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Synthesis, characterization, potentiometry, and antimicrobial studies of transition metal complexes of a tridentate ligand

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Complexes of Cu(II), Ni(II), Co(II), Mn(II), and Fe(III) with the tridentate Schiff base, 4-hydroxy-3(1-{2-(benzylideneamino)-phenylimino}-ethyl)-6-methyl-2H-pyran-2-one (HL)derived from 3-acetyl-6-methyl-(2H)-pyran-2,4(3H)-dione (dehydroacetic acid or DHA). o-phenylenediamine, and benzaldehyde were characterized by elemental analysis, molar conductivity, magnetic susceptibility, thermal analysis, X-ray diffraction, IR, ¹H-NMR, UV-Vis spectroscopy, and mass spectra. From analytical data, the stiochiometry of the complexes was found to be 1:2 (metal:ligand) with octahedral geometry. The molar conductance values suggest nonelectrolytes. X-ray diffraction data suggest monoclinic crystal systems. IR spectral data suggest that the ligand is dibasic tridentate with ONN donors. To investigate the relationship between formation constants of metal complexes and antimicrobial activity, the dissociation constants of Schiff base and stability constants of its binary metal complexes have been determined potentiometrically in THF-water (60:40) at $30 \pm 1^{\circ}$ C and at 0.1 mol L⁻¹ NaClO₄ ionic strength. The potentiometric titrations suggest 1:1 and 1:2 complexation. Antibacterial and antifungal activities in vitro were performed against Staphylococcus aureus, Escherichia coli, Aspergillus niger, and Trichoderma with determination of minimum inhibitory concentrations of ligand and metal complexes. The structure-activity correlation based on stability constants of metal complexes is discussed. Activity enhances upon complexation and the order of activity is in accord with the stability order of metal ions.

Keywords: Tridentate ligand; Potentiometry; Antimicrobial activity; MIC; Metal complexes

1. Introduction

Heterocyclic aromatic compounds like benzimidazoles and benzothiazoles possess physiological activities with fungicidal, insecticidal, antimicrobial, and anesthetic properties. Dehydroacetic acid (DHA) is a heterocyclic compound which is a potential

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chelating agent [1] and shows promising fungicidal and antibacterial activities [2, 3]. It is also a versatile starting material for the synthesis of a wide variety of heterocyclic ring systems [4] which show enhanced biological activities. Schiff bases and their metal complexes exhibit a wide range of biological activities and structures. In view of the importance of DHA and its metal complexes, it is worthwhile to synthesize Schiff bases of DHA and their metal complexes. Little attention has been given to tridentate Schiff bases of DHA containing ONN donors. In continuation of our study [5–8], we report the synthesis of a tridentate Schiff base formed by condensation of DHA, *o*-phenylenediamine, and benzaldehyde. Complexes of Cu(II), Ni(II), Co(II), Mn(II), and Fe(III) with this ligand have been prepared and characterized by physicochemical methods.

