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SYNTHESIS CHARACTERIZATION AND ANTIMICROBIAL STUDIES ON NITROGEN AND OXYGEN-BASED BI DENTATE MANNICH BASE LIGAND OF TRANSITION METAL COMPLEXES

A. M. Anusuya * and B. S. Krishna

Department of Chemistry, Sapthagiri College of Engineering Affiliated to Visveswaraya Technological University, Bangalore - 560057, Karnataka, India.

Keywords:

Heterocyclic molecules melt condensation, Mannich base, Transition metals, and antimicrobial activities

Correspondence to Author:
A. M. Anusuya

Assistant Professor, Department of Chemistry, 14/5, Chikkasandra, Hesaraghatta main Road, Sapthagiri College of Engineering Affiliated to Visveswaraya Technological University, Bangalore - 560057, Karnataka, India.

E-mail: anujathin11@gmail.com

ABSTRACT: 1-{3-[2, 3dihydro-1H-imidazol-1-yl (8-hydroxyquinolin-7-yl) methyl] phenyl-l} ethanon, nitrogen and oxygen-based bi-dentate mannich base heterocyclic ligand synthesized and complexed with biologically significant transition metals like copper, cobalt, nickel, and zinc by the melt condensation three-component one-pot synthesis. All the synthesized potential compounds characterized by spectral methods by using NMR, IR, UV-visible mass, and elemental analysis. The antimicrobial analysis investigated for all the synthesized compounds using some bacterial and fungal cultures used by the disc diffusion method, and the activity proved in proportion with the standard drugs used as a reference. The main significant part of the work involved in mannich base reaction of one-pot synthesis three-component reactions prove better synthetic procedure and improved product yield. The ligand and the complexes of transition metals proved better microbial activities of biologically important and to prove the efficiency of the present work. Continuation of research work is to investigate significant heterocyclic molecules and transition metal complexes to prove potential microbial activities play an important role in pharmaceutical and biological applications.

INTRODUCTION: The innovative drug discovery and efficiency of biological activity is the interest of the pharmacological era, so there is great importance for the synthesis of structurally and quantitatively significant drug molecules. Transition metals exhibit variable oxidation state, and such properties possess therapeutic value in the field of medicinal chemistry [1-2]. The coordination behavior of the structurally derived compounds mainly depends on the multi chelating and complexation behavior such a potential biological molecule prepared by the process of mannich base reaction, which gives significant molecules of biological interest [3-4].

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The hydroxy Quinoline which has potential chelating properties complexes with many of metal ions on protonation of hydroxyl group and the Quinoline nitrogen coordinate to form bi liganding sites such two molecules of 8-hydroxy Quinoline molecule to form tetradentate complexes with transition metal ions to respond to bacterial and fungal action to be used in the treatment of bacterial and fungal infectious deceases is the important part of this research work studied with the use of various bacterial and fungal culture uses with the disc diffusion method [5-8]. The benzene ring fused with 4, 5 positions of imidazole is called as benzimidazole. Benzimidazole is sparingly soluble in water but more soluble in organic solvents, the basic nature of pyridine nitrogen makes to accept hydrogen [9]. Many substituted benzimidazole structures are the source of natural compounds like vitamin B12, and such compounds are of biologically active compounds against bacteria, fungi and viruses.

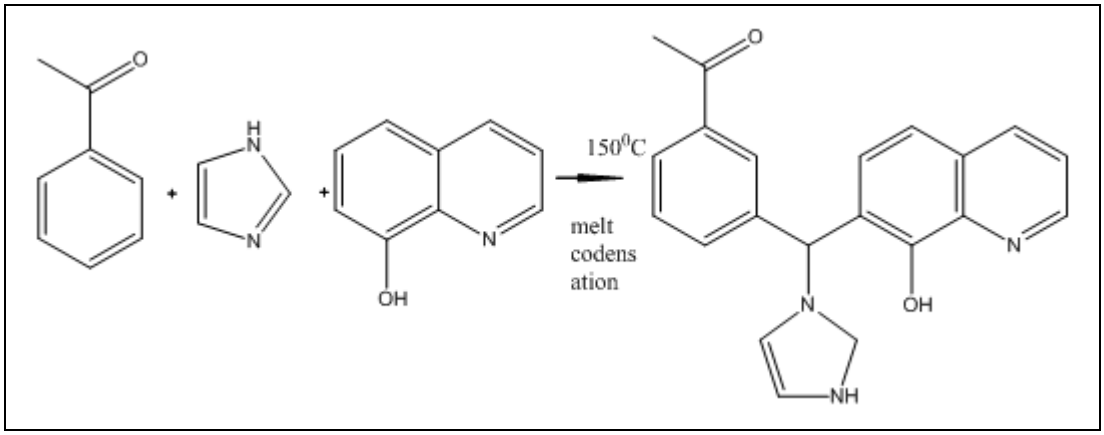
Benzimidazole has amphoteric behavior by loss or gain of proton [10]. Due to the diverse range of biological, analytical, and industrial application, mannich base coordination chemistry plays a very important role for Pharmacists and industrialists [11]. Nitrogen-containing heterocyclic compounds are the important class of chemotherapeutic and biologically active compounds for various bacterial and fungal microorganisms [12-13].

