ANTIOXIDANT AND ANTI-MICROBIAL ACTIVITY STUDY OF SYNTHESIZED COPPER, NICKEL AND ZINC METALS SCHIFF BASE DERIVATIVE OF SALICYLALDEHYDE

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ABSTRACT

Organometallic compounds conjugates play a vital role in new drug discovery, in which Schiff base is useful as a ligand in consideration with different metals. Schiff base mostly encouraged due to its versatile activity due to the presence of a unique Imine (C=N) group. An attempt has been taken to synthesize a Schiff base by using salicylaldehyde and ethylene diamine which further design for the incorporation of salts of Cu, Ni and Zn metals separately. The ligand and its metal complexes have been carried out several characterization studies like elemental analysis, molar conductance, UV, IR and ¹H NMR. DPPH antioxidant potential and antimicrobial effect against four species *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Staphylococcus aureus* have been done with the ligand and all its metal complexes. The result revealed that metal incorporation in the Schiff base ligand enhanced the antioxidant potential as well as remarkable antimicrobial effect.

Keywords: Organometallic, Schiff Base, DPPH, Metal Complexes, Antioxidant.

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INTRODUCTION

In recent years, there has been a considerable effort towards the preparation of new materials containing polyfunctional units (ligands) capable of binding the metal ions. Imine (C=N) Schiff base compounds are possessing broad-spectrum activity¹⁻⁶ and metal conjugates of its (Schiff base) derivatives exhibited remarkable biological activity including antioxidant, antitumor, antibacterial and antiviral activity.⁷ The metal incorporation always plays an important role in a different physiological process. Good numbers of organic compounds not only bearing organic mode of action but also activated as well as a biotransformed form of action due to conjugation of metals through metabolism.

Schiff base derivatives play an important role in various disease conditions. Multidentate ligands are the substance containing at least two donor atoms often separated by atom-to-atom chains. Since carbon has a greater tendency to form chains, it is often used to link the donor atoms, for instance by an alkylene chain to form chelating ligand. A metal complex $M_nL_xA_y$ (where M = Metal, L = Multidentate ligand, A = Monodentate ligand) is formed when its coordination is substituted i.e $n = px + y$. Where p = denticity of the chelating ligand.⁸ The donor atom in the ligand is the atoms with a high electron-donating ability such as N, O, S etc. Metals (Copper, Nickel and Zinc) incorporation in Schiff base has been previously attempted and successfully established as potential as an antibacterial and analgesic activity.⁹ Transition metal complexes coordinated to tetradentate Schiff base have been studied mainly because of their ease of preparation, flexibility and versatility in term of chemical properties, geometry, coordination sites and cause of substitution. Complexes of Schiff base ligand have been studied for another cause that is for their dioxide intake and oxidative catalysis.¹⁰

In the present study, an attempt has been made to evaluate the antioxidant activity of the metal complexes of Schiff bases derivatives and compared them with standard compounds. The evaluation of antioxidant activities has been done with a series of *in-vitro* models. The characterization of the structure was done

through CHN elemental analysis, UV, FTIR, Molar conductance, and ¹H NMR study. The coordination of the metal to ligands (1:1 or 1:2) in this study also lean on different parameters such as PH, temperature, reagent medium, etc.

Fig.-1: Schiff Base Ligand

Fig.-2: Metal-Ligand Complex

EXPERIMENTAL

Materials and Instrumentation

The chemicals and solvents used were of A.R. grade. By using capillaries, melting points were determined followed by apparatus from SISCO. The compound purity was determined through thin layer chromatography (TLC). JASCO FTIR 410 spectrophotometer was used to determine IR spectra (Ker, cm⁻¹). ¹H NMR (CDCl₃) on a Bruker DPX 300-MHz spectrometer in which internal standard TMS was being used. UV spectrum measurements were carried out by Jasco V-600. C, H and N analysis was performed by Euro EA (Italy) analyzer.

