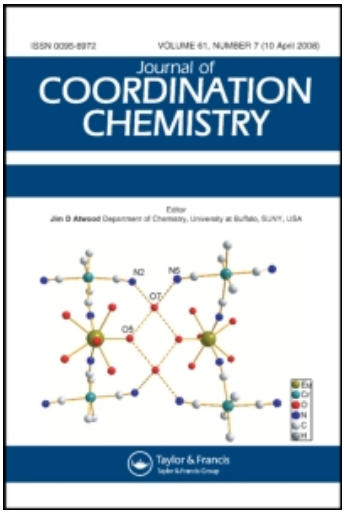

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Synthesis, spectral and antimicrobial studies of a novel macrocyclic ligand containing a piperazine moiety and its binuclear metal complexes

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Synthesis, spectral and antimicrobial studies of a novel macrocyclic ligand containing a piperazine moiety and its binuclear metal complexes

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A novel macrocycle 1,16-diaza-7,10-diamino-6,11-dioxo-1,17-bis[2′-hydroxy-5′-aminobenzyl]-piperazine-4,12-cyclododecadiene, [H_4L] has been synthesized by a multistep process. The interaction of 5-amino salicylic acid, piperazine and formaldehyde in ethanol gave PC-1, which was reduced into a chloro-derivative PC-2. PC-2 by reacting with ethylenediamine gave a new macrocyclic ligand titled [H_4L]. Its binuclear complexes with Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) ions have also been synthesized. The ligand and all metal complexes have been characterized by elemental analysis, IR, ^{1}H NMR, ^{13}C NMR and U.V.Visible spectroscopy. Molar conductance and magnetic moment measurements have also been determined. Microanalytical data revealed 1 : 2 molar ratio of ligand to metal in all the complexes. The spectral and magnetic data indicate that Mn(II), Co(II), Ni(II) complexes show octahedral geometry with two water molecules while Cu(II) and Zn(II) complexes exhibit square planar and tetrahedral environments, respectively. The compounds show significant inhibitory activity against seven bacteria and seven fungi.

Keywords: Piperazine; Ligand; Binucleating complexes; Antibacterial; Antifungal

1. Introduction

A wide variety of ligands such as Schiff bases, multidentate amines, crown ethers and porphyrins have been extensively studied [1–5]. The coordination chemistry of amide group has received much attention due to its diverse behavior and its role in biological processes [6, 7]. Many ligands employed in the synthesis of amides are derived from salicylaldehyde. Biological activities of these compounds are influenced significantly by metal coordination [8]. Coordination compounds have various applications such as catalysts [9, 10], pharmaceutical agents, antitumor [11], anticancer, antibacterial, anticonvulsive, antifouling and as corrosion inhibitors. Investigations on metal mediated ligand–ligand interactions revealed that these interactions can be categorized as hydrophilic, hydrophobic, or electrostatic depending on their chemical and physical characteristics [12]. Such complexes containing transition metal ions play a vital role

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in many catalytic reactions of metalloenzymes as well as in supporting structures of many proteins [13].

Drug resistance to the presently available classes of antibiotics has become a worldwide medical problem [14]. Chelating of the ligand by metals and its correlation with biologically active constituents offers the possibility for design of novel antibiotics [15]. We have synthesized a new class of metal complexes containing piperazine, because some piperazine-containing derivatives [16] are known to constitute a novel class of mixed D_2/D_4 receptor antagonists [17, 18] and substituted piperazine compounds exhibit a wide spectrum as antifilarial [19], antiamoebic [20] and spermicidal agents.

As s part of our continuing efforts to synthesize and characterize first row transition metal chelates using amide based ligands, we describe here the synthesis, spectral and antimicrobial studies of a macrocyclic ligand containing a piperazine and its binuclear Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes. All the synthesized compounds were investigated for their antibacterial activity against *Bacillus subtilis, Bacillus megaterium, Staphylococcus aureus, Escherichia coli*, *Salmonella typhi, Pseudomonas aeruginosa, Shigella boydii* and for antifungal activity against *Candida albicans, Trichophyton* sp., *Aspergillus flavus, Aspergilllus niger, Fusarium* sp., *Mucor* sp., *penicillium* sp. During the investigation, it has been observed that the metal complexes show better antimicrobial and antifungal activity than the ligand.

