single crystals

Lattice parameters	BTCdCl crystal	BTZnCl crystal
Empirical formula	C2 H8 Cd Cl2 N4 S2	C2 H8 Cl2 N4 S2 Zn
Formula weight	335.54	288.51
Crystal system	Orthorhombic	Orthorhombic
Space group	$Pmn2_1$	P n m a
Unit cell dimensions	a = 13.1107(3) Å;b = 5.8145(3) Å;c= 6.4833(6)Å; α= β= γ = 90°	a=12.9995(16)Å;b=12.7309(16)Å c = 5.8842(6) Å ; α= β= γ = 90°
Volume	494.24(5) $Å^3$	973.8(2) $Å^3$
Z	2	4
Density	2.255 Mg/m^3	1.968 Mg/m3
Absorption coefficient	3.119 mm^{-1}	3.445 mm^{-1}
Crystal size	0.200 x 0.150 x 0.100 mm^3	0.350 x 0.300 x 0.300 mm

Table 2: Bond angles and bond lengths of BTZnCl and BTCdCl single crystals

BTCdCl Bonds	BTCdCl length[Å]	BTZnCl Bonds	BTZnCl length[Å]	BTCdCl Bonds	BTCdCl Angles[°]	BTZnCl Bonds	BTZnCl Angles[°]
C(1)-N(2)	1.314(3)	Zn(1)-Cl(1)	2.2697(10)	N(2)-C(1)-N(1)	117.75(18)	Cl(1)-Zn(1)-Cl(2)	106.04(5)
C(1)-N(1)	1.314(3)	Zn(1)-Cl(2)	2.3010(10)	N(2)-C(1)-S(1)	123.74(17)	Cl(1)-Zn(1)-S(1)	110.54(3)
C(1)-S(1)	1.718(2)	Zn(1)-S(1)	2.3337(7)	S(1)-Cd(1)-Cl(2)	106.19(18)	Cl(2)-Zn(1)-S(1)	108.48(2)
N(1)-H(1)	0.88(2)	Zn(1)-S(1) #1	2.3337(7)	S(1)-Cd(1)-Cl(2)	106.19(18)	N(1)-C(1)-N(2)	118.0(2)
N(1)-H(2)	0.88(2)	S(1)-C(1)	1.711(2)	C(1)-N(1)-H(2)	120(2)	N(2)-C(1)-S(1)	118.0(2)
N(2)-H(3)	0.87(2)	N(1)-C(1)	1.304(3)	H(1)-N(1)-H(2)	116(2)	S(1)-Zn(1)-S(1)1	112.51(4)
N(2)-H(4)	0.87(2)	N(1)-H(1N1)	0.859(18)	C(1)-N(2)-H(3)	123(3)	C(1)-S(1)-Zn(1)	108.47(8)
S(1)-Cd(1)	2.5070(6)	N(1)-H(2N1)	0.839(17)	C(1)-N(2)-H(4)	116(3)	C(1)-N(1)-H(1N1)	125(2)
Cd(1)-S(1)1	2.5070(6)	N(2)-C(1)	1.307(4)	H(3)-N(2)-H(4)	121(3)	C(1)-N(2)-H(1N2)	124(3)
Cd(1)-Cl(2)	2.5158(9)	N(2)-H(1N2)	0.847(18)	C(1)-S(1)-Cd(1)	109.87(8)	C(1)-N(2)-H(2N2)	118(2)
Cd(1)-Cl(1)	2.5494(9)	N(2)-H(2N2)	0.836(18)	S(1)-Cd(1)-S(1)	128.37(3)	H(1N2)-N(2)-H(2N2)	118(3)

Table 3: Hydrogen bond geometry of BTCdCl and BTZnCl single crystals

D-H...A		d(D-H)		d(H...A)		d(D...A)		<(DHA)	
BTCdCl	BTZnCl	BTCdCl	BTZnCl	BTCdCl	BTZnCl	BTCdCl	BTZnCl	BTCdCl	BTZnCl
N(1)-H(1)...Cl(2)	N (1)-H (1)… Cl(2)	0.88(2)	0.85(18)	2.38(2)	2.32(2)	3.24(2)	3.17(2)	170(3)	175(3)
N(1)-H(2)...Cl(1)	N (1)-H (2)…. Cl(1)	0.88(2)	0.83(17)	2.86(2)	2.34(2)	3.62(2)	3.17(2)	146(3)	170(30
N(2)-H(3)...Cl(1)	N (2)-H (1)…. Cl(1)	0.87(2)	0.84(18)	2.59(2)	2.41(2)	3.40(2)	3.35(2)	157(3)	165(3)
N(2)-H(4)...Cl(1)	N(1)-H(2) ….Cl(1)	0.87(2)	0.83(18)	2.74(2)	2.42(2)	3.52(2)	3.25(2)	151(3)	168(3)

Antimicrobial analysis

Table 4: Antimicrobial screening activity of BTZnCl and BTCdCl crystals.

Compound	Organism	Minimum Zone of Inhibition (mm) Concentration (µg/ml) *				Control*
		25	50	75	100	
BTZnCl	*Staphylococcus*	36±0.01	39±0.03	41±0.04	44±0.02	20±0.01
BTCdCl	*Staphylococcus*	31±0.03	33±0.02	36±0.03	38±0.04	18±0.03
BTZnCl	*E.Coli*	32±0.01	34±0.03	38±0.04	40±0.01	18±0.02
BTCdCl	*E.Coli*	30±0.04	33±0.02	35±0.03	37±0.01	17±0.03
BTZnCl	*Candida albicans*	38±0.02	40±0.01	43±0.04	45±0.03	20±0.01
BTCdCl	*Candida albicans*	35±0.03	37±0.04	39±0.02	42±0.01	20±0.03

*** mean±SD**

Antioxidant analysis

Table 5: Assessment of *invitro* antioxidant activity of BTZnCl and BTCdCl crystals

Sample	Concentration (µg / ml)	Control (Ethanol)*	Absorption sample(a.u)*	Absorption control(a.u)*	Inhibition ratio (%)*	IC_{50*}
BTZnCl	25	1.42±0.04	0.64±0.04	0.9±0.04	87± 0.31	07±0.4
	50	1.42±0.01	0.62±0.02	0.9±0.02	89± 0.11	
	75	1.42±0.02	0.58±0.04	0.9±0.03	93± 0.23	
	100	1.42±0.03	0.54±0.02	0.9±0.01	98± 0.12	
BTCdCl	25	1.42±0.02	0.82±0.04	0.9±0.03	67± 0.10	22 +0.2
	50	1.42±0.04	0.80±0.02	0.9±0.01	69± 0.23	
	75	1.42±0.01	0.78±0.04	0.9±0.02	71± 0.32	
	100	1.42±0.03	0.75±0.02	0.9±0.03	74± 0.14	
L-Ascorbic Acid	5	1.42±0.01	1.06±0.01	0.9±0.04	50± 0.10	10 ±0.3
	10	1.42±0.03	0.94±0.03	0.9±0.01	55± 0.31	
	15	1.42±0.02	0.85±0.04	0.9±0.03	61± 0.24	
	20	1.42±0.03	0.77±0.02	0.9±0.02	75± 0.13	

***mean±SD**

Cytotoxicity analysis

Table 6: Cytotoxicity activity of BTZnCl and BTCdCl Crystals

Concentration(µg/mL) *	Control	1	10	50	100	300	500	IC50
Cell inhibition BTZnCl (mm)*	**100**	94.48±0.02	67.67±0.01	48.11±0.03	42.02±0.01	25.43±0.02	6.73±0.03	40.02±0.01
Cell inhibition BTCdCl (mm)*	**100**	97.33±0.03	76.79±0.01	62.66±0.02	55.82±0.01	35.55±0.03	22.57±0.01	44.83±0.02

***mean±SD**

Single crystal XRD analysis

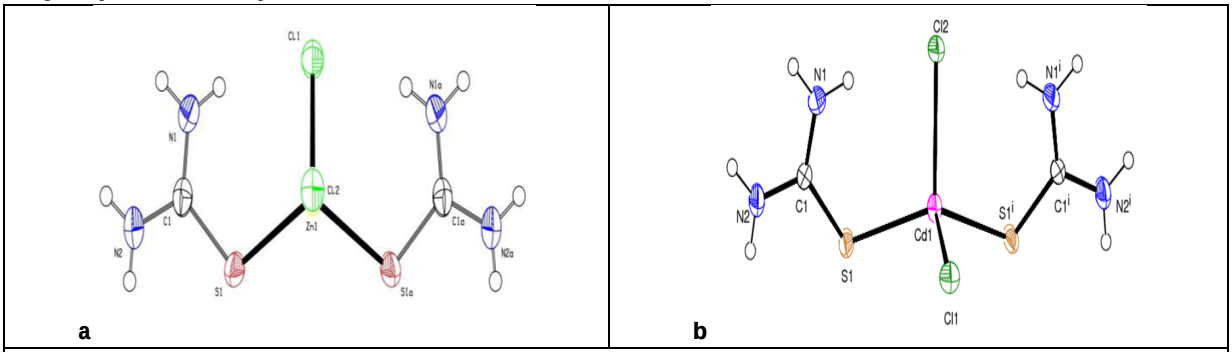

Fig.1: Atom numbering arrangement of (a) BTZnCl and (b) BTCdCl single crystals

Optical absorption analysis

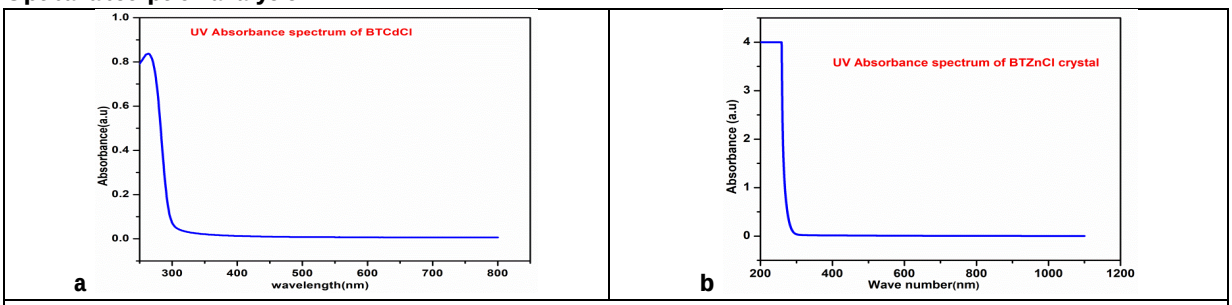

Fig.2. UV-Vis studies on Absorbance of (a): BTCdCl and (b): BTZnCl single crystals.

Solubility analysis

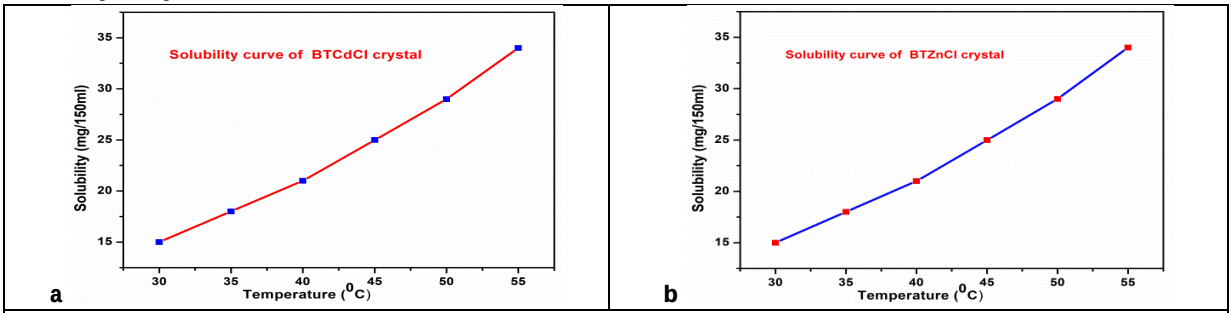

Fig.3. Solubility graph of (a): BTCdCl and (b): BTZnCl single crystals

Antimicrobial analysis

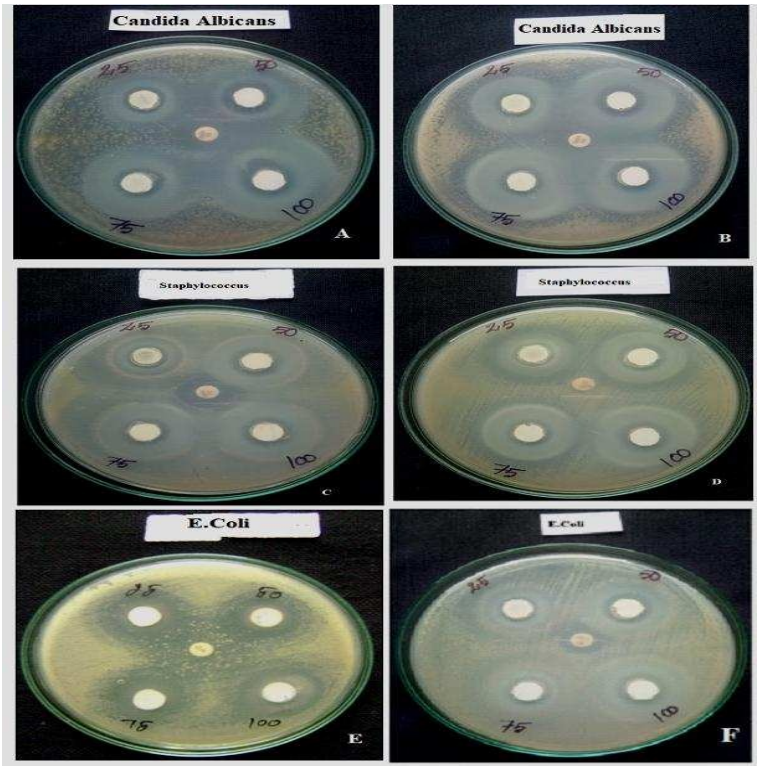

Fig.4. Antimicrobial activity against (A): *Candida albicans*, (C): *Staphylococcus*, (E): *E.Coli* of BTZnCl and (B): *Candida albicans*, (D): *Staphylococcus*, (E) *E.Coli* of BTCdCl crystals