2. Experimental

2.1. Materials and methods

DHA (purity > 99%) was purchased from E. Merck and used as supplied. o-Phenylenediamine and benzaldehyde of AR grade used for synthesis of ligand were obtained from Acros Organics and Sisco, respectively. AR grade metal nitrates of S.D. Fine were used for complex preparation. Spectral grade solvents were used for spectral measurements. The carbon, hydrogen, and nitrogen contents were determined on a Perkin Elmer (2400) CHNS analyzer. IR spectra (4000-400 cm⁻¹) were recorded on a Jasco FT-IR-4100 spectrometer using KBr pellets. ¹H-NMR spectra of the ligand were measured in CDCl₃ using TMS as an internal standard. The TG/DT analyses were recorded on a Perkin Elmer TA/SDT-2960 at 10 degrees min⁻¹. X-ray diffraction (XRD) was recorded on a Philips 3701 powder diffractometer employing Cu-Ka radiation ($\lambda = 1.541$ Å). The UV-Vis spectra of the complexes were recorded on a Jasco UV-530 spectrophotometer. Magnetic susceptibility measurements of the metal complexes were done on a Gouy balance at room temperature using Hg $[Co(SCN)_4]$ as a calibrant. Molar conductances were measured on an Elico CM-180 conductometer using 1 mmol L^{-1} solutions in DMSO. Elico digital pH meter (model LI-127) equipped with a CL-51B combined electrode was used for pH measurements, calibrated against standard buffers (pH 4.02 and 9.18) before measurements. The pH readings were corrected for organic-aqueous media. Titrations were performed in a double-walled glass cell in nitrogen at ionic strength of $0.1 \text{ mol } L^{-1}$ (NaClO₄); solutions were titrated pH-metrically against (0.2N) NaOH. The system used for potentiometric measurements and calculations has been described previously [9]. Potentiometric titrations were carried out at $30 \pm 1^{\circ}$ C. THF used in this study obtained from E. Merck was further distilled by known literature method [10]. THF: water (60:40) solutions were used as solvent for potentiometric studies. All metal ion solutions were prepared from their AR grade metal chlorides and standardized by known literature methods. A standard 0.2N NaOH solution (E. Merck) was used for titrations. Standard solutions of (AR grade), HClO₄, and NaClO₄ $(1.0 \text{ mol } L^{-1})$ were prepared and standardized by known methods [10]. The ligand solution $(0.1 \text{ mol } L^{-1})$ was prepared in distilled THF.



4-hydroxy-3(1-{2[{benzylideneamino} phenylimino) ethyl}-6-methyl-2H-pyran 2-one

Scheme 1. Synthesis of ligand.

2.2. Preparation of ligand

2.2.1. Step I. The ligand was prepared by modification of reported methods [11–13] (scheme 1). In a 50 mL solution of 0.001 mol (0.168 g) of DHA [3-acetyl-6-methyl-(2H)-pyran-2,4(3H)-dione], 0.001 mol (0.108 g) of *o*-phenylenediamine was refluxed in super dry ethanol for 3 h, then cooled to room temperature. On cooling, white mono-Schiff base precipitated in 80% yield.

2.2.2. Step II. The intermediate (0.001 mol; 0.258 g) was then refluxed with 0.001 mol (0.10 mL) of benzaldehyde in super dry ethanol for 6 h. The precipitate thus formed was filtered, dried in vacuum over CaCl₂, and recrystallized from ethanol (yield 72%).

2.3. Preparation of complexes

To a hot methanolic solution (25 mL) of ligand (0.02 mol), methanolic solution (25 mL) of metal nitrate (0.01 mol) was added with constant stirring. The pH was adjusted to 7.5–8.5 by adding 10% alcoholic ammonia solution and refluxed for 3 h. The precipitated metal complex was filtered off while hot and washed with hot methanol, petroleum ether, ethyl acetate, and dried over calcium chloride in a vacuum desiccator (yield 65%).

	Antibacterial activity $(mg mL^{-1})$				Antii	Antifungal activity (mg mL ⁻¹)			
	E. coli		Staphylococcus aureus		A. niger		Trichoderma		
Compound	0.5	1	0.5	1	0.5	1	0.5	1	
Ciprofloxin/control	40	45	42	44	75	72	65	60	
ΗĹ	15	17	09	11	65(13)	60(17)	45(31)	27(55)	
$Cu(L)_2$	27	29	18	25	42(44)	10(86)	30(54)	20(67)	
$Ni(L)_2$	10	16	13	18	45(40)	13(82)	32(51)	22(63)	
$Co(L)_2$	20	22	14	20	55(31)	18(75)	36(45)	24(60)	
$Mn(L)_2$	25	27	16	23	54(28)	22(69)	45(31)	27(55)	
$Fe(L)_2$	22	24	15	22	53(29)	20(72)	40(38)	25(58)	

Table 1. Antibacterial activity of compounds (diameter of inhibition zone in mm) and antifungal activity weight (mg) (% inhibition) of the ligand and complexes.

2.4. Antimicrobial activity

Antibacterial activity of free ligand, its metal complexes, the metal salts, and control (DMSO) was tested *in vitro* against Gram-positive bacteria (*S. aureus*) and Gramnegative bacteria (*Escherichia coli*) by paper disc method [8]. Sterile (10 mm diameter) Whatman no. 42 paper discs were soaked in different concentrations of ligand/ complexes (0.5 and 1 mg L⁻¹) in DMF, dried, and then placed on nutrient agar plates. The plates were then incubated for 24 h at 37°C and the inhibition zone around each disc was measured. The results obtained were compared with Ciprofloxin. Three replicates were taken and average value is given in table 1.

