

Synthesis, Characterization And Biological Screening Of Binuclear Complexes Of Terephthaldehyde Based Ligand With Zn(II), Cd(II), Hg(II) And Mn(II)

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ABSTRACT

In the presence of 2-3 drops of glacial acetic acid and reflux for approximately 7 hours, the Schiff base was synthesized by the reaction of 2-amino-3-hydroxypyridine and terephthaldehyde, with a transition temperature of 183 °C, and the color was brown. By vaporizing the mixture for approximately 9 hours, the chemical reactions of Zn (II) acetate, Cd (II), Hg (II), Mn (II) chloride were conducted at 1:2 molarities with the Schiff base, which resulted in colored metal (II) complexes. In the air, the synthesized complexes were stable except manganese and were solid in state. Various spectroscopic techniques such as UV/Vis, ¹H-NMR, FT-IR, have characterized the ligand and synthesized complexes. All the complexes have melting point between the range 126-298 °C. The synthesized complexes were soluble in organic solvents like DMSO. The molar conductivity values showed the non-electrolytic nature of all the synthesized metal (II) complexes. Values fall in the range 1.70 to 5.37 μS/cm⁻¹. FT-IR spectra demonstrated that ligand act as bidentate during complex formation. In the ligand spectrum of FT-IR spectroscopy, characteristic bands were observed at 3309.9 cm⁻¹ for -OH spectrum. In the UV spectra, Intra-ligand transitions were observed for ligand 232 nm while charge transfer transitions were absent for ligand. In ¹H-NMR spectra of the ligand, signal of -OH bond was present with a value of 10.38 ppm but disappeared in all the synthesized complexes. Hence this disappearance of -OH signal in the spectra of all newly synthesized complexes got cleared that complexation occurred in metal complexes. The singlet proton peak was observed at 8.120 ppm for ligand. σ-OH peak for ligand was found at 10.38 ppm and its disappearance in the complexes showed chelation of the ligand with metal (II) complex. The synthesized complexes and the free ligand were screened against bacterial strains of G+ bacteria (*S. aureus*) and G- bacteria (*E. coli*) to check their potential in antibacterial activities. Biological activities results have demonstrated that all complexes were strongly biologically active against selected bacterial strains. The bacterial data proved that the synthesized complexes were better than free ligand.

Keywords: Schiff base, Metal(II) complexes, Spectroscopic characterization, Chelation, Antibacterial activity

Introduction

In biological processes, inorganic compounds play critical roles, and it has been established that many organic compounds used in medicine are activated or bio transformed by metal ions metabolism. Schiff bases are classified as organic ligands derived from the condensation reactions of primary or secondary amines and corresponding aldehydes or ketones ($RCH=NR$, where R and R represent alkyl/or aryl substitutes) [1].

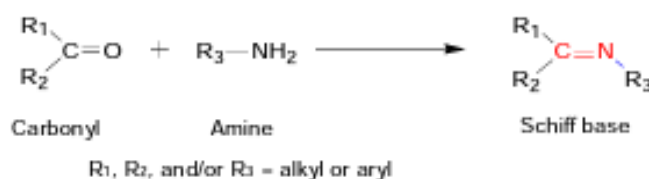


Figure 1: General procedure for Schiff bases formation

These compounds were reported by a German Chemist Hugo Schiff in 1864 and therefore referred to his name. Schiff bases may serve as monodentate, bidentate, tridentate or tetradentate ligands depending upon the number of donor atoms present in the molecule [2]. They can make chelates (typically five or six-membered) on reaction with metal ion. Schiff bases are considered a very important class of organic ligands possessing diverse applications. Schiff base ligand plays a central role in transition metal coordination chemistry and biochemistry [3]. The Schiff base metal complexes are used as metal enzymes, catalyst, material chemistry and biomimetic chemistry. The binuclear complexes have greater cleaving efficiency than mononuclear complexes. Copious transition metal complexes with polydentate Schiff bases containing nitrogen, oxygen, or Sulphur donor atoms contribute immensely in biological systems [4]. These complexes exhibit applications in clinical, analytical and industrial processes. Studies on transitional metal compounds of Schiff base ligands have been of great significance due to their spectral properties and wide applications [5]. These complexes are used as model molecules for biological oxygen carrier systems. Such compounds display promising pharmacological properties as anti-bacterial, antifungal, anti-cancer, antioxidant, antimalarial, anti-inflammatory, antiviral and anti-proliferative properties [6]. In the past recent years, a large number of binuclear Schiff base metal complexes has been synthesized and characterized. The binuclear complexes have greater cleaving efficiency than mononuclear complexes. The pharmacophore potential of SBs is because of their ability to form complex compounds with metal ions in the active center of many enzymes involved in metabolism [7]. Pyridine-based ligands are currently employed in structurally simple medications such as sulpha pyridine used in pneumococcal pneumonia, and death rates have been lowered by 25 to 6 percent. Schiff base ligands generated from the pyridine moiety and their copper derivatives are employed in chemotherapy drugs. 2-amino-3-hydroxy pyridine plays a crucial function in anti-inflammatory drugs [8]. Several Schiff base ligands derived from pyridine derivatives and their metal (II) complexes have also been shown to inhibit tumor growth. Although Schiff bases containing a heterocyclic moiety have biological activity, the studies on 2-amino-3-hydroxy pyridine Schiff base are less extensive. 2-amino-3-hydroxy pyridine is of interest

since its Schiff bases can act as a bidentate N, O donor forming five membered rings [9].

In humans, zinc complexes have catalytic and structural functions in an estimated 300 enzymes, an example being carboxypeptidase A. Zn complexes seem very attractive mainly because zinc (II) is significantly non-toxic at higher doses compared with other metals (Fe, Cu, Hg, etc.), and then because zinc complexes undergo rapid ligand exchange, are able to promote Lewis acid activation and can play a part in the catalysis of hydrolytic reactions, such as hydrolysis and cleavage of DNA, thus exerting an anti-cancer activity [10, 11]. Cadmium complexes have attracted considerable interest due to pharmacological importance including anti-microbial agents, DNA binding affinity and anticancer activities. Mercury (II) compounds are used in numerous expanses including polymers, cosmetics, paper, dyes, fluorescent lamps and to a lesser extent in batteries [12]. Mercury has been used as a constituent in bactericides, antiseptics, skin ointment, and laxatives; toxicity of mercury and its compounds are well known. Manganese is also a good complexing agent with oxygen- and nitrogen-containing ligands; therefore, the study of the biological properties of its complexes is an actual task [13]. Manganese compounds can act as antioxidants against superoxides (O_2^-), which are produced as a part of normal metabolism in human body [14].

In the present work, we reported the synthesis, characterization and biological studies of Cd (II), Zn (II), Hg (II) and Mn (II) complexes derived from the newly synthesized ligand 2,2'-((1E,1E)-(1,4-phenylenebis(methanylylidene))bis(azaznylylidene))bis(pyridine-3-ol).

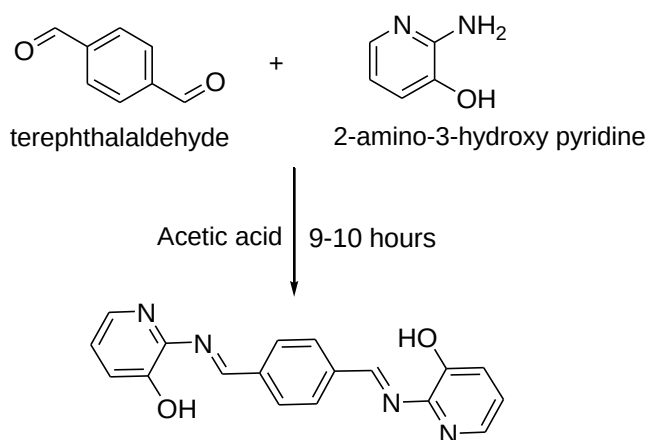
Experimental section

Method and materials

Terephthaldehyde, 2-amino-3-hydroxypyridine, glacial acetic acid, zinc (II) acetate, cadmium (II) chloride, mercury (II) chloride and manganese (II) chloride were obtained from Aldrich. Reagents are of high quality and analytical grade which were used for experimental work without purification. Solvents like ethanol, chloroform, methanol, DMSO and acetone were also purchased from Sigma Aldrich (UK).