Antioxidant analysis

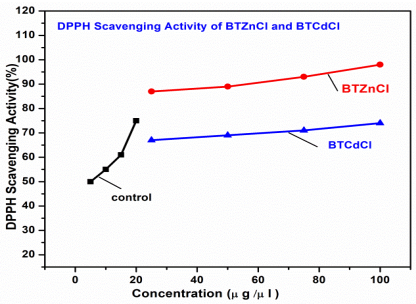

Fig.5. DPPH Scavenging Activity of BTZnCl and BTCdCl crystals

Cytotoxicity analysis

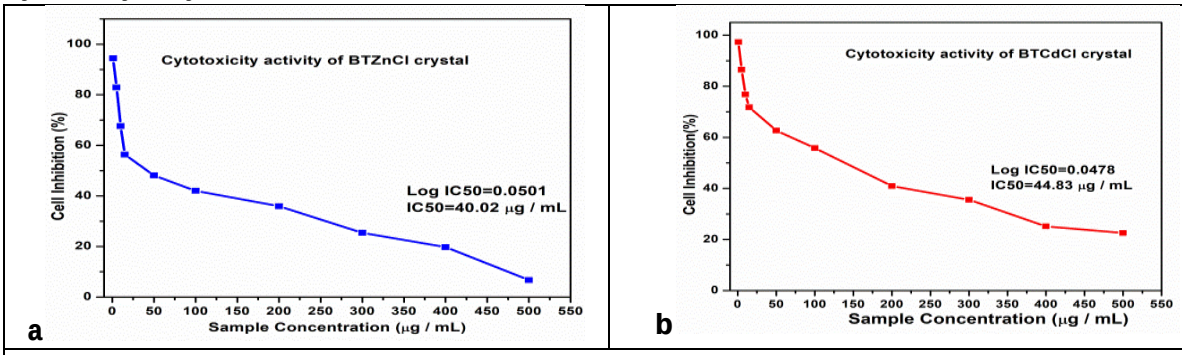

Fig .6. Graphical repersentation for Cytotoxicity Vs. HeLa Cell line of (a): BTZnCl and (b): BTCdCl Crystals

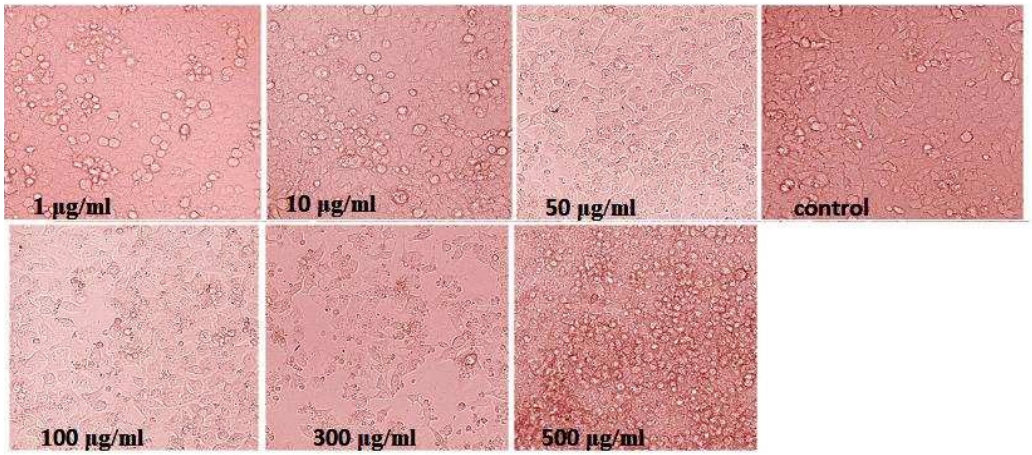

Fig.7. Cytotoxicity Vs HeLa Cell line of BTZnCl Crystal

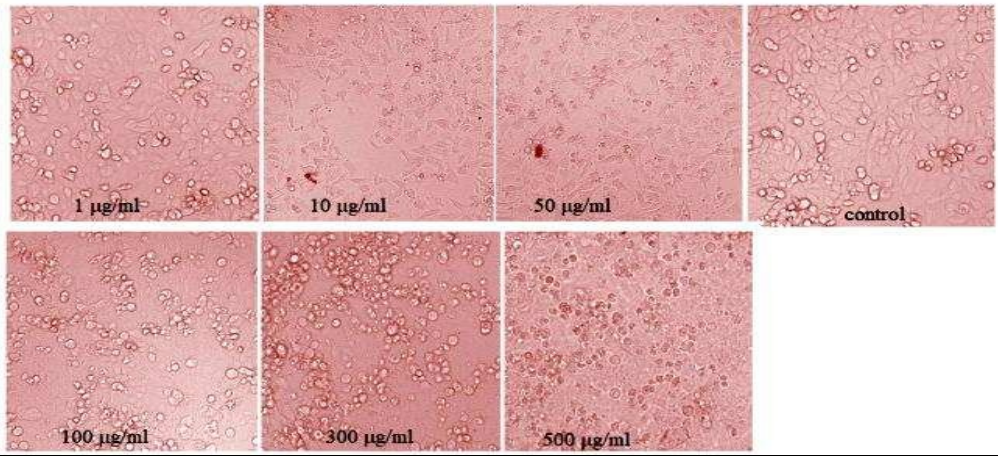

Fig 8. Cytotoxicity Vs HeLa Cell line of CuNaT Crystal

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RESEARCH ARTICLE

Burden of Acute Kidney Injury among Cardiac Surgery Patients

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ABSTRACT

Acute kidney injury (AKI) is a common complication following cardiac surgery, occurring in up to 30% of patients postoperatively. The incidence of acute kidney injury after cardiac surgery (CS-AKI) ranges from 33% to 94% and is associated with a high incidence of morbidity and mortality. Currently, there are no effective therapies proven to modify AKI in patients undergoing cardiac surgery. The aim of the study was to determine the frequency of acute kidney injury in patients undergoing cardiac surgery & outcome in post-cardiac surgery acute kidney injury patients. A descriptive case series study was conducted upon a sample of 95 patients undergoing cardiac surgery were selected as per AKI criteria, increase in Serum Cretinine by ≥1.5 times from baseline within seven days of surgery. History was taken for duration of disease and comorbids like Diabetes Mellitus, hypertension and smoking status. Height and weight will be measured in meters and kg respectively. Serum creatinine was assessed every day till seven days and an increase ≥1.5 times from baseline were considered positive for AKI. The mean age of the patients was 60.39 ± 12.8 years ranging from 40-75 year. The mean BMI of the patients was 26.8±4.6 ranging from 18.75-32. The mean duration of disease of the patients was 17.8±6.5 ranging from 1-30. Out of 107 patients, 72 (75.8%) were males, and 23(24.27%) were females. Male predominance was present. Most of the patients were overweight 41(43.2%). Most common cause of risk of acute kidney injury was followed by hypertension 85(89%), diabetic 52(54.7%), smoking 16(16.8%) as appropriate. 31(33%) patients having acute kidney injury. Mortality rate found only in 16(16.8%) respectively. This study confirms that acute renal failure is one of the major complications of cardiac surgery, identifies the risk factors, and suggests that optimizing cardiac output and reducing CPB time could improve the outcome of patients.

Keywords: Mortality Rate, Acute Kidney Injury, Cardiac Surgery.

INTRODUCTION

Acute renal failure (ARF) still remains a major complication after cardiac surgery. Even minor changes in serum creatinine are related to an increase morbidity and mortality. As recently shown by Chertow et al [1], ARF "per se" is an independent determinant of mortality as much as cardiac arrest. The true incidence of acute renal failure in patients undergoing cardiac surgery is still unknown because different authors have used different nomenclature to define ARF. To sort out this lack of uniformity in 2004 the Acute Dialysis Quality Initiative Group (ADQI) published the Rifle criteria [2]. Acute Kidney Injury post cardiac surgery (AKI-CS) is associated with substantial morbidity and mortality independent of all other factors [2]. Post-operatively even minimal changes in serum creatinine are associated with a substantial decrease in survival as observed in a study that showed 30 day mortality of up to 32.5% with a rise in serum creatinine of more than 0.5 mg/dl [3]. Various risk factors acting through perturbed blood pressure, inflammation and nephrotoxicity have been identified for AKI-CS that may help us risk stratify patients and manage them with renal protective strategies and drugs. The AKI is defined according to the Risk-Injury-Failure-Loss- End stage (RIFLE) and Acute Kidney Injury Network (AKIN) criteria [4, 5].

The incidence of AKI-CS across various studies have been estimated and is about 14% with 1-2% of these patients requiring dialysis (AKI-D) [6]. The development of AKI-CS is associated with a significant increase in infectious complications, an increase in hospital stay, and greater mortality when compared with patients without AKI-CS.(7) Staging of patients according to the rise in serum creatinine may quantify the risk of AKI-CS. A study on 29,388 individuals who underwent cardiac surgery showed that the magnitude of creatinine increase, class I (1-24%), class II (25-49%), class III (50-99%), or class IV (≥100%), was associated with greater incidence of CKD (hazard ratios of 2.1, 4.0, 5.8, and 6.6, respectively). It also increased the risk of CKD progression, and mortality [8]. Elevated pre-operative serum creatinine is predictive of the risk for ARF-D (about 10 to 20% in patients with a baseline pre-operative creatinine 2.0 to 4.0 mg/dl and 25 to 28% if >4.0 mg/dl).(2) However, the relationship between GFR and serum creatinine is nonlinear and GFR may decrease by more than 50% from normal before a significant rise in serum creatinine occurs; therefore small changes in creatinine reflect a significant reductions in GFR [9]. Preoperative proteinuria is an independent predictor of adverse outcomes in patients undergoing cardiac surgery and suggests higher risk for AKI [10]. Pre-operative anemia, perioperative RBC transfusions, and post-operative reexploration are independently and strongly associated with AKI-CS [11]. Anemic patients presenting for cardiac surgery are more susceptible to transfusion-related AKI than non-anemic patients (6.6% versus 3.2%) hence, interventions that reduce perioperative transfusions may protect them against AKI [12, 13]. In a retrospective observational study on 4,836 consecutive patients undergoing cardiac surgery, modification of RIFLE by staging of patients requiring acute renal replacement therapy (RRT) in the failure class-F was shown to improve predictive value. Applying AKIN without correction of serum creatinine for fluid balance may lead to over-diagnosis of AKI (poor positive predictive value) [14]. The aim of the study was to mitigate the burden of AKI among patients undergoing cardiac surgery and to determine the predictors of AKI amongthese patients after surgical procedure.

METHODOLOGY

A descriptive case series study was conducted at the Cardiac Surgery Department of Tabba Heart Institute, Karachi for 6 months. The sample size of 95 was calculated using the single population proportion formula keeping the proportion of AKI post cardiac surgery (p) as 14% (6), 95% Confidence level (CL) and 7% Absolute precision (d). All patients aged between 40 to 75 years presented for cardiac surgery at the study setting were included in the sample based on non- probability consecutive sampling technique. The patients with serum creatinine level within the optimal range (men 0.5-1.5 mg/dL and women 0.6-1.2 mg/dL) and those with the duration of cardiac illness within one month (angiography showing more than 70% stenosis of one or more arteries) were eligible for inclusion. While the known cases of dengue and malaria, those with preoperative dialysis dependency, the ones who underwent infrequent procedures like heart transplantation, ventricular assist device placement, and complex congenital

abnormality repair and those with missing preoperative or postoperative creatinine values were excluded from the study sample.