Preparation of Ligands

[Synthesis of Ligand (H₂L)] Salicylaldehyde was purified by standing with powered CaCO₃ followed by distillation. To the solution, 24.4 gm (0.2mol) of purified 100 cm³, boiling 95 % ethanol was added 6.01 gm (0.2mol) ethylenediamine in a ratio 1:1 with constant stirring. Within 5 minute, a bright yellow crystalline solid was obtained (Fig.-1). The reaction mixture was cooled and filtered dried out on an adsorbent paper.¹¹

Preparation of H₂L Metal Complexes

To an ethanolic solution of the ligand-1 (H₂L), was mixed with metal ions (M) (Cupric sulphate/ acetate of Nickel/Zinc) in ethanol, in which H₂L and M ratio 1:1 followed by dropwise addition of perchloric acid (PH=6), was heated in water bath with constant stirring for 6 hrs. Then the resultant solution was kept overnight. The precipitated solid was filtered and dried in a desiccator recrystallize from acetonitrile. After 3 days, the formation of colored structure compounds was filtered, followed with methanol washing and dried in vacuum. Melting point and TLC were carried for purity to check the synthesized compounds (Fig.-2). The structure of the newly formed metal-ligand complexes were confirmed by using CHN elemental analysis, UV, FTIR, Molar conductance and ¹H NMR study which depicted in Table-1 and 2.

Free Radical Scavenging Activity by 1, 1-Diphenyl-2-Picrylhydrazyl (DPPH): The antioxidant activity by DPPH was studied with spectrophotometric as per the reported literature with little modification.¹² 0.1 mmol of DPPH solution was prepared and an aliquot of 1 ml of this solution was mixed with 3 ml of a solution of H₂L and its metal solution at different concentrations 10-50 µg/ml separately. The mixture solutions were incubated for 30 minutes in dark condition and then the absorbance was taken at 517 nm against the blank solution.

$$\% \text{ DPPH Scavenging Effect} = (1 - A_t/A_c) \times 100$$

Where, A_c = Absorbance control at 517 nm containing all the reagent except the test compounds

A_t = Absorbance test containing reagent with a metal-ligand complex solution

Antibacterial Activity

The antibacterial activity was screened for all synthesized metal-ligand complex against *Staphylococcus aureus*(S.a), *Enterococcus faecalis*(E.f), *Pseudomonas aeruginosa*(P.a), *Klebsiella pneumonia* (K.p) in standard agar well diffusion method.¹¹

RESULTS AND DISCUSSION

Schiff base compounds and their derivative metal complexes are air-stable, colored, organic solvent-soluble but insoluble in water. The result of the elemental analysis is satisfactory and can well be

correlated with finding value calculated as depicted molecular formula indicated to synthesized metal complexes. This metal to ligand complex reflecting 1:1 stoichiometries which were depicted in Table-1. The non-electrolyte characteristics ML were well established by the molar conductance studies. The UV spectral study of the H_2L exhibited two high-intensity bands lying at 364.5 and 273.5 nm assigned to transition respectively. In ML, shifting of intense sharp bands were observed CuL lying 394 and 269 nm, NiL lying 374.5 and 266 nm, ZnL lying 402 and 265 nm respectively. The remarkable shifting of absorption spectrum from H_2L to ML may be featured to the sharing of lone pairs of the nitrogen atoms of the H_2L to the metal.¹³⁻¹⁵

In H_2L , an intense ligand absorption band at 1286 cm^{-1} due to C-N stretching frequency assigned which is lowered by $10-95\text{ cm}^{-1}$ in complex spectra. This may be indicated as the existence of azomethane coordination of the ligand. The tetradentate ligand showed absorption at $3300-3394\text{ cm}^{-1}$ which may be assigned to hydrogen-bonded O-H in-plane stretching vibration.¹⁶⁻¹⁸ The dissipated intense band in the ML resulting bond formation involvement. The ligand shows intense absorption at 1286 cm^{-1} which may be assigned to C-N stretching frequency is lowered by $3-95\text{ cm}^{-1}$ in the spectra of the complexes which may be due to coordination of Schiff base by azomethane nitrogen. The appearance of the new band at $733-760\text{ cm}^{-1}$ and $543-648\text{ cm}^{-1}$ indicating the formation of M-N and M-O bonds and water molecule coordination respectively (Fig.-5). The HNMR study were evaluated in both ligands as well as their complexes by using TMS as a reference in DMSO solvent (Fig.-3 and 4). For the aromatic ring protons that showed characteristics signals in the range 6.7-7.18 ppm. This was also checked for the respective metal complexes that produced multiple signal bonds as well. The important characteristics of ML showed a signal at 10.63 ppm indicating coordination of aromatic ring resulting deprotonation. The measurement of molar conductance in DMSO at room temperature has found 10^{-3} M which also depicted in the table. The antioxidant potential was showed that metal complexes of ligand greater potential than Schiff base ligand and followed the order of inhibition $ZnL > NiL > CuL > H_2L$.