EXPERIMENTAL:

Materials and Methods: All the chemicals and solvents used were AR grade. The micro elemental analyses were performed using a caroler 1108 CHN analyzer. Metals were estimated by conventional wet chemical analysis. FT-IR spectral measurements were made with a Bruker FTIR spectrometer as KBr pellets. Mass spectra were recorded using Maldi Mass spectrometer IISER Pune. 1H NMR-600MHZ Using DMSO d6 as a solvent.

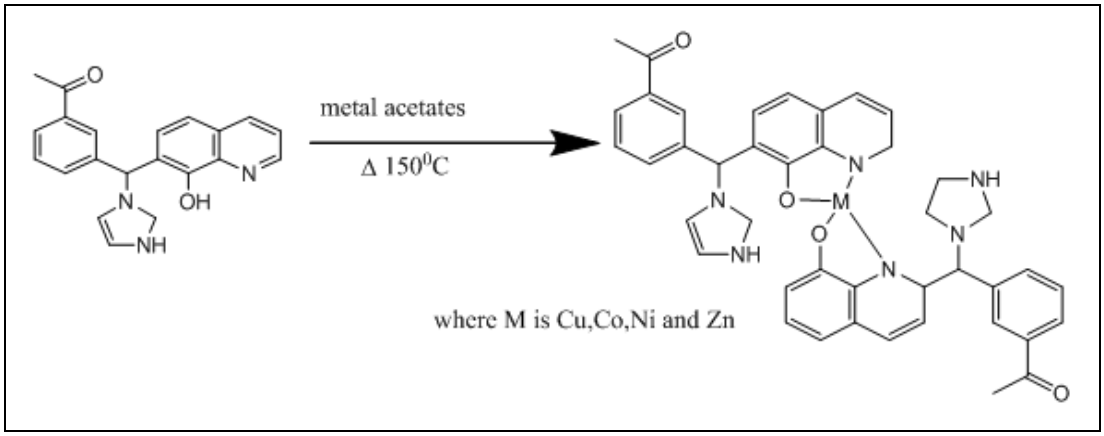
General Procedure:

Synthesis of ligand: 1-{3-[2, 3dihydro-1H-imidazol-1-yl (8-hydroxyquinolin-7-yl) methyl] phenyl-l} ethanone: Equimolar amount of benzaldehyde (1.061 g), imidazole (0.6807 g) and 8-hydroxyquinoline (1.45g) weighed and subjected for melt condensation at the different duration of 12 h, 15 h, 22 h and 24 h the product formed were confirmed by using thin-layer chromatography and finally the product recrystallized using ethanol repeatedly and washed with acetone. The synthesized mannich base and transition metal complexes analyzed by physical and spectral methods like NMR, UV-Visible, mass spectra, and elemental analysis [14-19].



SCHEME-1: 1-{3-[2,3-DIHYDRO-1H-IMIDAZOL-1-YL(8-HYDROXYQUINOLIN-7-YL)METHYL]PHENYL}ETHANONE

Preparation of Metal Complexes of Ligand: To the stirred solution of prepared mannich base ligand equivalent amount of 0.5 g of copper, cobalt, nickel, and zinc acetate added dropwise and allowed to mixed at the room temperature for 1 h followed by refluxing over a period of 5 h. The precipitate formation observed and confirmed by thin-layer chromatography and repeatedly washed with acetone and water and dried, the expected yield calculated as 80-90% [20-23].



SCHEME 2: SYNTHESIS OF COPPER, COBALT, NICKEL AND ZINC COMPLEXES OF THE LIGAND

RESULTS AND DISCUSSION:

Spectral Characterisation of Ligand:

1-{3-[2, 3dihydro-1H-imidazol-1-yl (8-hydroxy-quinolin-7-yl) methyl] phenyl} ethanone: IRKBr, 3347 cm^{-1} (C=N), 825 cm^{-1} (NH), 783 cm^{-1} (C-N). NMR (600 MHz, DMSO-$d_6$ppm): 9.58 (s, OH), 8.16 (N=C), 6.26 (aromatic CH), 7.18-7.29 (aromatic Hs). Mass: m/z, 345.15 (100%), 346.15 (23.0%), 347.15 (3.1%), 346.14 (1.1%). UV-Visible: 330 nmn-Π*, m/z: 345.15 (100%), 346.15 (23.0%), 347.15 (3.1%), 346.14 (1.1%).

Spectral Characterisation of Complexes of Copper, Cobalt Nickel and Zinc Complexes of Ligand: [24, 25]

Cu-L Complex: 1705.18 cm^{-1} (C=O), 1570.54 cm^{-1} (aromatic CH), 1498 cm^{-1} (C=N), 1446.67 cm^{-1} (C=C), 711.12 cm^{-1} (M-N), 824.08 cm^{-1} (M-O). H-NMR, 500 MHZ DMSO(d6): 10.01 (s, Aromatic CH or aldehyde group), 9.58 (Phenolic OH), 8.16 (S, NH imidazole), 6.26 (s, carbonyl proton), 8.12, 8.06, 8.01 (aromatic H), 5.08-5.20 (aliphatic proton). UV-Visible; 330 nm Π-Π*. m/z, 753.23 (100.0%), 754.23 (46.0%), 755.22 (44.6%), 756.23 (21.1%), 755.23 (12.2%), 757.23 (5.0%) 754.22 (2.2%) 756.24 (1.5%).

