

Antimicrobial Activities Of Schiff Base Metal Complexes Of 4-Amino Antipyrine

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ABSTRACT:

A novel series of transition metal complexes of Co(II), Cu(II), and Zn(II) have been synthesized from their corresponding metal chloride and macrocyclic Schiff base ligand derived from, 4-aminoantipyrine, thiophene-2-carboxyaldehyde. Several tools like elemental analysis, FI-IR, UV-Vis, ¹H NMR, ¹³C NMR, ESR have been used to obtain the chemical structures of synthesized transition metal complexes. The antimicrobial screening test indicates that the metal complexes of Cu(II) have good antimicrobial activity than the other metal complexes.

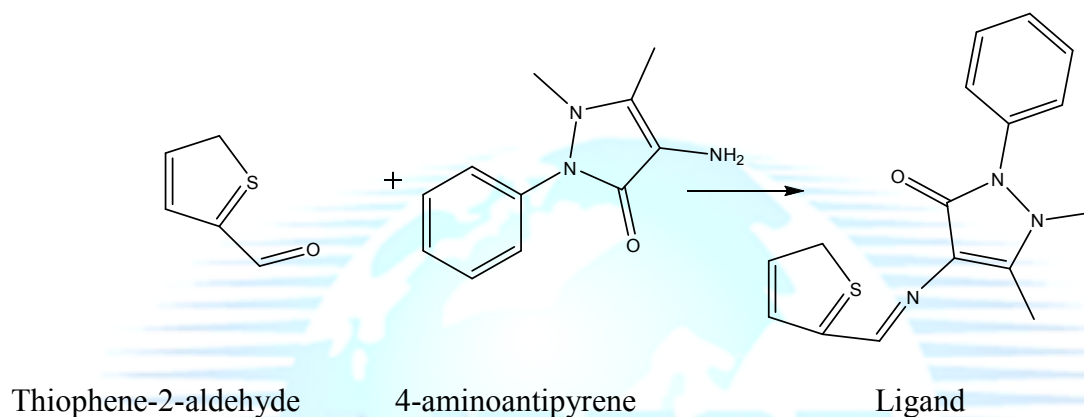
Key words: Schiff bases, Coordination compounds, Antibacterial , Antifungal

1.INTRODUCTION

Schiff bases are the condensation product of an amino compound with an active carbonyl compound. Schiff bases are considered as very important class of organic ligands which have wide application for many biological aspects [1] . In azomethines derivatives the C=N linkages are essential for biological activity, several azomethines were reported to possess remarkable antibacterial, antifungal, activities [2,3]. Schiff bases and their complexes were recently found to have significant and biological activity [4]. Amino acid based schiff bases is very effective metal chelators and their metal complexes are models for a number of important biologicals [5] . The literature reveals that schiff base ligands are excellent coordinating ligands because of the high stability of the coordination compounds, their good solubility in common solvents and the flexibility in varying the chemical environment about C=N group.[6,7] The present work are the study of Cu(II), Co(II), Zn(II) metal complexes of the Schiff base derived from

thiophene-2- carboxyaldehyde and 4-amino antipyrene .Synthesis, characterization and antimicrobial activities of above metal complexes are reported.

Figure 1



2. EXPERIMENTAL

2.1 Materials and Methodology

All chemicals and solvents used were of analar grade. All metal (II) salts were used as chloride. The UV-Visible spectra of all complexes were recorded on a Shimadzu UV-1800 spectrophotometer. The ^1H and ^{13}C NMR spectra were recorded using Bruker instrument using TMS as internal standard. IR spectra were recorded in KBR pellet medium on a perkin-Elmer 783 spectrophotometer.

2.2 SYNTHESIS OF SCHIFF BASES

The Schiff base was synthesized by condensation of thiophene-2- carboxyaldehyde and 4-amino antipyrene (1:1) molar ratio dissolved in ethanol. The resulting reaction mixture refluxed for 48 hrs. The brown precipitate of ligand obtained was filtered, washed with ethanol, finally dried.

2.3 SYNTHESIS OF METAL COMPLEXES

Ligands were dissolved in absolute ethanol and ethanolic solutions of metal salts were mixed dropwise in 1:2 (M:L) ratio. The mixture was refluxed for 2hrs and left to cool to room temperature. The product formed was filtered, washed with ethanol and ether. The samples were dried.