Synthesis of Schiff base ligands

Terephthaldehyde (1 g), 2-amino-3-hydroxypyridine (0.82 g) and glacial acetic acid about 2-3 drops were put together in methanol (40 mL) and the resultant mixture was refluxed for 9-10 hours and then reaction mixture was filtered. Brownish colored precipitates were obtained. The solid product obtained was soluble in ethanol, DMSO and insoluble in chloroform and acetone [15].



2,2'-((1E,1'E)-(1,4-phenylenebis(methanylylidene)))bis(azanylylidene))bis(pyridin-3-ol)

Figure 2: Synthesis of Schiff base ligand (**HL**)

Synthesis of complex 1

For preparation of Zn (II) complex, (0.2 g) terephthalaldehyde (0.16 g) 2-amino-3-hydroxypyridine, glacial acetic acid was dissolved in methanol (40 mL). Reaction was refluxed for some time. Then a Stoichiometric amount of Zn (II) acetate (0.55 g) in 1:2 molar ratio was added in above solution. The resulting solution was refluxed for 5-6 hours. TLC was used to check progress of reaction. After completing reaction, solution mixture was evaporated in open air to get the product [16].

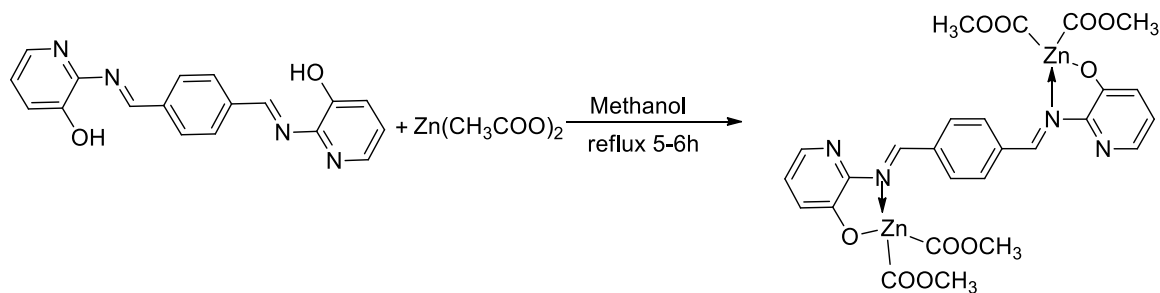


Figure 3: Synthesis of complex 1

Synthesis of complex 2

For the preparation of Cd (II) complex, (0.2 g) terephthalaldehyde (0.16 g) 2-amino-3-hydroxypyridine in methanol (40 mL) Then reaction was refluxed for some hours. Then (0.05 g) of sodium metal was added into the flask and was refluxed for about 30 mints. After this a stoichiometric amount of CdCl₂·2H₂O (0.64 g) in 1:2 (L:M) ratio was added in the above solution. Refluxing time for the reaction was 8-10 hours. When reaction was completed, then the above solution was evaporated gradually in air to get the solid product. Dark brown colored crystals were obtained [17].

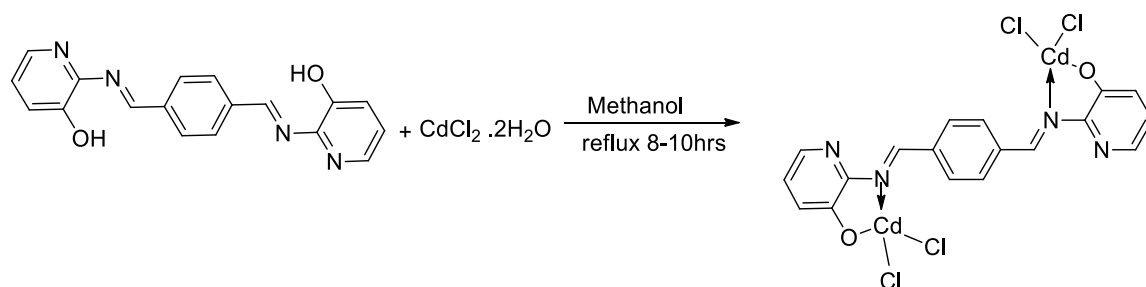


Figure 4: Synthesis of complex 2

Synthesis of complex 3

(0.2 g) Terephthaldehyde, (0.16 g) 2-amino-3-hydroxypyridine and glacial acetic acid were dissolved in methanol (40 mL) to prepare the complex. Then reaction was refluxed for some time. Then (0.05 g) of sodium metal was added into the flask and was refluxed for about 30 mints. After this a stoichiometric amount of Hg (II) chloride (0.8 g) in 1:2 ratio was added in above mixture. Reaction was refluxed for about 8-10 hours. Progress of reaction was checked by thin layer chromatography [18].

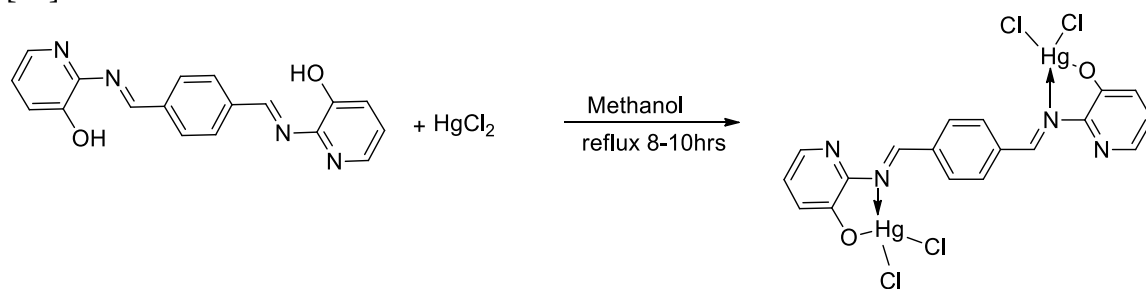


Figure 5: Synthesis of complex 3

Synthesis of complex 4

For the preparation of Mn (II) complex, (0.2 g) terephthaldehyde (0.16 g) 2-amino-3-hydroxypyridine, glacial acetic acid about 2-3 drops were put together in methanol (40 mL) in 250 mL round bottom flask. Reaction was refluxed for some time. Then (0.05 g) of sodium metal was added into the flask and was refluxed for about 30 mints. After this a stoichiometric amount of MnCl₂·4H₂O chloride (0.58 g) in 1:2 ratio was added in the above solution. The solution was refluxed for 10 hours. TLC was used to check the progress of reaction [19].

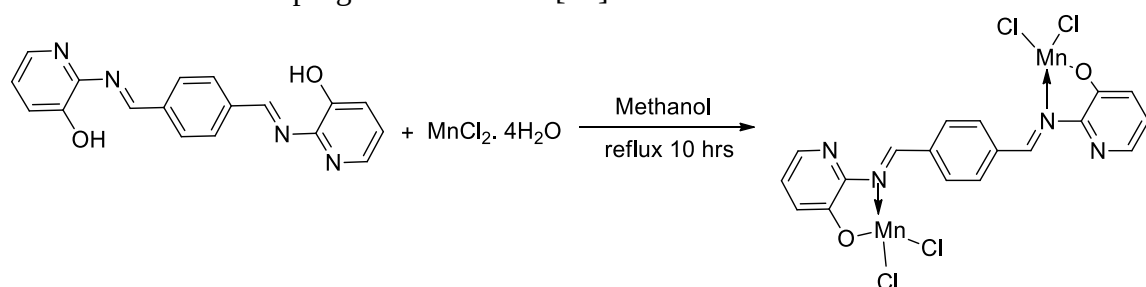


Figure 6: Synthesis of complex 4

Biological activities

Antimicrobial activity

The in vitro biological screening activities of the investigated compounds were examined against the gram-negative bacteria (*Escherichia coli*) and gram-positive bacteria (*Staphylococcus aureus*) by the well diffusion route using agar nutrient as the medium. While antifungal effect was carried out using potato dextrose agar as medium against (*Aspergillus flavus* and *Aspergillus niger*). The stock solutions were made ready by dissolving the compounds in DMSO. In a typical process, a well was made with the help of borer on the nutrient medium plate which was formerly inoculated with microorganisms. The well was made full of the various concentrations of test solution using a micropipette and incubated at 37 °C for 24 h (bacteria) and 48 h (fungus). During incubation time, the test solution transpired, and the growth of the inoculated microorganisms was affected. Antimicrobial activity was indicated by the presence of obvious zones of inhibition around the wells. The zone of inhibition was evaluated in mm [20].