Co-LComplex: IR KBr cm^{-1}, 2888.34 cm^{-1} (aromatic NH), 1610.11 cm^{-1} (aromatic C=O), 785 (aromatic C=C) 1366.72 cm^{-1} (M-O), 787 cm^{-1} (M-N). UV-visible- 313 nm Π-Π*. m/z, 749.23 (100.0%), 750.23 (48.2%), 751.24 (10.3%), 752.24 (1.9%), 751.23 (1.8%).

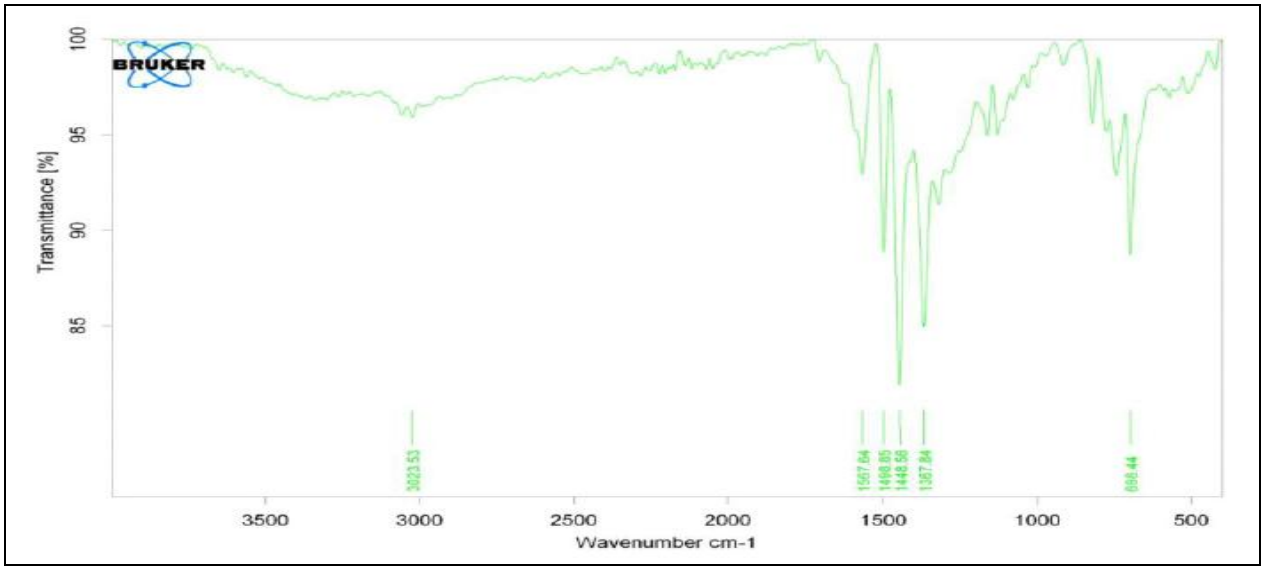


FIG. 1: IR SPECTRA OF LIGAND

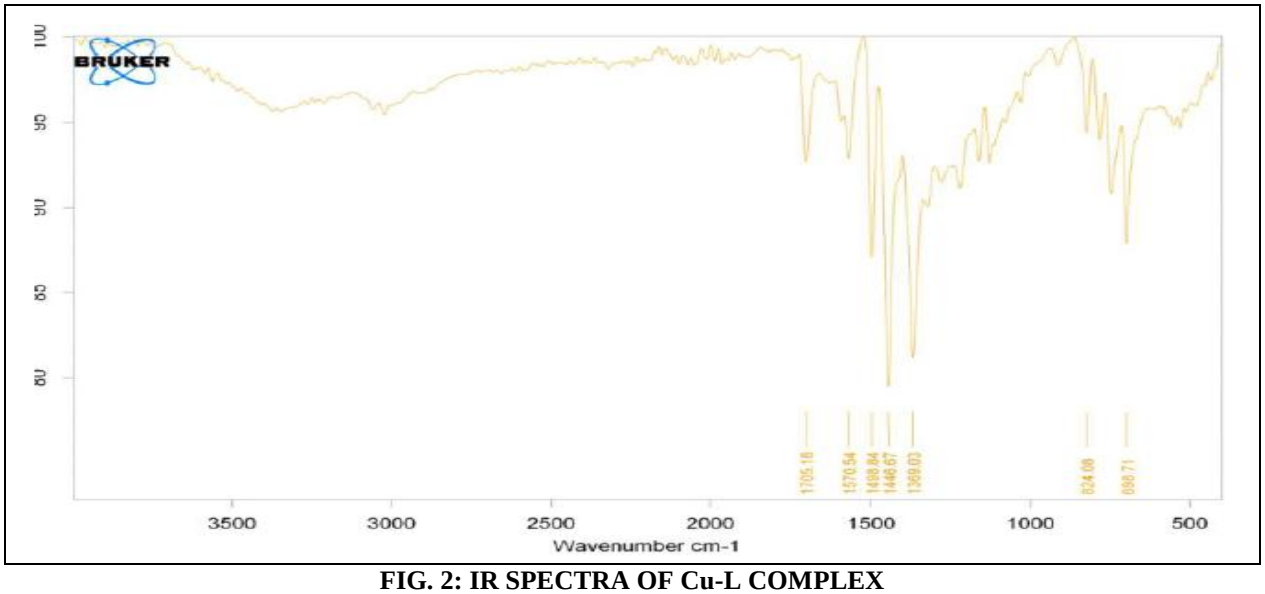


FIG. 2: IR SPECTRA OF Cu-L COMPLEX

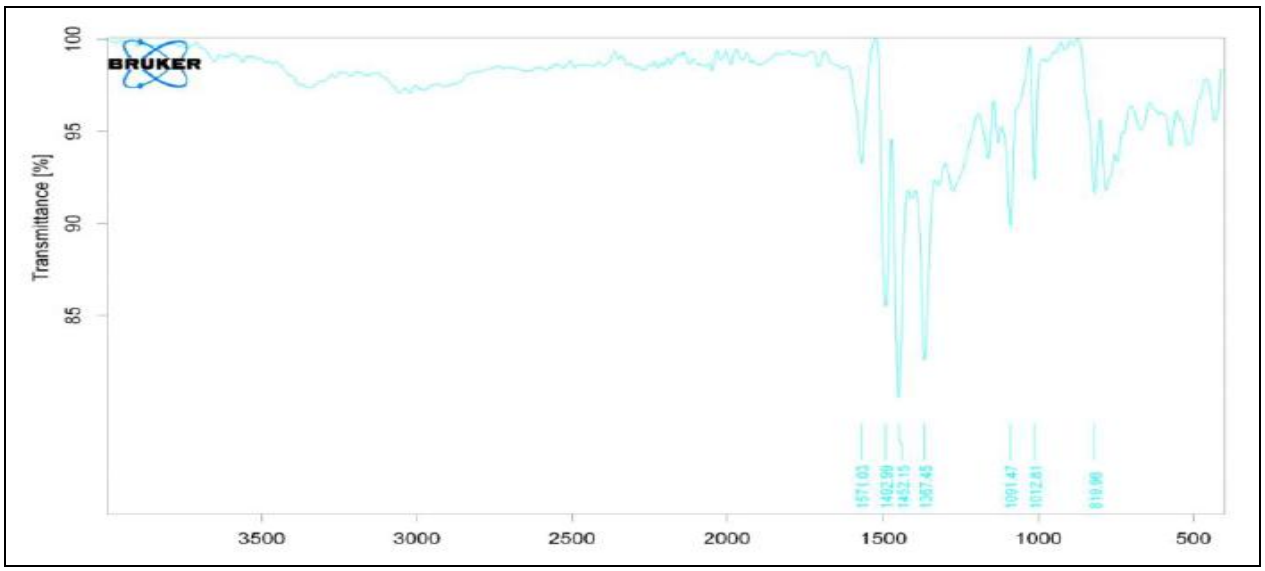


FIG. 3: IR SPECTRA OF Co-L COMPLEX

