



Original article

Biological activity studies on metal complexes of novel tridentate Schiff base ligand. Spectroscopic and thermal characterization

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ABSTRACT

Metal complexes of novel Schiff base (HL) ligand, prepared via condensation of 4-aminoantipyrine and 2-aminophenol, are prepared. The ligand is characterized based on elemental analysis, mass, IR and ^1H NMR spectra. Metal complexes are reported and characterized based on elemental analyses, IR, ^1H NMR, solid reflectance, magnetic moment, molar conductance, ESR spectra and thermal analyses (TG, DTG and DTA). From the elemental analyses, 1:1 [M]:[ligand] complexes are prepared with the general formulae $[\text{M}(\text{L})\text{Cl}(\text{H}_2\text{O})_2] \cdot y\text{H}_2\text{O}$ ($\text{M} = \text{Mn}(\text{II}), \text{Co}(\text{II}), \text{Ni}(\text{II}), \text{Cu}(\text{II}), \text{Zn}(\text{II})$ and $\text{Cd}(\text{II}), y = 3-4$), $[\text{Fe}(\text{L})\text{Cl}_2(\text{H}_2\text{O})] \cdot 3\text{H}_2\text{O}$ and $[\text{Th}(\text{L})\text{Cl}(\text{H}_2\text{O})_2]\text{Cl}_2 \cdot 3\text{H}_2\text{O}$. The molar conductance data reveal that all the metal chelates are non-electrolytes (except Th(IV) complex, it is 2:1 electrolyte). IR spectra show that HL is coordinated to the metal ions in a uninegatively tridentate manner with NNO donor sites of the azomethine-N, amino N and deprotonated phenolic-O. From the magnetic and solid reflectance spectra, it is found that the geometrical structures of these complexes are octahedral. The thermal behaviour of these chelates shows that the hydrated complexes losses water molecules of hydration in the first step followed immediately by decomposition of the anions and ligand molecules in the subsequent steps. The activation thermodynamic parameters are calculated from the DTG curves using Coats–Redfern method. The synthesized ligand, in comparison to its metal complexes is screened for its antibacterial activity against bacterial species, *Escherichia coli*, *Pseudomonas putida*, *Exiguobacterium acetylicum* and *Bacillus simplex*. The activity data show that the metal complexes to be more potent/antibacterial than the parent Schiff base ligand against one or more bacterial species.

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1. Introduction

There is a continuing interest in metal complexes of Schiff bases. Because of the presence of both hard nitrogen or oxygen and soft sulphur donor atoms in the backbones of these ligands. They readily coordinate with a wide range of transition metal ions yielding stable and intensely coloured metal complexes, some of which have been shown to exhibit interesting physical and chemical properties [1] and potentially useful biological activities [2]. Many reports are available for the preparation and properties of model copper complexes which mimic copper-containing metalloproteins such as hemocyanine and tyrosinase. Two noticeable properties of copper proteins are an intense absorption band [3] near 600 nm and relatively high copper(II)/copper(I) reduction potentials [1]. Attention was particularly focused on their correlation with the active site of metalloenzymes and metalloproteins

containing dinuclear metalcenters in order to elucidate the factors that determine the reversible binding and activation of O_2 in various natural oxygen transport systems and mono- and dioxygenases and to mimic their activity [3]. Schiff bases [4] were still regarded as one of the most potential group of chelators for facile preparations of metallo-organic hybrid materials. In the past two decades, the properties of Schiff base metal complexes stimulated much interest for their noteworthy contributions to single molecule-based magnetism, material science [5], catalysis of many reactions like carbonylation, hydroformylation, oxidation, reduction and epoxidation [6], their industrial applications [7], complexing ability towards some toxic metals [8]. The interest in Schiff base compounds as analytical reagents is increasing since they enable simple and unexpensive determinations of different organic and inorganic substances [9]. The high affinity for the chelation of the Schiff bases towards the transition metal ions is utilized in preparing their solid complexes.

Schiff bases derived from condensation of various aldehydes with 4-aminoantipyrine [10–12] or 2-aminophenol [13–18] were reported. The ligands and their complexes were prepared and

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characterized by their elemental analysis, TG, IR and electronic spectral studies, molar conductance and magnetic susceptibility measurements. The antimicrobial activities of the ligands and their metal complexes were detected on Gram-positive, Gram-negative bacteria and on fungi. The antimicrobial activity of the organic ligands increased several folds on chelation as compared to the ligand molecule alone [10–18].

The present study describes the coordination behaviour of novel Schiff base derived from the condensation of 4-aminoantipyrine with 2-aminophenol (HL) towards some transition elements, which may help in more understanding of the mode of chelation of HL towards metals. For this purpose the complexes of Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Th(IV) ions with HL are studied in solution and in the solid state. The stability constants are evaluated and structure of the studied complexes is elucidated using elemental analyses, IR, ^1H NMR, solid reflectance, magnetic moment, ESR, molar conductance, and thermal analyses measurements. The biological activity of the parent Schiff base and its metal complexes is reported.

2. Experimental

2.1. Materials and reagents

All chemicals used were of the analytical reagent grade (AR), and of highest purity available. They included 4-aminoantipyrine (Sigma) and o-aminophenol (Sigma). $\text{Cu(II)Cl}_2 \cdot 2\text{H}_2\text{O}$ (Sigma), $\text{Co(II)Cl}_2 \cdot 6\text{H}_2\text{O}$ and $\text{Ni(II)Cl}_2 \cdot 6\text{H}_2\text{O}$ (BDH); MnCl_2 (Sigma), ThCl_4 (Aldrich), $\text{ZnCl}_2 \cdot 2\text{H}_2\text{O}$ (Ubichem), $\text{CdCl}_2 \cdot 2\text{H}_2\text{O}$ (Sigma) and $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (Prolabo) were used. Organic solvents used included absolute ethyl alcohol, diethyl ether and dimethylformamide (DMF). Sodium chloride (Adwic), tryptone (Oxoford), Yeast extract (Oxoford) and agar (Adwic) were also used. These solvents were either spectroscopically pure from BDH or purified by the recommended methods [22]. Hydrogen peroxide and chloride, carbonate and hydroxide salts of sodium (A.R.) were used. Hydrochloric and nitric acids (Merck) were used. De-ionized water collected from all glass equipments was usually used in all preparations.

2.2. Solutions

Fresh stock solution of 5.0×10^{-3} M HL was prepared by dissolving the accurately weighed amount of HL (0.368 g/L) in the appropriate volume of absolute ethanol. 5.0×10^{-3} M Stock solutions of the metal salts (Fe(III), 0.271 g/L; Co(II), 0.238 g/L; Ni(II), 0.238 g/L; Cu(II), 0.218 g/L; Zn(II), 0.219 g/L; Cd(II), 0.20 g/L; Mn(II), 0.170 g/L and Th(IV), 0.316 g/L) were prepared by dissolving the accurately weighed amounts of the metal salts in the appropriate volume of de-ionized water. The metal salt solutions were acidified and standardized by the recommended procedures [22]. Dilute solutions of the metal ions and Schiff base under study of 2.5×10^{-6} M, 1.0×10^{-6} M, 2.5×10^{-5} M, 1.0×10^{-5} M, and 1.0×10^{-4} M were prepared by accurate dilution.

For potentiometric studies, all solutions of metal ions were prepared by dissolving the calculated amount of their salts in the least amount of water, then ethanol was added to the appropriate volume.

Standard 0.1 N sodium carbonate solution was prepared from dried sodium carbonate. 0.1 N hydrochloric acid was prepared and standardized using sodium carbonate. 1.00 M sodium chloride solution was also prepared. A 1:1 sodium hydroxide solution was prepared from A.R. product and stored in a well steamed waxed tall glass cylinder for some days with occasional shaking to obtain a carbonate free sodium hydroxide solution. The clear solution was filtered through a sintered glass funnel G4. Solutions of the

required molarities were prepared by dilution and then standardized by recommended procedure [19].