The preparation of metal oxides followed this route: First of all, Petri plates were made by (20 mL) of sterile Muller Hinton Agar for bacteria and (20 mL) of potato dextrose agar in case of yeast. The 24 h prepared test cultures of inoculums were swabbed on the top of the sclerotic media and left to dry for 10 min. Previously prepared metal oxides nanoparticles impregnated nipping at the different concentrations of 10 and 20 (mg/mL) for bacteria and fungi were placed aseptically on sensitivity plates with suitable controls. Ciprofloxacin was used as an antibacterial standard drug. The loaded discs were put on the surface of the medium and left for 30 min at room temperature for compound diffusion. Ciprofloxacin was used as positive control for bacteria and Fluconazole was utilized as positive control for fungi. After that all the plates were incubated for 24 h at 37 °C for bacteria and 28–35 °C for fungi, respectively. The sensibility was registered by measuring the clear zone of growth inhibition of agar surface around the discs in millimeter [18].

Antioxidant Assay

It has been recognized that bio-molecular oxidation can harm human cells. Free radicals can promote oxidative chain reactions. As an outcome, antioxidants play a vital role in slowing down the oxidative process by scavenging free radicals and preventing damage to cell membrane. Antioxidants' efficiency is determined because of their capacity to scavenge free radicals. In recent times, it has been proved that metal-based antioxidants are more effective at protecting living cells from the oxidative stress. Synthetic antioxidants have replaced natural antioxidants because they are less expensive and more effective than natural oxidants. Various research on metal complexes and Schiff bases and their revealed that ROS were efficient scavengers. Research using the 2,2-diphenyl-1-picrylhydrazyl free radical scavenging technique was conducted to evaluate the compound's antioxidant capabilities built on their radical scavenging capacities. An unusual electron is obtained by DPPH and employed for scavenging activity. A well-balanced free

radical called DPPH will accept an electron or a proton in order to transform into the well-balanced diamagnetic compound hydrazine. A material with the capacity to deliver hydrogen atoms or electrons can convert DPPH's radical purple hue into its spectrophotometrically observable non-radical yellow color [21].

Result and Discussion

Synthesis of Schiff base ligand and its metal (II) complexes

The Schiff base was prepared by the reaction of terephthalaldehyde and 2-amino-3-hydroxypyridine for 9 hours reflux in 40 mL methanol. The ligand has sharp melting point 183 °C. Schiff base obtained was brown in color. The Schiff base was stable in air and 64 % yield was obtained. The metal (II) complexes were synthesized by using Schiff base in methanol in 1:2 (ligand: metal) molar ratio with salt solution zinc(II) acetate, cadmium(II), mercury(II) and manganese(II) chloride. The synthesized metal (II) complexes have sharp melting points ranging from 126-298 °C. They were obtained in maximum yield (64-86 %). They were stable, non-hygroscopic except manganese (II) complex. They were also partially soluble in most organic solvents like CHCl_3 , CH_3OH , $\text{C}_2\text{H}_5\text{OH}$, $\text{C}_2\text{H}_3\text{N}$, as well as fully dissolved in DMSO. Molar conductance data revealed that ligand as well as metal (II) complexes were non-electrolyte in nature. The physical data of ligand and the metal (II) complexes such as solubility, color, percentage yield, molecular formula, molecular weight, melting point and elemental analysis were given in Table 1.

Molar conductance

Molar conductance values of the ligand and metal (II) complexes were checked in DMSO (0.001M). Conductance values of complexes were noted at room temperature. Conductivity meter was calibrated with the solutions of standard potassium chloride electrolytes [22]. The molar conductance values of the complexes lie in the range 1.70 to 5.37 $\mu\text{S}/\text{cm}^{-1}$ which is quite lower than that expected for an electrolyte and reveal their non-electrolytic nature [23]. Molar conductance data of the ligand and metal (II) complexes were given in Table 2.

Table 1: Physical data of synthesized ligand and its metal (II) complexes

Complex No.	Reactant 1	Reactant 2	Molecular formula	Molecular weight (g)	Melting point (°C)	% Yield	Color	Solubility ethanol, DMSO	Elemental analysis, % calculated (Found)		
									C	H	N
HL	$\text{C}_8\text{H}_6\text{O}_2$	$\text{C}_5\text{H}_6\text{N}_2\text{O}$	$\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_2$	318.33	183	36	Brown	Soluble	75.26 (75.11)	4.92 (4.40)	19.65 (19.50)
1	$\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_2$	$\text{Zn}(\text{CH}_3\text{COO})_2$	$\text{C}_{27}\text{H}_{22}\text{ZnN}_4\text{O}_{10}$	682.26	126	86	Black	Soluble	82.80 (82.02)	6.43 (6.20)	10.73 (10.60)
2	$\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_2$	$\text{CdCl}_2 \cdot 2\text{H}_2\text{O}$	$\text{C}_{27}\text{H}_{22}\text{CdN}_4\text{O}_{10}$	776.32	160	64	Dark brown	Soluble	82.81 (82.04)	6.45 (6.01)	10.74 (10.54)
3	$\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_2$	HgCl_2	$\text{C}_{27}\text{H}_{22}\text{HgN}_4\text{O}_{10}$	955.68	298	82	Black	Soluble	82.83 (82.00)	6.47 (6.11)	10.72 (10.23)
4	$\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_2$	$\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$	$\text{C}_{27}\text{H}_{22}\text{MnN}_4\text{O}_{10}$	661.38	-	-	Black	Soluble	82.85 (82.70)	6.49 (6.54)	10.73 (10.14)

Table 2: Conductometric data of ligand and its synthesized metal (II) complexes

Sr. No.	Complexes	Molar conductance $\mu\text{S}/\text{cm}^{-1}$
1	HL	2.30
2	Complex 1	1.70
3	Complex 2	5.19
4	Complex 3	4.11
5	Complex 4	5.37

Characterization of the ligand and its synthesized metal (II) complexes

The ligand and newly synthesized metal (II) complexes were characterized by various spectroscopic methods e.g., UV-visible, ^1H -NMR and FT-IR.

Uv-Visible Spectroscopy

The UV-Vis spectra were recorded in DMSO (0.001M) in the region of 200-500 nm. In electronic spectra of ligand, the wide range of bands were due to intra-ligand transitions results from electronic interaction between the metal and the ligand which involves either a metal to ligand or ligand to metal electron transfer. Charge transfer transitions appeared due to ligand to metal complexation. The $\pi \rightarrow \pi^*$ transition was observed for a ligand at the wavelength of 235-280 nm. The bands observed in the region of 235-250 nm were due to $\pi \rightarrow \pi^*$ transition. The absorption bands were observed in the range of 310 nm due to $n \rightarrow \pi^*$ transition from imine group corresponding to the ligand or metal complexes. In Zn(II) complexes $n \rightarrow \pi^*$ transition in C=N bond shifted from 302 to 314 nm after binding to the Zn metal center [24].