The study protocol was approved by Research Evaluation Unit (REU), College of Physicians & Surgeons of Pakistan (CPSP). The study purpose, procedure, risks and benefits were clearly explained to all the participants and they were required to provide written informed consent before inclusion. Ethical guidelines were followed and patient's confidentiality were ensured. The data was collected using a structured questionnaire inquiring the baseline demographics, disease duration and information regarding the existing comorbidities like Diabetes Mellitus (DM), Hypertension (HTN). All the patients underwent cardiac surgery with Cardiopulmonary Bypass (CPB), performed by experienced consultant. The serum creatinine level was assessed daily for seven days and increase in serum creatinine ≥1.5 times from baseline were considered as AKI. The AKI patients were then followed for 7 days. The statistical analysis was performed using SPSS version 17.0, age, disease duration, Body Mass Index (BMI) were displayed as mean ± SD while gender, DM, HTN, AKI, mortality and other categorical variables were given as frequency and percentages. Effect modifiers like age groups, gender, DM, HTN, smoking status, BMI and duration of disease were dealt through stratification. Post stratification chi square test were applied keeping level of significance at 0.05.

RESULTS

The present study was conducted at the Department of surgery, Tabba Heart Hospital over a sample of cardiac surgery 95 patients. The mean age of the patients was 60.39 $\pm$ 12.8 years and meanBMIwas found to be 26.8±4.6 kg/m^2 ranging from 18.75-32. The mean duration of disease of the patients was 17.8±6.5. Out of 107 patients, 72(75.8%) were males, and 23 (24.27%) were females.Most of the patients were overweight (43.2%) and 89% were hypertensive, 54.7% were diabetic and 16.8% were smokers. Around 33% patients had AKI and the associated mortality was reported among 16.8%. The relationship of AKI with mortality outcome, comorbidities and other baselines characteristics was also assessed and it was found that there was significant association between age, gender, co-morbidities, mortality and AKI ($p<0.05$).

DISCUSSION

AKI is a significant cause of morbidity and mortality after cardiac surgery. Clinical risk factors that predicted AKI in this study include hypertension, diabetes mellitus, and smoking status; these are similar to previous reports [15]. Acute kidney injury (AKI) following cardiac surgery (AKICS) is associated with increased postoperative (post-op) morbidity and mortality. Acute renal failure (ARF) still remains a major complication after cardiac surgery.(4) Even minor changes in serum creatinine are related to an increase morbidity and mortality. As recently shown by Chertow et al. [1,16,17]. ARF "per se" is an independent determinant of mortality as much as cardiac arrest. The true incidence of acute renal failure in patients undergoing cardiac surgery is still unknown because different authors have used different nomenclature to define ARF. To sort out this lack of uniformity in 2004 the Acute Dialysis Quality Initiative Group (ADQI) published the Rifle criteria [4]. Acute renal failure (ARF) is one of the most serious complications of cardiac surgery. Its incidence varies between 1 and 30%. ARF requiring renal replacement therapy (ARF-RT) develops in 1% to 5% of patients and is associated with a very high mortality [17,18]. This study confirms that ARF is one of the most severe complications of cardiac surgery and, when renal replacement therapy is needed, mortality is markedly increased. In the present study, ARF incidence is in accordance with previous reports [19]. A higher incidence of ARF in valvular surgery and combined valvular-CABG surgery was noted. The risk of ARF after cardiac surgery ranges from 1 % to 30%, depending on the criteria used to define this complication whereas 1% to 5% of patients develop severe disease [1]. The incidence of acute renal failure has decreased after cardiac surgery due to clinicians' awareness of its pathophysiology, preoperative management strategies, and the reduced inflammatory response associated with modern CPB (coated circuits and reduced bypass time) [5] Nonetheless, mortality remains

high, greater than 50% in most series of patients requiring RRT despite improvements in intensive care and RRT technology. In the Chertow et al study (1) the overall operative mortality was 63.7% in patients with ARF-RT. By analyzing data from a large cohort study of cardiac surgery patients, Chertow et al., (1) showed that ARF independently influences outcome, and except for cardiac arrest, it is associated with the highest increase in mortality. The present data are comparable showing a mortality rate of 46.2% (ARF) and 63.8% (ARF-RT).Same exact results were found in my study the mortality rate in acute renal failure group were found high 13 (81.25%) out of 16 patients respectively. Age is still a controversial risk factor; a number of studies reported that ARF is more likely to develop in older patients as confirmed by this present study, but some others did not con- firm it. [7,12-14] Elderly patients are susceptible to many forms of ARF because the aging kidney loses functional reserve and the ability to withstand acute insults is compromised. Older patients may have a reduced ability to cope with reduced circulation.

CONCLUSION

Acute renal failure (100% creatinine increase) developed in 30% patients, the mortality was found among 16.8%. Sex, age, diabetes, smoking, hypertension, BMI were independently associated with acute renal failure. This study confirms that acute renal failure is one of the major complications of cardiac surgery, identifies the risk factors, and suggests that optimizing cardiac output and reducing CPB time could improve the outcome of patients at high risk of acute renal failure.

REFERENCES

1. Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med. 1998;104(4):343-8.
2. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clinical journal of the American Society of Nephrology. 2006;1(1):19-32.
3. Lassnigg A, Schmidlin D, Mouhieddine M, Bachmann LM, Druml W, Bauer P, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. Journal of the American Society of Nephrology. 2004;15(6):1597-605.
4. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure–definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Critical care. 2004;8(4):R204.
5. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Critical care. 2007;11(2):R31.
6. Palomba H, De Castro I, Neto A, Lage S, Yu L. Acute kidney injury prediction following elective cardiac surgery: AKICS Score. Kidney international. 2007;72(5):624-31.
7. Kumar AB, Suneja M. Cardiopulmonary bypass-associated acute kidney injury. Anesthesiology. 2011;114(4):964.
8. Ishani A, Nelson D, Clothier B, Schult T, Nugent S, Greer N, et al. The magnitude of acute serum creatinine increase after cardiac surgery and the risk of chronic kidney disease, progression of kidney disease, and death. Archives of internal medicine. 2011;171(3):226-33.
9. McIlroy DR, Wagener G, Lee HT. Biomarkers of Acute Kidney InjuryAn Evolving Domain. The Journal of the American Society of Anesthesiologists. 2010;112(4):998-1004-998-.
10. Coca SG, Jammalamadaka D, Sint K, Philbrook HT, Shlipak MG, Zappitelli M, et al. Preoperative proteinuria predicts acute kidney injury in patients undergoing cardiac surgery. The Journal of thoracic and cardiovascular surgery. 2012;143(2):495-502.
11. Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Cheng DC, Crowther M, et al. Acute kidney injury after cardiac surgery focus on modifiable risk factors. Circulation. 2009;119(4):495-502.

12. Karkouti K, Wijeysundera DN, Yau TM, McCluskey SA, Chan CT, Wong P-Y, et al. Influence of erythrocyte transfusion on the risk of acute kidney injury after cardiac surgery differs in anemic and nonanemic patients. Anesthesiology. 2011;115(3):523-30.
13. Karkouti K, Wijeysundera DN, Yau TM, Mc Cluskey SA, Chan CT, Wong P-Y, et al. Influence of Erythrocyte Transfusion on the Risk of Acute Kidney Injury After Cardiac Surgery Differs in Anemic and Nonanemic Patients. Survey of Anesthesiology. 2012;56(4):164-5.
14. Englberger L, Suri RM, Li Z, Casey ET, Daly RC, Dearani JA, et al. Clinical accuracy of RIFLE and Acute Kidney Injury Network (AKIN) criteria for acute kidney injury in patients undergoing cardiac surgery. Crit Care. 2011;15(1):R16.
15. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clin J Am SocNephrol. 2006;1(1):19-32.
16. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol. 2005;16(11):3365-70.
17. Chertow GM, Lazarus JM, Christiansen CL, Cook EF, Hammermeister KE, Grover F, et al. Preoperative renal risk stratification. Circulation. 1997;95(4):878-84.
18. Fortescue EB, Bates DW, Chertow GM. Predicting acute renal failure after coronary bypass surgery: cross-validation of two risk-stratification algorithms. Kidney Int. 2000;57(6):2594-602. Chew S, Mar W, Ti L. Association of ethnicity and acute kidney injury after cardiac surgery in a South East Asian population. Br J Anaesth. 2012:aes415.

Table 1: Demographic characteristics of the study population

Variables		Mean ± SD (Range)
Age (Years)		60.39±12.8 (40-75)
BMI (kg/m^2)		26.8±4.6 (18.75-32)
Disease Duration (Days)		17.8±6.5 (1-30)
		n(%)
Gender	Male	23(24.2)
	Female	72(75.8)
Age group	40 to 55 years	23(24)
	56 to 70 years	54(75)
	>70 years	18(19)
BMI	Underweight	5(5.3)
	Normal	34(35.8)
	Overweight	41(43.2)
	Obese	15(15.8)
Comorbidities	Hypertension	85(89)
	Diabetes	52(54.7)
Smoking	Yes	32(34)
	No	63(66)
AKI	Present	31(33)
	Absent	64(67)
Outcome (mortality)	Yes	16(16.8)
	No	79(83.2)

*AKI- Acute Kidney Injury

Table 2: Relationship of AKI with mortality, comorbidities and other baselines characteristics

Variables		AKI		p-value
		Present	Absent	
Gender	Male	25(26.3)	47(49.5)	0.001*
	Female	6(6.3)	17(17.9)	
Hypertension	Yes	22(23.2)	63(66.3)	0.001*
	No	9(9.5)	1(1.1)	
Diabetic	Yes	28(29.5)	15(15.8)	0.001*
	No	3(3.2)	49(51.6)	
Smoking	Yes	12(12.6)	20(21.1)	0.001*
	No	19(20)	44(46.3)	
BMI	Underweight	1(1.1)	4(4.2)	0.027*
	Normal	5(5.3)	29(30.5)	
	Overweight	19(20)	22(23.2)	
	Obese	6(6.3)	9(9.5)	
Age (Years)	40-55	5(5.3)	18(18.9)	0.015*
	56-70	24(25.3)	30(31.6)	
	>70	2(2.1)	16(16.8)	
Mortality	Yes	13(81.25)	3(18.75)	0.001*
	No	18(22.78)	61(77.21)	

*AKI- Acute Kidney Injury

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RESEARCH ARTICLE

Studies on the Role of Environmental Factors in the Development of Fungal Diseases of Cassava Crops

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ABSTRACT

Cassava is one of the major tuber crop belongs to the family Euphorbiaceae. Cassava plant gives the third highest yield of carbohydrates per cultivated area among crop plants. In tropics, cassava is the third most important source of calories, after rice and maize. This work examined the role of environmental factors affecting the cassava crops. The study was carried out in fungal disease incidence was predominant due to relative humidity, wind, precipitation, temperature and moisture content. These factors favours the fungal disease incidence in tuber crops like cassava, The result shows that weather data obtained from Namakkal district and weather variables was determined with the help of multiple regression studies.

Keywords: Fungi, Cassava, Diseases incidence, Weather, Factors

INTRODUCTION

Cassava is a staple food for millions of people in several regions particularly in developing countries. Cassava is originated in North-East Brazil. India occupies fifth place in cassava cultivation,The first four being Brazil,Zaine, Nigeria and Indonesia. Thailand and India are the major cassava growing countries in Asia. Thailand is the world's largest exporter of cassava products. In India it is cultivated mainly in Kerala, Tamilnadu, Karnataka and Andhra pradesh. Kerala and Tamilnadu account for about 80% of the total average of The crop in India. In Tamilnadu during 2011, cassava is cultivated in an area of 1.96 lakh hectares with the production of 38.8% lakh tones. Tamilnadu state stands first (64%) in respect of cassava production and also processing of cassava into starch and sago. Cassava is cultivated in major 14 districts including Namakkal (21%), Dharmapuri (19%), Salem (15%), Vilupuram (14%), Trichy (9%), Erode (5%), and Thiruvannamalai (5%) in an area of 1.21 lakh hectare. Cassava produces bulky storage roots with about 80% carbohydrate concentration. The leaves constitute a good vegetables

rich in protein, vitamins and minerals. Cassava leaves and roots, if properly processed, can provide balanced diet protecting millions of African children against malnutrition. It's potentials in the fight against hunger and food insecurity is documented (Gregory *et al.,* (2000). Cassava ranks among the highest most important food crop world wide and highest food crop produced in the developing countries. Cassava is used in the preparation of flour, rava, macroni, papad instant noodles, vermicelli and etc., cassava starch is a thickner and stabilizerin fruit pies, soups, pudding, breads, sauces, soy and meat products. It serves as raw materials for bakery industries, starch for textile industries, adhesive glucose for pharmaceutical industries and ethanol for brewery and bottling industries. This study therefore intends to find out the cassva is affected by various fungal pathogens like *Fusarium*, *Phytophthora*, *Pythium*, *Aspergillus niger* and *Rhizopus*. For this factors like biotic and abiotic factors played necessary role.Abiotic factors include wind, rainfall, precipitation, relative humidity and temperature. Fungal incidence and the weather, climatic variable and interrelated (Sharon *et al,* 2002). The weather variables will eventually affected by the host and the pathogen. Therefore the present investigation was undertaken to find out the climatic condition in Namakkal district and three years of weather data was collected.