2.3. Instruments

pH measurements were carried out using 716 DMS Titrino Metrohm connected with 728 Metrohm Stirrer. Elemental microanalyses of the solid chelates for C, H and N were performed at the Microanalytical Center, Cairo University. The analyses were repeated twice to check the accuracy of the analyzed data. The molar conductance of solid chelates in DMF was measured using Sybron-Barnstead conductometer (Meter-PM.6, $E = 3406$). Infrared spectra were recorded on a Perkin-Elmer FT-IR type 1650 spectrophotometer in wave number region $4000\text{--}200\text{ cm}^{-1}$. The spectra were recorded as KBr pellets. The solid reflectance spectra were measured on a Shimadzu 3101pc spectrophotometer. The molar magnetic susceptibility was measured on powdered samples using the Faraday method. The diamagnetic corrections were made by Pascal's constant and $\text{Hg[Co(SCN)}_4\text{]}$ was used as a calibrant. The mass spectra were recorded by the EI technique at 70 eV using MS-5988 GC-MS Hewlett-Packard instrument in the Microanalytical Center, Cairo University. The ^1H NMR spectra were recorded using 300 MHz Varian-Oxford Mercury. The deuterated solvent used was dimethylsulphoxide (DMSO) and the spectra extended from 0 to 15 ppm. The thermal analyses (TGA and DTA) were carried out in dynamic nitrogen atmosphere (20 mL min^{-1}) with a heating rate of $10^\circ\text{C min}^{-1}$ using Shimadzu TG-50H and DTA-50H thermal analyzers.

2.4. Procedures

2.4.1. Potentiometric measurements

The potentiometric measurements were carried out at 25°C and ionic strength $\mu = 0.1$ M by the addition of appropriate amounts of 1.0 M sodium chloride solution. The pH-meter was calibrated before each titration using standard buffers.

The ionization constants of the investigated Schiff base and the stability constants of its metal chelates with Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Th(IV) ions were determined potentiometrically using the technique of Sarin and Munshi [20]. For this purpose three solution mixtures of total volume 50 mL were prepared. Thus,

- (A) 3 mL of standard HCl (around 0.10 M) + 5 mL of 1.0 M NaCl + 25 mL ethanol and the volume is completed up to 50 mL with distilled water.
- (B) 3 mL of 0.10 M HCl + 5 mL of 1.0 M NaCl + 25 mL of 0.001 M of ethanolic solution of the Schiff base and the volume being complete to 50 mL with distilled water.
- (C) 3 mL of 0.10 M HCl + 5 mL of 1.0 M NaCl + 25 mL of 0.001 M of ethanolic solution of the Schiff base + 5 mL 0.001 M metal ion solution and the volume being completed to 50 mL with distilled water.

The above three mixtures were titrated potentiometrically against standard sodium hydroxide solution (0.10 M). The molarities of HCl and NaOH were checked every day before the titrations. The appropriate volume of ethanol was added so as to keep the ratio 50% (v/v) ethanol/water, constant to ensure the complete solubilities of the Schiff base during the titration. The three curves obtained were referred to as: (A) acid titration curve, (B) ligand titration curve and (C) complex titration curve. The ionization constant of the ligand is calculated using the equation used by Irving and Rossotti [21]. The metal–ligand stability constants were

Table 1
Analytical and physical data of HL ligand and its metal complexes.

Compound	Colour (yield) %	M.p. (°C)	% Found (calcd)				$\mu_{\text{eff.}}$ (B.M.)	$\Lambda_m \Omega^{-1} \text{mol}^{-1} \text{cm}^2$
			C	H	N	M		
HL	Brown (89)	180 ± 2	69.19 (69.39)	6.40 (6.12)	19.25 (19.05)	–	–	–
$\text{C}_{17}\text{H}_{18}\text{N}_4\text{O}$								
$[\text{Mn}(\text{L})\text{Cl}(\text{H}_2\text{O})_2] \cdot 3\text{H}_2\text{O}$	Black (75)	>300	43.22 (43.08)	5.81 (5.70)	12.01 (11.83)	11.80 (11.61)	5.21	9.85
$\text{C}_{17}\text{H}_{27}\text{ClMnN}_4\text{O}_6$								
$[\text{Fe}(\text{L})\text{Cl}_2(\text{H}_2\text{O})] \cdot 3\text{H}_2\text{O}$	Black (71)	>300	41.79 (41.46)	5.27 (5.08)	11.39 (11.38)	11.55 (11.38)	5.43	13.10
$\text{C}_{17}\text{H}_{25}\text{Cl}_2\text{FeN}_4\text{O}_5$								
$[\text{Co}(\text{L})\text{Cl}(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O}$	Black (75)	>300	41.49 (41.17)	5.74 (5.85)	11.48 (11.30)	11.77 (11.91)	5.87	8.05
$\text{C}_{17}\text{H}_{29}\text{CoClN}_4\text{O}_7$								
$[\text{Ni}(\text{L})\text{Cl}(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O}$	Black (75)	>300	40.95 (41.17)	5.98 (5.85)	11.23 (11.30)	12.01 (11.91)	4.13	9.65
$\text{C}_{17}\text{H}_{29}\text{ClNiN}_4\text{O}_7$								
$[\text{Cu}(\text{L})\text{Cl}(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O}$	blue (83)	>300	40.53 (40.80)	5.73 (5.80)	10.91 (11.20)	12.55 (12.70)	2.15	12.15
$\text{C}_{17}\text{H}_{29}\text{CuClN}_4\text{O}_7$								
$[\text{Zn}(\text{L})\text{Cl}(\text{H}_2\text{O})_2] \cdot 3\text{H}_2\text{O}$	Black (61)	>300	42.20 (42.19)	5.55 (5.58)	11.27 (11.58)	13.33 (13.44)	Diam.	7.09
$\text{C}_{17}\text{H}_{27}\text{ClN}_4\text{O}_6\text{Zn}$								
$[\text{Cd}(\text{L})\text{Cl}(\text{H}_2\text{O})_2] \cdot 3\text{H}_2\text{O}$	Brown (71)	>300	38.52 (38.45)	5.45 (5.09)	10.32 (10.56)	21.31 (21.11)	Diam.	8.50
$\text{C}_{17}\text{H}_{27}\text{CdClN}_4\text{O}_6$								
$[\text{Th}(\text{L})\text{Cl}(\text{H}_2\text{O})_2]\text{Cl}_2 \cdot 3\text{H}_2\text{O}$	Brown (75)	>300	28.59 (28.20)	4.01 (4.13)	7.75 (7.74)	32.32 (32.07)	Diam.	135.7
$\text{C}_{17}\text{H}_{29}\text{Cl}_3\text{N}_4\text{O}_6\text{Th}$								

calculated using methods applied for computing successive stability constants [22].

2.4.2. Synthesis of Schiff base (HL)

Hot solution (60 °C) of 4-aminoantipyrine (5.0 g, 24.88 mmol) was mixed with hot solution (60 °C) of *o*-aminophenol (2.71 g, 24.88 mmol) in 50 mL ethanol. The resulting mixture was left under reflux for 2 h and the formed solid product was separated by filtration, purified by crystallization from ethanol, washed with diethyl ether and dried in a vacuum over anhydrous calcium chloride. The brownish yellow product was produced in 89% yield for HL.

2.4.3. Synthesis of metal complexes

The metal complexes of the Schiff base HL was prepared by the addition of hot solution (60 °C) of the appropriate metal chloride (1.0 mmol) in an ethanol–water mixture (1:1, 25 mL) to the hot solution (60 °C) of the Schiff bases (0.294 g HL, 1.0 mmol) in the same solvent (25 mL). The resulting mixture was stirred under reflux for 1 h whereupon the complexes precipitated. They were collected by filtration and purified by washing with an ethanol–water mixture (1:1) and diethyl ether. The analytical data for C, H and N were repeated twice.

2.4.4. Determination of the metal content of the chelates

An accurately weighed portion of the different chelates ranged from 10 to 30 mg was placed in Kjeldahl flask. A measured volume of concentrated nitric acid ranged from 5 to 10 mL was added initially to the powdered chelates, to start the fast wet oxidation digestion. This mixture had been digested by a gradual heating with dropping of H_2O_2 solution. This treatment was conducted until most of the powdered complexes were diminished and the remained solution had the colour of the corresponding metal salt. This solution was diluted up to 50 mL with bidistilled water and the metal content was determined by titration against standard EDTA solution at a suitable pH value using the suitable indicator.

2.4.5. Biological activity

It is carried out using susceptibility test method. 0.5 mL spore suspension (10^{-7} – 10^{-8} spore/mL) of each of the investigated organisms was added to a sterile agar medium just before

solidification, then poured into sterile petri dishes (9 cm in diameter) and left to solidify. Using sterile cork borer (6 mm in diameter), three holes (wells) were made in each dish, then 0.1 mL of the tested compounds dissolved in DMF (100 $\mu\text{g/mL}$) were poured into these holes. LB agar media (it is a suitable media for most bacteria and it composed of sodium chloride (10 g/L), tryptone (10 g/L), yeast extract (10 g/L) and agar (15 g/L)) surfaces were inoculated with four investigated bacteria (2 Gram-positive and 2 Gram-negative) then, transferred to a saturated disk with a tested solution in the center of Petri dish (agar plates). Finally, the dishes were incubated at 37 °C for 48 h where clear or inhibition zones were detected around each hole. 0.1 mL DMF alone was used as a control under the same condition for each organism and by subtracting the diameter of inhibition zone resulting with DMF from that obtained in each case, both antibacterial activities can be calculated as a mean of three replicates [23].