The absorption spectrum of Zn (II) complex exhibited a charge transfer transition with the absorption maximum located at 314 nm. The electronic spectra of Hg (II) complex showed two main intra-ligand transition between 200 and 500 nm. The first (245 nm) and second (260 nm) absorptions are assigned to $\pi \rightarrow \pi^*$ transition of the aromatic ring. The band at 310 nm involves ($\pi \rightarrow \pi^*$) transition of the C=O and C=N groups; the longer wavelength band can be assigned to charge transfer transition. In the spectrum of Hg (II) complex there is no d-d transitions observed because the Hg (II) cation has d^{10} electron configuration [25].

The electronic spectrum of the Cd (II) complex exhibited bands related to the ligand ($\pi \rightarrow \pi^*$), ($n \rightarrow \pi^*$) transitions at 230 and 285 nm, respectively. The additional band at 315 nm was assigned to the charge-transfer transition. No ligand field transitions are observed because of the filled d orbital. Since the d^{10} configuration affords no crystal field stabilization, the stereochemistry depends on the size and polarizing power of the M (II) cation and steric requirement of the ligand [26].

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Table 3: UV-Vis data of the ligand and metal (II) Complexes

Sr. No.	Complex number	Intra-ligand transition (nm)	Charge-transfer transition (nm)
1	HL	235, 280	-
2	Complex 1	235, 250	310
3	Complex 2	272	314
4	Complex 3	245, 260	310
5	Complex 4	230, 285	315

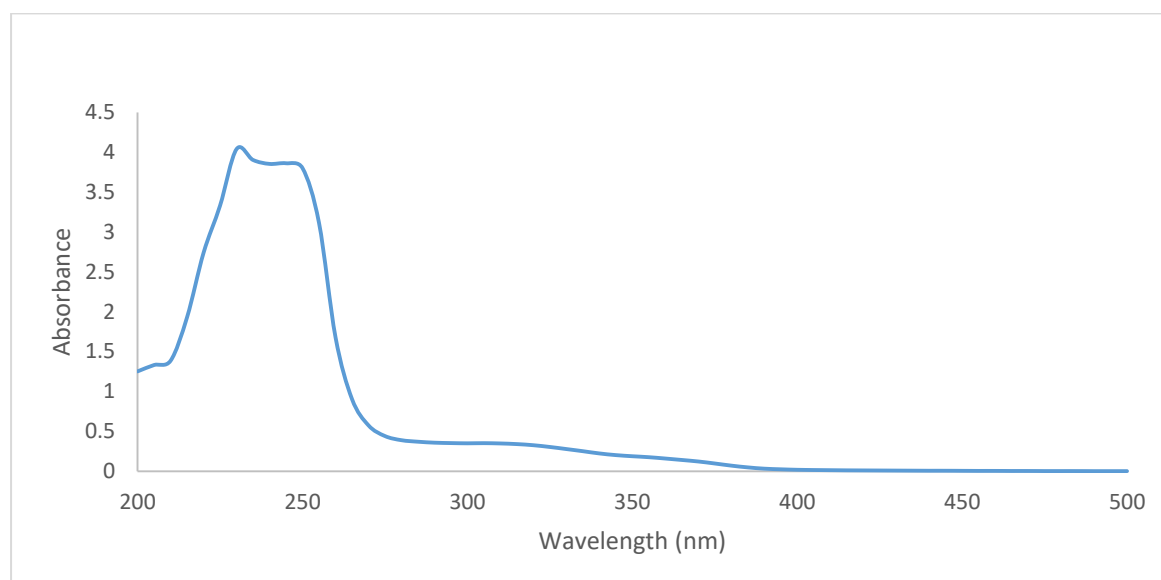


Figure 7: UV-Vis spectrum of Schiff base (HL)