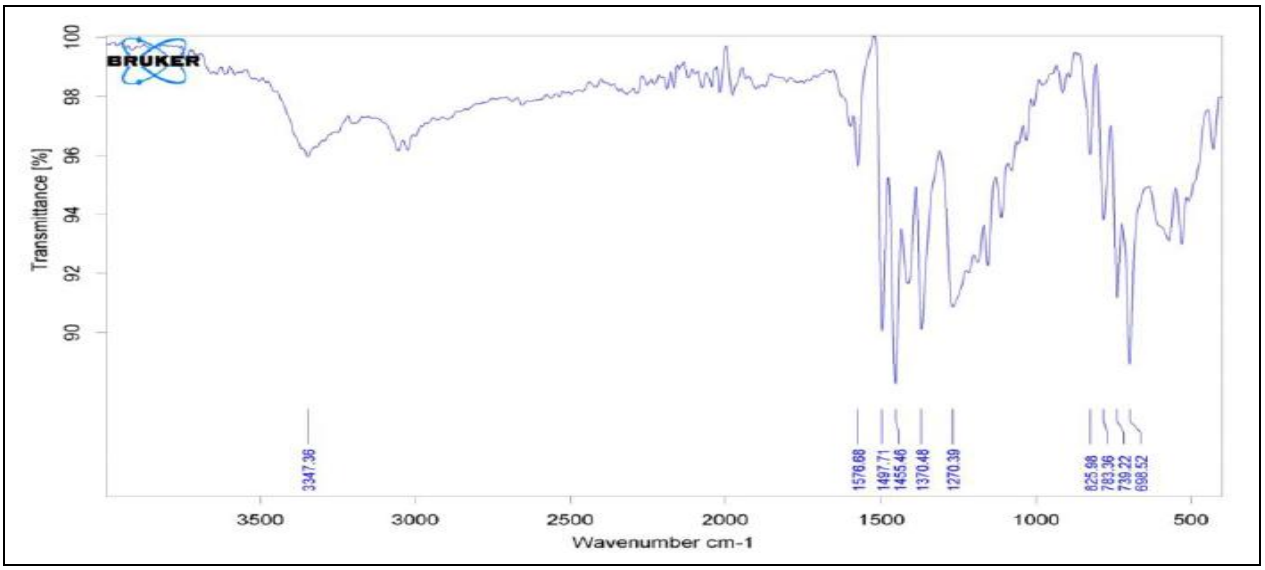


FIG. 4: IR SPECTRA OF Ni-L COMPLEX

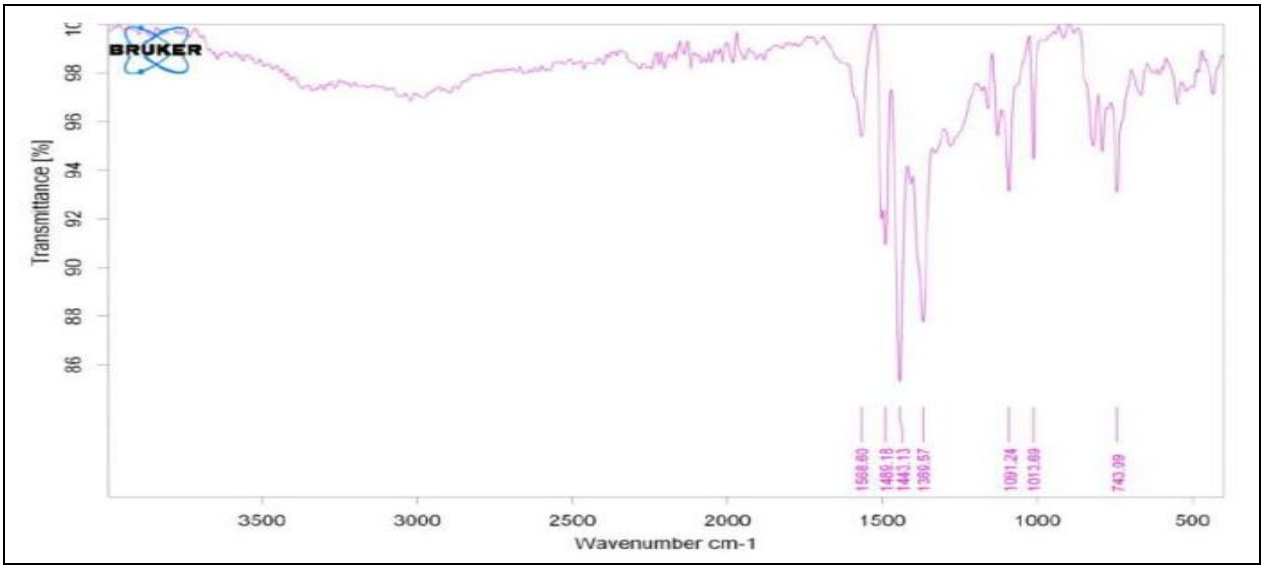


FIG. 5: IR SPECTRA OF Zn-L COMPLEX

Ni-L Complex: IR KBr cm^{-1} 2884.54 cm^{-1} (aromatic NH), 1610.94 cm^{-1} (carbonyl C=O), 1514.75 cm^{-1} (C=N), 1451.6 cm^{-1} (C=C), 1364.52 cm^{-1} (C-N), 786.57 cm^{-1} (M-N), 1159.20 (M-O). UV-visible-330 nm Π-Π*. Mass m/z: 748.23 (100.0%), 749.23 (47.6%), 750.23 (39.5%), 751.23 (19.7%), 750.24 (11.2%), 752.23 (5.4%), 752.22 (5.4%), 752.22 (2.9%), 751.24 (1.9%), 764.22 (1.4%).

Zn-L Complex: IR KBr disc cm^{-1}, 2886.43 cm^{-1} (aromatic NH), 1605.36 (carbonyl C=O), 1556.42 cm^{-1} (C=N), 145.12 cm^{-1} (C-N), 746.54 cm^{-1} (M-N), 1146.24 cm^{-1} (M-O). UV-visible-313 nm n-Π* Mass, m/z: 754.22 (100%), 756.22 (58.4%), 755.23 (46.0%), 758.22 (39.3%), 757.22 (35.8%), 759.22 (18.5%), 756.23 (11.2%), 758.23 (10.3%), 760.23 (4.3%), 757.23 (2.4%), 759.23 (2.3%), 7.2 (2%), 760.22 (2.0%).