3. Results and discussion

3.1. Characterization of Schiff base

3.1.1. Elemental analyses of the Schiff base

The novel Schiff base is prepared and subjected to elemental analyses, mass and IR spectral analyses. The results of elemental analyses (C, H, N) with molecular formula and the melting point are presented in Table 1. The results obtained are in good agreement with those calculated for the suggested formula and the melting point is sharp indicating the purity of the prepared Schiff base. The structure of the Schiff base under study is as shown in Fig. 1.

The structure of HL is also confirmed by IR and ^1H NMR spectra, which will be discussed in detailed manner with metal complexes latter.

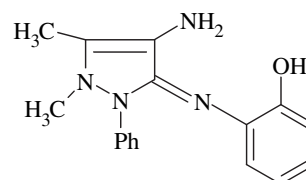
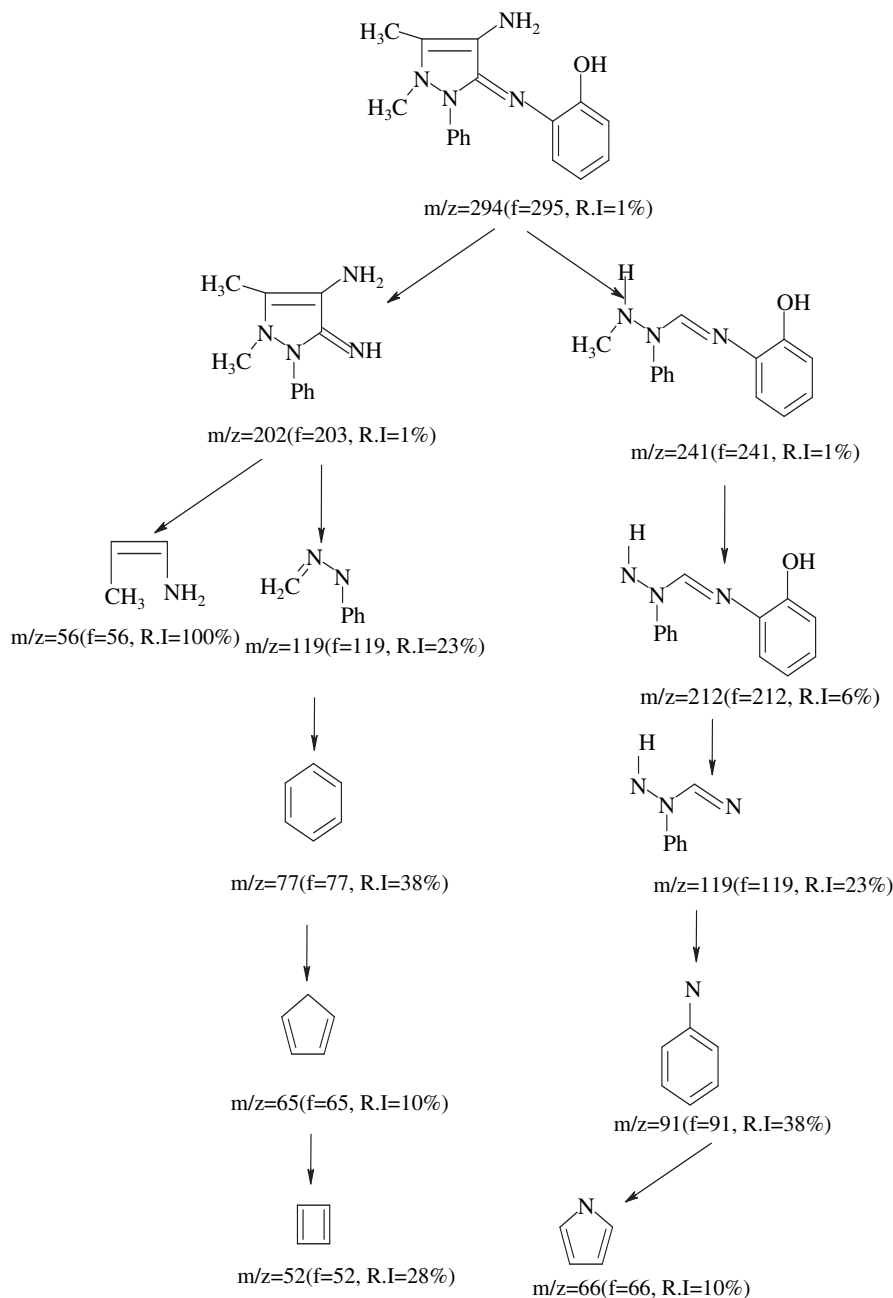


Fig. 1. Structure of Schiff base (HL).



Scheme 1. Mass fragmentation pattern of HL.

3.1.2. Mass spectrum of the Schiff base

The electron impact mass spectra of HL ligand is recorded and investigated at 70 eV of electron energy. The mass spectrum of the studied Schiff base is characterized by moderate to high relative intensity molecular ion peaks. It is obvious that, the molecular ion peaks are in good agreement with their suggested empirical formula as indicated from elemental analyses (Table 1).

The different pathways of the fragments of the parent molecular ion peaks are given in Scheme 1. Fragments at $m/z = 56$ (R.I. = 100%, base peak) may be due to $C_3H_7N_3$ ion. The other molecular ion peaks appeared in the mass spectrum (abundance range from 1–100 %) are attributed to the fragmentation of HL molecule obtained from the rupture of different bonds inside the molecule as shown in Scheme 1.

3.1.3. Potentiometric determination of the ionization constant of Schiff base

The ionization constant of the ionizable groups in Schiff base under investigation is determined by a method similar to that described by Sarin and Munshi [20].

The average of protons associated with the ligand (\bar{n}_A) at different pH values is calculated utilizing acid and ligand titration curves. The pK_a values can be calculated from the curves obtained by plotting \bar{n}_A versus pH. The formation curves are found between 0 and 1. This indicates that the ligand has one dissociable proton from OH group. The pK_a values can be calculated also by plotting $\log(\bar{n}_A/1 - \bar{n}_A)$ versus pH whereby a straight line is obtained intersecting the x-axis at the pK_a value. The pK_a value is found to be 9.30 which can be attributed to the ionization of the phenolic-OH proton from HL ligand.

Table 2
Cumulative data of $\log \beta_1$ and $\log \beta_2$ values for complexes.

Ion	HL									
	$\log \beta_1$				$-\Delta G^\circ$ (kJ mol ⁻¹)	$\log \beta_2$				$-\Delta G^\circ$ (kJ mol ⁻¹)
	A	B	M			A	B	C	M	
Mn(II)	9.55	9.69	9.62	54.9		18.16	18.53	18.48	18.39	70.6
Fe(III)	9.58	9.78	9.68	55.0		18.58	18.72	18.84	18.71	71.0
Co(II)	9.56	9.72	9.64	54.9		18.43	18.63	18.68	18.63	70.9
Ni(II)	9.58	9.77	9.68	55.0		18.69	18.78	18.96	18.81	71.1
Cu(II)	9.59	9.81	9.70	55.1		18.72	18.86	19.04	18.87	71.2
Zn(II)	9.57	9.75	9.66	55.0		18.20	18.57	18.66	18.48	70.7
Cd(II)	9.60	9.87	9.74	55.2		18.30	18.63	18.78	18.57	70.8
Th(IV)	9.61	9.97	9.79	55.3		18.79	18.97	19.10	18.95	71.3

Where: (A) Interpolation at half values method. (B) Correction – term method. (C) Mid – Point method. (M) Mean

The free energy change, ΔG° , was also calculated and is found to be 54.04 KJ mol⁻¹. The negative value indicates the spontaneous character of association reaction.

3.1.4. Potentiometric determination of the stability constants

The stability constants of the Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Th(IV) complexes with HL ligand are determined potentiometrically using the method described by Sarin [20] and Bjerrum [24]. The formation curves of the investigated complexes are obtained by plotting a graph between average number of ligands attached per metal ion (\bar{n}) and free ligand exponent (pL). Values of \bar{n} and pL are calculated as previously mentioned. The maximum \bar{n} values calculated for metal–ligand system are found to be not exceed two indicating the possibilities of formation of 1:1 and 1:2 (metal:ligand) complexes. The mean $\log \beta_1$ and $\log \beta_2$ values for complexes of Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Th(IV) ions with HL are listed in Table 2.