2. Experimental

2.1. *Materials*

Reagent grade and HPLC grade solvents and chemicals were used during the experiments. Dimethylsulphoxide (DMSO), dimethyformamide (DMF), methanol and other solvents were distilled under reduced pressure prior to their use. Ethylenediamine, piperazine, 5-aminosalicylalhehyde (E. Merck. India Ltd.) and metal acetates were used as received. Nutrient medium (agar) was purchased from Hi-Media (India). The above-mentioned microorganism strains for antimicrobial activities were collected from the Dept. Of Microbiology, All India Institute Of Medical Sciences (AIIMS), New Delhi.

2.2. *Measurements*

Elemental analysis (C, H and N) was performed on a Perkin-Elmer Model-2400 elemental analyzer (CDRI, Lucknow). The percentage of metal was determined by complexometric titration against EDTA after decomposing with concentrated nitric acid. The FT-IR spectra were recorded on a Perkin-Elmer infrared spectrophotometer Model 621 in the range of 4000–400 cm^{-1} by using KBr pellets. Nuclear magnetic resonance spectra (^{1}H-NMR and ^{13}C-NMR) were recorded on a JEOL–GSX-300 MHz, DPX–100 FT-NMR spectrometer using DMSO-d_6 as a solvent and tetramethylsilane (TMS) as internal standard. Electronic spectra of the synthesized complexes were recorded in DMSO by using a Perkin-Elmer Lambda EZ-201 spectrophotometer. The solubility of the complexes in various solvents was checked at room temperature.

Magnetic susceptibilities of the complexes were measured at room temperature on a Faraday balance having a facial strength of 7000 kg, using $Hg[Co(SCN)_4]$ as calibrant. The anti-microbial activities of these compounds were observed on different bacteria and fungi and are reported according to their growth profile.

3. Synthesis

3.1. *Synthesis of precursor compound, PC-1*

1,4-bis-[2′-hydroxy-3′-(carboxy)-5′-aminobenzyl] piperazine (PC-1) was prepared by the condensation of 5-amino salicylaldehyde with para-formaldehyde and piperazine in acidic medium. A solution of 5-amino salicylaldehyde 13.68 g (0.2 mol) in 50 mL of water was slowly added to 80 mL of ethanol solution containing piperazine 8.6 g (0.1 mol) and para-formaldehyde 6.4 g (0.4 mol). The resulting solution was stirred for 30 min and then added to 100 mL ethanol/acetic acid (2 : 1 v/v). This resulting solution was refluxed for 5 h. The reaction was monitored by TLC using chloroform as an eluent. Excess solvent was removed by distillation under reduced pressure and extracted with $CHCl_3$. Yellow precipitate was filtered and washed by petroleum ether and dried at room temperature. Yield, 26.2 g, 63%, m.p. 176°C.

^{1}H NMR (300 MHz, δ ppm, from TMS in DMSO) 12.5 (s, 2H, –COOH), 10.3 (s, 2H, OH), 4.8 (s, 4H, $–NH_2$), 3.52 (s, 4H, Ar–CH_2–N<), 6.85–7.13 (s, 4H, Ar), 2.53 (t, 8H, piperazine). FTIR (KBr pellets, ν in cm^{-1}) 3446 (OH), 3350 (NH_2), 2650 (OH, acid), 1760 (C=O acid), 1560 (Aromatic), 1320 (C–N tertiary). Elem. Anal. (%), Calcd C (57.69), H (5.76), and N (13.46), Found C (57.70), H (5.78), and N (13.47).

3.2. *Synthesis of precursor compound, PC-2*

1,4-bis-[2′-hydroxy-3′-(chlorocarboxy)-5′-aminobenzyl] piperazine, PC-2 was synthesized by the reaction of thionyl chloride and PC-1. $SOCl_2$, 17.5 g (0.47 mol) was added dropwise into PC-1, 15.05 g (0.0362 mol) in a 250 mL three-necked, round-bottom flask with constant stirring. Thus obtained wooden color solution was refluxed for 2 h. The solution was cooled at room temperature and then the deposited yellow solid was filtered, washed with methanol and diethyl ether and dried in vacuum under reduced pressure at 60°C for 3 h. Yield, 29.38 g, 65%, m.p. 185°C.