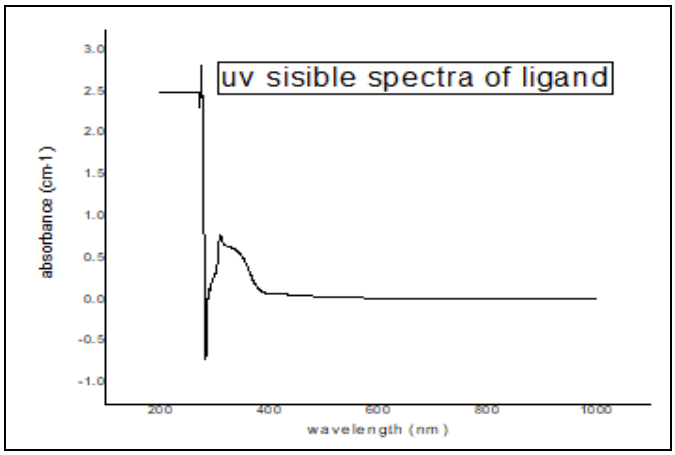


FIG. 6: UV VISIBLE SPECTRA OF LIGAND

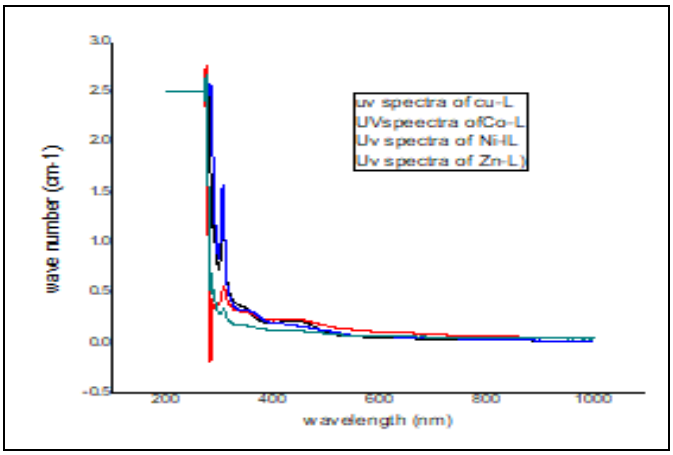


FIG. 7: UV VISIBLE SPECTRA OF Cu, Co, Ni & Zn COMPLEX

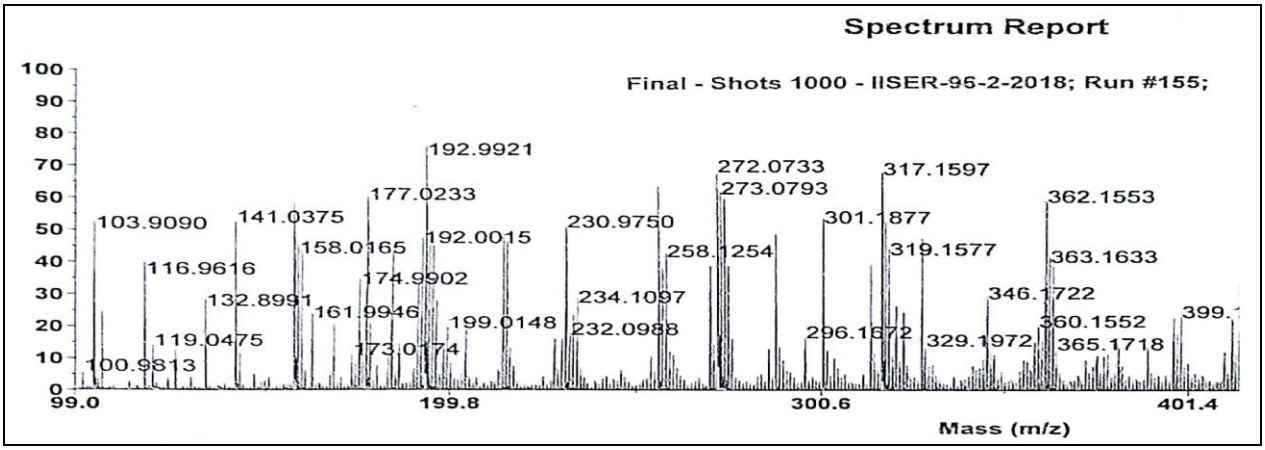


FIG. 8: MASS SPECTRA OF LIGAND

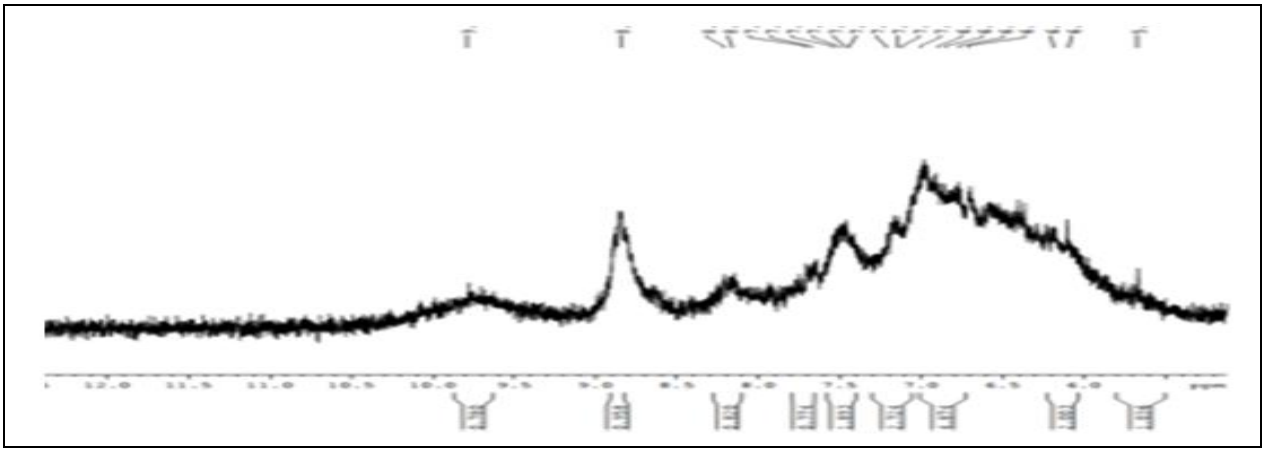


FIG. 9: H-NMR SPECTRA OF LIGAND

Physico-chemico Characterisation of Ligands and Complexes:

TABLE 1: ELEMENTAL ANALYSIS

Ligand and complexes	Formula weight & yield percentage	Yield percentage	Elemental analysis				
			C Calculated (found)	N Calculated (found)	O Calculated (found)	H Calculated (found)	M Calculated (found)
L_{1-}	345.15	78	73.011	12.17	9.27	5.50	
$C_{21}H_{19}N_3O_2$			73.03	12.16	9.26	5.54	
L_1-Cu	754.33	80	66.91	11.15	8.49	5.04	8.43
$C_{42}H_{38}CuN_6O_4$			66.87	11.14	8.48	5.08	8.42
L_1-Co	749.23	82	67.26	11.21	8.54	5.07	7.85
$C_{42}H_{38}CoN_6O_4$			67.28	11.20	8.05	5.11	7.86
L_1-Ni	748.23	76	67.35	11.22	8.55	5.07	7.844
$C_{42}H_{38}N_6NiO_4$			67.31	11.21	8.54	5.11	7.83
L_1-Zn	754.22	82	66.82	11.13	8.48	5.03	8.66
$C_{42}H_{38}N_6ZnO_4$			67.71	11.11	8.46	5.07	8.65

Antimicrobial Studies of Ligand and Complexes: *Escherichia coli* and *Staphylococcus aureus* bacterial cultures were used for antimicrobial studies followed by disc diffusion method for which molten agar culture media prepared and incubated at 45 °C then the agar was poured into Petridis allowed to solidifies in which 5 diameter holes were punched and each of the holes filled with 50 & 100 mg/ml of teas solution with respect to standard antibacterial drug ciprofloxacin. All the petridishes were autoclaved and subjected for antifungal confirmation followed by the same disc diffusion procedure by using *Aspergillus niger* and *Candida albicans* with reference of the standard amphotericin-B antifungal drug for which potato-dextrose agar culture media prepared at a temperature of 37 °C over a period of 48 h then all the observed bacterial and fungal inhibition activity measured and tabulated in **Table 2** [26-28].

TABLE 2: ANTIMICROBIAL STUDIES

Compounds	*Escherichia coli*		*Staphylococcus aureus*		*Aspergillums niger*		*Candida albicans*	
	50 mg/ml	100 mg/ml	50 mg/ml	100 mg/ml	50 mg/ml	100 mg/ml	50 mg/ml	100 mg/ml
Ligand	16	20	26	22	18	20	20	22
Co-ligand complex	17	23	11	12	10	18	20	27
Cu-Ligand complex	22	27	12	17	18	22	17	29
Ni-Ligand complex	19	22	17	29	14	19	10	11
Zn-ligand complex	14	17	20	22	22	27	20	23
ciprofloxacin	-	22	-	27	-	-	-	-
Amphotericin-B	-	-	-	-		12		17

CONCLUSION: Biologically potential mannich base ligand prepared by Multicomponent one-pot synthesis followed by melt condensation of benzaldehyde, imidazole, and 8-hydroxyquinoline with the objective of antimicrobial biological application it's observed and tabulated that synthesized ligand and its transition metal complexes exhibited inhibition zone of bacterial and fungal culture. In our earlier work, we studied with the multicomponent of substituted benzaldehyde, benzimidazole, and 8-hydroxy-quinoline by which antimicrobial activity was not exhibited.

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CONFLICTS OF INTEREST: The author has no conflict of interest regarding the publication of this article.

REFERENCES:

1. Sebastian A and Suvaikin MY: Synthesis, characterization and antimicrobial activity of 2-(dimethylaminomethyl) soindoline-1, 3-dione and its cobalt (II) and nickel(II) complexes. Advances in Applied Science Research 2012; 3(1): 45-50.
2. Mazumder MMU, Sukul A, Saha SK, Chowdhury AA and Mamun Y: A comprehensive *in-vitro* biological investigation of metal complexes of tolfenamic acid. Alexandria Journal of Medicine 2019; 54(1): 23-26.