The complex-forming abilities of the transition metal ions are frequently characterized by stability orders. The order of stability constants is found to be: Mn(II) < Co(II) < Ni(II) < Cu(II) > Zn(II) in accordance with Irving and Williams order [25,26] for divalent metal ions of the 3d series. It is clear from Table 2 that the stability of Cu(II) complexes is larger as compared to the other metal ions of 3d series. Under influence of the ligand field, Cu(II) (3d⁹) will receive some extra stabilization [27] due to tetragonal distortion of

octahedral symmetry in their complexes. The Cu(II) complexes will be further stabilized due to Jhan–Tellar effect [28].

One would expect a bigger difference between $\log K_1$ and $\log K_2$ values in such a ligand because of possible steric hindrance to the linking of the second ligand to the metal ion. The small difference may be due to trans-structure.

The free energy of formation, ΔG° , accompanying the complexation reaction has been determined at 25 °C. The results are given in Table 2. From the table, it is apparent that the negative values of ΔG° show that the driving tendency of the complexation reaction is from left to right and the reaction proceeds spontaneously.

3.1.5. Composition and structures of Schiff base complexes

The solid complexes are subjected to elemental analyses (C, H and N, metal content), infrared spectral studies (IR), nuclear magnetic resonance (¹H NMR), magnetic studies, molar conductance and thermal analyses (TG, DTG and DTA), to identify their tentative formulae in a trial to elucidate their molecular structures. The biological activity of the Schiff base ligand and its metal chelates is studied against antibacterial organisms.

3.1.6. Elemental analyses of the complexes

The results of elemental analyses, Table 1 are in good agreement with those required by the proposed formulae.

3.1.7. Molar conductance measurements

The results given in Table 1 show that the Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) complexes have a molar conductivity values in the range 7.09–13.10 Ω⁻¹ mol⁻¹ cm² (Table 1) which indicates the non-ionic nature of these complexes and they are considered as non-electrolyte. Th(IV) complex is found to have molar conductance value of 135.7 Ω⁻¹ mol⁻¹ cm² indicating that it is ionic and of the type 2:1 electrolyte [29].

3.1.8. IR spectral studies

The data of the IR spectra of Schiff base ligand (HL) and its complexes are listed in Table 3. The IR spectra of the complexes are compared with those of the free ligand in order to determine the coordination sites that may be involved in chelation. There are some guide peaks, in the spectra of the ligand, which are of good help for achieving this goal. The position and/or the intensities of

Table 3
IR data (4000–400 cm⁻¹) of HL ligand and its metal complexes.

Compound	$\nu(\text{OH})$ (phenolic)	$\nu(\text{NH}_2)$	$\nu(\text{C}=\text{N})$ (azomethine)	$\delta(\text{NH}_2)$	$\delta(\text{OH})$	$\nu(\text{C}-\text{O})$	$\nu(\text{M}-\text{N})$ (azomethine)	$\nu(\text{M}-\text{N})$ (amino)	$\nu(\text{M}-\text{O})$
HL	3431m	3375m, 3330m	1648m	1589m	1404s	1270m	–	–	–
C ₁₇ H ₁₈ N ₄ O									
[Mn(L)Cl(H ₂ O) ₂]·3H ₂ O	3405br	Disappear	1625m	1593m	1406s	disappear	431w	503w	585s
C ₁₇ H ₂₇ ClMnN ₄ O ₆									
[Fe(L)Cl ₂ (H ₂ O)]·3H ₂ O	3391br	Disappear	1605m	1547m	1405s	1286s	459w	504w	589s
C ₁₇ H ₂₅ Cl ₂ FeN ₄ O ₅									
[Co(L)Cl(H ₂ O) ₂]·4H ₂ O	3402br	Disappear	1621m	1495m	1424m	disappear	430w	503w	593w
C ₁₇ H ₂₉ CoClN ₄ O ₇									
[Ni(L)Cl(H ₂ O) ₂]·4H ₂ O	3405br	3245br	1616m	1570m	1401w	1255s	450s	502s	588s
C ₁₇ H ₂₉ ClNiN ₄ O ₇									
[Cu(L)Cl(H ₂ O) ₂]·4H ₂ O	3420br	3172sh	1622m	1596m	1411m	disappear	462w	503w	553w
C ₁₇ H ₂₉ CuClN ₄ O ₇									
[Zn(L)Cl(H ₂ O) ₂]·3H ₂ O	3431br	3231br	1614sh	1564m	disappear	1276s	454w	505w	592w
C ₁₇ H ₂₇ ClN ₄ O ₆ Zn									
[Cd(L)Cl(H ₂ O) ₂]·3H ₂ O	Disappear	3244br	1615sh	1563m	disappear	1272s	451w	504s	593s
C ₁₇ H ₂₇ CdClN ₄ O ₆									
[Th(L)Cl(H ₂ O) ₂]·Cl ₂ ·3H ₂ O	Disappear	3241br	1615m	1597m	Disappear	1253s	455w	501s	587w
C ₁₇ H ₂₉ Cl ₃ N ₄ O ₆ Th									

sh = sharp, m = medium, br = broad, s = small, w = weak

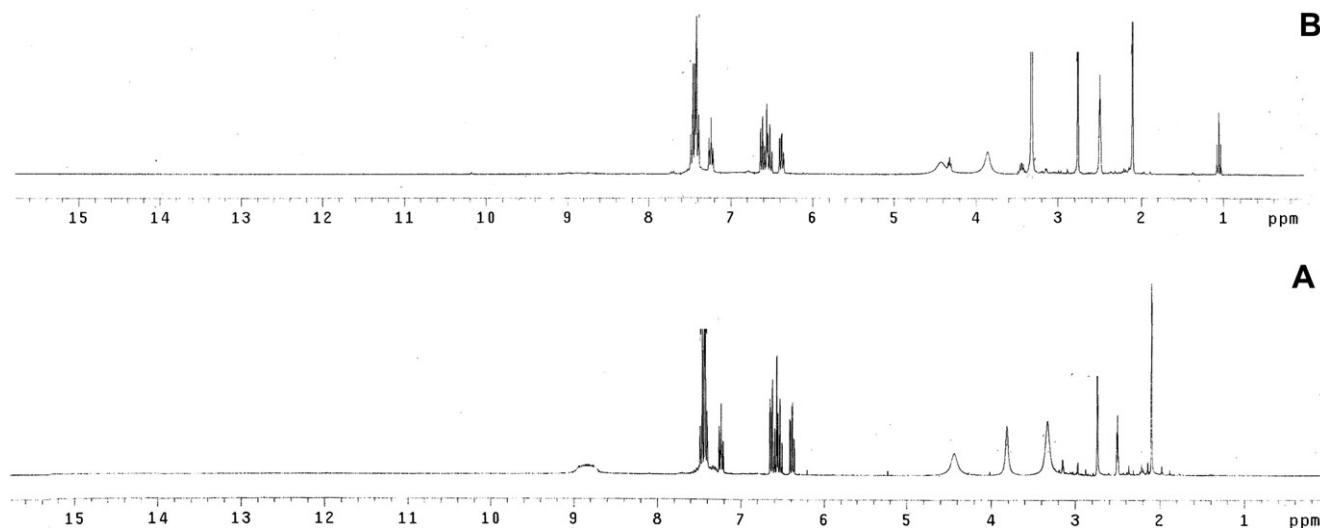


Fig. 2. ^1H NMR spectra of (A) HL and (B) Cd(II) complex.

these peaks are expected to be changed upon chelation. These characteristic peaks are listed in Table 3. Upon comparison it is found that:

- (1) The $\nu(\text{C}=\text{N})$ stretching vibration of the azomethine is found in the free ligand at 1648 cm^{-1} . This band is shifted to higher or lower wavenumbers in the complexes indicating the participation of the azomethine nitrogen in coordination [30].
- (2) The IR spectrum of HL shows a medium broad band at 3375 and 3330 cm^{-1} which attributed to NH_2 of the amino group. The existence of water of hydration and/or water of coordination in the spectra of the complexes render it difficult to get conclusion from the NH_2 group of the HL ligand, which will be overlapped by those of the water molecules. The participation of the NH_2 group is further confirmed by clarifying the effect of chelation on the in-plane bending, $\delta(\text{NH}_2)$ vibration. The shift of this band, from 1589 cm^{-1} in the free HL ligand to $1495\text{--}1597\text{ cm}^{-1}$ in the complexes indicates the participation of the NH_2 group in complex formation [31].
- (3) The IR spectrum of the HL ligand shows a broad band at $3431\text{--}3391\text{ cm}^{-1}$, which can be attributed to the phenolic-OH group. This band is still broad in all complexes, which renders it difficult to attribute to the involvement of phenolic-OH group in coordination. The involvement of the deprotonated phenolic-OH group in chelation is confirmed by the blue-shift of the $\nu(\text{C}-\text{O})$ stretching band, observed at 1270 cm^{-1} in the free ligand, to the extent of $2\text{--}17\text{ cm}^{-1}$ in the complexes [32]. Also the participation of the OH group is apparent from the disappearance (in Mn(II), Co(II) and Cu(II) complexes) or shift in position of the $\delta(\text{OH})$ in-plane bending at 1404 cm^{-1} in the free ligand by $1\text{--}20\text{ cm}^{-1}$ in the remaining complexes [33].
- (4) New bands are found in the spectra of the complexes in the regions $553\text{--}593$ (hydroxyl O), which are assigned to $\nu(\text{M}-\text{O})$ stretching vibrations for HL metal complexes. The bands at $430\text{--}460$ in HL metal complexes have been assigned to $\nu(\text{M}-\text{N})$ of the azomethine mode. The $\nu(\text{M}-\text{N})$ bands due to amino group appeared at $502\text{--}505\text{ cm}^{-1}$ [31].

Therefore, from the IR spectra, it is concluded that HL behaves as a uninegative tridentate ligand with NNO donor sites coordinating to the metal ions via the azomethine N, deprotonated phenolic-O and amino N atoms.

3.1.9. ^1H NMR spectra

A survey of literature revealed that the NMR spectroscopy has been proved useful in establishing the nature and structure of many Schiff base as well as its complexes in solutions. The ^1H NMR spectra of Schiff base (HL) and its Cd(II) complex are recorded in d_6 -dimethylsulfoxide (DMSO) solution using tetramethylsilane (TMS) as internal standard. The ^1H NMR spectra of the Schiff base HL and its diamagnetic Cd(II) complex are shown in Fig. 2 and the chemical shifts of the different types of protons are listed in Table 4.

The spectrum of the complex is examined in comparison with those of the parent Schiff base. Upon examinations it is found that:

- (1) The OH signal, appeared in the spectrum of HL ligand at 8.90 ppm (Table 4), completely [32] disappeared in the spectrum of its Cd(II) complex indicating that the OH proton is removed by the chelation with metal ion.
- (2) The signal observed at 4.432 ppm for HL ligand is assigned to NH_2 protons. This signal is found at 3.857 for Cd(II) complex. This indicates that the NH_2 group is coordinated to the Cd(II) ion without proton displacement.

Therefore, it is clear from these results that the data obtained from the elemental analyses, IR and ^1H NMR spectral measurements are in agreement with each other.

3.1.10. Magnetic susceptibility and electronic spectral studies

The diffused reflectance spectrum of the Mn(II) complex shows three bands at $21,739\text{--}21,980\text{ cm}^{-1}$ assignable to $^4\text{T}_{1g} \rightarrow ^6\text{A}_{1g}$, $^4\text{T}_{2g}(\text{G}) \rightarrow ^6\text{A}_{1g}$ and $^4\text{T}_{1g}(\text{D}) \rightarrow ^6\text{A}_{1g}$ transitions, respectively [31,34].

Table 4

^1H NMR spectral data of the Schiff base and its metal chelates.

Compound	Chemical shift, (δ) ppm	Assignment
HL	8.90	(S, 1H, OH)
	6.358–7.485	(m, 9H, 5ArH and 4 phenolic-H)
	4.432	(br, 2H, NH_2)
	2.739	(S, 3H, N- CH_3)
	2.096	(S, 3H, C- CH_3)
[Cd(L)Cl(H ₂ O) ₂] \cdot 3H ₂ O	6.353–7.488	(m, 9H, 5ArH and 4 phenolic-H)
	3.857	(br, 2H, NH_2)
	2.762	(S, 3H, N- CH_3)
	2.107	(S, 3H, C- CH_3)

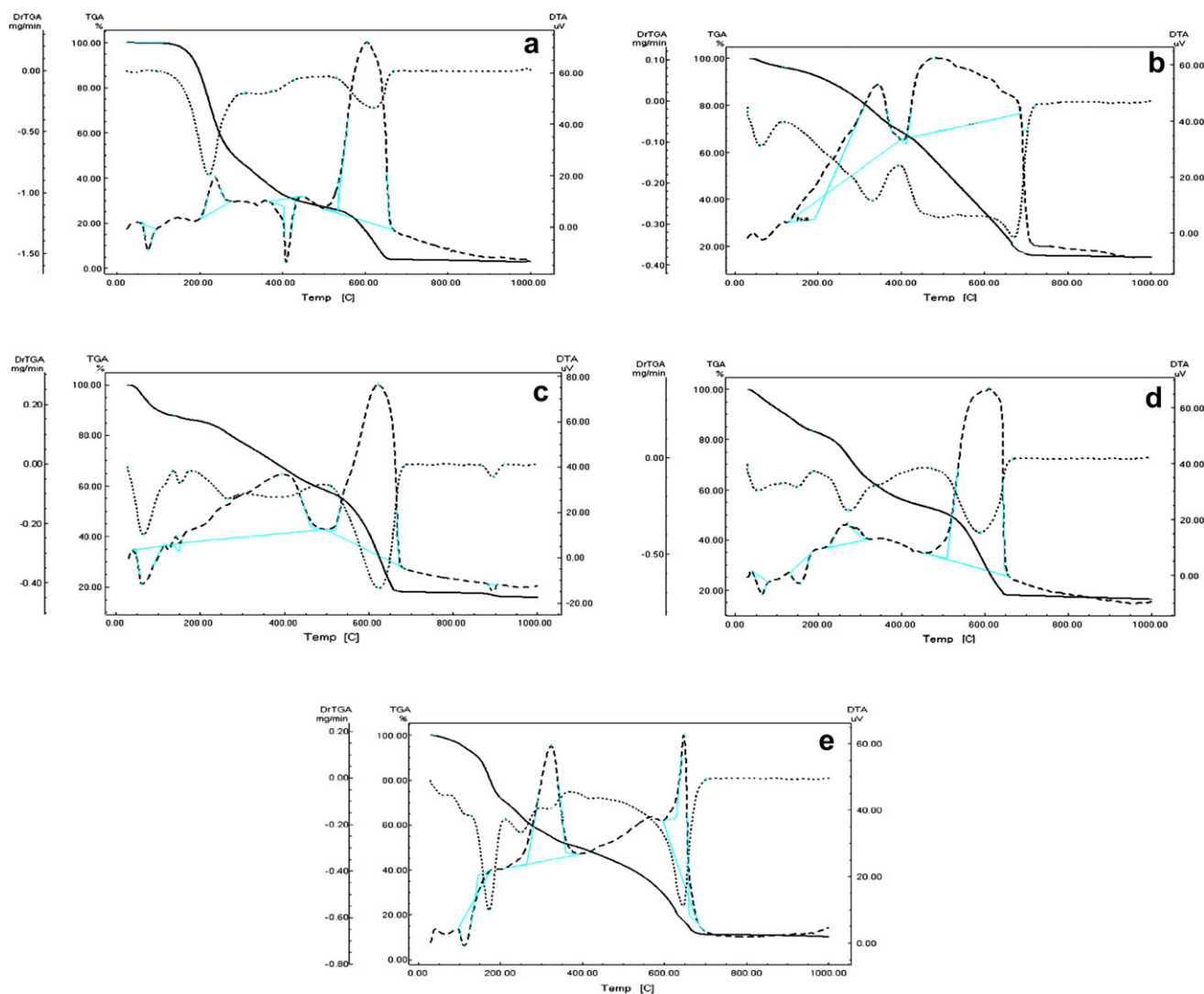


Fig. 3. Thermal analysis of HL ligand and its complexes. (a) HL ligand, (b) Fe(III), (c) Co(II), (d) Ni(II), (e) Cu(II) complexes.

The magnetic moment value is found to be 5.21 B.M. which indicates the presence of Mn(II) complex in octahedral structure.

From the diffused reflectance spectrum it is observed that, the Fe(III) chelate exhibits a band at $21,959\text{ cm}^{-1}$, which may be assigned to the ${}^6A_{1g} \rightarrow T_{2g}(G)$ transition in octahedral geometry of the complex [35]. The ${}^6A_{1g} \rightarrow {}^5T_{1g}$ transition appears to be split into two bands at $17,455\text{ cm}^{-1}$ and $12,950\text{ cm}^{-1}$. The observed magnetic moment of Fe(III) complex is found to be 5.43 B.M. Thus, the complex formed has the octahedral geometry involving d^2sp^3 hybridization in Fe(III) ion [34]. The spectrum shows also a band at $25,290\text{ cm}^{-1}$ which may attribute to ligand to metal charge transfer.