The free ligand, its metal complexes, metal salts, and control (DMSO) were screened for antifungal activity against the fungi *Aspergillus niger* and *Trichoderma* at 0.5 and 1 mg L^{-1} by mycelial dry weight (MDW) method [14]. The cultures of fungi were purified by single spore isolation technique. The glucose nitrate (GN) medium was used for growth of fungi. The mycelial biomass was then dried along with filter paper in an oven at $65 \pm 5^{\circ}$ C to constant weight, cooled, and finally weighed. The MDW was obtained by subtracting the weight of mycelium-free filter paper from final dry weight [15]. Three replicates of each treatment were repeated in all experiments. The MDW was corrected each time by subtracting the dry weight obtained from incubated flask under similar experimental conditions. The yields of MDW (mg) are presented in table 1. The percentage error was found to be ± 0.01 . The percent decrease in MDW to the test compound in each case was calculated and tabulated in terms of average percentage inhibition. The results indicate that the ligand and its metal complexes arrested the growth of fungi.

2.5. Minimum inhibitory concentration

Minimum inhibitory concentration (MIC) is the lowest concentration of an antimicrobial that inhibits visible fungal growth [16–18]. The MIC of fungi was determined by using MDW method by preparing different concentrations of test solutions (0.5, 0.75, 1, and 1.25 mg mL^{-1}). GN medium (50 mL) was taken in clean conical flasks and wrapped with paper and sterilized in an autoclave at 121° C for 30 min. Different concentrations

Compound	E. coli	S. aureus	A. niger	Trichoderma	
Ciprofloxin/control	40(0.25)	42(0.25)	50(1.5)	35(1.25)	
HL	15(0.5)	09(0.5)	20(1.5)	07(1.25)	
$Cu(L)_2$	27(0.5)	18(0.5)	05(0.75)	04(0.75)	
$Ni(L)_2$	10(0.5)	13(0.5)	07(1)	07(1)	
$Co(L)_2$	20(0.5)	14(0.5)	11(1)	08(1)	
$Fe(L)_2$	22(0.5)	15(0.5)	10(0.75)	09(1)	
$Mn(L)_2$	25(0.75)	16(0.75)	05(1.25)	11(1)	

Table 2. MIC $(mg mL^{-1})$ of the ligand and metal complexes against the bacterial and fungal inhibition zones.

of the ligand and metal complexes as prepared above were added in the conical flasks in which target fungi *A. niger* and *Trichoderma* were added. The conical flasks were incubated immediately at 37°C for 7 days. The MDW was obtained and the MIC values calculated are depicted in table 2.

The MIC of ligand and its metal complexes against Gram-positive and Gramnegative bacteria (*S. aureus* and *E. coli*) were determined by paper disc method in nutrient agar media. The compounds were tested at concentrations 0.25, 0.5, 0.75, 1, and 1.25 mg mL⁻¹ in DMSO. All experiments were conducted in triplicate and the same MIC value was obtained. These MIC values are compared with Ciprofloxin as standard in table 2.

3. Results and discussion

3.1. Elemental analysis

The analytical data of ligand and metal complexes are given in table 3. The elemental analyses show 1:2 (metal:ligand) stoichiometry for the solid complexes, corresponding with [ML₂], where M = Cu(II), Ni(II), Co(II), Mn(II), and Fe(III). The magnetic susceptibilities of all complexes at room temperature were consistent with octahedral geometry. The metal complex solutions in DMSO show low conductances which support their nonelectrolyte nature.

3.2. ¹H-NMR spectra

¹H-NMR spectra of the ligand in CDCl₃ show signals at $\delta 2.11$ (s, C6–CH₃), $\delta 2.54$ (s, 3H, N=C-CH₃), $\delta 5.83$ (s, 1H, C5–H), 6.9–7.9 (m, 9H, phenyl), $\delta 8.71$ (s, 1H, N=C–H), and $\delta 15.86$ (s, 1H, enolic OH of DHA moiety). The structure of the ligand is shown in figure 1.