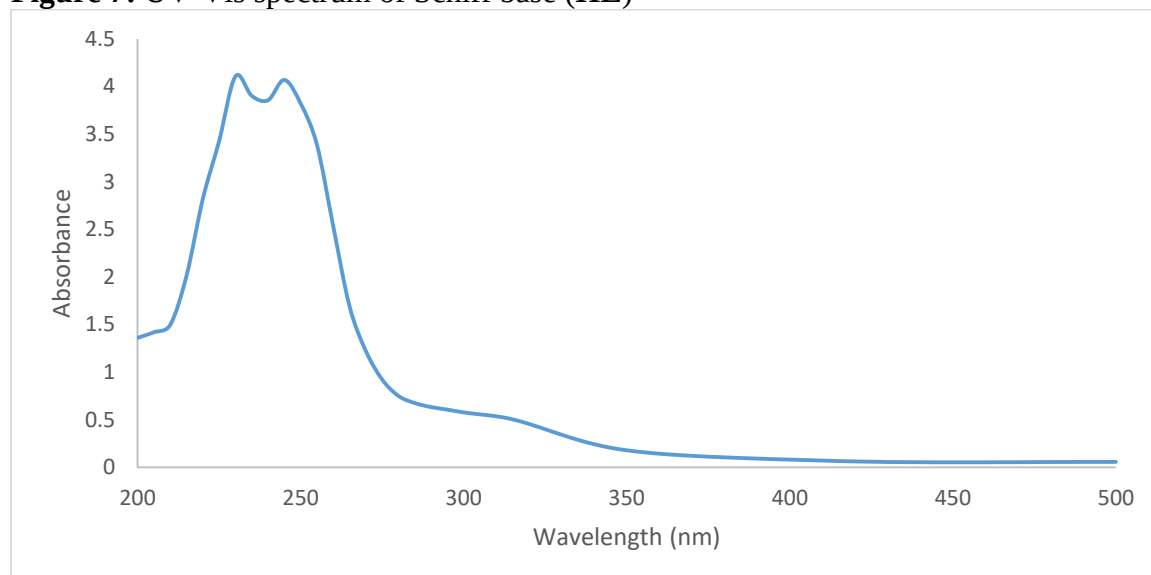


Figure 8: UV-Vis spectrum of Cd (II) complex

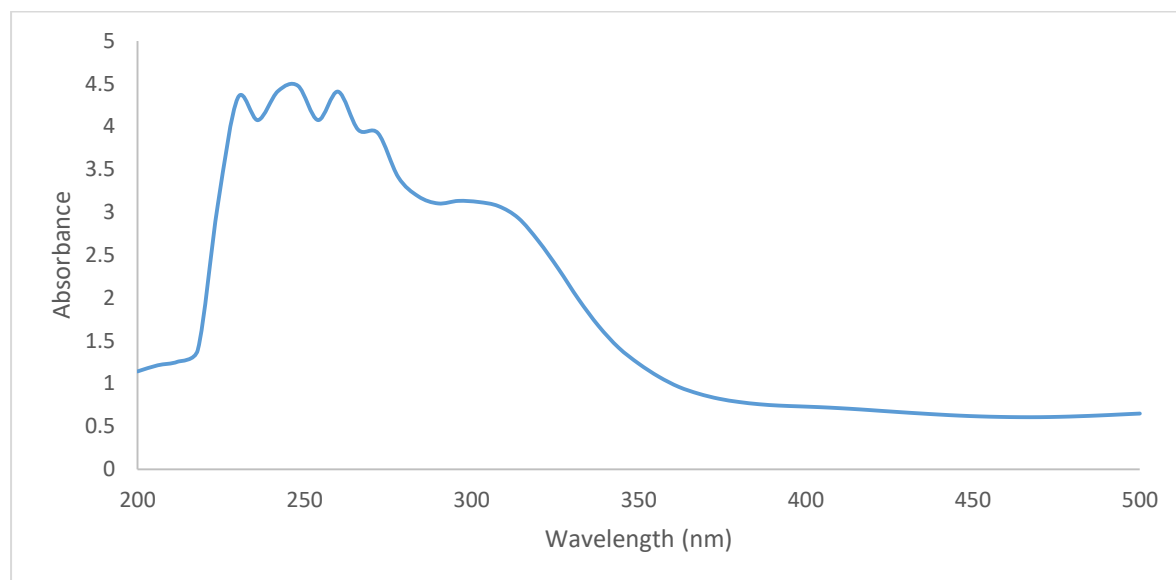


Figure 9: UV-Vis spectrum of Zn (II) complex

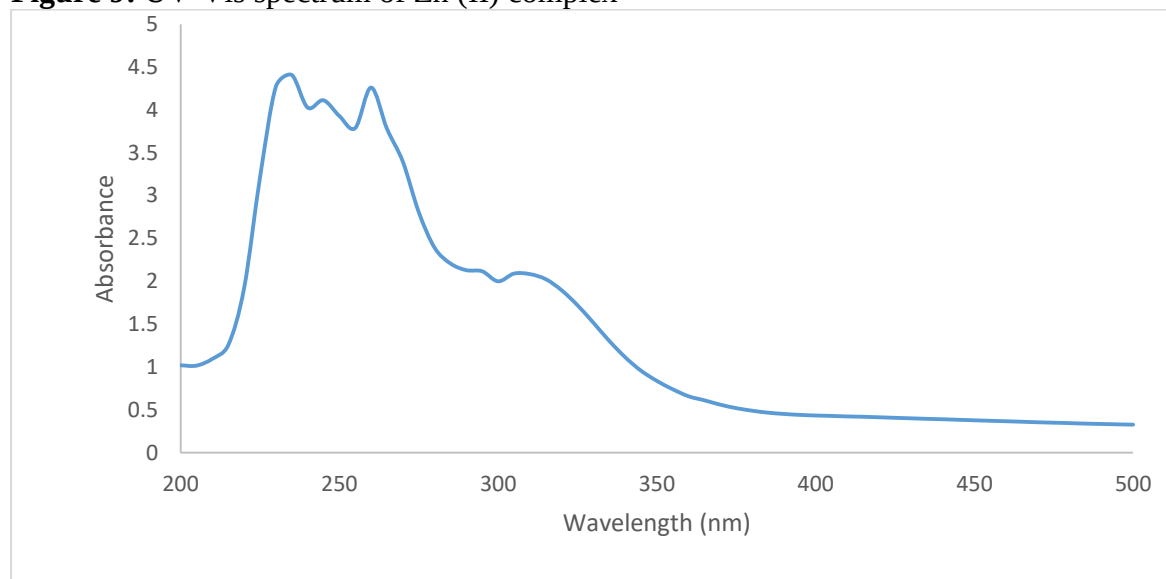


Figure 10: UV-Vis spectrum of Hg (II) complex

¹H-NMR spectroscopy

The characteristics signals in ¹H-NMR spectra of the ligand and newly synthesized complexes were recorded in DMSO-d₆ solution. Tetramethyl silane was used as an internal reference at room temperature. Based on their multiplicity and intensity patterns, values were assigned to different protons given in Table 4. The integration of the spectra was according to the number of protons present on each fragment. All the protons present in the ligand and synthesized metal (II) complexes were identified in position and number with the protons calculated from incremental method.

Comparison of the Chemical shifts shows that the signal due to the phenolic proton (OH) is absent in the complexes, suggesting coordination of the phenolic oxygen to the metal after deprotonation. The azomethine proton at 8.120 ppm in the ligand appeared at 8.119–8.224 ppm in the complexes, this supports the coordination of azomethine nitrogen to metal. These conclusions are also supported by IR spectral data. The comparison of $^1\text{H-NMR}$ spectra of Schiff base ligand and their corresponding complexes confirmed the coordination of ligands with metal ion. In $^1\text{H-NMR}$ spectra of Schiff base ligands, a sharp singlet signal at δ 10.38 ppm ascribed to phenolic–OH proton near to azomethine carbon atom and one singlet signal at δ 8.120 ppm due to azomethine proton ($-\text{CH}=\text{N}-$) was observed. On complexation, these singlets remained almost unaltered which showed the non-participation of these phenolic protons. The complexation was confirmed by shifting of azomethine protons signal in ligand spectra from δ 8.120 to δ 8.119 ppm in the complexes' spectra and disappearance of a singlet due to phenolic proton near to azomethine group which was present in spectra of ligands [27]. The doublet (d) appeared at 7.410–7.470 ppm and was assigned to protons 1 and 6 of the ligand. Multiplet (m) appeared at 7.624–7.725 ppm and were assigned to proton 2 and 7 of the metal (II) complex. Doublet appeared at 8.110–8.28 ppm was assigned to 3 and 8 protons of the ligand. While carbon 4,5,9,10 have multiplet (m) peaks appeared at 8.37–8.59 ppm for a ligand. The same trend with minor changing in values was followed by metal complexes. The $^1\text{H-NMR}$ spectra of ligand and complexes were given in Table 4.

The peak appeared at 10.38 ppm in the spectra of ligand (HL) assigned to OH and disappeared in the spectra of complexes showed that the coordination of metal occurs at oxygen atom of Schiff base ligand [28].

Table 4: $^1\text{H-NMR}$ of ligand (HL) and its metal complexes

Complexes	-OH	-CH=N	Proton 1,6	Proton 2,7	Proton 3,8	Proton 4,5,9,10
HL	10.38 (s)	8.120 (s)	7.410–7.470 (d)	7.508–7.561 (m)	8.110–8.28 (d)	8.37–8.59 (m)
Complex 1	-	8.119 (s)	7.342–7.359 (d)	7.624–7.725 (m)	7.922–7.948 (d)	8.119–8.36 (m)
Complex 2	-	8.125	7.26–7.39 (d)	7.29–7.62 (t)	7.920–7.940 (t)	8.28–8.56 (m)
Complex 3	-	8.150	7.342–7.59 (d)	7.554–7.598 (t)	7.725–7.922 (t)	8.07–8.14 (m)
Complex 4	-	8.225	7.410–	7.508–	7.591–	8.10–

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		7.470 (d)	7.564 (t)	7.595 (t)	8.29 (m)
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Multiplicity is denoted here as: s= singlet, d= doublet, t= triplet, m= multiplet

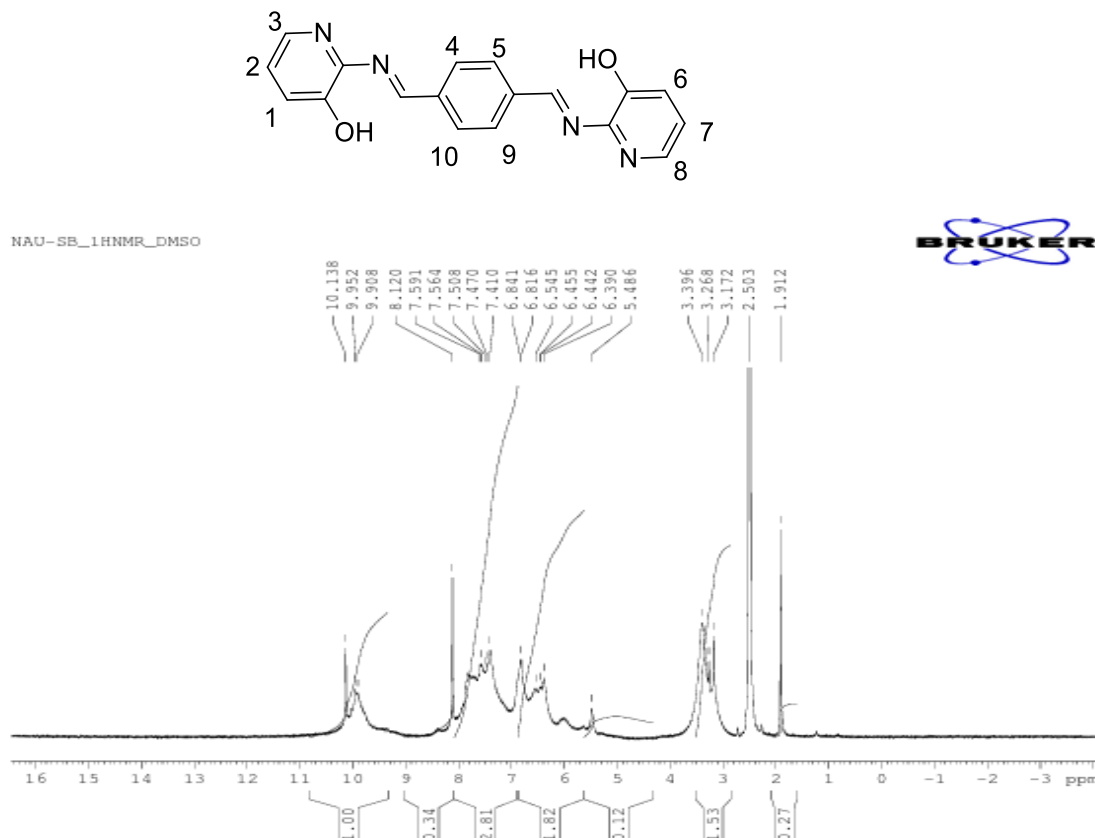


Figure 11: ¹H-NMR spectrum of Schiff base (HL)