The Ni(II) complex reported herein is found to has a room temperature magnetic moment value of 4.13 B.M.; which are in the normal range observed for octahedral Ni(II) complexes ($\mu_{\text{eff}} = 2.9\text{--}3.3\text{ B.M.}$) [36]. The electronic spectrum, in addition to show the $\pi\text{--}\pi^*$ and $n\text{--}\pi^*$ bands of the free ligand, displays three bands, in the solid reflectance spectra at $\nu_1: 13,887\text{ cm}^{-1}$; ${}^3A_{2g} \rightarrow {}^3T_{2g}$; $\nu_2: 16,277\text{ cm}^{-1}$; ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and $\nu_3: 22,452\text{ cm}^{-1}$; ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$. The 10Dq value is found to be $13,977\text{ cm}^{-1}$, again confirming the octahedral configuration of the chelate [34]. The spectrum shows also a band at $27,173\text{ cm}^{-1}$ which may attribute to ligand to metal charge transfer.

The electronic spectrum of the Co(II) complex gives three bands at $13,077$, $16,651$ and $21,903\text{ cm}^{-1}$ wavenumber regions. The region at $27,027\text{ cm}^{-1}$ refers to the charge transfer band. The bands observed are assigned to the transitions ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ (ν_1), ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ (ν_2) and ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$ (ν_3), respectively, suggesting that there is an octahedral geometry around Co(II) ion [34,37]. The magnetic susceptibility value is found to be 5.87 B.M. (normal range for octahedral Co(II) complexes is 4.3–5.2 B.M.), which is an indicative of octahedral geometry [31].

The reflectance spectrum of the Cu(II) chelate consists of a broad, low intensity shoulder band centered at $16,050$ and $22,056\text{ cm}^{-1}$. The 2E_g and ${}^2T_{2g}$ states of the octahedral Cu(II) ion (d^9) split under the influence of the tetragonal distortion and the distortion can be such as to cause the three transitions ${}^2B_{1g} \rightarrow {}^2B_{2g}$; ${}^2B_{1g} \rightarrow {}^2E_g$ and ${}^2B_{1g} \rightarrow {}^2A_{1g}$ to remain unresolved in the spectra [31]. This assignment is in agreement with the general observation that Cu(II) d–d transitions are normally close in energy [31]. The magnetic moment value of 2.15 B.M. falls within the range normally observed for octahedral Cu(II) complexes [38]. A moderately intense peak observed at $26,395\text{ cm}^{-1}$ is due to ligand to metal charge transfer transition [34].

Table 5
Thermoanalytical results (TG, DTG and DTA) of HL ligand and its metal complexes.

Complex	TG range (°C)	DrTG _{max} (°C)	n*	Mass loss Found (calcd.) %	Total mass loss	Assignment	Metallic residue	DTA
HL	25–275	200	1	52.04 (52.19)	100.0 (100.4)	- Loss of C ₆ H ₅ NO, C ₂ H ₈ N.	–	50(–), 75(+), 125(–), 180(+), 225(–), 275(+), 340(+), 360(–), 410(+), 450(–), 500(+), 610(–).
	275–525	370	1	26.19.78 (26.36)		Loss of C ₆ H ₅ . Loss of C ₃ N ₂ .		
	525–1000	620	1	21.77(21.8)				
(1)	30–200	60	1	7.00 (7.32)	83.85 (83.89)	- Loss of 2H ₂ O -Loss 2HCl and C ₂ H ₈ O - Loss of C ₁₅ H ₁₁ N ₄ O _{0.5} .	½Fe ₂ O ₃	40(–), 60(+), 110(–), 125(+), 350(–), 400(+), 475(–), 650(+).
	200–400	330	1	24.62 (24.41)				
	395–720	670	1	51.91(51.58)				
(2)	30–175	65	1	14.00 (14.13)	84.88 (84.84)	- Loss of 4H ₂ O. -Loss of HCl and C ₂ H ₁₀ O ₂ - Loss of C ₁₁ H ₁₁ N ₄ .	CoO	40(–), 60(+), 110(–), 125(+), 140(–), 150(+), 400(–), 500(+), 625(–), 900(+).
	175–510	155, 395	1	30.18 (30.31)				
	510–685	625	1	40.17 (40.40)				
(3)	30–160	50	1	14.00 (14.52)	84.91 (83.68)	- Loss of 4H ₂ O - Loss of HCl, 2H ₂ O, C ₂ H ₈ N. - Loss of C ₁₅ H ₈ N ₃ .	NiO	40(–), 60(+), 125(–), 160(+), 200(–), 270(–), 320(+), 460(+), 600(–).
	160–470	150,270	1	23.93 (23.86)				
	471–665	590	1	46.44 (45.30)				
(4)	50–290	170,250	2	28.90 (28.50)	84.10 (84.61)	- Loss of 4H ₂ O, 2H ₂ O, HCl. - Loss of C ₆ H ₅ and C ₂ H ₆ . -Loss of C ₉ H ₅ N ₄ .	CuO	40(–), 75(+), 100(–), 125(+), 175(–), 325(–), 375(+), 575(–), 630(–).
	290–375	325	1	21.40 (21.91)				
	375–700	650	1	33.80(34.20)				

n* = number of decomposition steps.

(–) = endothermic, (+) = exothermic.

(1) [Fe(L)Cl₂(H₂O)] · 3H₂O, (2) [Co(L)Cl(H₂O)₂] · 4H₂O, (3) [Ni(L)Cl(H₂O)₂] · 4H₂O, (4) [Cu(L)Cl(HO)₂] · 4H₂O.

The complexes of Zn(II), Cd(II) and Th(IV) are diamagnetic and according to the empirical formulae of these complexes, an octahedral geometry is proposed.

3.1.11. Electron spin resonance spectra

The ESR spectrum of the Cu(II) complex at room temperature exhibits anisotropic signals with $g_{\parallel} = 2.201$ and $g_{\perp} = 2.030$ which is characteristic for axial symmetry [39]. Since the g_{\parallel} and g_{\perp} values are closer to 2 and $g_{\parallel} > g_{\perp}$ suggesting a tetragonal distortion around the Cu(II) ion corresponding to elongation along the four-fold symmetry Z-axis [40]. The trend $g_{\parallel} > g_{\perp} > g_e$ (2.0033) shows that the unpaired electron localized in the $d_{x^2-y^2}$ orbital of the Cu(II) ion in complex [41]. In addition, exchange coupling interaction between two Cu(II) ions is explained by Hathaway expression $G = (g_{\parallel} - 2)/(g_{\perp} - 2)$. When the value $G < 4.0$, a considerable exchange coupling is present in solid complex ($G = 1.686$) [39]. Kivelson and Neiman showed that for an ionic environment g_{\parallel} is normally 2.3 or larger, but for covalent environment g_{\parallel} are less than

2.3. The g_{\parallel} value for the Cu(II) complex is 2.201, consequently the environment is covalent.

The ESR spectra of the solid Co(II), Ni(II) and Zn (II) complexes at room temperature do not show ESR signal because the rapid spin lattice relaxation of the Co(II) and Ni(II) broadness the lines at higher temperatures [39] and the diamagnetic nature of the Zn (II) complex. The ESR spectrum of the Fe(III) complex shows two signals observed at g values 2.271 and 3.991. These values can be respected as the signal of high spin state of the Fe(III) ($S = 5/2$) [39].