2.4 ANTI MICROBIAL ACTIVITY

The antimicrobial activity were determined for the investigated compounds against the bacteria E.Coli, S.aureus and fungus A.niger, and Candida albicans well diffusion method using agar nutrient as the medium. The stock solution was prepared by dissolving the compounds in DMSO and serial dilutions of the compounds were prepared in sterile distilled water to determine the minimum inhibition concentration (MIC). The nutrient agar medium was poured into petri plates. A suspension of the tested microorganism (0.5ml) was spread over the solid nutrient agar plates with the help of the spreader. Different dilutions of the stock solutions were applied to the 10mm diameter sterile disc. After evaporating the solvent, the disc was placed on the inoculated plates. The petri plates were placed at low temperature for 2 hours to allow the diffusion of the chemical and then incubated at a suitable optimum temperature for 30 -36 hours. The diameter of the inhibition zone was measured in millimeters.

3 RESULTS AND DISCUSSION

The metal complexes were solid and non-hygroscopic. The molar conductance values at room temperature and 10^{-3} M dilution in DMSO showed that all complexes are non-electrolytic in nature. The infrared spectrum of HL ligand exhibits a band of 1593cm^{-1} assignable to $\nu(\text{C}=\text{N})$ of the azomethine group and intense bands at $(1491, 1405)\text{cm}^{-1}$ corresponding to C=C stretching of the thiophene rings.[8,9].The comparison of the positions of these bands of those observed in the infrared spectra of its Co(II), Cu(II), Zn(II) complexes indicated that the band at 1593cm^{-1} did not show a marked shift, this discussed that azomethine group unshared in the complexation toward Co(II), Cu(II), Zn(II) ions . The presence of very sharp band of the range $612-529\text{cm}^{-1}$ indicated the formation of M-N bond involving N atom of Pyridine ring [10,11] in this way ligands are behaving in bidentate manner coordinating through carboxylate ion, N atom of pyridine ring and N atom of azomethine group.

Table -1 Analytical data of metal complexes

Compound	Colour	M.P($^{\circ}\text{C}$)	Molar conductance
[Cu(HL) ₂]Cl ₂	Light brown	>100	121
[Co(HL) ₂]Cl ₂	Brown	>100	98
[Zn(HL) ₂]Cl ₂	Brown	>100	141

The observed medium intensity band of 911 cm^{-1} in the free HL ligand which is ascribed to thiophene ring vibration [8], shifted to lower values for the two HL complexes, suggesting the involvement in the sulphur atom in the bonding with the metals ions[9] The band assigned to the stretching of $\nu(\text{C-S})$ is similarly shifted to lower frequencies. This also confirms that the sulphur atom is taking part in the complex formation.

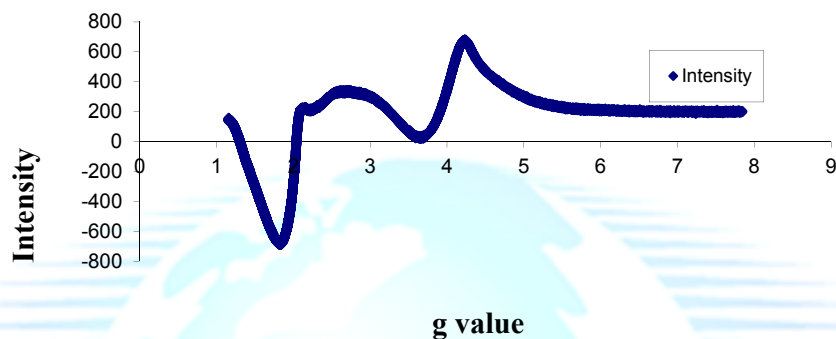
Upon the electronic spectrum of the HL Schiff base ligand the two essential absorption bands were observed at 309nm ,(360 and 550) nm and assigned to the transitions $n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$, respectively.[10,11] These transitions were existed also of the spectra of the complexes, but they shifted to different lower intensities, confirming the confirming the coordination of the ligand to the metal ions. In UV-Vis, spectra the weak band should be at 400-500nm are due to to charge-transfer (ct) band in the complexes which are absence in the HL.