3.3. FT-IR spectra

The IR spectrum of free ligand shows bands at 3060–3300, 1698, 1657, 1354, and 1212 cm^{-1} assignable to intramolecular hydrogen-bonded v(OH), lactone carbonyl

				Contents (found/calcd) (%)				
Compound	Molecular formula (formula weight)	Color	Melting point (°C)	С	Н	N	М	$(\Omega^{-1} cm^2 mol^{-1})$
HL	$C_{21}H_{18}N_2O_3$ 346.379	Yellow	162	72.80/72.81	5.20/5.40	8.00/8.10	-	-
$Cu(L)_2$	C ₄₂ H ₃₄ N ₄ O ₆ Cu 754.31	Green	280	66.90/66.87	4.50/4.60	7.50/7.42	8.50/8.42	12.02
$Ni(L)_2$	C ₄₂ H ₃₄ N ₄ O ₆ Ni 749.454	Yellow	285	67.40/67.31	4.60/4.57	7.50/7.47	8.50/8.98	25.05
$Co(L)_2$	C ₄₂ H ₃₄ N ₄ O ₆ Co 749.697	Brown	200	67.60/67.56	4.60/4.50	7.55/7.48	7.50/7.39	15.03
Fe(L) ₂	C ₄₂ H ₃₄ N ₄ O ₆ Fe 746 61	Brown	264	67.60/67.56	4.60/4.40	7.55/7.45	7.50/7.40	11.02
$Mn(L)_2$	C ₄₂ H ₃₄ N ₄ O ₆ Mn 745.70	Brown	270	67.10/67.65	4.60/4.39	7.60/7.50	9.20/9.00	10.02

Table 3. Analytical and physical data of the ligand and its metal complexes.



Figure 1. Resonance structure of ligand.

 $\nu(C=O)$, methyl azomethine $\nu(C=N)$, arylazomethine $\nu(C-N)$, and phenolic $\nu(C-O)$ stretching modes, respectively [19, 20]. In IR spectra of metal complexes, the absence of a weak broad band at 3060–3300 cm⁻¹ indicates deprotonation of the intramolecular hydrogen-bonded OH on complexation. This is supported by shift to higher energy in phenolic $\nu(C-O)$ [14]. The $\nu(C=N)$ shifts to lower value with respect to free ligand denoting that nitrogen of azomethine is coordinated to metal, supported by shift to higher energy in $\nu(C-N)$. IR spectra of metal complexes show bands at 457–540 cm⁻¹ which can be assigned to $\nu(M-O)$ and $\nu(M-N)$, respectively [21]. From the above facts, it is evident that coordination takes place *via* azomethine nitrogen and phenolic OH of the ligand.

3.4. Electronic absorption spectra and magnetic studies

Electronic spectra of Cu(II) complex in DMSO show bands (ε in L mol⁻¹ cm⁻¹) at 13,513(740), 16,339(612), and 25,641(366) cm⁻¹ assignable to a ${}^{2}E_{g} \rightarrow {}^{2}T_{2g}$ transition

Complex	Ligand field splitting energy (Dq cm ⁻¹)	Racah interelectronic repulsion parameter (B cm ⁻¹)	Covalent factor (β)	β (%)	ν_{2}/ν_{1}	LFSE (kcal mol ⁻¹)
Cu(L) ₂	1351.3	96.06	_	_	-	38.512
$Ni(L)_2$	936.32	843.57	0.8103	23.40	1.584	26.685
$Co(L)_2$	1016.26	913.97	0.9412	6.23	1.832	28.963
$Fe(L)_2$	126,582	788.63	0.7769	22.30	1.496	36.075
$Mn(L)_2$	1385.042	648.04	0.6743	32.56	1.760	39.473

Table 4. Ligand field parameter of the complexes.