3.2. Thermal analyses (TG, DTG and DTA) of Schiff base

The TG curve of Schiff base HL, (Fig. 3a), refers to three stages of mass losses at temperature ranges from 100 to 750 °C (Table 5). These stages involved mass losses of 100.0 % calcd (found 100.35 %). These mass losses may be due to the successive losses of C₁₇H₁₈N₄O at the given temperature ranges. Fig. 3a shows the DTA curves

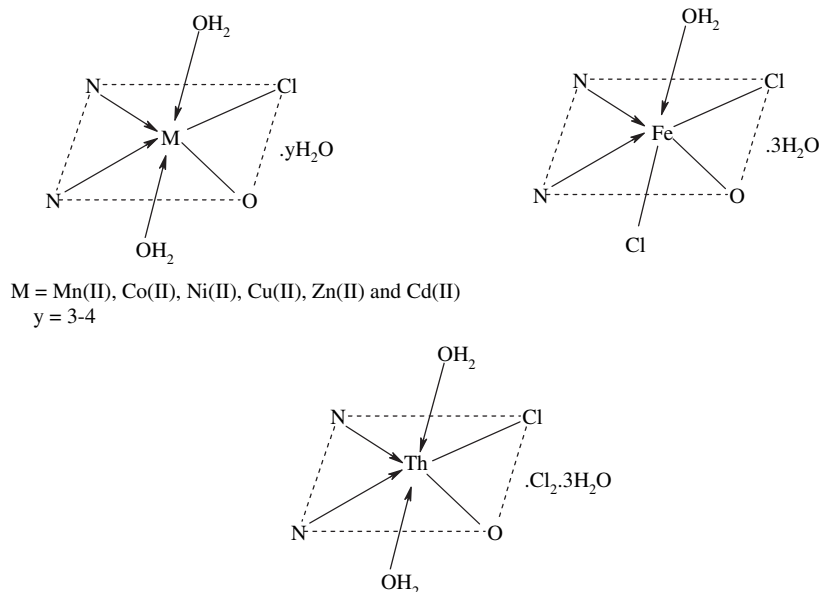


Fig. 4. Proposed structures of HL metal complexes.

Table 6

Thermodynamic data of the thermal decomposition of HL ligand and its metal complexes.

Complex	Decomp. Temp. (°C)	E^* kJ mol ⁻¹	A s ⁻¹	ΔS^* kJ mol ⁻¹	ΔH^* kJ mol ⁻¹	ΔG^* kJ mol ⁻¹
HL	25–200	21.36	5.85×10^7	-93.90	19.49	40.63
	200–600	37.07	2.01×10^7	-107.0	33.97	73.83
	600–1000	218.7	9.41×10^{11}	-21.81	213.6	227.1
(1)	30–120	50.87	5.62×10^6	-103.0	50.34	56.95
	120–400	36.06	2.00×10^7	-106.2	33.26	68.93
	400–800	69.86	8.77×10^6	-118.8	64.26	144.2
(2)	30–150	46.81	9.24×10^5	-118.8	46.22	54.63
	150–300	72.27	9.15×10^5	-130.0	70.04	105.0
	300–500	218.4	2.76×10^3	-181.4	3.07	68.72
	500–1000	214.4	4.01×10^{11}	-29.10	209.1	227.5
(3)	30–110	52.44	1.01×10^7	-97.04	51.96	57.46
	110–300	77.80	5.78×10^8	-71.59	76.54	87.42
	300–600	42.02	1.22×10^7	-108.6	39.74	69.57
	600–1000	179.6	6.73×10^9	-62.49	174.7	211.7
(4)	30–120	35.14	1.28×10^6	-123.6	33.68	55.44
	180–430	121.3	1.65×10^{11}	-28.85	119.2	126.6
	460–620	76.20	4.61×10^6	-123.8	70.79	151.2

which show 6 exothermic peaks at 50, 125, 225, 360, 450 and 610 °C and 6 endothermic peaks at 75, 180, 275, 340, 410 and 500 °C.

3.3. Thermal analyses (TG, DTG and DTA) of the metal chelates

Fig. (3) and Table 5 show the TG, DTG and DTA results of thermal decomposition of Schiff base chelates. From these results it can conclude that:

The thermogram of Fe(III) chelate shows three decomposition steps within the temperature range from 30 to 720 °C. The first two steps of decompositions within the temperature range 30–400 °C corresponds to the loss of water molecules of hydration, the coordinated water, HCl and C₂H₆O with a mass loss of 7.32% (calcd 7.90%) and 24.62% (calcd 24.41%). The subsequent step (400–720 °C) corresponds to the removal of the organic part of the ligand leaving metal oxide as a residue. The overall weight loss amounts to 83.85% (calcd 83.89%). The DTA data are listed in Table 5 and represented graphically in Fig. 3b. It is clear from these data that these mass losses are accompanied by exothermic 40, 110, 350 and 475 °C and endothermic 60, 125, 400, 650 °C peaks.

The TG curve of the Co(II) chelate is shown in Fig. 3c and listed in Table 5. It decomposes in three steps in the temperature range 30–800 °C. The first step is the loss of the hydrated water with mass loss of 14.00% (calcd 14.13%). The 2nd and 3rd steps correspond to the removal of coordinated water, HCl molecules and the residue of ligand with mass loss of 70.35% (calcd 70.71%). These steps are accompanied by exothermic peaks at 40, 110, 140, 400 and 625 °C. Also these steps are accompanied by endothermic peaks at 60, 125, 150, 500 and 900 °C.

The TG curve of the Ni(II) chelate shows three stages of decomposition within the temperature range of 30–800 °C. The first stage at 30–160 °C corresponds to the loss of water molecules of hydration, while the subsequent (2nd and 3rd) stages involve the loss of coordinated water, HCl and ligand molecules. The overall weight loss amounts to 84.91% (calcd 83.68%). The DTA data are listed in Table 5 and represented graphically in Fig. 3d. It is clear from these data that these mass losses are accompanied by exothermic (40, 125, 200, 270 and 600 °C) and endothermic (60, 160, 320 and 460 °C) peaks.

On the other hand, [Cu(L)Cl(H₂O)₂]·4H₂O chelate exhibits three decomposition steps (Fig. 3e). The first step in the temperature

range 30–290 °C in which the complex losses the hydrated and coordinated water and HCl molecule with estimated mass loss = 28.90% (calcd 28.50%) (Table 5). The total mass losses of the decomposition steps were 84.10% (calcd 84.61%), leaving CuO as a residue. The DTA data are listed in Table 5 and represented graphically in Fig. 3e. It is clear from these data that these mass losses are accompanied by (6) exothermic and (3) endothermic peaks for HL at (40, 100, 175, 325, 575 and 630 °C) and (75, 125 and 375 °C).

3.4. Structural interpretation

The structures of the complexes of HL Schiff base with Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Th(IV) ions are confirmed by the elemental analyses, IR, ¹H NMR, molar conductance, magnetic moment, solid reflectance, mass and thermal analyses data. Therefore, from the IR spectra, it is concluded that HL behaves as a uninegative tridentate ligand with NNO sites coordinating to the metal ions via the azomethine N, deprotonated phenolic-O and amino N. From the molar conductance data of the complexes (Λ_m), it is concluded that the complexes of HL ligand are considered as non-electrolytes except Th(IV) complex, which it was 2:1 electrolyte. The ¹H NMR spectra of the free ligand shows that the OH signal, appeared in the spectrum of HL ligand at 8.90 ppm completely disappeared in the spectrum of its Cd(II) complex indicating that the OH proton is removed by the chelation with Cd(II) ion. On the basis of the above observations and from the magnetic and solid reflectance measurements, octahedral geometry is suggested for the investigated complexes. The structure of the complexes is shown in Fig. 4.

3.5. Biological activity

The main aim of the production and synthesis of any antimicrobial compound is to inhibit the causal microbe without any side effects on the patients. In addition, it is worthy to stress here on the basic idea of applying any chemotherapeutic agent which depends essentially on the specific control of only one biological function and not multiple ones. The chemotherapeutic agent affecting only one function has a highly sounding application in the field of treatment by anticancer, since most anticancers used in the present time affect both cancerous diseased cells and healthy ones which in turns affect the general health of the patients. Therefore, there is a real need for having a chemotherapeutic agent which controls only one function. In testing the antibacterial activity of these compounds we used more than one test organism to increase the chance of detecting antibiotic principles in tested materials. The sensitivity of a microorganism to antibiotics and other antimicrobial agents is determined by the assay plates which are incubated at 37 °C for two days for bacteria. All of the tested compounds show a remarkable biological activity against two Gram-positive and two Gram-negative bacteria. The data are listed in Table 6 and shown in Fig. 5. On comparing the biological activity of the Schiff base and its metal complexes with the standard (cefepime), the following results are obtained:

(a) Using *B. simplex* bacteria (G⁺):

The biological activity of Co(II), Cu(II), Zn(II), Cd(II), Th(IV) and Fe(III) complexes is higher than that of the free HL ligand and standard cefepime. While, Mn(II) and Ni(II) complexes have the same biological activity of HL ligand and higher than that of cefepime. The biological activity of the complexes are found to follow the order Co(II) = Cu(II) = Zn(II) = Cd(II) = Th(IV) > Fe(III) > HL = Mn(II) = Ni(II) > cefepime.