3. Patil SS, Ganesh A, Thakur, Manzoor and Shaikh: Synthesis, characterization, and antibacterial studies of mixed ligand dioxouranium complexes with 8-hydroxyquinoline and some amino acids. International Scholarly Research Network 2011; 168539: 1-6.
4. AL-Noor TH, Jarad AJ and Obaid A: Synthesis, Characterization and antibacterial activity of mixed ligands complexes of some metal ions with 2-aminophenol and tributylphosphine. Research Journal of Pharmaceutical, Biological, and Chemical Sciences 2017; 8(3): 132-39.
5. Camellia FK, Kader A, Alam MA, Zahan MKE and Islam MS: Synthesis, characterization and antimicrobial studies of three new Mo (VI) Mixed Ligand Complexes 2018; 4: 1-5.
6. Vashi RT, Patel SB and Kadiya HK: Synthesis, Characterization and Antimicrobial Activity of Metal Chelates of 2-[(8-hydroxyquinoline) - 5-aminomethyl]-3-(4-Bromophenyl)-3(H) - -quinazoline-4-one. Der Pharma Chemica 2012; 4(4): 1506-11.
7. Dixit RB and Patel JA: spectrophotometric determination of paracetamol drug-using 8-hydroxyquinoline. International Journal of Pharmaceutical Sciences and Research 2014; 5(6): 2393-97.
8. Ibrahim MA, Awad, Aref AM, Hafez AAA and Hassan K: Transition Metal Complexes of Azo-8-Hydroxyquinoline Derivatives as Antimicrobial Agents. Journal of the Chinese Chemical Society 1989; 36: 107-14.
9. Nadia A, El- Wakiel, Hala F, Rizk, & Seham a Ibrahim: Synthesis and characterization of metal complexes of azo dye based on 5- nitro- 8- Hydroxyquinoline and their applications in dyeing polyester fabrics. Appl Organometal Chem 2017; 31(10): 1-7.
10. Hofmann K: the chemistry of Heterocyclic compounds-Imidazole and its derivatives - Part I. by Inter-Science Publishers. Inc, New York, 1953; Chapter VIII: 24-7.
11. Walla R, Murray WJ, Knutson G and Diaz A: nomenclature, physical properties and electrolytic behavior of benzimidazole. Arne J Chem. Soc 1966; 88: 1962-8.
12. Sathya, Muthukumar C, Ramesh M, Sebastian A, Sebastian A and Suvaikin MY: synthesis, characterization and antimicrobial activity of manganese(II) and nickel(II) complexes of 7-diethylaminobenzyl-8-hydroxyquinoline. Journal of Advances in Chemistry 2016; 4: 4324-32.
13. Jain CVM, Reddy RP, Halder M, Singh S, Kumar R, Wasudeo SG, Singh PP, Khan SI, Jacob MR, Tekwani BL and Jain R: Synthesis and biological evaluation of 8-quinolinamines and their amino acid conjugates as broad-spectrum anti-infective. ACS Omega 2018; 3(3): 3060-75.
14. Mohammed A, Abdel-Amid N, Maher F and Farghaly: A synthesis and antibacterial action of certain quinoline derivatives. Collection of Czechoslovak Chemical Communications 1992; 57(7): 1547-52.
15. Ujjinamatada RK, Bayer's, Borowski P and Hosmane RS: An analogue of AICAR with dual inhibitory activity against WNV and HCV NTPase/helicase: synthesis and in vitro screening of 4-carbamoyl-5-(4, 6-diamino-2, 5-dihydro-1, 3, 5-triazin-2-yl) imidazole-1-beta-D-ribofuranoside. Bioorg Med Chem Lett 2007; 17(8): 2285-8.
16. Rajpurohit Sangeetha, Garg SP and Sah P: Synthesis, spectral characterization and antimicrobial studies of novel imidazole derivatives. Ind J Het Chem 2005; 15: 129.
17. Ghorai MK, Das K, Kumar A and Das A: A convenient synthetic route to 2-aryl-N-tosylazetidines and their ZnX2 (X = I, OTf) mediated regioselective nucleophilic ring opening reactions synthesis of c-iodoamines and tetra-hydropyrimidines. Tetrahedron Letters 2006; 47: 5393-97.
18. Nasresfahani Z, Kassaee MZ, Nejati-Shendi M, Eidi E and Taheri Q: Mesoporous silica nanoparticles (MSNs) as an efficient and reusable nanocatalyst for synthesis of β-amino ketones through one-pot three-component Mannich reactions. RSC Adv 2016; 6: 32183-88.
19. Anusuya AM and Krishna BS: Synthesis characterization and biological applications of some heterocyclic molecules of Transition metal complexes. International Journal of Scientific Research and Review 2019; 7(5): 182-90.
20. Wang R, Chen JZ, Zheng XA, Kong R, Gong SS and Sun Q: Hafnium (IV) triflate as a potent catalyst for selective 1-O-deacetylation of per acetylated saccharides. Carbohydrate Research 2017; 455: 114-18
21. Kong R, Han SB, Wei JY, Peng XC, Xie ZB, Gong SS and Sun Q: Highly efficient synthesis of substituted 3,4-Dihydropyrimidin-2-(1H)-ones (DHPMs) catalyzed by Hf(OTf)4 Mechanistic insights into reaction pathways under metal Lewis acid catalysis and solvent-free conditions. Molecules 2019; 2: 364.
22. Lu C, Eskandari A, Cressey PB and Suntharalingam K: Cancer stem cell and bulk cancer cell active Copper (II) complexes with vanillin schiff base derivatives and naproxen. Chemistry 2017; 23(47): 11366-74.
23. Andiappan K, Sanmugam A, Deivanayagam E, Karuppasamy K, Kim HS and Vikraman D: *In-vitro* cytotoxicity activity of novel Schiff base ligand-lanthanide complexes. Sci Rep 2018; 8(1): 3054.
24. Kumaravel G, Ponya Ultra P and Raman N: Exploiting the biological efficacy of benzimidazole based Schiff base complexes with l-Histidine as a co-ligand combined molecular docking, DNA interaction, antimicrobial and cytotoxic studies. BioorgMed Chem 2018; 77: 269-79.
25. Mumtaz A, Zaib S, Zahoor F, Nawaz MAH and Saeed A: Synthesis, characterization and biological activities of creatinine amides and creatinine Schiff bases. Med Chem 2017; 13(2): 196-03.
26. Unver Y, Deniz S, Celik F, Akar Z, Kucuk M and Sancak K: Synthesis of new 1,2,4-triazole compounds containing Schiff and Mannich bases (morpholine) with antioxidant and antimicrobial activities. J Enzyme Inhib Med Chem 2016; 31: 89-95.
27. Petrović VP, Simijonović D, Milovanović VM and Petrović ZD: Acetophenone Mannich bases: study of ionic liquid catalyzed synthesis and antioxidative potential of products. R Soc Open Sci 2018; 5(11): 181232.
28. De Moraes Gomes PAT, Pena and LJ: Isatin derivatives and their antiviral properties against arboviruses a review Mini Rev Med Chem 2019; 19(1): 56-62.
29. Vandana K, Marathakam A, Thushara BS and Rajitha K: A review on isatin derivatives with diverse biological activities. World J Pharm Res 2017: 6: 318-22.

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