MATERIALS AND METHODS

Geographical Location

Namakkal districtis one of the 38 districts in the state of Tamilnadu. It lies between 11000"and 11036"North latitude and 77028"and 78030"East longitude.The altitude of the districtis 300 metres above MSL. It is located in the interior parts of Tamilnadu. Geographical area of the districtis 3363.35sq.km.

Preparation of field

Cassava is a tropical root crop, Mostly plough the field 4-5 times to get a fine tilth. The soil depth should be at least 30cm. Cassava can tolerates a wide range of soil pH 4.5 to 8.0.

Methods of cultivation

The Cassava plant is a woody plant with erect stems and spirally arranged simple lobed leaves with petioles up to 30 cm in length. Cassava mostly propagated vegetatively [stem cuttings]. A stake length of 25 to 30 cm should be beneficial and shallow planting allows producing more number of roots. Plant the setts vertically with buds pointing upward on thes Sides of ridges and furrows. Irrigated and non branched types require 75cm×75 cm (17,777 setts), semi branched and branched type requires 90×90cm (12,345 setts) for best tuber yield.

Major varieties of Cassava

There are many improved cassava varieties being cultivated in different taluks of Namakkal district. The following the important varieties among all, CO 1, CO2, CO3, Tapioca YTP 1, Mulluvadi1, H-97, Sree Apoorva, Sree Prabha , Sree Vijaya, Sree Harsha, Sree Sahya and Sree Visakham.

Irrigation Management

The famous Cauvery River flows along the Western and southern Boundaries of the district. Well irrigation is the main source of irrigation covering nearly 91% of irrigated area of the district from 78780 open wells and 5071 Bore wells. Canal irrigation which covers 8% Ground water potential of the district is very poor. In cassva crops, First irrigation is given at the time of planting. Life irrigation is given on the 3rd day followed by once in 7-10 days 3rd Month and once in 20-30 days upto 8th month.

Manuring

Applied 25t/ha FYM and incorporate at the time of ploughing. Applied 45: 90:120: kg NPK/ha as basal and 45:120 kg NK/ ha on 90 days after planting during earthing up.

Design

No.of locations per land use system : 03
No.of sites per location :03
No.of replications per site :02
Design: Stratified Random Sampling .

Sample collection

The present study was carried out the impacts of climate change on cassava. We sampled the infected leaves of Cassava Mulluvadi variety were collected and placed in plastic bag. These variety is cultivated are mostly red and black soils. Mulluvadi variety is a irrigated crops grows upto 9 to 12 months.The tuberous roots were carefully exposed, and a tuber diameter 30 - 80 mm was removed and stored in a plastic bag. Upon return to the laboratory, the samples were stored in a refrigerator (4^{o}c) until analysis the next day. Fine roots were collected from plants at the time of excavation of tuberous roots and stored in 70% ethanol for later analysis. The samples were collected from the study sites at Namakkal district and were isolated on potato dextrose agar medium and the fungal pathogens were identified. Among the fungal organisms. *A.niger*, *Fusarium* and *Rhizopus* found abundant in the selected cassava. The factors which influenced the growth of microorganisms like pH, temperature, relative Humidity and Rainfall was studied from the period 2017 to 2019 periodically. The Meterological data was compared with the percentage of infection depending upon the maximum and minimum mean temperature, rainfall of relative Humidity in all the three years of infection percentage was calculated accordingly are recorded. For this weather parameters have been collected from the Indian Meterological data, Chennai.

Data analysis

Therefore the present investigation was undertaken to find out the climatic condition in Namakkal district and three years of weather data was collected. The average annual Rainfall at Namakkal district are recorded from 2017 to 2019 minimum 4mm and maximum 222mm respectively. Average annual temperature ranged from miniumum 18.5^{o}C and maximum 38.2^{o}C. Average humidity ranged from minium 24.6% and maximum 98.4%.

RESULT AND DISCUSSIONS

From the study it shows that fungal incidence (abundance and richness like brown leaf spot, root rot disease) were clearly affected by weather showing large differences among habitats. Weather parameters differed considerably in the amount of variance explained in the richness and abundance of the habitat. As reported by several times previously, both moisture and temperature were important for fungal incidence. All the weather variables averaged over the growing season of cassava crops were positively high related to measures of fungal prevalence were reported and coincided with the works of Hardwick et al., (1998) and Timmer *et al.,(*2000). Were of the same conclusion that these data are consistent with the studies of crop plants that suggest dew duration, relative humidity and temperature are critical parameters for predicting the disease extent.

This study has been carried out on the basis effect of meteorological parameters on the high incident pathogens that affects cassava crops are *Aspergillus niger*, *Fusarium* and *Rhizopus* in the order of their disease severity and pathogenicity obtained. Multiple regression was used since we want to predict the value of a disease incidence based on the value of two or more other weather factors. In the multiple regression model equation of Y on $x_1, x_{2.....} x_k$ is given by $Y = b_0 + b_1 x_1 + b_2 x_2$. So once the multiple regression equation has been constructed. We can check the co-efficientof determination (R2) and R2 always lies between 0 and 1. It shows that climatological factors have strong

correlation with ($p<0.001$) the pathogenicity of fungi and their impact on the severely of diseases. Since the present study clearly give an idea that the fungal pathogens appear to have abiotic requirements for the growth of the many fungi which also coincides with the studies carried out by Jones (1998), Harris on *et al.,* (1994), Griffin (1994) and Colhoun (1973). They were of the opinion that it is likely that fungal pathogens would show correlations with climatic conditions that parallel those reported in this study. Various factors influence changes by the global climate (Pachaori and Reisinger,2007 and Pachauri et al.,2014) and change influence all the three major elements of disease triangle *viz.,* pathogen,host and environment (Legreve and Duveille (2010), Rosenzweig and Tubiello (2007), Ghini et al ., (2008) and Chakraborty 2011) reported that changes in temperature and extreme. Weather phenomena and significantly affected the crop growth and production by causing fungal diseases by promoting its incidence, prevalence and severity was similar with present study.

CONCLUSION

Multiple regression equation that fitted with certain weather factors was determined to predict the disease incidence in cassava crop with respect to the collected weather data from Namakkal district ie.

Y= 35.60 + 1.26 max – 3.08T min + 0.42R max + 0.61 Hmin–0.00186 rain fall for cassava.

High temperature, high relative humidity and moderate rainfall have a positive influence on the disease incidence. These results suggest the predictive equation framed confirms the influence of weather in the progression of the disease.

REFERENCES

1. Chakrobothy,S.,and Newton, A.C.2011.Climatechange, plant diseases and food security an over view. Plant pathology, 60:2-14.
2. Colhoun J: Effect of environmental factor on plant disease. Annu RevPhytopath. 1973.11: 343-363
3. Ghini,R, Harmada, E,Bettiol,W.2008. Climate change and plant disease. Scientia Agricola (Piracicaba, Brazil), 65:98–107.
4. Griffin DH, ed:Fungal physiology.NewYorkWileyLiss1994.
5. Gregory,J.Scott,Mark W.Rosegrant and Claudia Kingler (2000) Roots and Tubers in the 21st Century.Trend, Projections and policy Options.Food ,Agriculture and Environment Discussion paper 31 .InternationalFood Policy Research Institute 20033 K Street, N.W;Washington D.C.20006-1002 USA.
6. HardwickNV:Diseases Forcasting. In: The epidemiology of plant diseases (Edited by DG Jones) Boston:Kluwer Academic Publishers.1998.207–230.
7. HarrisonJG, LoweR, Williams NA: Humidity and fungal diseases of plants problems. In:Ecology of plant pathogens (Edited by : JP Bakeman, B Williamson) Walling ford CAB International 1994, 79–97.
8. JonesD: TheEpidemiologyofPlantDiseases,Boston:KluwerAcademicPublishers: 1998.
9. Legreve,A,andDuvieller,E.2010.Preventing potential diseases and pest epidemics under a changing climate, p.50-70 in M.P.Reynolds (ed.),Climate change and crop production,Wallingford,CABI.
10. Pachaori, R and Reisinger, A.(Eds.) 2007. Climate change 2007 synthesis report. The global, climatic change is expected negatively affect agriculture production.
11. Pachauri, R.K. ,Allen, M.R., Barros, V.R., Broome,J., Cramer,W., Chirst, R.,Chruch, J.A.,Clarke ,L., Dahe,Q., Dasgupta,P., Dubash, N.K, (Edenhofer,O.,Elgizouli,I.,Field,C.B., Forster,P., Friedlingstein, P., Fuglestvedt, J., Gomez–Echeverri,L., Hallegatte,S., Hergerl, G.,Howden, M.Jiang,K., JimenezCisneroz,B., Kattsov,V., Lee,H., Mach,K.J., Marotzke, J.,Mastrandrea, M.D., Meyer,L., Minx,J., Mulugetta,Y., O'Brien.K., Oppenheimer,M.,Pereira,J.J., PichsMadruga,R., Plattner, G.K., Portner,H.O., Power,S.B., Preston,B.,

Ravindranath,N.H., Reisinger,A., Riahi,K., Rusticucci,M., Scholes,R., Seyboth,K., Sokana,Y., Stavins,R., Stocker,T.F., Tschakert,P., VanVauren,D and Van Ypserl, J.P. 2014. Climate change 2014. GroupI, II and III to the fifth assessment report of the inter governmental panel on climate change. Switzerl and Geneva.

12. Rosemzweig, C, and Tubiello, F.N.2007. Adaptation and mitigation strategies in agriculture: ananalysis of potential synergies. Mitigation and adaptation. Strategies for global change, 12:855–873.
13. SharonM Talley, Phyllis DColey and ThomasA Kursar, The effects of weather on fungal abundance and richnesss among 25 communities in the inter mountain west,2002.
14. Timmer LW, Darhower HM, ZitkoSE Peever TL,Ibanez AM. Bushong PM: Environmental factors affecting the severity of Alter naria brown spot of citrus and their potential use in timing fungicide applications. Plant disease 2000.84:638-643.