and charge transfer. Electronic spectral data coupled with observed magnetic moment of 1.84 B.M. suggests octahedral geometry [22]. Ni(II) complex displays bands at 12,562(1068), 17,482(674), and 25,641(386) cm⁻¹ assignable to ${}^{3}A_{2g} \rightarrow {}^{3}T_{2g}(F)$, ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(F)$, and ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(P)$, respectively. These electronic transitions along with magnetic moment 2.92 B.M. suggest octahedral geometry for Ni(II) complex [23, 24]. The Co(II) complex shows three bands at 10,162(984), 18,621(537), and 25,575(391) cm⁻¹ assignable to ${}^{4}T_{1g}(F) \rightarrow {}^{4}T_{1g}(P)$, ${}^{4}T_{1g}(F) \rightarrow {}^{4}A_{2g}$, and ${}^{4}T_{1g}(F) \rightarrow {}^{4}A_{2g}$ ${}^{4}T_{1g}(P)$ transitions, respectively. These transitions and observed magnetic moment of 4.7 B.M. indicate high spin octahedral complex [25, 26]. Fe(III) complex exhibits bands at 12,658(790), 18,940(528), and 30,864(324) cm⁻¹ assignable to ${}^{6}A_{1g} \rightarrow {}^{4}T_{1}(D)$, ${}^{6}A_{1g} \rightarrow {}^{4}T_{1}$, and ${}^{6}A_{1g} \rightarrow {}^{4}T_{2g}$, respectively. The observed magnetic moment of 5.85 B.M along with electronic transitions corresponds to octahedral geometry [27-30]. For Mn(II) complex, the observed magnetic moment of 5.7 B.M. and the spectral bands at 16,611(722), 24,390(410), and 26,881(372) cm⁻¹ assignable to ${}^{6}A_{1g} \rightarrow {}^{4}T_{1}(G)$, ${}^{6}A_{1g} \rightarrow {}^{4}T_{2g}(G)$, and ${}^{6}A_{1g} \rightarrow {}^{4}E_{g}$, respectively, indicate octahedral geometry [31, 32]. The calculated values of ligand field splitting energy (10 Dq), Racah interelectronic repulsion parameter (B), covalent factor (β), ratio ν_2/ν_1 , and ligand field stabilization energy (LFSE), given in table 4, support the proposed geometry for all the complexes.

3.5. XRD study

The X-ray diffractograms of the metal complexes were scanned from 5° to 100° at wavelength 1.543 Å. The diffractogram and associated data depict 2θ values for each peak, relative intensity, and interplanar spacing (*d*-values). The diffractogram of Ni(II) complex shows 12 reflections with maxima at $2\theta = 23.07^{\circ}$ corresponding to a *d*-value of 3.855 Å. The diffractogram of Co(II) complex shows nine reflections with maxima at $2\theta = 23.16^{\circ}$ corresponding to *d*-value of 3.83 Å, whereas the diffractogram of Mn(II) complex shows 26 reflections with maxima at $2\theta = 89.95^{\circ}$ corresponding to *d*-value of 1.089 Å. The XRD pattern of these complexes with respect to major peaks having relative intensity greater than 10% have been indexed by using a computer program [33]. The above indexing method also yields Miller indices (hkl), unit cell parameters, and unit cell volume. The unit cell of Ni(II) complex yielded values of lattice constants, a = 10.053, b = 8.571, and c = 9.830 Å and unit cell volume, V = 394.253 (Å)³; Co(II), a = 16.038 Å, b = 4.285 Å, c = 10.692 Å and unit cell volume, V = 734.170 (Å)³; Mn(II),

a = 14.223 Å, b = 5.196 Å, c = 7.754 Å and unit cell volume, V = 568.562 (Å)³. The condition $a \neq b \neq c$ and $\alpha = \gamma = 90^{\circ} \neq \beta$ required for the compounds to be monoclinic were tested and found to be satisfactory for Ni(II), Co(II), and Mn(II) complexes. Hence, it can be concluded that these metal complexes show monoclinic crystal system. Experimental density values of the complexes were determined by using specific gravity method [34] and found to be 1.877, 1.021, and 2.326 gcm⁻³ for Ni(II), Co(II), and Mn(II) complexes, respectively.