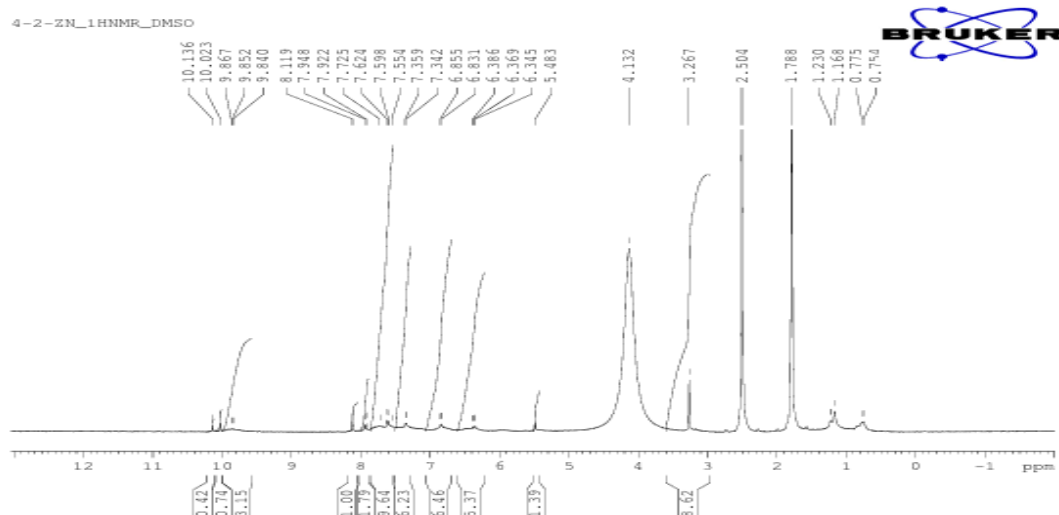


Figure 12: ¹H-NMR spectrum of Zn (II) metal complex

3.4.3. FT- IR
Infra-red spectra of compounds were recorded in the range of 500–4000 cm⁻¹. In these spectra the absorptions for important functional groups like C=N, C-H and O-H were observed. The IR spectrum of ligand has the bands in the region 3550-3450

cm^{-1} due to $\nu(\text{OH})$, in the region 2900 cm^{-1} due to $\nu(\text{-C-H})$ and in the region $1690\text{--}1550 \text{ cm}^{-1}$ due to $\nu(\text{C=N})$. The ligands possessed two potential donor sites, phenolic oxygen and the azomethine nitrogen. The ligands exhibited characteristic bands for (C=N) at 1686 cm^{-1} . Bonding of the azomethine is indicated by the shift of (C=N) to lower frequency $1618\text{--}1600.9 \text{ cm}^{-1}$ in the complexes. During complex formation deprotonation of the ligand has taken place and $\delta(\text{N-H})$ disappears in the spectra of complexes. It revealed that the nitrogen of azomethine forms the bond with the metal in the complex [29].

The IR spectrum of the Schiff base showed a peak at 1686 cm^{-1} characteristics of the $\nu(\text{C=N})$ group. No bands characteristic of free carbonyl or free amine were observed. The above information strongly suggested that the proposed ligand framework is formed. The IR spectra of the metal complexes also show new bands in the $669.1\text{--}794.2 \text{ cm}^{-1}$ region, which are probably due to the formation of M-O bond. The formation of M-O bond is supported the appearance of weak bands in the spectrum of complexes [30]. Bonding through phenolic oxygen after deprotonation is revealed by the disappearance of (OH) phenolic bands at 3309 cm^{-1} for complexes and the appearance of bands due to (C=N) at much lower frequencies ($1618\text{--}1600.9 \text{ cm}^{-1}$) in the complexes. HL exhibited bands for C=N at 1686 cm^{-1} , which remain changed to lower values in the complexes, indicating that this group participated in coordination. The metal ions chelated to the ligand through ON donor sites of nitrogen atom of azomethine group and oxygen atom of phenol group to confirm the formation of all metal(II) complexes [31].

Table 5: FT-IR data (cm^{-1}) of the ligand and its Cd (II), Hg (II), Zn (II) and Mn (II) complexes

Complex No.	$\nu(\text{O-H})$	$\nu(\text{C-H})$	$\nu(\text{C=N})$	$\nu(\text{M-O})$
HL	3309.9	2830.9	1686.6	-
1	-	2920.4	1600.9	669.1
2	-	2927.8	1636.8	794.2
3	-	2372.5	1630.4	756.1
4	-	2849.5	1618.1	625.2

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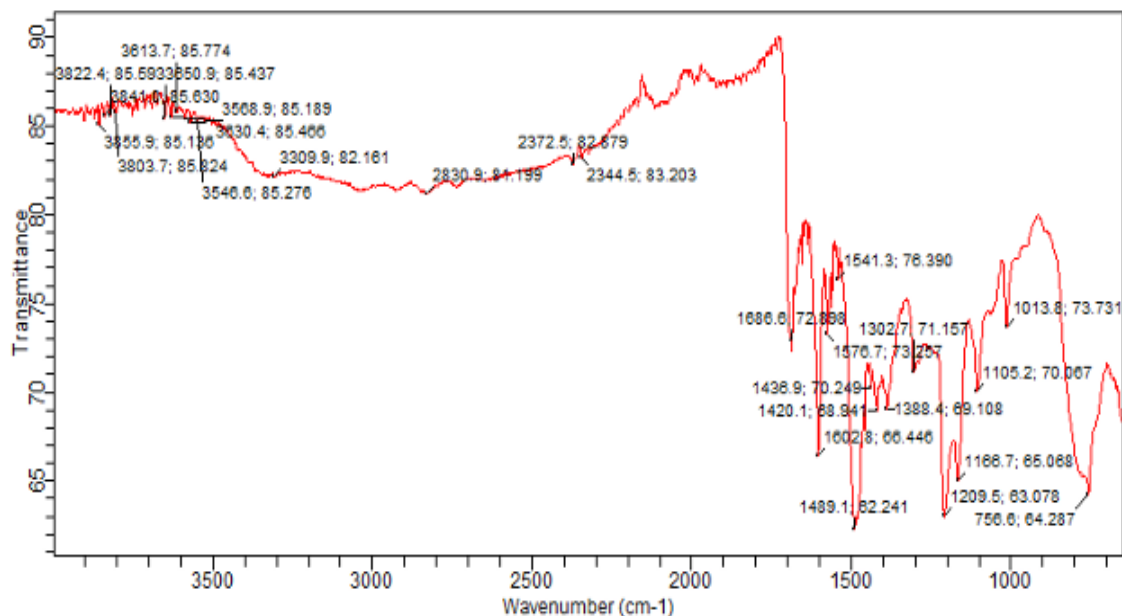


Figure 13: FT-IR spectrum of Schiff base (HL)