^{1}H NMR (300 MHz, δ ppm, from TMS in DMSO). 10.3 (s, 2H, OH), 4.8 (s, 4H, −NH), 3.52 (s, 4H. Ar–CH_2–N<), 6.85–7.13 (s, 4H Ar), 2.53 (8H, piperazine). FTIR (KBr pellets, ν cm^{-1}) 3446 (OH), 3350 (NH), 2650 (OH acid), 1760 (C=O acid), 1560 (C=C, Ar), 1320 (C–N tertiary). Elem. Anal. (%) Calcd C (52.98), H (4.85), and N (12.36). Found C (53.07), H (4.78), and N (12.37).

3.3. *Synthesis of macrocyclic ligand (H_4L)*

The amide-based macrocycle was synthesized by the condensation of ethylenediamine with PC-2. Yellow powder of PC-2, 9.04 g (0.02 mol) was dissolved in 20 mL

of pyridine (py). A solution of 1.33 mL (0.018 mol) of ethylendiamine in 15 mL py was added to the precursor solution. The mixture was refluxed for 10 h resulting in a brown precipitate. Following filtration, the precipitate was washed several times with methanol and diethyl ether and then dried *in vacuo*.

3.4. *Preparation of metal complexes type M_2L and $M_2L \cdot 2H_2O$*

Dinuclear metal complexes were prepared by reaction of H_4L and metal acetate hydrate in 1 : 2 molar ratio according to the reported method [21]. $Ni(acae)_2$ 8.23 g (0.02 mol) in 40 mL of ethanol was added to a round bottom flask containing 4.20 g (0.1 mol) of ligand in 40 mL ethanol. This mixture was refluxed for 8 h. The resulting parrot green precipitate was filtered, washed with ethanol and diethyl ether and then dried *in vacuo* at 50°C for 3 h.

Dinuclear complexes of Mn(II), Co(II), Cu(II) and Zn(II) were prepared by similar procedure to the Ni(II) complex.

4. Results and discussion

4.1. *Chemistry*

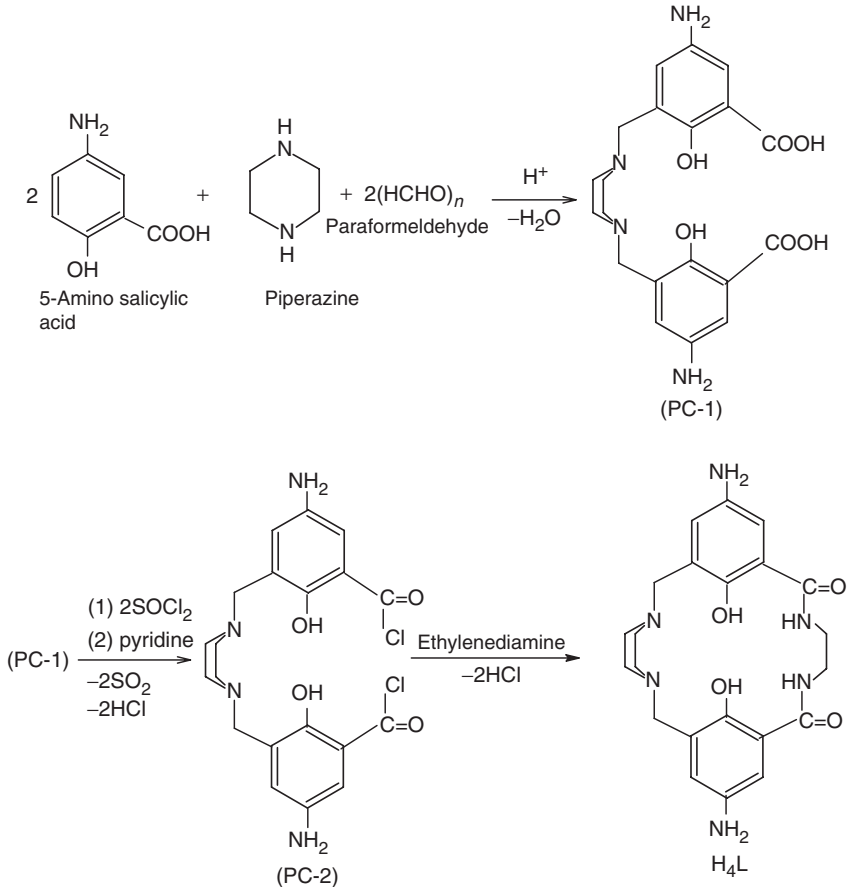
A condensation reaction occurred with 5-aminoslicylaldehyde, piperazine and paraformaldehyde yielding 1,4-bis-[2′-hydroxy-3′-(carboxy)-5′aminobenzyl] piperazine (PC-1) in acidic medium. The formation of PC-1 was confirmed by spectral data *viz*. ^{1}H NMR, ^{13}C NMR and FTIR. The piperazine nitrogen shows a band at 1320 cm^{-1} due to C–N stretching of a tertiary amine. PC-1 was soluble in polar solvents like methanol, ethanol, chloroform, etc but insoluble in nonpolar solvents.