Table1: Weather data at namakkal district for the year 2017

S.NO	Month	MaxTemp	MinTemp	MaxRH	MinRH	WS	RFmm	Cassava
1.	Jan	32.19	20.87	76.29	36.77	3.40	3	61
2.	Feb	24.86	19.93	70.75	27.18	2.36	NIL	52
3.	Mar	36.71	24.32	76.42	34.87	6.40	6	45
4.	Apr	39.63	27.23	70.57	30.13	3.65	12	48
5.	May	37.81	26.58	75.16	38.55	4.36	108	40
6.	Jun	36.03	26.03	75.13	40.13	6.28	27	50
7.	Jul	36.42	25.87	74.32	39.06	2.48	15	61
8.	Aug	34.58	24.34	80.52	49.19	5.23	153	76
9.	Sep	33.65	24.02	83.77	56.83	11.40	277	72
10.	Oct	32.65	23.94	84.13	59.45	9.25	142	82
11.	Nov	32.07	22.43	83.23	57.43	10.48	89	76
12.	Dec	30.84	20.01	79.55	52.19	3.25	79	70

Table 2: Weather data at Namakkal district for the year – 2018

S.NO	Month	MaxTemp	MinTemp	MaxRH	MinRH	WS	RFmm	Cassava
1.	Jan	31.55	18.39	77.65	43.58	2.5	1	77
2.	Feb	30.56	17.08	66.32	31.52	2.46	7	66
3.	Mar	36.23	22.16	74.01	32.48	3.42	13	74
4.	Apr	36.35	24.53	68.47	36.97	5.35	3	68
5.	May	36.52	24.14	83.06	52.58	6.39	78	70
6.	Jun	35.37	24.82	81.04	62.01	11.07	34	71
7.	Jul	34.99	24.05	81.58	51.01	9.61	29.7	70
8.	Aug	34.86	23.95	83.61	50.32	10.97	65.8	78
9.	Sep	34.59	23.28	87.07	52.17	5.8	166.2	80
10.	Oct	32.95	22.66	92.71	61.03	4.19	133.9	84
11.	Nov	32.10	22.40	86.10	58.40	6.40	120.5	75
12.	Dec	31.40	20.34	91.20	56.35	5.20	78	81

Table2 : Weather data at namakkal district for the year – 2019

S.NO	Month	MaxTemp	MinTemp	MaxRH	MinRH	WS	RFmm	Cassava
1.	Jan	32.10	17.79	91.55	49.06	5.61	NIL	65
2.	Feb	35.18	21.43	89.96	42.39	7.50	NIL	66
3.	Mar	37.09	23.34	84.94	37.61	7.74	NIL	55
4.	Apr	37.76	25.41	79.56	37.93	6.73	88	46
5.	May	37.70	24.53	79.67	48.77	6.64	73.2	75
6.	Jun	36.28	24.18	81.56	50.63	9.93	84.2	54
7.	Jul	35.69	24.54	79.87	47.67	13.6	6.2	70
8.	Aug	33.92	23.74	84.58	55.41	12.3	92.8	76

9.	Sep	32.68	22.98	87.01	57.05	7.04	222.6	78
10.	Oct	32.25	22.79	89.70	63.03	3.80	220.2	80
11.	Nov	31,91	21.91	91.02	65.09	3.33	95	82
12.	Dec	30.08	20.24	91.32	67.12	4.51	83.5	79

Table 4. Derivation of Co–efficient of Determination (R2) Form Prediction of Overall Incidence of Cassava Crops to the Collected Weather Data from Namakkal

Strain Name	Y formula
Cassava	35.60+1.26Tmax-3.08Tmin+0.42 Rmax+0.60Hmin-0.00186

R2=0.96,0.99+0.98 respectively $p < 0.001$
where Y is the sum fungal disease incidence.

Figure 1: Cassava root rot is caused by *Aspergillus niger*

Figure 2: Cassava brown leaf spots caused by *Cercosporidium henningsii.*

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RESEARCH ARTICLE

Anticancer Activity of Isolated Fractions from *Cardiospermum halicacabum* Methanol Leaf Extract on Human Hepatocellular Carcinoma (HepG-2) Cells

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ABSTRACT

The current work was designed to examine the anticancer activity of isolated fractions from *C. halicacabum* methanol leaf extract on human hepatocellular carcinoma (HepG-2) cells. Of the five fractions *viz*., MAF, MCF, MEF, MHF and MMF, the MMF showed highest reduction in cell viability both at 24 h and 48 h treatments. The presence of secondary metabolites in methanol-methanol fraction of *C. halicacabum* has a potential role in causing an inhibition of cell viability.

Keywords: *C. halicacabum*, Isolated Fractions, MTT, HepG-2 Cells.

INTRODUCTION

Cancer is a word that is used to consign to a number of circumstances where the body's cells start to develop and reproduce in an out of control mode. This fast growth of cancerous cells is recognized as a malignant cancer. These cells can then occupy and wipe out healthy tissue, as well as organs [1-6]. The commonness of cancer contributes considerably towards the worldwide trouble of illness [7, 8]. Hepatocellular carcinoma is the major type of primary liver cancer that is almost the same in morbidity and death. HCC is the third top cause of cancer mortalities globally. Around 745,500 citizens die of liver cancer each year [9, 10]. Conventional treatment isn't always possible to offer sufficient relief for chemotherapy and radiotherapy side effects. This might be the reason why quite a few cancer patients are looking for help from the complementary health sector [11]. Herbal remedies happens to be more and more conventional and their practice is prevalent. Authorized policy and pharmaco-vigilance relating to herbal goods are still wanting evidence to authenticate their effectual usage in liver diseases [12]. Various parts of *C.*

halicacabum are used in the conventional remedy for healing of rheumatism, lumbago, cough, hyperthermia, nervous diseases, stifness of limbs *etc.* Many pharmacological studies have been completed with various parts of *C. halicacabum* plant to display its medicinal effect. *C. halicacabum* has Anti-arthritis, anti-inflammatory, anti-pyretic, gastric ulcer, anti-hyperglycaemic, anticancer, anti-apoptotic and antioxidant activity [13-17, 3-5]. The *flavone* isolated from *C. halicacabum* was investigated for the antioxidant and hepatoprotective activity in *Wistar albino* rats [18, 19]. Isolation of anxiolytic principle from ethanolic root extract of *C. halicacabum* shows the presence of *Cardiospermin* a cyanogenic glucoside [20]. *Mucilage* has been isolated from aerial part of *C. halicacabum* and it possesses many biological activities [21]. Still there is no report on isolation of active fractions from *C. halicacabum* leaf extracts, and hence the current study was undertaken to isolate the active fractions from methanol leaf extract of *C. halicacabum* and explore its efficacy against human hepatocellular carcinoma (HepG-2) cells. This work will be helpful for the discovery of new drugs in the field of plant medicine against cancer.

MATERIALS AND METHODS

Our previous work on aqueous, chloroform and methanol extracts of *Cardiospermum halicacabum* revealed that methanol extract showed profound effect on HepG-2 cells [4]. Based on our previous studies, we selected methanol extract for isolation of active compounds.

Preparation of methanol extract

The leaves of *C. halicacabum* were separated and shade dried and compressed to powder form using mortar and pestle. Exactly 50 g of dried leaf powder was soaked in methanol in a container at room temperature (1:10 w/v) for 72 h. The extract was filtered via Whatman No 1 filter paper and the deposit was extracted at 45-55ºC under dropping pressure using vacuum rotary evaporator (ROLEX). The extract was quantified and the concentrated crude extract was further subjected to isolation of fractions [4].

Isolation of fractions from methanol extract of *C. halicacabum*

Liquid-liquid extraction was used as the method for fractionation. A thick methanol extract of the *C. halicacabum* leaf (20 g) was dissolved in double-distilled water (50 ml). The extract solution was inserted into a separating funnel, and then, hexane solvent was added with a volume ratio of 3:1 with the double distilled water (aqueous). Furthermore, it was shaken for a while until the two solutions were mixed into one phase. The mixture was allowed to remain until the aqueous phase and the hexane phase were separated into two phases. The hexane phase was collected in a beaker. This process was repeated 2 times until the hexane phase was almost clear. The fractionation was continued as mentioned above for chloroform, ethyl acetate and methanol also, by adding the respective solvent to the remaining extract in the separating funnel, (150 ml respective solvent and 50 ml of distilled water in 3:1 proportion). Then, each fraction was evaporated using a rotary evaporator and water bath until the viscous fractions of methanol-aqueous fraction (MAF), methanol-chloroform fraction (MCF), methanol-ethyl acetate fraction (MEF), methanol-hexane fraction (MHF) and methanol-methanol fraction (MMF) were obtained [22].

Anticancer activity of isolated fractions (MTT)

MTT analyse was used to measure the cell viability of HepG-2 cells by Mosmann (1983) method [23]. HepG-2 cells (1×10^4 cells/ml) were plated in 96 wells in the midst of DMEM containing 10% FBS. HepG-2 cells were incubated 24 h below 5% CO_2 and 95% O_2 at 37°C. The medium was removed, washed with PBS and new serum free medium was added and set aside in an incubator for 1 h. Following starvation, the cells were treated with MAF, MCF, MEF, MHF and MMF at different concentrations such as 1.56, 3.12, 6.25, 12.5, 25, 50 and 100 µg/ml and incubated for 24 h and 48 h. Subsequently, 5.0 mg/ml MTT dye (10 µl) was added to each wells and incubated for 4 h. Following incubation, the supernatant was aspirated and DMSO (100 µl) was added to solubilise the crystals. A micro plate reader was used to assess the OD at 570 nm for each wells. Percentage of viability was determined as follows:

$$\text{Cell viability (\%)} = \frac{\text{Optical Density of Experimental value}}{\text{Optical Density of Control value}} \times 100$$

Cytomorphological studies

The morphological changes of MAF, MCF, MEF, MHF and MMF treated HepG-2 cells were assessed. HepG-2 cells (1×10^6 cells/ml) were plated in 100 mm plates and incubated for 24 h. Then the culture media was removed, and fresh MAF, MCF, MEF, MHF and MMF (50% inhibitory concentration) were added and incubated for 48 h. Following incubation, the fixed HepG-2 cells were visualized under inverted microscope (RTC-99) at 10 X.

Statistical analysis

The data of MTT were subjected to statistical treatment and Mean and SE (Standard Error) of six individual values was calculated. The significance of the data was analyzed by Two Way ANOVA using GraphPad Prism 5. The differences were consider as significant at $p<0.001$ level.

RESULTS AND DISCUSSION

Based on our previous studies on anticancer activity and phytochemical profiling of *C. halicacabum* leaf extracts, which clearly demonstrated that methanol leaf extract have strong anticancer activity against HepG-2 cells. At 48 h of incubation, methanol leaf extract recorded an IC_{50} value of 18.04 µg/ml, followed by aqueous and chloroform extracts with per cent inhibition of 103.02 µg/ml and 32.32 µg/ml, correspondingly [4]. From the above results, methanol leaf extract of *C. halicacabum* was taken for fractionation along with its anticancer activity against human hepatocellular carcinoma (HepG-2) cells. The anticancer activity of MAF, MCF, MEF, MHF and MMF of *C. halicacabum* methanol leaf extract against HepG-2 cells for 24 and 48 h was carried out by MTT. Cell viability inhibition was observed at various concentrations (0 (untreated HepG-2 cells), 1.56, 3.12, 6.25, 12.5, 25, 50 and 100 µg/ml). The per cent cell viability was observed at 24 h and 48 h of all the five fractions. The untreated normal HepG-2 cells were 100% viable, while, MAF, MCF, MEF, MHF and MMF treated HepG-2 cells for 24 h recorded a per cent reduction of -5.408 at 1.56 µg/ml and -43.632 at 100 µg/ml concentration in MAF, -9.485 at 1.56 µg/ml and -56.629 at 100 µg/ml concentration in MCF, -4.861 at 1.56 µg/ml and -52.314 at 100 µg/ml concentration in MEF, -5.135 at 1.56 µg/ml and -47.964 at 100 µg/ml concentration in MHF and -11.358 at 1.56 µg/ml and -65.311 at 100 µg/ml concentration in MMF (Table 1 and Figure 1). On the other hand, cell viability of MAF, MCF, MEF, MHF and MMF treated HepG-2 cells for 48 h recorded a per cent reduction of -7.307 at 1.56 µg/ml and -51.754 at 100 µg/ml concentration in MAF, -16.251 at 1.56 µg/ml and -70.714 at 100 µg/ml concentration in MCF, -13.257 at 1.56 µg/ml and -65.055 at 100 µg/ml concentration in MEF, -12.186 at 1.56 µg/ml and -61.521 at 100 µg/ml concentration in MHF and -27.356 at 1.56 µg/ml and -91.049 at 100 µg/ml concentration in MMF (Table 2 and Figure 2).

In the current investigation, the incubation time and cell viability were inversely proportional. Statistical analysis of the data by Two Way ANOVA revealed that data were found to be significant. The data overall indicates that methanol-methanol fraction exhibited highest activity in causing reduction in per cent cell viability. The fifty percent inhibition of cell viability (IC_{50}) was obtained at 139.197 µg/ml in MAF, 62.884 µg/ml in MCF, 84.233 µg/ml in MEF, 112.112 µg/ml in MHF, and 31.611 µg/ml in MMF at end of 24 h incubation. Similarly, the end of 48 h Incubation, the IC_{50} value was 88.852 µg/ml in MAF, 17.196 µg/ml in MCF, 29.799 µg/ml in MEF, 46.465 µg/ml in MHF, and 9.112 µg/ml in MMF. The accurate median incubatory concentration (IC_{50}) of all the fractions for 24 h and 48 h is specified in Table 3. Thus, MMF showed superior action when compared to other fractions. The morphological observation of HepG-2 cells was carried out in 10 X amplification and presented in Figure 3. The untreated HepG-2 cells indicated intermittent blended and polygonal cell morphology. On contrary, treatment with IC_{50} concentration of MAF, MCF, MEF, MHF and MMF for 48 h brought the contraction of polygonal HepG-2 cells and made it spherical in shape as a

fiddle. The cell shrinkage expanded logically and it was dosage and time-subordinated. The rate of decrease was high in MMF than other fractions.