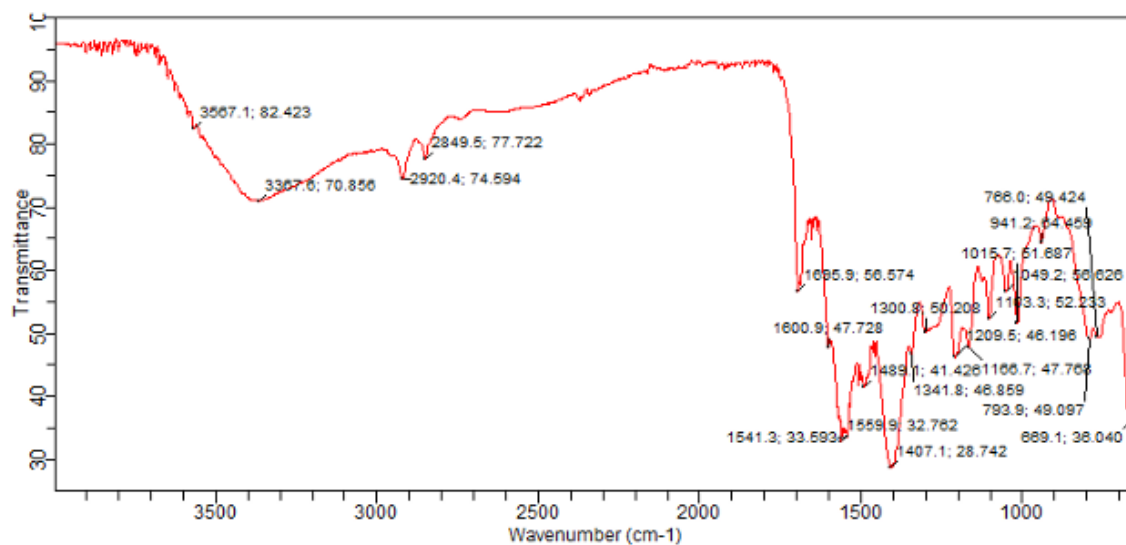


Figure 14: FT-IR spectrum of Cd (II) complex

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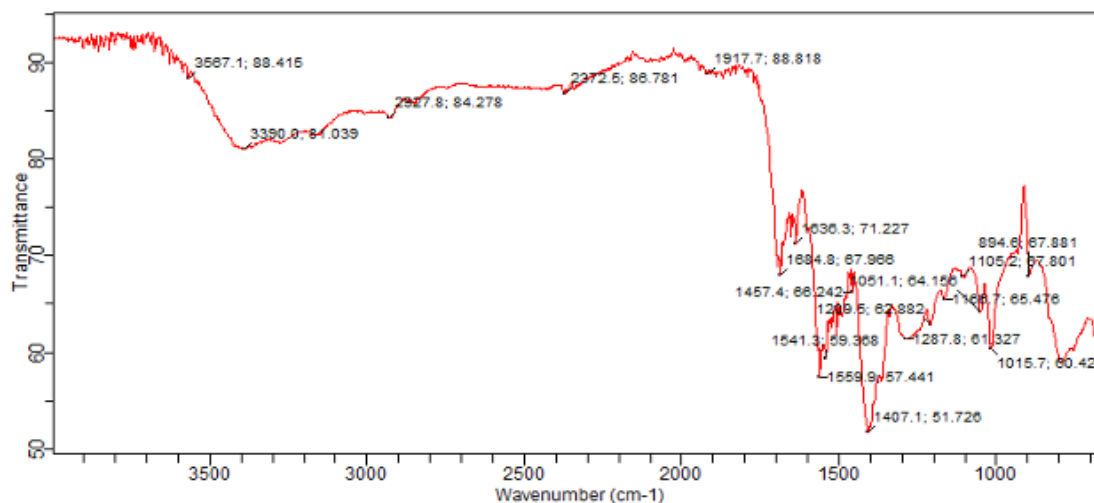
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Figure 15: FT-IR spectrum of Hg (II) complex

Biological activities

Antimicrobial activity

The synthesized ligand and its transition metal (II) complexes were screened in vitro for their antibacterial activities against *Escherichia coli* and *Staphylococcus aureus* bacterial strains using the well diffusion method. Well diffusion method was used because of its convenience, efficiency, and low cost. Stock solutions (10 mg/mL) were prepared for the ligand and its metal (II) complexes. Solvent (DMSO) was used as control for each dilution. Bacteria were sub-cultured in a nutrient agar medium. Standard antibacterial drugs (Ciprofloxacin) were used as positive controls for comparison with the ligand and the synthesized metal complexes [32].

The ability of the Schiff base ligand and its metal (II) complexes to inhibit the growth of the bacteria was compared to that of the known standard antibacterial drug, (Ciprofloxacin). Schiff base ligand and its metal (II) complexes demonstrated abilities to inhibit bacterial growth. Research has shown that coordination of a ligand, with the potential to inhibit bacterial growth, evokes antibacterial growth inhibition ability.

The mercury (II) complex had the highest activity against *E. coli* and *S. aureus*, while the Cd (II) complex was slightly higher activity than the ligand against *E. coli*. The Mn (II) complex had a slightly active than the ligand against both bacterial strains. Zinc (II) complex performed better than the ligand against *S. aureus* at 10 mg/mL. It was worth mentioning that the Schiff base and its metal (II) complexes inhibited the growth of Ciprofloxacin-resistant *E. coli* and *S. aureus*. Overall, the inhibition zones of the Schiff base ligand and its metal (II) complexes at different concentrations showed that the complexes had enhanced bactericidal activity than the ligand and the standard drug Ciprofloxacin against all the bacterial strains studied. The antibacterial activities of the metal complexes were directly proportional to their concentration. The increase in the antibacterial activity of the metal (II) complexes may be because of the metal ion on the normal state of the bacterial cell process. Research has shown that the structural components possessing

additional (C=N) bond with nitrogen and oxygen donor systems inhibit enzyme activity due to their deactivation by metal coordination. Thus, there is hope that these metal (II) complexes could reasonably be used in designing more potent antibacterial agents for the treatment of some common diseases caused by *E. coli* and *S. aureus* [33].

A similar procedure was followed for the antifungal activity of the above ligand and metal (II) complexes against two fungi namely, *Aspergillus niger* and *Aspergillus flavus*. Well diffusion method was used, and the well size was 8 mm, growth medium was potato dextrose agar media. All the plates were incubated at 32 °C for 48 hours. Results were in triplicate of inhibition zone (mm). Cd (II) complexes showed higher antifungal activity compared to ligand. Hg (II) complex was slightly higher active than the ligand against *Aspergillus niger* and *Aspergillus flavus*. The uncoordinated atoms with the ligands enhance the activity of the complexes. These results suggested that the antifungal activity is affected by the ligand, metal and the solvent used for investigation of the antifungal activity. The antimicrobial activities were calculated as mean±SD of three replicates (Table 6 and 7). The zones of inhibition (Figures 16 and 17) [34].

Table 6: Antibacterial data of ligand and metal (II) complexes

Complexes	Bacterial inhibition zone (mm)	
	<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>
HL	12±0.5	13±0.5
Hg (II)	24±0.9	27±0.9
Cd (II)	22±0.5	15±0.5
Mn (II)	23±0.5	20±0.5
Standard	28±0.9	27±0.5

Table 7: Antifungal data of ligand and metal (II) complexes

Complexes	Fungal inhibition zone (mm)	
	<i>Aspergillus flavus</i>	<i>Aspergillus niger</i>
HL	11±0.8	12±0.5
Hg (II)	22±0.9	30±0.6
Cd (II)	30±0.5	32±0.5
Mn (II)	21±0.5	26±0.5
Standard	6±0.0	6±0.0

Sample strength= 10 mg/mL

Positive control= Ciprofloxacin (CF)