PC-1 was reacted with thionyl chloride in pyridine solution and converted into corresponding acid chloride derivative, 1,4-bis-[2′-hydroxy-3′-(chlorocarboxy)-5′-aminobenzyl] piprazine, PC-2 (scheme 1). Formation of PC-2 was confirmed by various spectral techniques.

Diamide macrocycle, H_4L was formed by the condensation of ethylenediamine and PC-2 compound. The formation of macrocycle was confirmed by various physico-chemical methods. Binuclear metal complexes of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) were prepared by the reaction of metal(II) salts and ligand in 2 : 1 molar ratio (scheme 2). These complexes were obtained in good yield. Two molecules of water in Mn(II), Co(II) and Ni(II) complexes are supported by microanalysis and spectral data (table 1).

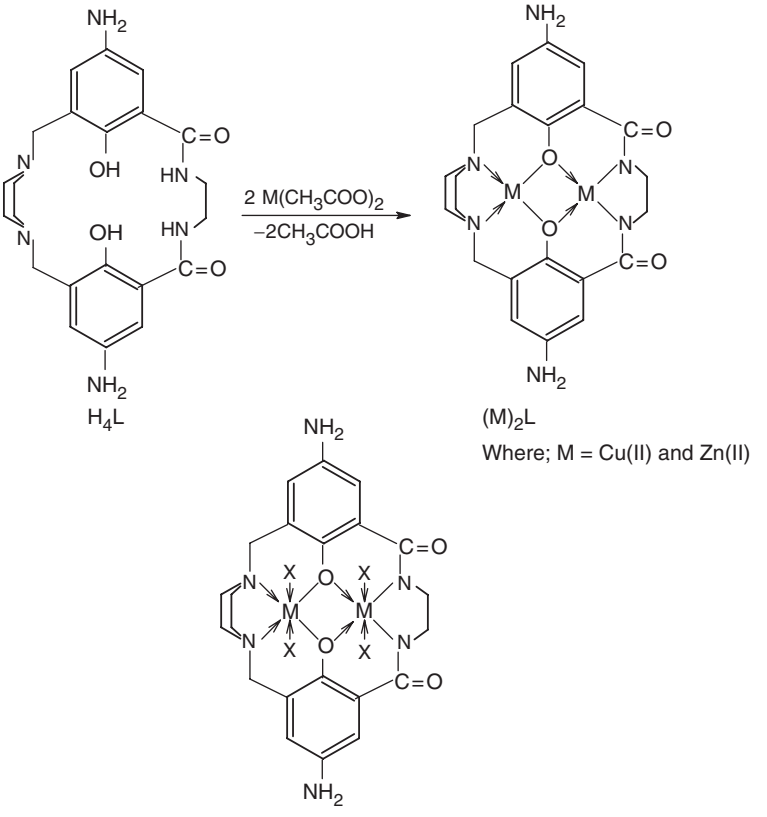
4.2. *IR spectra*

The most significant IR bands of the ligand and binuclear metal complexes with their assignments are listed in table 2. The spectra of free ligand showed a broad medium intensity band in the region of 3430–3235 cm^{-1} due to ν(N–H) stretching vibration of amine and amide groups along with the merging of (O–H) stretching [22].