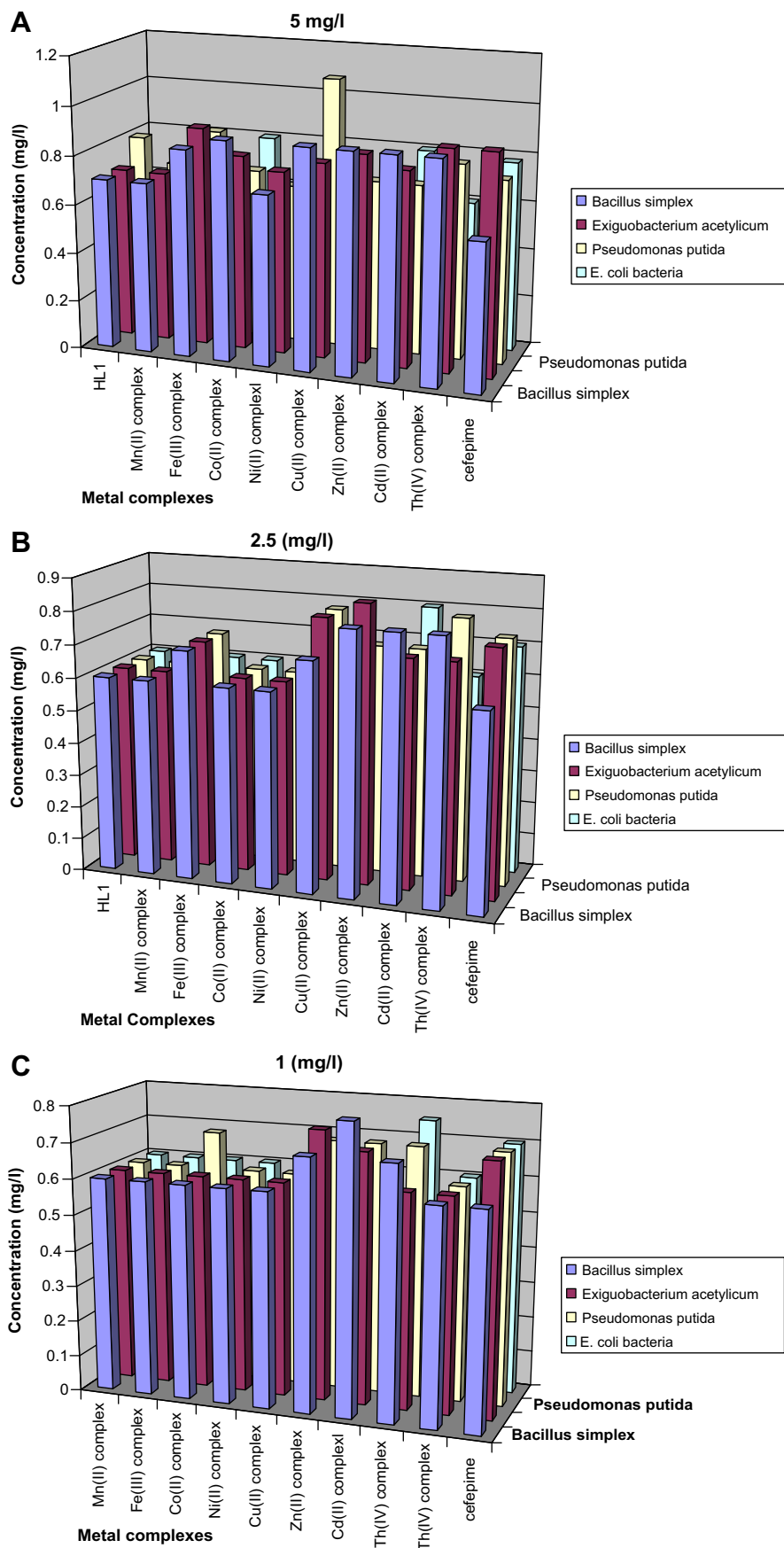


Fig. 5. Biological activity of HL and its complexes at (A) 5 ppm, (B) 2.5 ppm and (C) 1 ppm.

Table 7

Biological activity of HL and its metal complexes.

Sample	<i>Bacillus simplex</i>			<i>Exiguobacterium acetylicum</i>			<i>Pseudomonas putida</i>			<i>E. coli</i>		
C, mg/L	5	2.5	1	5	2.5	1	5	2.5	1	5	2.5	1
HL	++	+	+	++	+	+	++	+	+	+	+	+
[Mn(L)Cl(H ₂ O) ₂]·3H ₂ O	++	+	+	++	+	+	++	+	+	+	+	+
[Fe(L)Cl ₂ (H ₂ O)]·3H ₂ O	++	++	+	++	++	+	++	++	++	+	+	+
[Co(L)Cl(H ₂ O) ₂]·4H ₂ O	++	+	+	++	+	+	++	+	+	++	+	+
[Ni(L)Cl(H ₂ O) ₂]·4H ₂ O	++	+	+	++	+	+	++	+	+	+	+	+
[Cu(L)Cl(H ₂ O) ₂]·4H ₂ O	++	++	++	++	++	+	+++	++	++	+	+	+
[Zn(L)Cl(H ₂ O) ₂]·3H ₂ O	++	++	++	++	++	++	++	++	++	+	+	+
[Cd(L)Cl(H ₂ O) ₂]·3H ₂ O	++	++	++	++	++	+	++	++	++	++	++	++
[Th(L)Cl(H ₂ O) ₂]Cl ₂ ·3H ₂ O	++	++	+	++	++	+	++	++	+	+	+	+
Cefepime	+	+	+	++	++	++	++	++	++	++	++	++

The test was done using the diffusion agar technique.

Inhibition values = 0.1–0.6 cm beyond control = +.

Inhibition values = 0.65–1.0 cm beyond control = ++.

Inhibition values = 1.1–1.5 cm beyond control = +++.

(b) *Exiguobacterium acetylicum* bacteria (G⁺)

The data listed in Table 6 show that the biological activity of the Cu(II) complex is higher than that of cefepime and HL ligand and the ligand has higher biological activity than that of the standard. The order of increasing the biological activity of the complexes are found to be Cu(II) > Fe(III) > HL = Th(IV) > cefepime > Mn(II) = Co(II) = Zn(II) = Cd(II) > Ni(II).

(c) using *Pseudomonas putida* bacteria (G⁻)

The biological activity of the HL ligand is found to be less than that of the cefepime standard, while Fe(III) and Th(IV) complexes are found to have activity equal to that of the standard and higher than the free ligand HL. It is found that the order of activity is as follows Fe(III) = Th(IV) = cefepime > Zn(II) > Co(II) = Cu(II) = Cd(II) > Ni(II) > HL = Mn(II).

(d) *Escherichia coli* bacteria (G⁻)

It is found that the biological activity for the standard is higher than that of the free ligand but less than that of the Cd(II) and Co(II) complexes which have the higher activity. The biological activity of the complexes follow the order Co(II) = Cd(II) > cefepime > HL = Mn(II) = Fe(III) = Ni(II) = Cu(II) = Zn(II) = Th(IV).

Also the data listed in Table 7 show that *E. coli* is inhibited by Co(II) and Cd(II) complexes. The importance of this lies in the fact that these complexes could be applied fairly in the treatment of some common diseases caused by *E. coli* e.g., Septicaemia, Gastroenteritis, Urinary tract infections and hospital acquired infections [42,43].

However, Fe(III), Co(II), Cu(II), Zn(II), Cd(II) and Th(IV) complexes of HL ligand are specialised in inhibiting Gram-positive and Gram-negative bacterial strains (*Bacillus simplex*, *P. putida* and *E. acetylicum*). The importance of this unique property of the investigated Schiff base complexes lies in the fact that, it could be applied safely in the treatment of infections caused by any of these particular strains.

Since almost all scientists working in the field of search for new antitumours depend basically on the line of antibiotics affecting Gram-negative bacteria [44–46], and since there are certain organisms which have proved to be difficult to treat and most of them are Gram-negative rods. It is therefore believed that all the complexes which are biologically active against both the Gram-negative strains may have something to do with the barrier function of the envelope of these Gram-negative strains activity, acting

in a way similar to that described by Brown [46] and Nikaido et al. [44]. Therefore, it is claimed here that the synthesis of these complexes might be recommended and/or established a new line for search to new antitumour particularly when one knows that many workers studied the possible antitumour action of many synthetic and semisynthetic compounds e.g., Hodnett et al. [46] and Hickman [47]. Such compounds may have a possible antitumour effect since Gram-negative bacteria are considered a quantitative microbiological method testing beneficial and important drugs in both clinical and experimental tumour chemotherapy [48].

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