3.6. Thermogravimetric studies

The Cu(II), Ni(II), and Co(II) complexes were chosen for thermal study. The TG/DT analyses were carried out from ambient temperature to 1000°C in nitrogen using α -Al₂O₃ as reference. The TG/DTA curves of these complexes show no weight loss up to 270°C, indicating the absence of coordinated water [35]. In the copper complex, the first decomposition step at $290-390^{\circ}$ C with mass loss (calculated = 29.70%; TG = 30.80%) as an exothermic peak $\Delta T_{max} = 337^{\circ}C$ in DTA attributed to decomposition of noncoordinated part of ligand. The second step from 460°C to 875°C corresponds to loss of the coordinated part of the ligand (calculated = 52.30%; TG = 52.30%) and finally, stable metal oxide CuO (calculated = 10.47%; TG = 9.20%). In the TG curve of nickel complex, the first step from 280°C to 495°C (calculated = 39.60%; TG = 40.70%) corresponds to decomposition of noncoordinated ligand. In DTA, an endothermic peak at 400°C was obtained. Second step at 425- 800° C (calculated = 29.59%; TG = 30%) is due to coordinated ligand. A broad exothermic peak in DTA was obtained at 518.67°C. Finally, stable nickel oxide was formed (calculated = 9.5%; TG = 9.96%). For cobalt complex, the first decomposition takes place from 280° C to 370° C (calculated = 54.00%; TG = 53.65%) due to decomposition of noncoordinated ligand with sharp exotherm at 340°C in the DTA curve. Second step from 380° C to 930° C (calculated = 31.20%; TG = 30.94%) indicates decomposition of coordinated ligand. The residues at the end of the decomposition corresponds to CoO (calculated = 9.70%; TG = 9.99%).

3.7. Potentiometry

Calvin–Bjerrum pH titration technique as modified by Irving and Rossotti [36] was used to determine proton–ligand and metal–ligand stability constants in THF–water mixture (60% v/v) at $30 \pm 1^{\circ}$ C. Irving and Rossotti method was used to calculate \bar{n}_A , \bar{n} , pK, and pL values from the pH titration curves. Protonation takes place in the initial stages of titrations because of the presence of azomethine nitrogen. The pK₁ and pK₂ were determined at $\bar{n}_A = 1.5$ and 0.5, respectively. The first stability constant pK₁, therefore, refers to the imine nitrogen. However, there are two imine nitrogens present in the ligand and only one pK value is displayed, suggesting that one is not involved in protonation. This may be attributed to intramolecular hydrogen bonding of nitrogen N^b (figure 1) which undergoes chelation with enolic OH of DHA and hence does not take part in protonation and deprotonation. Therefore, the pK₁ value (2.93) shown by the ligand is due to the protonation of N^a. The second pK observed at 9.83 in the ligand is due to dissociation of enolic proton which is sufficiently acidic due to the resonance effect. All the metals form 1:1 and 1:2 chelates with this ligand. The 1:1 and 1:2 chelates are formed in a simultaneous process in all the systems. Hence, the method of least squares has been used for getting accurate values of $\log k_1$ and $\log k_2$. The values of $\log k_1$, $\log k_2$, and $\log \beta$ for Cu(II) are 10.05, 9.61, and 19.67; Ni(II), 10.02, 8.79, and 18.82; Co(II), 9.83, 3.89, and 13.72; Fe(III), 9.15, 3.38, and 12.54; and Mn(II), 9.09, 3.50, and 12.40, respectively.

Coordination of metal ion with ligand takes place *via* protonated nitrogen and oxygen of the enolic group (figure 2). The order of stability constants is Cu > Ni > Co > Fe > Mn which is in agreement with Irving–Williams order [36].

3.8. Antimicrobial activity

The Schiff base HL and its metal complexes were evaluated for antimicrobial activity against one Gram-positive bacteria (S. aureus), a Gram-negative bacteria (E. coli) and fungi A. niger and Trichoderma. The antimicrobial activities are presented in table 1, showing that the free ligand and all metal complexes exhibit antibacterial activity against both strains. Metal complexes exhibit higher activity than free ligand under identical experimental conditions. Antimicrobial inhibitions were compared with the activity of Ciprofloxin as a standard and all compounds were less than the standard. The metal salts used for synthesis of complexes exhibit negligibly small antimicrobial activities [37–40]. Enhancement of activity of ligand after chelation can be explained on the basis of Overtones and Tweedy's concepts [41]. Inhibition was found to increase with increasing concentration of metal complex. The results showed that the Cu(II) complex exhibits higher activity against each class of organism. The activity is related to the nature and structure of the complexes [42, 43]. The higher activity of copper complex may be attributed to its higher stability constants. The ferric and manganese complexes show activity comparable to the copper complex. However, nickel complex shows low activity against E. coli as compared to S. aureus. All the reported complexes and ligand show more activity against Gram-negative E. coli than Gram-positive S. aureus.