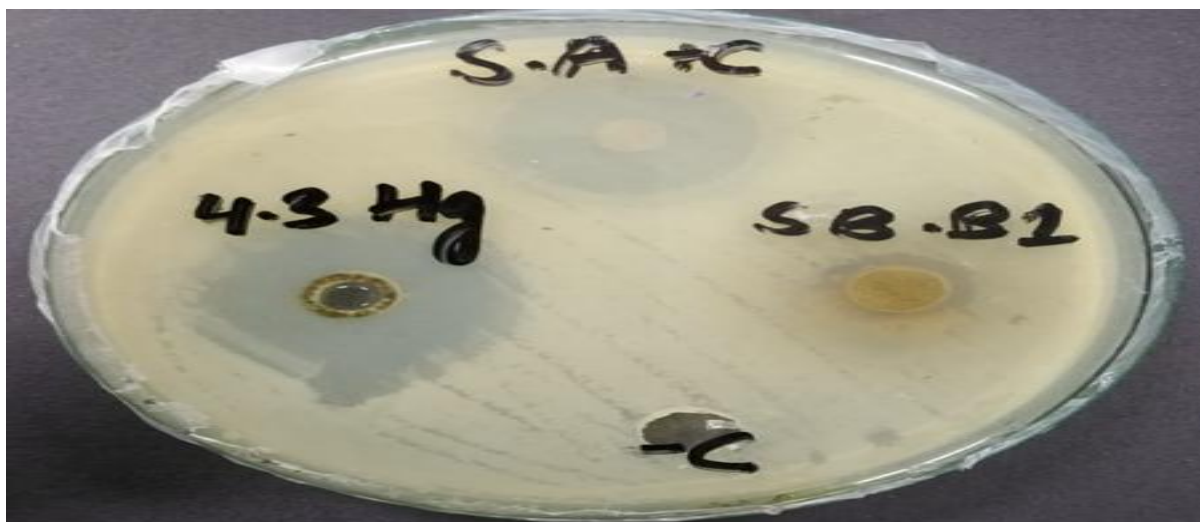


Figure 16: Antibacterial activity of ligand and Hg (II) complex

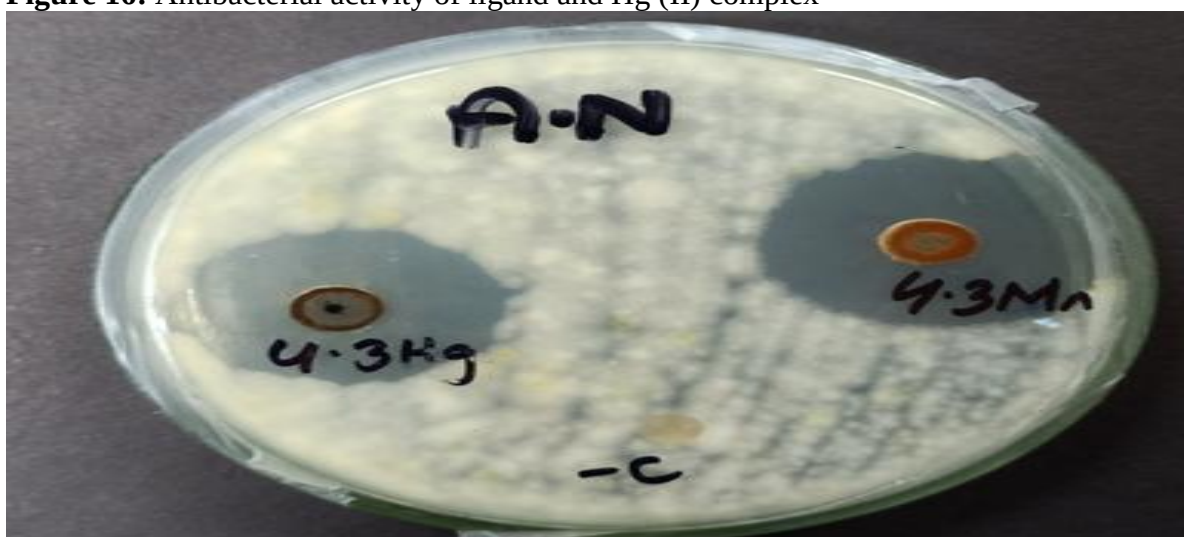


Figure 17: Inhibition zone of Hg (II) and Mn (II) metal complexes

Antioxidant activity

The antioxidant evaluation was carried out for all synthesized compounds at different concentrations with DPPH radical, using ascorbic acid as a standard. The maximum absorption of a stable DPPH[•] was at 517 nm in methanol. The decrease in absorption of radicals of DPPH at 517 nm may therefore be calculated because of its reduction. The percentage scavenging activity of the compounds was found to increase with an increase in concentration. The synthesized compounds showed an enhanced behavior as a radical scavenger compared to the standard ascorbic acid scavenging capacity. The scavenging activity of Schiff bases was found on the basis of the presence of electron-withdrawing groups which got enhanced on complexation as complexes are good hydrogen radical or electron donors for DPPH radical [35].

On ligation, azomethine hydrogen is very easy to abstract due to its highly acidic nature resulting in increasing the stability of complexes due to the presence of

electron-withdrawing group and dispersal of negative charge on the phenyl ring. The most active Schiff base ligand exhibited 86.11 % scavenging activity at lower concentrations and 92.57 % inhibition at higher concentrations but on ligation, the scavenging power gets enhanced from 93.8 % to 95.7 % for its cadmium complex. The order of antioxidant activity exhibited by the complexes was found to be Cd (II) > Zn (II) > Mn (II) which can be explained by the potential of the samples to infringement the free radical sequence by donation of a hydrogen atom. Hence, the concluded results of the present study showed that all complexes showed good antioxidant activity but cadmium(II) complexes are the most potent with lowest IC₅₀ values and bring to bear a hopeful treatment for the curative purpose of pathological diseases occurring due to oxidative stress [28].

Table 8: DPPH scavenging activity of ligand and its metal (II) complexes

Compound	Concentration (µg/mL)	DPPH scavenging activity (%)
HL	50	86.11
	100	87.32
	150	90.51
	200	92.57
Zinc(II)	50	88.11
	100	89.32
	150	91.51
	200	92.52
Cadmium (II)	50	93.8
	100	94.9
	150	95.4
	200	95.7
Ascorbic acid	50	96.8
	100	97.09
	150	97.6
	200	97.8

DPPH= 1,1-diphenyl-2-picrylhydrazyl

Conclusion

In the presence of 2-3 drops of glacial acetic acid and reflux for approximately 7 hours, the Schiff base was synthesized by the reaction of 2-amino-3-hydroxypyridine and terephthalaldehyde, with a transition temperature of 183 °C, and the color was brown. By vaporizing the mixture for approximately 9 hours, the chemical reactions of Zn (II) acetate, Cd (II), Hg (II), Mn (II) chloride were conducted at 1:2 molarities with the Schiff base, which resulted in colored metal (II) complexes. In the air, the synthesized complexes were stable except manganese and were solid in state. Various spectroscopic techniques such as UV/Vis, ¹H-NMR, FT-IR, have characterized the ligand and synthesized complexes. All the complexes have melting point between the range 126-298 °C. The synthesized complexes were soluble in organic solvents like DMSO. The molar conductivity values showed the

non-electrolytic nature of all the synthesized metal (II) complexes. Values fall in the range 1.70 to 5.37 $\mu\text{S}/\text{cm}^{-1}$

FT-IR spectra demonstrated that ligand act as bidentate during complex formation. In the ligand spectrum of FT-IR spectroscopy, characteristic bands were observed at 3309.9 cm^{-1} for -OH spectrum. In the UV spectra, Intra-ligand transitions were observed for ligand 232 nm while charge transfer transitions were absent for ligand. In ^1H -NMR spectra of the ligand, signal of -OH bond was present with a value of 10.38 ppm but disappeared in all the synthesized complexes. Hence this disappearance of -OH signal in the spectra of all newly synthesized complexes got cleared that complexation occurred in metal complexes. The singlet proton peak was observed at 8.120 ppm for ligand. σ -OH peak for ligand was found at 10.38 ppm and its disappearance in the complexes showed chelation of the ligand with metal (II) complex. The synthesized complexes and the free ligand were screened against bacterial strains of G+ bacteria (*S. aureus*) and G- bacteria (*E. coli*) to check their potential in antibacterial activities. Biological activities results have demonstrated that all complexes were strongly biologically active against selected bacterial strains. The bacterial data proved that the synthesized complexes were better than free ligand.

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