According to Zhi-Zhong *et al*. (2016), the five fractions of *P. niruri* 75% EtOH extract such as petroleum ether fraction, $CHCl_3$ fraction, EtOAc fraction, *n*-BuOH fraction and water fraction showed antitumor activity against SMMC7721, Bel7402, and Chang-liver (HeLa) cells [24]. Similar study of Abouelela *et al*. (2018) reported that, methanol fraction of *C. pentandra* against HepG-2 and MCF-7 cells, the IC_{50} values of methanol fraction of *C. pentandra* against the HepG-2 and MCF-7 cells were 14.895 µg/mL and 18.859 µg/mL, correspondingly [25]. The cytotoxicity assay of methanol extract from root bark and ethyl acetate fraction from stem bark of *Pseudocedrela kotschyi* exhibited noticeable anticancer effect with IC_{50} value of 87.36 µg/ml and 21.53 µg/ml on HeLa cancer cell and 101.51 µg/mL and 38.46 µg/mL on RD cell. The isolated crude saponins from *P. kotschyi* also gave the IC_{50} values of 5.28 µg/mL and 81.52 µg/mL against RD cell lines and IC_{50} values of 1.05 µg/mL and 86.8 µg/mL for MCF-7 cancer cell lines [26]. Thus the reports of the above authors support the findings of this work. Medicinal plants both from land and sea, as well as bioactive compounds isolated from them, have found usefulness in the management of several diseases, as well as cancer [27-30]. The plant secondary metabolites are off the record into four major categories as per the British Nutrition Foundation [31]. These four major groups include terpenoids (carotenoids, sterols, cardiac glycosides and plant volatiles), phenolics (lignans, phenolic acid, tannins, coumarins, lignins, stilbenes and flavonoids), nitrogen containing compounds (non-protein amino acids, cyanogenic glucosides and alkaloids) and sulphur containing compounds (GSH, GSL, phytoalexins, thionins, defensins and lectins) [32]. Several active compounds such as flavonoids, diterpenoids, triterpenoids, and alkaloids have been reported to possess anticancer activity [33, 34]. Methanol extract of *C. halicacabum* leaf showed the presence of carbohydrates, flavonoids, protein, quinines, saponins, tannins terpenoids and triterpenoids [4]. This clearly indicates that the secondary metabolites from Methanol-Methanol fraction of *C. halicacabum* have contributed to the anticancer activity.

CONCLUSION

In conclusion, the Methanol-Methanol Fraction (MMF) of *C. halicacabum* has confirmed hopeful anticancer properties against human hepatocellular carcinoma (HepG-2) cells. Increasing knowledge, promotion, and consumption of *C. halicacabum* for communal benefits are extremely encouraged. In future, isolation of pure bio active compounds is needed to find out the effectiveness of the *C. halicacabum* to serve as natural cytotoxic agent in cancer patient.

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REFERENCES

1. Gatzemeier U, Heckmayr M, Neuhauss R, Schlüter I, Pawel JV, Wagner H, *et al*. Phase II Study with Paclitaxel for the Treatment of Advanced Inoperable Non-small Cell Lung Cancer. Lung Cancer 1995; 12(2): 101-106.
2. Paridaens R, Biganzoli L, Bruning P, Klijn JGM, Gamucci T, Houston S, *et al*. Paclitaxel versus Doxorubicin as First-line Single-agent Chemotherapy for Metastatic Breast Cancer: A European Organization for Research and Treatment of Cancer Randomized Study with cross-over. J Clin Oncol 2000; 18(4): 724.
3. Rajesh S, Sivakumari K, Ashok K. *In Silico* Docking of Selected Compound from *Cardiospermum halicacabum* Linn. Leaf against Human Hepatocellular Carcinoma (HepG-2) Cell Line. Int J Comput Bioinfo In Silico Model 2016a; 5(2): 780-786.
4. Rajesh S, Sivakumari K, Ashok K, Abitha AR. Anticancer Activity of *Cardiospermum halicacabum* Leaf Extracts against Hepatocellular Carcinoma Cell Line (HepG-2). World J Pharm Sci 2016b; 5(3): 1133-1154.

5. Rajesh S, Sivakumari K, Ashok K, Abitha, AR. Anti-cancer Activity of *Cardiospermum halicacabum* Linn. Leaf Extracts against Human Breast Cancer Cell Line (MCF-7). Eur J Biomed Pharmaceu Sci 2016; 3(10): 213-222.
6. Hemalatha G, Sivakumari K, Rajesh S, Shyamala Devi K. Phytochemical Profiling, Anticancer and Apoptotic Activity of Graviola (*Annona muricata*) Fruit Extract against Human Hepatocellular Carcinoma (HepG-2) Cells. Int J Zool Appl Biosci 2020; 5(1): 32-47.
7. Kamangar F, Dorez GM, Anderson WF. Patterns of Cancer Incidence, Mortality and Prevalence across Five Continents: Defining Priorities to Reduce Cancer Disparities in Different Geographic Regions of the World J Clin Oncol 22006; 24(14): 2137-2150.
8. Weir HK, Thun MJ, Hankey BF, Ries LAG, Howe HL, Wingo PA, *et al*. Annual Report to the Nation on The Status of Cancer, 1975-2000, Featuring The Use of Surveillance Data for Cancer Prevention and Control. J Nat Cancer Inst 2003; 95(17): 1276-1299.
9. Ho C, Wang C, Mattu S, Destefanis G, Ladu S, Delogu, S. *et al*. AKT (v-akt Murine Thymoma Viral Oncogene Homolog 1) and N-Ras (Neuroblastoma Ras Viral Oncogene Homolog) Co-activation in The Mouse Liver Promotes Rapid Carcinogenesis by Way of mTOR (Mammalian Target of Rapamycin Complex 1), FOXM1 (Forkhead Box M1)/SKP2, and c-Myc Pathways. Hepatol 2012; 55: 833-845.
10. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. J Clin 2015; 65: 87-108.
11. Cassileth BR, Lusk EJ, Strouse TB, Bodenheimer BA. Contemporary, Unorthodox Treatments in Cancer Medicine: A Study of Patients, Treatments and Practitioners. Ann Intern Med 1984; 101: 105-112.
12. Rajaratnam M, Prystupa A, Lachowska-Kotowska P, Załuska W, Filip R. Herbal Medicine for Treatment and Prevention of Liver Diseases. J Pre-Clin Clin Res 2014; 8(2): 55-60.
13. Asha VV, Pushpangadan P. Antipyretic Activity of *Cardiospermum halicacabum*. Indian J Exp Biol 1999; 37: 411-414.
14. Boonmars T, Khunkitti W, Sithithaworn P. *In-vitro* Antiparasitic Activity of Extracts of *Cardiospermum halicacabum* against Third-stage Larvae of *Strongyloides stercoralis*. Parasitol Res 2005; 95: 417-419.
15. Sheeba MS, Asha VV. *Cardiospermum halicacabum* Ethanol Extract Inhibits LPS Induced COX-2, TNF-alpha and iNOS Expression, which is mediated by NF-kappa B Regulation, in RAW264.7 Cells. J Ethnopharmacol 2009; 124: 39-44.
16. Veeramani C, Pushpavalli G, Pugalendi KV. Antihyperglycaemic Effect of *Cardiospermum halicacabum* Linn. Leaf Extract on STZ-induced Diabetic Rats. J Appl Biomed 2008; 19-26.
17. Rajesh S, Sivakumari K, Ashok K. Antioxidant potential of isolated fractions from methanol leaf extract of Cardiospermum halicacabum. J Adv Sci Res 2020; 11(Suppl 5): 13-16.
18. Rupesh Kumar M, Kavitha K, Basu SK. Antioxidant and Hepatoprotective Effect of Flavanone from *Cardiospermum halicacabum* N. against Acetaminophem Induced Hepatotoxicity in Rats. J Pharm Res 2012; 5(1): 544-547.
19. Jeyadevi R, Sivasudha T. Anti-arthritic Activity of the Indian Leafy Vegetable *Cardiospermum halicacabum* in Wistar Rats and UPLC–QTOF–MS/MS Identification of the Putative Active Phenolic Components. Inflam Res 2013; 62: 115-126.
20. Kumar R, Murugananthan G, Nandakumar K, Talwar S. Isolation of Anxiolytic Principle from Ethanolic Root Extract of *Cardiospermum halicacabum*. Phytomed 2011; 18: 219-223.
21. Fatima Grace X, Latha S, Shanthi S, Seethalakshmi D, Chamundeeswari PKM. Isolation and Characterisation of *Cardiospermum halicacabum* Mucilage. Int J Green Pharm 2011; 5(4): 314-317.
22. Aranya M, Hiroyuki A, Worapong K, Toshihiro A, Worapaka M, Jiradej M. Potent Antiproliferative Effect on Liver Cancer of Medicinal Plants Selected from the Thai/Lanna Medicinal Plant Recipe Database ''MANOSROI III''. Evide-Based Compl Altern Med 2015; 1-11.
23. Mosmann T. Rapid Colorimetric Assay for Cellular Growth and Survival: Application to Proliferation and Cytotoxicity Assays. J Immunol Methods 1983; 65(2): 55-63.
24. Zhi-Zhong Z, Liang-Hua C, Shao-Song L, Yuan D, Guo-Hua Z, Yue G. *et al*. Bioguided Fraction and Isolation of the Antitumor Components from *Phyllanthus niruri* L. BioMed Res Int 2016; 1-7.

25. Abouelela ME, Orabi MAA, Abdelhamid RA, Abdelkader MSA, Darwish FMM. Chemical and Cytotoxic Investigation of Non-Polar Extract from *Ceiba Pentandra* (L.) Gaertn: A Study Supported by Computer Based Screening. J Appl Pharmaceu Sci 2018; 8(7): 057-064.
26. Taiwo OE, Abolaji AA, Jone OM. Cytotoxicity Studies of the Extracts, Fractions, and Isolated Compound of *Pseudocedrela kotschyi* on Cervical Cancer (HeLa), Breast Cancer (MCF-7) and Skeletal Muscle Cancer (RD) Cells. Pharmacogn Res 2017; 9(1): 46-50.
27. Ayyad SE, Ezmirly ST, Basaif SA, Alarif WM, Badria AF, Badria FA. Antioxidant, Cytotoxic, Antitumor, and Protective DNA Damage Metabolites from the Red Sea Brown Alga *Sargassum* sp. Pharmacogn Res 2011; 3(3): 160-165.
28. Khanavi M, Gheidarloo R, Sadati N, Ardekani MR, Nabavi SM, Tavajohi S. Cytotoxicity of Fucosterol Containing Fraction of Marine Algae Against Breast and Colon Carcinoma Cell Line. Pharmacogn Mag 2012; 8: 60-64.
29. Jayaprakash P, Sivakumari K, Ashok K, Rajesh S. Designing siRNA for Silencing Polo-like Kinase 1 (PLK1) Gene of Prostate Cancer. IJCERT 2017; 4(2): 25-32.
30. Mohamad Sitheek A, Sivakumari K, Rajesh S, Ashok K. Anti-proliferative effect of durian fruit (*Durio zibethinus*) against HL-60 cells and its phytochemical analysis. J Adv Sci Res 2020; 11(Suppl 5): 174-181.
31. Goldberg G. Plants: Diet and health. The report of a British nutrition foundation task force. Oxford Ames Iowa Blackwell Science for the British Nutrition Foundation 2003; 347.
32. Mazid M, Khan TA, Mohammad F. Role of Secondary Metabolites in Defence Mechanisms of Plants. Biol Med 2011; 3(2): 232-249.
33. Adebayo AH, Tan NH, Akindahunsi AA, Zeng GZ, Zhang YM. Anticancer and Antiradical Scavenging Activity of *Ageratum conyzoides* L. (Asteraceae). Pharmacogn Mag 2010; 6: 62-66.
34. Chahar MK, Sharma N, Dobhal MP, Joshi YC. Flavonoids: A Versatile Source of Anticancer Drugs. Pharmacogn Rev 2011; 5(9): 1-12.