Scheme 1. Synthesis of the ligand (H_4L).

These bands involve symmetric and asymmetric stretching of primary amine ($-NH_2$ group) and amide –NH– group. In metal complexes these bands undergo downward shift by 20–25 cm^{-1}. This indicates the coordination of amide N to metal ion [23]. Furthermore it is reasonable to expect hydrogen bonding between hydroxyl hydrogen and carbonyl oxygen, strengthened by broadening of the band and it's shifting from the normal position (3730–3520 cm^{-1}) for free O–H. Two strong bands were observed at 2950–2840 cm^{-1} assigned to C–H stretching of CH and CH_2 groups in all the compounds. The spectrum of the ligand showed a strong band at 1655 cm^{-1}, which is fairly certain to C=O stretching vibration [24]; this band occurs in all the complexes at lower frequency (1625–1610 cm^{-1}) compared to the ligand. The band at 1470 cm^{-1} is assigned to the δ (C–H) bending of >N–CH_2–CH_2–N< [25]. The presence of coordinated water molecules in the Mn(II), Co(II), and Ni(II) complexes was further confirmed by appearance of bands in the region 1600–1540 cm^{-1} for δHOH deformation and in 670–650 cm^{-1} for the rocking modes of coordinated water [26]. In metal complexes ν(O–H) and ν(N–H) of amide disappear, which may suggest the participation of these groups in coordination. The participation of the *oxygen*



Scheme 2. Synthesis of metal complexes.

Table 1. Physical and elemental analysis data of the ligand and its binuclear metal complexes.

Ligand/Complexes	Molecular formula	Dec. P.[a] (°C)	Yield (%)	Elemental analysis (%)			
				C	H	N	M
H_4L	$C_{22}H_{28}N_6O_4$	198[b]	63	60.00	6.36	19.00	–
				(60.03)	(6.35)	(19.03)	–
$(Mn)_2L \cdot 2H_2O$	$C_{22}H_{32}(Mn)_2N_6O_8$	210	72	42.72	5.17	13.59	17.87
				(42.75)	(5.16)	(13.57)	(17.90)
$(Co)_2L \cdot 2H_2O$	$C_{22}H_{32}(Co)_2N_6O_8$	216	75	42.18	5.11	13.42	18.82
				(42.19)	(5.13)	(13.47)	(18.86)
$(Ni)_2L \cdot 2H_2O$	$C_{22}H_{32}(Ni)_2N_6O_8$	225	73	42.21	5.11	13.43	18.77
				(42.23)	(5.15)	(13.44)	(18.80)
$(Cu)_2L$	$C_{22}H_{24}(Cu)_2N_6O_8$	218	72	46.71	4.26	14.92	22.55
				(46.73)	(4.26)	(14.95)	(22.60)
$(Zn)_2L$	$C_{22}H_{24}(Zn)_2N_6O_8$	213	70	46.59	4.23	14.82	23.04
				(46.53)	(4.78)	(14.61)	(23.09)

The calculated, (Found) values. [a]Dec. P. Decomposition Point. [b]Melting Point.

Table 2. The IR spectral bands and their assignments of the ligand and complexes.