Where M = Cu(II), Ni(II), Co(II), Mn(II)

Where M' = Fe(III)

Figure 2. Structures of metal complexes.

Antibacterial activity can be ordered as $Cu(L)_2 > Mn(L)_2 > Fe(L)_2 > Co(L)_2 > Ni(L)_2$, similar to earlier observations [44]. These complexes do not show strong concentration dependence of antimicrobial activity as compared to the antifungal activities of the same complexes. The relation between chelation and toxicity is very complex, expected to be a function of steric, electronic, and pharmakinetic factors along with mechanistic pathways [44]. Stability constants, solubility, particle size, size of metal ion, and magnetic moments may also be responsible for the antimicrobial activity of the complexes [45, 46]. Attempts to show a relationship between stability constants and antimicrobial activity of the complexes proved futile.

Investigation of antifungal activity of the ligand and its metal complexes revealed that all the metal chelates are more toxic than the ligand (table 1). The antifungal activity is enhanced several times on being coordinated with metal. Antifungal activity of these complexes increases as the stability of the complex increases. The activities of these complexes follow the order Cu > Ni > Co > Fe > Mn which is exactly same as the order of stability constants of these complexes. Comparison of activities shows that the copper complex is more active than the ligand against *A. niger*. Activity of ligand against *Trichoderma* increases after chelation; however, the extent of increase is less than that of *A. niger*.

3.9. Minimum inhibitory concentration

The inhibitory potential of the compounds were further investigated by determining the MIC values. The observed inhibition of growth (mm) and MIC $(mgmL^{-1})$ are presented in table 2.

The copper complex is most potent against both bacterial strains compared to other metal complexes. Copper complex showed a MIC of 0.5 mg mL^{-1} against *E. coli* and *S. aureus* with the highest zone of inhibition at 27 and 18 mm. The Fe(III), Co(II), and Ni(II) complexes showed zones of inhibition at 22, 20, and 10 mm, respectively, for MIC 0.5 mg mL^{-1} against *E. coli* and 15, 14, and 13 mm zones against *S. aureus*. Mn(II) complex shows higher MIC of 0.75 mg mL^{-1} with zone of inhibitions of 22 and 15 mm against the two bacterial strains. However, the MIC shown by all the compounds is much higher than that of Ciprofloxin but lower than the free ligand.

For antifungal activity, the observed MDW (mg) and MIC (mg mL⁻¹) are presented in table 2. Copper complex has significant growth inhibition of both the fungal strains and lowest MDW of 5 and 4 mg with an MIC of 0.75 mg mL^{-1} against *A. niger* and *Trichoderma* indicating its strong antifungal activity. All other complexes showed an MIC of 1.0 mg mL^{-1} against both fungal species. The order of activity in terms of their MIC values is Cu > Ni > Co > Fe > Mn against *A. niger* and *Trichoderma*. MIC of all the complexes is less than the ligand and control DMF.

4. Conclusion

On the basis of physicochemical and spectral data discussed above, octahedral geometry for Cu(II), Ni(II), Co(II), Mn(II), and Fe(III) complexes is proposed. IR spectra show the ligand as a dibasic, ONN tridentate, coordinating *via* phenolic oxygen

and imino nitrogen. Thermal study reveals that the complexes are thermally stable. XRD study suggests monoclinic crystal system for Co(II), Ni(II), and Mn(II) complexes. The ligand and its metal complexes are biologically active; antibacterial activity shows that the copper complex is more biologically active. Antifungal activity of these complexes increases in the order of increase in stability constants of metal complexes. The same trend has been found for MIC.

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