Table 1: Per cent cell viability of HepG-2 cells for 24 h when treated with various fractions

Concentration	MAF	MCF	MEF	MHF	MMF
Control	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00
1.56 µg/ml	94.59 ± 0.66* (-5.408)	90.52 ± 0.77* (-9.485)	95.14 ± 0.92* (-4.861)	94.87 ± 0.75* (-5.135)	88.64 ± 1.04* (-11.358)
3.12 µg/ml	90.26 ± 0.90* (-9.740)	82.14 ± 1.36* (-17.857)	84.84 ± 1.19* (-15.161)	89.71 ± 0.64* (-10.287)	77.53 ± 1.05* (-22.473)
6.25 µg/ml	84.83 ± 0.31* (-15.174)	73.98 ± 0.45* (-26.020)	75.89 ± 0.88* (-24.103)	85.10 ± 0.61* (-14.897)	69.92 ± 0.45* (-30.075)
12.5 µg/ml	78.05 ± 0.36* (-21.952)	66.12 ± 0.79* (-33.878)	67.49 ± 1.13* (-32.512)	75.61 ± 0.57* (-24.389)	60.98 ± 0.74* (-39.017)
25 µg/ml	71.30 ± 1.02* (-28.705)	58.01 ± 0.70* (-41.992)	60.18 ± 0.75* (-39.824)	67.77 ± 1.01* (-32.230)	52.58 ± 0.75* (-47.418)
50 µg/ml	64.49 ± 0.57* (-35.509)	52.31 ± 0.32* (-47.699)	55.02 ± 0.62* (-44.976)	60.44 ± 0.55* (-39.559)	42.82 ± 0.61* (-57.184)
100 µg/ml	56.37 ± 0.61* (-43.632)	43.37 ± 0.98* (-56.629)	47.69 ± 0.45* (-52.314)	52.04 ± 0.59* (-47.964)	34.69 ± 0.67* (-65.311)

Values are mean ± S.E. of six individual observations.
Values in parentheses are per cent change over control.
- Denotes per cent decrease over control.
* Denotes that values are significant at $p < 0.001$.

Table 2: Per cent cell viability of HepG-2 cells for 48 h when treated with various fractions

Concentration	MAF	MCF	MEF	MHF	MMF
Control	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00
1.56 µg/ml	92.69 ± 0.90* (-7.307)	83.75 ± 0.79* (-16.251)	86.74 ± 1.17* (-13.257)	87.81 ± 0.99* (-12.186)	72.64 ± 0.87* (-27.356)
3.12 µg/ml	88.09 ± 0.84* (-11.904)	71.82 ± 0.76* (-28.179)	73.99 ± 0.68* (-26.012)	79.95 ± 0.76* (-20.049)	62.89 ± 1.19* (-37.113)
6.25 µg/ml	80.24 ± 0.96* (-19.762)	62.89 ± 1.01* (-37.100)	66.93 ± 0.83* (-33.067)	73.44 ± 0.30* (-26.558)	54.47 ± 0.58* (-45.531)
12.5 µg/ml	72.63 ± 0.61* (-27.369)	52.84 ± 0.58* (-47.157)	57.73 ± 0.81* (-42.266)	67.51 ± 1.01* (-32.495)	44.71 ± 0.59* (-55.289)
25 µg/ml	64.24 ± 0.87* (-35.756)	45.28 ± 0.71* (-54.725)	51.51 ± 0.89* (-48.489)	59.07 ± 0.39* (-40.929)	33.33 ± 1.22* (-66.668)
50 µg/ml	56.11 ± 0.85* (-43.887)	38.75 ± 0.44* (-61.247)	43.64 ± 0.84* (-56.359)	48.51 ± 0.89* (-51.494)	21.96 ± 0.72* (-78.043)
100 µg/ml	48.25 ± 0.86* (-51.754)	29.29 ± 0.73* (-70.714)	34.95 ± 0.88* (-65.055)	38.48 ± 0.45* (-61.521)	8.95 ± 0.58* (-91.049)

Values are mean ± S.E. of six individual observations.
Values in parentheses are per cent change over control.
- Denotes per cent decrease over control.
* Denotes that values are significant at $p < 0.001$.

Table 3: IC_{50} values of various fractions against HepG-2 cells

Fraction	Time	
	24 h	48 h
Methanol-Aqueous (MAF)	139.197 µg/ml	88.852 µg/ml
Methanol-Chloroform (MCF)	62.884 µg/ml	17.196 µg/ml
Methanol-Ethyl acetate (MEF)	84.233 µg/ml	29.799 µg/ml
Methanol-Hexane (MHF)	112.112 µg/ml	46.465 µg/ml
Methanol-Methanol (MMF)	31.611 µg/ml	9.112 µg/ml

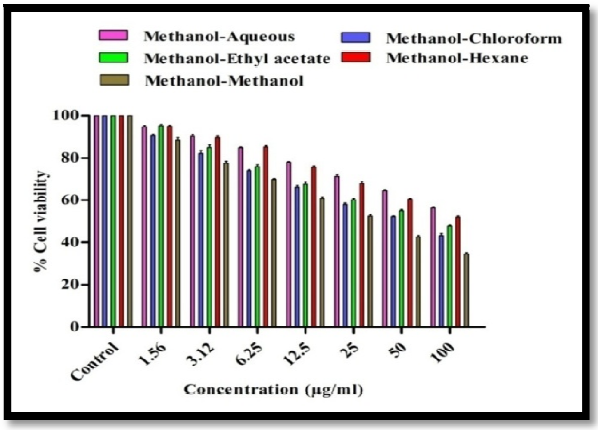

Figure. 1: Per cent cell viability of Hep-G2 cells for 24 h when treated with various fractions

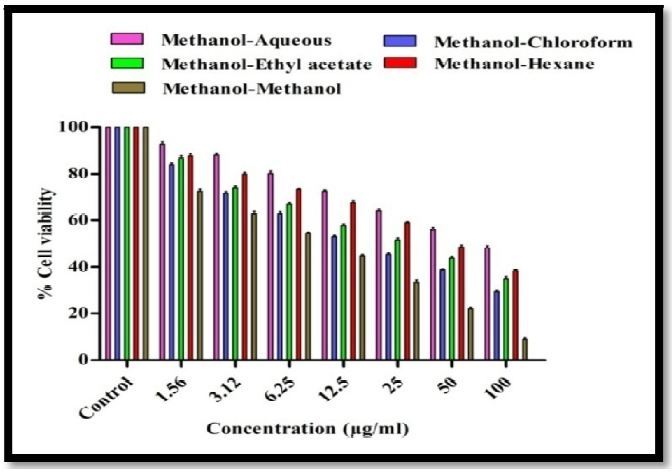

Figure. 2: Per cent cell viability of Hep-G2 cells for 48 h when treated with various fractions

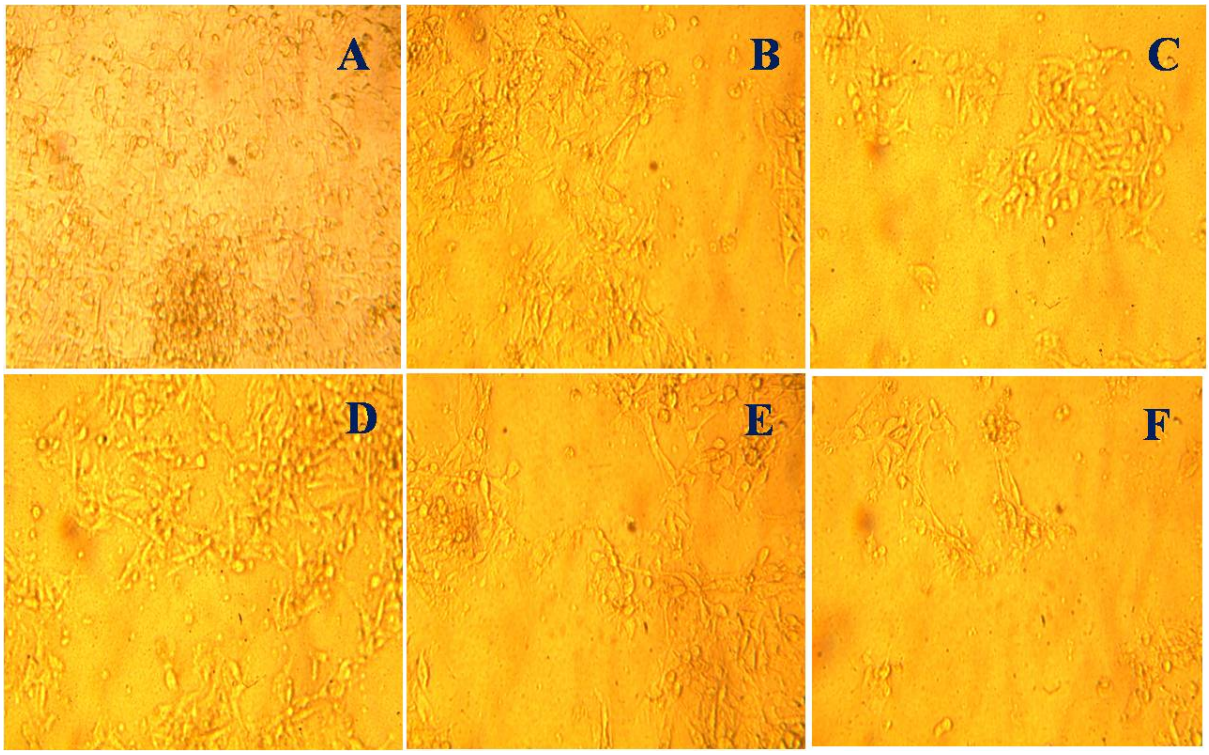

Figure. 3: Cytomorphology of HepG-2 cells when treated with IC_{50} concentrations of various fractions of *C. halicacabum* at 10 X magnification. ((A) Control, (B) Methanol-Aqueous, (C) Methanol-Chloroform, (D) Methanol-Ethyl acetate, (E) Methanol-Hexane, and (F) Methanol-Methanol).

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RESEARCH ARTICLE

Contemplating the Conceptualization of Mental Toughness

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ABSTRACT

The study is an attempt to understand the concept of mental toughness in relation to sports and in general. To do this, the study will explore diverse ideas, conceptualizations, and interpretations of mental toughness across various disciplines. The study will be exhaustive neither establish a specific approach to reach a common research consensus. Instead, it will strive to reveal the complexity that surrounds the notion of mental toughness. The proliferation of peer-reviewed articles and various literature on mental toughness met the eligibility criteria for inclusion in review and textual analysis is done in study. The study reveals the lack of idea clarity of mental toughness and how its basic precepts have been underexplored. The finding of this study supports the concept of clarity of mental toughness and provides future directions for research.

Keywords: Mental Toughness, Sports, Personality Attributes, Competition, Performance etc.

INTRODUCTION

Personality is a spiritual integrity that brings together the traits of a sports person. This emphasizes the individual physical structure and psychological orientation such as intelligence, mental sturdiness, emotions, reactions, information and values of a person (Adasal, 1979). The wholesome attribution of personality is very important for performance in sports competitions and in general to lose or win the game. Different things and abilities affect competitions. The winning ones are generally at a higher level of mental skills (Weinburg and Gould, 2015). The abled people are brought to an efficient level by the coordination of different mental elements that are required for an activity. Many psychological elements are important factors to determine the success and failure in general and in sports up to a great extent.

Mental toughness is one of the most used but underexplored terms in sports psychology (Graham, Hanton and Cannaughton, 2002). In the available literature, various things associated with the concept of mental toughness and performance is gained (Gibson, 1998; Goldberg, 1998). Loehr (1982) stated in a study that robust athletes are having innumerable behavior which constructs them emotionally strong and stable. There are two skills from this point of view is firstly the efficient use of energy in a crisis context and secondly to think sensibly about pressures, problems and appropriate behavior in the situation of competition. However, mental durability can be defined as a personal character as well as a mental state (Kroll, 1967; Gibson, 1998). According to Cattell (1957), mental toughness emerges as a hard, mature, realistic, independent and timid behavioral dimension. Gibson (1998) contends that mental sturdiness pertains to self-efficacy and inner control focus.

The attention towards expertise mental sturdiness over the past decade has gathered instructional movement. Scholastics have developed the research from exceptional perspectives initiated by the means of the basic inquiry, “What is this called as mental toughness?” (Jones et al., 2002). There is little need to survey this group of information here, as extensive reviews exist both within this volume and elsewhere (Crust, 2008; Gucciardi et al., 2009; Connaughton et al., 2008).However, this section returns to the fundamental inquiry that “What is mental toughness?” and the argument that scholastics appear to have adopted a genuinely nearsighted way to deal with the use of reasonable research practices. Diverse individuals simplify mental toughness relying upon their own understanding and connections inside their own social world. In this manner, the expression "mental toughness" may mean something other than what's expected to various individuals (reliant upon age gatherings, sex, societies) and is apparently translated distinctively inside various situational conditions (for example sports execution, managing difficulty, career destruction, being disabled or lasting sadness).

Statement of the Problem

The role of this work was to visualize diverse notions of mental toughness. The reason for this examination was to review the quantitative writing on mental toughness in relation to competitive standards, accomplishment level, and execution (competitive and non-competitive) in sport and in general. The current research tried to detect the variety inthe concept of mental toughness for various individuals across different sporting and non-sportingsettingsin the world..