3.1 ESR SPECTRA

The ESR spectra were recorded in DMSO at liquid nitrogen temperature. The spectra of complexes exhibit a set of four well-resolved signals at low field and one or two signals are high field corresponding to $g_{\parallel}$ and $g_{\perp}$ respectively. The $g_{\parallel}$ and $g_{\perp}$ values are computed from the spectrum using the tetracyano ethylene free radical as the 'g' marker. Kivelson and Nieman [12] have reported that $g_{\parallel}$ value is less than 2.3 for covalent character and is greater than 2.3 for ionic character of the metal ligand bond. The trend $g_{\parallel} > g_{\perp} > 2.0023$, suggest that the unpaired electron lies predominantly in the dx^2-dy^2 orbital characteristic of octahedral geometry of Co & Cu(II) complexes [13]. The g average value for these complexes is greater than 2 indicating the covalent character of metal –ligand bond. The ESR parameters $g_{\parallel}$ and $g_{\perp}$ of the complexes and the energies of d-d transitions are used to evaluation the dipolar interaction [14] . A typical ESR spectra of Cu (II) complexes shown in the below figure.

If G values less than 4 indicates considerable exchange interaction in the solid complexes. The above reported complex showed G values less than 4 indicating the exchange interaction in complexes. Furthermore, Masa cesi et al [15] reported that $g_{\perp}$ is 2.4 for copper oxygen bonds and 2.3 for copper-nitrogen bonds. For the complexes reported here, $g_{\parallel}$ values between 2.3-2.4 which further confirms, the presence of mixed copper-nitrogen and copper-oxygen bonds in these chelates complexes.

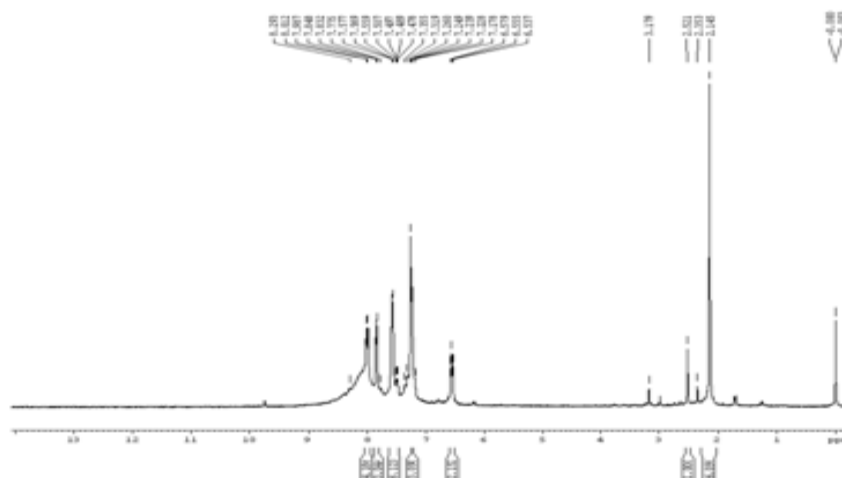
Figure- 2



3.2 NMR SPECTRA

The NMR spectral data of the ligand is given in experimental Sections 2.2. The ^1H and ^{13}C -NMR spectrum of the ligand is shown in Figs. 3a and 3b. As shown in Fig. 2a, it is observed that the signal for azomethine proton ($>\text{CH}=\text{N}-$) in the ligand appears as a singlet at 8.512 ppm. The peaks at 1.288 and 2.596 ppm are assignable to the isopropyl $-\text{CH}-$ and $-\text{CH}_3$ protons, respectively. The aromatic ring protons are observed in the 7–8 ppm range as expected. The ^{13}C -NMR spectrum of Schiff base ligand shows a peak at 162.427 ppm characteristic of azomethine carbon.

Figure -3

Fig.3. (a) ^1H -NMR spectrum of the Schiff base ligand (L).