Compounds	Assignments (cm^{-1})								
	ν(OH) and ν(NH)	ν(Ar–CH)	ν_s(CH)	ν_{as}(CH)	ν(C=O)	ν(C=C)	ν(C–N)	ν(M–O)	ν(M–N)
H_4L	3430–3235	3050	2950	2860	1655	1560	1380	–	–
$(Mn)_2L \cdot 2H_2O$	3400–3210	3055	2940	2840	1640	1550	1375	530	425
$(Co)_2L \cdot 2H_2O$	3415–3220	3050	2940	2860	1625	1540	1378	536	418
$(Ni)_2L \cdot 2H_2O$	3415–3218	3052	2946	2865	1630	1565	1365	532	422
$(Cu)_2L$	3405–3225	3050	2942	2860	1630	1563	1375	520	408
$(Zn)_2L$	3420–3205	3054	2940	2864	1610	1560	1368	514	415

ν_s, symmetric; ν_{as}, asymmetric.

of hydroxyl group and *nitrogen* of amide group in all complexes is further supported by the appearance of prominent peaks of ν(M–O) and ν(M–N) at 536–514 cm^{-1} and 425–408 cm^{-1} respectively [27].

4.3. *^{1}H NMR spectra*

Additional structural information can be deduced from ^{1}H NMR spectra. Spectra of the ligand and its Zn(II) complex were taken in DMSO-d_6. The amino protons (NH_2) of the ligand are observed at 6.45 ppm merging with aromatic protons; however in the Zn(II) complex these are shifted slightly downfield and observed at 6.36 ppm. Ligand spectrum revealed a singlet at 10.42 ppm, attributed to the single proton of the hydroxyl OH group, which disappears in the complex, strongly suggesting that the hydroxyl group has deprotonated upon coordination. The methylene protons of ethylenediamine and piperazine showed their resonances at 3.02 ppm and 2.40 ppm, respectively [28]. The aromatic region is a set of multiplets in the range 6.53–7.30 ppm [29]. Amide protons at 7.23 ppm in ligand, do not appear in the Zn(II) complex confirming that amide N is coordinated to metal ion through deprotonation.

4.4. *^{13}C NMR spectra*

The ^{13}C-NMR spectrum of Zn(II) complex has a number of peaks. Most resemble those of their respective precursor except for the carbonyl group adjacent to the aromatic ring and some aromatic carbon peaks. Precursor compound, PC-2 exhibits the carbonyl peak of amide at 176 ppm, shifted significantly to 169 and 165 ppm in ligand H_4L and its Cu(II) complex respectively. This indicates that the condensation takes place at carboxyl halide with ethylenediamine in the formation of ligand, H_4L. Other signals at 35.6, 55.4 and 52.2 ppm assigned to >N–CH_2–CH_2–N<, Ar–CH_2–N< and –NH–CH_2–CH_2–NH– respectively [30]. The peaks of the aromatic carbons appear between 140–153 ppm. The peaks of coordination sites and aromatic carbons of the macrocyclic ligand are shifted downfield after formation of the binuclear complexes, which strongly indicate the coordination of the metal ion in the ligand cavity.

4.5. *Magnetic susceptibility*

The magnetic moment values of the complexes, summarized in table 3, support octahedral geometry for Mn(II), Co(II), and Ni(II) complexes, square planar for Cu(II) and tetrahedral geometry for Zn(II) complexes. The magnetic moment of the Co(II) complex in the present study was found to be 4.20 μ_s, [31] indicating the high spin octahedral geometry. This higher μ_s value than that of the calculated value 3.88μ_s [$\sqrt{n(n+2)}$] of the Co(II) complex is attributed to orbital contributions [32]. Theoretically it is often sufficient to treat the spin-orbit-coupling (SOC) as a weak perturbation. However, strictly speaking magnetism is a relativistic effect and may require a full relativistic treatment. The octahedral Ni(II) complex shows two unpaired electrons, 2.96μ_s, between 2.9–3.4μ_s for octahedral geometry, [33]. The d^5 Mn(II) complexes generally are high spin because of additional stability of high field d subshell. The magnetic moment value was found to be 6.96 μ_s in the present study. The magnetic moment value of Cu(II) was found to be in the expected range of square planar geometry at 1.80 μ_s indicating one free electron. The tetrahedral Zn(II) complexes are diamagnetic.