Fig.-3: HNMR Study of New Synthesize Schiff Base Ligand

Fig.-4: HNMR Study of Metal (Zn)-Schiff Base Ligand

Fig.-5: FTIR Study of Metal (Zn)-Schiff Base Ligand

Table-1: Colour, Elemental Analysis and ¹HNMR Spectral Data H₂L, CuL, NiL, ZnL

Compounds	Colour	Elemental Analysis %: Found		¹ HNMR		
		N	M	Ar-H	NH	OH
H ₂ L	Bright Yellow	10.30 (10.43)	-----	6.7-6.65	7.19	10.64
CuL	Greenish Transparent	8.44 (8.49)	19.29 (19.27)	7.7-7.6	8.42	-----
NiL	Reddish Yellow	8.62 (8.55)	18.09 (18.08)	7.3-7.4	8.33	-----
ZnL	Whitish Transparent	8.39 (8.45)	19.71 (19.73)	6.8-6.7	8.47	-----

Table-2: IR, Molar Conductance and Electronics Spectral Data of H₂L, CuL, NiL, ZnL

Compounds	IR Spectral Data (cm ⁻¹)					Molar Conductance (S cm ² , mol ⁻¹)	UV Data u-u*	N-u*
	OH	C-N	C-N	M-N	M-O			
H ₂ L	1281	1663	1550	-----			362	272
CuL	1190	1650	1598	735	580	6.11	389	270
NiL	1282	1634	1578	748	647	7.53	371	259
ZnL	1191	1644	1599	766	541	9.81	401	273

Table-3: Compounds Screening of Antimicrobial Effect by Agar Diffusion Method

Compound	MF	ZI of S.a (mm) 100µg/ml	ZI of P.a (mm) 100µg/ml	ZI of K.p (mm) 100µg/ml	ZI of E.c (mm) 100µg/ml
H ₂ L	C ₁₆ H ₁₆ N ₂ O ₂	10	13	14	18
CuL	C ₁₆ H ₁₄ N ₂ O ₂ Cu	17	14	15	22
NiL	C ₁₆ H ₁₄ N ₂ O ₂ Ni	13	15	18	17
ZnL	C ₁₆ H ₁₄ N ₂ O ₂ Zn	15	17	24	21
STD	Ampicillin trihydrate	26.4	25.3	26.2	25.6
Solvent	DMF	00	00	00	00

The evaluation result of antioxidant potential of all tested compound as depicted in Fig.- 6 showed that Zn and Ni coordinated complex having more effective as compared to the other Schiff base and Cu complex

which can be compared to that of standard BHT.¹⁹ The order potential was as followed: BHT>ZnL>NiL>CuL> L. The ligand and synthesized new metal complexes were also evaluated for antibacterial activity for which CuL and ZnL were showed good inhibitory activity against gram negative strain *E. coli* in comparison with H₂L and NiL showed in Table-3, however H₂L and NiL appreciable inhibitory effect on gram-negative strain *K.pneumoniae*.²⁰⁻²²

Fig.-6: DPPH Radical Scavenging Activity of H₂L, CuL, NiL and ZnL

CONCLUSION

The result of the above study reveals that all the metal complexes having appreciable antioxidant potential which could be the reason for its antimicrobial effect against the specific species. There is a great scope of the study for future research upon these metal complexes using this Schiff base ligand.

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