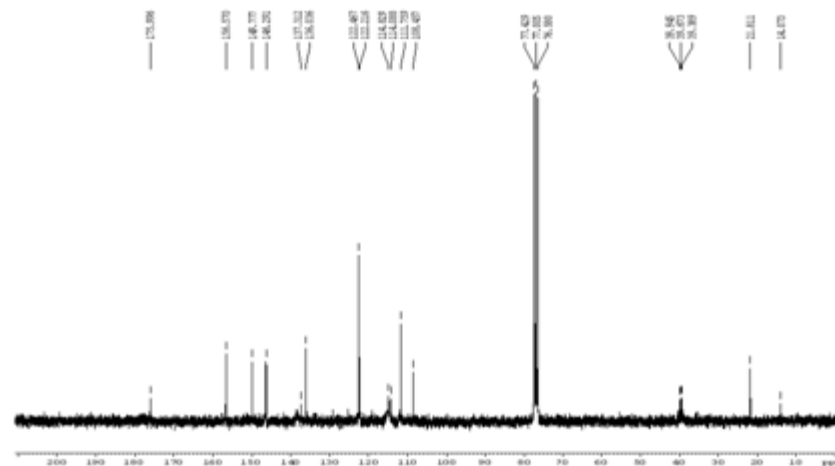


Fig.3. (b) ^{13}C -NMR spectrum of the Schiff base ligand (L).

3.3 BIOLOGICAL STUDIES:

The antibacterial activity of the Schiff base and its Co(II), Cu(II), Zn(II) complexes against gram positive (*Staphylococcus aureus*) and gram –negative(*Escherichia coli*) and two strains of fungus (*Aspergillus Flavus* and *Candida albicans*) were studied.[16,17] The antibacterial and antifungal results shown in table- 3 and fig All the Schiff base complexes individually exhibited varying of inhibitory effect on the growth of the tested bacterial species.[18] Table-3 shows that the activity of the schiff base complexes became more pronounced when coordinated with the metal ions. The enhanced activity of the metal complexes may be due to the increased lipophilic nature of the complexes arising due to chelation. It is probably due to faster diffusion of the chelates as a whole through the cell membrane or due to the chelation theory. The biological activity of the complexes follow the order. Antibacterial effect: Cu(II)>Co(II),Zn(II) and antifungal Cu(II)>Co(II),Zn(II).

Table-3 Results of antibacterial assay and anti fungal assay

Diameter of inhibition zone <10 : weak,

Diameter of inhibition zone between 10 and 16 : Moderate,

Diameter of inhibition zone >16 : Significant

TABLE-2

Antibacterial data of Schiff base metal complexes

Category	Salmonellatyphi (series 1)	Klebsiella Pneumonia (series 2)	Staphylococci aureus (series 3)
Standard(Amikacin)	17	18	16
Ligand	16	16	17
[Cu(HL) ₂]Cl ₂	16	10	R
[Co(HL) ₂]Cl ₂	10	R	10
[Zn(HL) ₂]CL ₂	10	10	12

*SD- Standard drug- Amikacin (Antibacterial)

Figure-4

Anti bacterial Schiff base metal complexes



Inhibition Zone of Salmonellatyphi



Inhibition Zone of Klebsiella pneumoniae



Inhibition Zone of Staphylococci aureus

Figure – 5 Anti fungal Schiff base metal complexes



Inhibition Zone of Candidiatrophicalis



Inhibition Zone of Aspergillus



Inhibition Zone of Candida albicans

TABLE- 3

Antifungal data of Schiff base metal complexes
 *SD- Standard drug- Ketakonazole (Antifungal)

Category	Candidiatrophicalis (Series 1)	Aspergillus (Series 2)	Candidaalbicans (Series 30)
Standard(Ketakonazole)	17	18	16
[Cu(HL) ₂]Cl ₂	16	16	16
[Co(HL) ₂]Cl ₂	14	R	15
[Zn(HL) ₂]Cl ₂	15	R	15

4. CONCLUSIONS

In this paper we proposed the synthesis, isolation of solid products and spectroscopic characterization of a new bi dentate schiff base derived from thiophene –2- carboxyaldehyde and 4-amino antipyrine its complexes with Co(II),Cu(II) Zn(II). It is tentatively proposed that the Schiff base ligand coordinates through nitrogen of the 4-amino antipyrine moiety and the sulphur of the thiophene ring forming the stable chelate ring structures. The complexes are biologically active and show enhanced antimicrobial activities compared to free ligand. The antimicrobial activities and Antifungal effect of the complexes follow the order Cu(II) > Co(II) > Zn(II).

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