4.6. *Electronic spectra and their parameters*

The electronic spectra of the synthesized complexes (10^{-3} M in DMSO) are tabulated in table 3. The Co(II) complex shows three bands at 7273, 14,285, and 19,638 cm^{-1} due to $^4T_{2g}(F) \leftarrow {}^4T_{1g}(F)$ (ν_1), $^4A_{2g}(F) \leftarrow {}^4T_{1g}(F)$ (ν_2), and $^4T_{1g}(P) \leftarrow {}^4T_{1g}(F)$ (ν_3), transitions, respectively, suggesting octahedral environment around Co(II) [34]. The $\nu_3 : \nu_2$ value for the compound is 2.70, leading to (from appropriate energy level diagram)

$$\frac{D_q}{B'} = 0.96 \tag{1}$$

and to,

$$^4T_{2g}(F) \leftarrow {}^4T_{1g}(F)/B' = 7273/B' = 8.2$$
$$B' = 887$$

Table 3. Electronic and magnetic properties of the metal complexes.

Complexes	Molar conductance ($\Omega^{-1}\,cm^2\,mol^{-1}$)	μ_{eff} (BM)	Frequency (cm^{-1})	Assignments	$10\,D_q$ (cm^{-1})	B (cm^{-1})	β	β%
			24,804	$^4A_{1g}(G) \leftarrow {}^6A_{1g}(F)$				
$(Mn)_2L \cdot 2H_2O$	26	6.96	21,250	$^4T_{2g}(G) \leftarrow {}^6A_{1g}(F)$	8547	777	0.80	20%
			18,650	$^4T_{1g}(G) \leftarrow {}^6A_{1g}(F)$				
			19,638	$^4T_{1g}(P) \leftarrow {}^4T_{1g}(F)$				
$(Co)_2L \cdot 2H_2O$	27	4.20	14,285	$^4A_{2g}(F) \leftarrow {}^4T_{1g}(F)$	8515	887	0.79	21%
			7273	$^4T_{2g}(F) \leftarrow {}^4T_{1g}(F)$				
			23,772	$^3T_{1g}(P) \leftarrow {}^3A_{2g}(F)$				
$(Ni)_2L \cdot 2H_2O$	18	2.96	16,090	$^3T_{1g}(F) \leftarrow {}^3A_{2g}(F)$	8565	874	0.81	19%
			13,984	$^3T_{2g}(F) \leftarrow {}^3A_{2g}(F)$				
			25,000	Charge transfer spectra				
$(Cu)_2L$	17	1.80	15,380	$^2E_g \leftarrow {}^2B_{1g}$				
$(Zn)_2L$	18	Diamagnetic						

now from (1)

$$D_q = 851.5.$$

Consequently, the spectral parameters of the compounds are: $10\,D_q = 8515\,cm^{-1}$, $B' = 887\,cm^{-1}$, $\beta = 0.79$. The reduction of the Racah parameter from the free ion value of $1120\,cm^{-1}$ to $887\,cm^{-1}$ and the value of β (0.79) indicate covalence in the compound. The Mn(II) complex exhibits three bands at 18,650, 21,250, and 24,804 cm^{-1} due to $^4T_{1g}(G) \leftarrow {}^6A_{1g}(F)$ (ν_1), $^4T_{2g}(G) \leftarrow {}^6A_{1g}(F)$ (ν_2), and $^4A_{1g}(G) \leftarrow {}^6A_{1g}(F)$ (ν_3) transitions, respectively [35]. The D_q/B of this complex is 1.1. The electronic parameter values are $10D_q = 8547\,cm^{-1}$, $B' = 777\,cm^{-1}$, $\beta = 0.8$. B' is reduced about 80.9% of the free ion value of Mn^{2+} ($960\,cm^{-1}$). The Ni(II) complex show three bands at 13,984, 16090, and 23,772 cm^{-1} assigned to the spin allowed transitions $^3T_{2g}(F) \leftarrow {}^3A_{2g}(F)$ (ν_1), $^3T_{1g}(F) \leftarrow {}^3A_{2g}(F)$ (ν_2), and $^3T_{1g}(P) \leftarrow {}^3A_{2g}(F)$ (ν_3), respectively suggesting an octahedral geometry. The $\nu_1 : \nu_2$ value for the present compound is 1.74 and corresponds to usual range (1.6–1.82) [36]. The spectral parameters are $10D_q = 8565\,cm^{-1}$, $B' = 874\,cm^{-1}$, $\beta = 0.81$, β^0 value is 19%. The reduction of Racah parameter from the free ion value of $1080\,cm^{-1}$ to $874\,cm^{-1}$ and β value of 0.81 indicate the covalent nature of the compound. The above discussion very strongly indicates octahedral geometry around the central metal ion in these three complexes, requiring occupation of two coordination sites by H_2O. The electronic spectra of the Cu(II) complex exhibit two bands at 15,380, and 25,000 cm^{-1}, due to $^2A_{1g} \leftarrow {}^2B_{1g}(F)$, and charge-transfer, respectively, indicating square planar geometry [37].