METHOD

Research Model

The study was a textual analysis of the conceptualization of mental toughness. It was a mixed method research aiming to define typical and existing concepts without the intervention of researcher and to make a conclusion about the diverse clarification of the notion of mental toughness.

What is Mental Toughness?

Mental toughness has the psychological edge that enables one to perform at peak most effort and potency throughout the stress that is placed on them throughout practice, training, or competition. In particular, when the demands are most prominent or the conditions are unfriendly. At whatever point the demands are the greatest is when the characteristics of mental toughness are the most obvious. A portion of the numerous qualities that are apparent when a player or an individual is mentally tough to include self-confidence, focus, self-motivation, calmness, composure, concentration, self-control, determination, poise, persistent, positive energy, and leadership.

This doesn't imply that the result is dependably a success, in many cases these properties can show up the most within a hardship, particularly a nearby loss to an intense rival or unfavorable conditions. Yet, after some time and with cautious preparing, the mental toughness of gifted players becomes known in titles won.

What is Mental Toughness in General?

Studies have revealed that the same phenomena can be seen jointly, even when looking at groups of people or even large organizations. However, the advantages of mental durability don't finish with performance alone. Individuals with great mental toughness are unmistakably bound to exhibit positive conduct. They create positive characteristics and an inspirational point of view. Rather than leaving an issue, they are bound to confront it and manage it in a positive way. Individuals with great mental quality quite often get the opportunity to enjoy a greater feeling of prosperity.

Studies have demonstrated a connection between mental strength and individual aspirations. Individuals with great mental toughness will, in general, be more goal-oriented than individuals who lack mental toughness. They seek to be superior to anything they at present are; they need advancements and they realize they can get them. Mental toughness is something which can be created, as can mental and passionate flexibility.

What is Mental Toughness in Sports?

Inside the sports, the word mental toughness is utilized by numerous coaches, players, and sports psychologists, and recently investigators have attempted to describe and understand the idea (Thelwell, Weston and Greenlees, 2005). Fourie and Potgieter (2001) were the first to recognize mental attributes which individuals viewed in relation to the idea of mental toughness in sport. A study was conducted on the 160 elite sportspersons and 131 expertise coaches from 31 individual and team sports (Gordon & Dimmock, Gucciardi, 2009). Participants content data was analyzed of written responses and came to the result that there were 12 main elements of mental toughness such as team unity, competitiveness, coping skills, preparation skills, motivation level, cognitive skills, confidence maintenance, physical and mental possession requirements, discipline and goal-directedness, mental hardiness, religious and ethical convictions (Gucciardi, Gordon et al., 2009).

A study conducted by Jones, Hanton et al., (2002) set out to explore the idea of mental toughness by concentrating on what fundamental attributes are required to become a mentally strong performer. Accordingly Jones et al., (2002), the academics selected 10 international players who participated in a focus group, interviews, and a rank order task. In this way, the exploration of the term mental toughness was characterized as:
Mental toughness is having the normal or created psychological edge that allows you to:

- In particular, be more steady and superior to anything your competitors in staying determined, concentrated, confident, and in control under a stressful situation.
- Generally, overcome your opponents with the varied requirements such as a way of life, training, and competition that sport puts on the performer.

Why Mental Toughness is important in Sports?

With regards to sports, having mental toughness is completely as imperative for players as physical fitness. It has been instituted that to bring a gold medal, mental toughness is an essential ingredient for any athlete. But what exactly is mental toughness. On the other hand, sports psychologist stat mental toughness as “the capacity to reliably perform toward the upper scope of your ability and skill by paying little attention to competition situations”. With a developing field of sports psychological study, more competitors are hoping to improve their psychological ability just as their physical exercise routines. There's a meager line that exists between intellectual strong sporting victory and in pressure failure. Some extraordinary athletes with mental toughness performing to the best of an individual athletes with high aspirations such as Michael Jordan, who has hit numerous match winning shots under the high pressure circumstances. These competitors couldn't perform at this dimension constantly without mental toughness. Point of fact, mental sturdiness is essential for competitors to accomplish the most ideal outcomes with regards to sports. In these instants, competitors must have the drive and inspiration to push through testing and pressure moments and proceed to progress.

“Try not to focus on Finishing. Concentrate on Finishing Well”

While investigating the insights of mental toughness, note that competitors shouldn't simply figure out how to keep making an uncommitted effort. Competitors need to stay similarly as connected and concentrated on carrying an excellent act in desperate circumstances. Regardless of whether somebody is dashing with time as the opponent or going up against different competitors, this sturdiness ought to enable the competitor to stay aggressive and at the front of the game, not only a nearness on the field.

Historical Perspective of Mental Toughness

The logical investigation of mental toughness, which has its developmental roots in identity search on "tough-mindedness" going back to the1950s, has gathered an empirical measure in recent years. Before this flow of research advancement, quite a bit of what was thought about mental toughness depended on circumstantial reports and scattered large through the media. The outcome was a various choice of definitions and clarifications of mental toughness up to a great extent incorporated a combination of helpful mental attributes (for example heartlessness to analysis) and mental abilities (for example excitement direction, perception).The theoretical misunderstanding made from this absence of consistency and comprehension brought about various helpful mental attributes being incorrectly named as mental toughness, especially as they depended on author's opinion somewhat to exact research. Encouragingly, empirical research on mental toughness has bloomed in the course of the recent decade, with autonomous but related streams of research concentrated on its conceptualization, valuation, and development.
The endeavor to define mental toughness was proposed by Raymond Cattell who recommended that it was a personality characteristic (Cattell, 1957). The idea of extreme mindedness was identified by Cattell, (1957) as one of the 16 essential source attributes which were estimated by his 16 personality factor inventory (16PF). The 16PF has been broadly utilized in psychological research, be that as it may, it has not been utilized in a game to quantify mental strength. Cattell (1957) visualized tough-mindedness as an essential trait which was a part of personality and numerous researchers followed toward this path (Kroll, 1967). In any case, it may be contended that this research isn't grounded in sound logical theory and more recently analysts have been arguing that it is important to understand mental toughness from a theoretical point of view (Clough and Earle, 2002).

Is Being Mentally Tough Always a Good Thing?

Mental toughness plays a significant role to be successful in strain circumstances whether it is in the field of sports or various areas of life. Mental toughness conquers self-doubt by reframing negative self-talk when the ambition is to compete. It insists on the goal with increased confidence. Mental toughness keeps an individual or an athlete a highly driven by sticking towards ambition and allows to tune out the unhelpful advice or criticism nearby and try to keep focused on making efficient decisions regardless of the feedback received nearby. Learning is ensured by mental strength that are the outcomes of mistakes by accepting responsibility for actions that assists in reaching closer towards the aim. Stepping outside from comfort zone is quite difficult and in this situation, mental toughness provides courage to face fears head-on with increasing discomfort tolerance that thrusts to move forward-facing despite distress. Generally, peoples with adequate self-worth or mental sturdiness are able to tolerate frequent failure without fear of ridicule. The all is the mental strength which is very helpful in regulating the emotions of an individual in general or in sports. The path to success is filled with high and low emotions up to a great extent and in the area mental toughness is the key to restraint the emotions as it develops resilience to life's inevitable obstacles or adverse circumstances. Mental toughness allows overcoming setbacks with confidence in life.

DISCUSSION AND CONCLUSION

Mental toughness is the umbrella term frequently utilized to define one's ability to deal viably with both significant ambushes on one's ordinary level of working and "consistently" challenges in the quest of high performance. Although certain studies have examined this common supposition, research in this space has, however, to be synthesized. After a review of the literature, the term mental toughness is very specific in nature but very broad in attributions related to it. It can be said that mental toughness is having developed psychological traits through varied

life experiences that enables an individual to be more consistent, determined, focused, confident, and in control under pressure. It can create the distinction between a victory and a defeat. Mental toughness allows an individual, on and off the field to be an extraordinary by his/her developed psychological capabilities that leads them to participate in an efficient and effective manner by optimizing their potentialities to a higher level of performance.

However there have been many studies focusing on trying to outline mental toughness, more work needs to be conducted due to variances in peoples understanding of the notion. Research needs to concentrate on attempting to outline mental toughness which is grounded in important theories. It should be known whether mental toughness is best concentrated from a sports general point of view or a sport specific viewpoint. As well as, more research needs to be conducted around the observational analysis of mental toughness behaviors so that sports psychologists can intervene and identify how to improve mental toughness (Crust, 2007). Future research could take a look at the connection between individual's cognitions and mental toughness (Crust, 2007). For instance, do mentally intense competitors show progressively positive self-talk in contrast with less mentally tough competitors. Most investigations concentrating on mental sturdiness have needed methodological variety and along these longitudinal examinations may profit analysts who are endeavoring to contemplate mental toughness. By focusing on developing this future research, this could help to build programs which will develop more mentally tough athletes for the future.

Even though ongoing headways in its conceptualization, estimation, and improvement are critical, mental toughness, as an insightful field of investigation, is still in its early stages when contrasted and crafted by literature on its key parts. Overall mental toughness is a significant domain within a sport, however much of the research which has been conducted is based on personal opinion rather than sound empirical research. Future researchers face the difficulties of investigating mental toughness in a more extensive context and more consideration is expected to take a look at how mentally intense people perform in all aspects of their life.

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Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

1. Jones, G., Hanton, S., & Connaughton, D. (2007). A framework of mental toughness in the world's best performers. *The Sport Psychologist*, *21*(2), 243-264.
2. Horsburgh, V. A., Schermer, J. A., Veselka, L., & Vernon, P. A. (2009). A behavioural genetic study of mental toughness and personality. *Personality and individual differeces*, *46*(2),100-105.
3. Golby, J., Sheard, M., & Lavallee, D. (2003). A cognitive-behavioural analysis of mental toughness innational rugby league football teams. *Perceptual and Motor skills*, *96*, 455- 462.
4. Malhotra, N., & Kaur, R. (2017). Mental Toughness in Relation with Mental Health of Sports Persons. *American Journal of Sports Science*, *5*(5), 31-34.
5. Singha, A. (2018). Effects of Yogic Practices on Mental Health and Mental Toughness Among Sports Persons. *International Journal of Adapted Physical Education & Yoga*, *3*(10), 1-7.

6. Lowe, L. M. (2018). *How do Adolescent Elite Athletes Adaptively Use Fear of Failure to Motivate Success?* (Doctoral dissertation, The Wright Institute).
7. Meggs, J., & Chen, M. A. (2018). Mental toughness and attributions of failure in high performing male and female swimmers.
8. Gucciardi, D. F. (2017). Mental toughness: progress and prospects. *Current Opinion in Psychology*, *16*,17-23.
9. Kazım, N. A. S., & Temel, V. (2018). Mental Toughness on athletes: The Interaction of the sports Type, Gender and Age. *The Journal of International Anatolia Sport Science*, *3*(2), 305-311.
10. Madrigal, L., Hamill, S. & Gill, D.L. (2013). Mind over matter: The development of the Mental Toughness Scale (MTS). *The Sport Psychologist*, *27*(1), 62-77.
11. Golby, J., & Sheard, M. (2004). Mental toughness and hardiness at different levels of rugby league. *Personality and Individual Differences, 37, 933-942.*
12. Jones, J. G., Hanton, S., & Connaughton, D. (2002). What is this thing called mental toughness? An investigation of elite performers. *Journal of Applied Sport Psychology, 14,* 205–218.
13. Connaughton, D., Hanton, S., & Jones, G. (2010). The development and maintenance of mental toughness in the world's best performers. *The Sport Psychologist*, *24*(2), 168-193.
14. Bull, S. J., Shambrook, C. J., James, W., & Brooks, J. E. (2005). Towards an understanding of mental toughness in elite English cricketers. *Journal of applied sport psychology*, *17*(3), 209-227.
15. Cowden, R. G., Crust, L., Jackman, P. C., & Duckett, T. R. (2019). Perfectionism and motivation in sport: The mediating role of mental toughness. *South African Journal of Science*, *115*(12), 57-63.
16. Akpinar, S., & Akpinar, Ö. (2018). The Relationship with the Personality and Mental Toughness at thletes. *Journal of International Social Research*, *11*(61).
17. Bull, S. J., Shambrook, C. J., James, W., & Brooks, J. E. (2005). Towards an understanding of mental toughness in elite English cricketers. *Journal of applied sport psychology*, *17*(3), 209-227.
18. Stamatis, A., & Papadakis, Z. (2018). What a Difference a Mentally-Toughening Off-Season Makes: A Case of NCAA DI Rowers.
19. Jones, G. (2002). What is this thing called mental toughness? An investigation of elite sport performers. *Journal of applied sport psychology*, *14*(3), 205-218.