4.7. *Antibacterial activity investigation*

4.7.1. Method. The agar diffusion method [38] is adopted for measuring the effectiveness of the compounds. Mueller Hinton agar was used as nutrient standard medium that allows growth of test microbes. Using this method, one species of bacteria is uniformly swabbed onto the nutrient agar in a petri dish. Compounds are then placed on paper discs. These discs are added to the surface of the agar. Petri dishes are now placed for incubation. During incubation, the compounds diffused from the disc containing the agent into the surrounding agar. Effective agents inhibit bacterial growth, and measurements are made to quantify the size of the zones of inhibition around the disc.

Antibacterial activity of the ligand and its metal complexes are studied against three gram positive and four gram negative bacteria and the results are presented in table 4. The highest zones of inhibition *i.e.* 27, 26, 25 and 24 mm were measured in *Salmonella typhi, Bacillus subtilis and Escherichia coli, Staphylococcus aureus*, and *Bacillus megaterium* in case of $(Cu)_2L$ complex. During the experiments, ligand and complexes show lowest inhibition zones *i.e.* 15 and 19 mm in case of *Shigella boydii and Pseudomonas aeruginosa*. Zn(II) complex show highest inhibition zone (24 mm) against *Pseudomonas aeruginosa and Bacillus subtilis*. Ni(II) and Co(II) complexes show intermediary inhibition zone against all the bacteria. The complexes show better antibacterial activity than their parental ligand and Cu(II) complex has maximum and Mn(II) complex has least antimicrobial effect. Analysis of variation with standard drug

Table 4. Antibacterial activity data for the ligand and its metal complexes.

Name of bacteria	Zone of inhibition[a] (mm) 50 μg mL^{-1}						
	Ligand	Mn(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	Kanamycin[b] (30 μg)
B. subtillis (+ve)	17	20	22	24	26	24	31
B. megaterium (+ve)	19	22	23	23	24	22	36
S. aureus (+ve)	19	21	23	23	25	23	29
E. coli (−ve)	18	23	22	21	26	24	32
S. typhi (−ve)	19	22	24	22	27	21	31
P. aeruginosa (−ve)	16	19	23	20	21	24	33
S. boydi (−ve)	15	20	21	20	20	21	30
DMSO[c]	–	–	–	–	–	–	–

[a] 18–30 mm significant active, 10–17 mm moderate active, <10 mm week active. [b] Standard drug (positive control). [c] Solvent (negative control).

Table 5. Antifungal activity data for the ligand and its metal complexes.

Name of fungi	Zone of inhibition[a] (mm) 100 μg mL^{-1}						
	Ligand	Mn(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	Miconazole[b]
C. albicans	17	20	23	24	23	22	28
Trichophyton sp.	20	23	24	25	26	25	32
A. flavus	16	21	22	21	24	21	34
A. niger	18	21	21	27	22	22	31
Fucerium sp.	16	23	23	25	23	25	31
Mucor sp.	17	20	21	24	21	23	34
Penicillium sp.	15	19	21	23	22	20	30
DMSO[c]	–	–	–	–	–	–	–

[a] 18–30 mm significant active, 10–17 mm moderate active, <10 mm week active. [b] Standard drug (positive control). [c] Solvent (negative control).

kanamycin (30 μg) showed that the inhibition effect of the complex on the bacteria growth is significant.

For antifungal activity (table 5) the highest inhibitory zone *i.e.* 27, 25 and 24 mm were measured in Ni(II) complex against *Aspergilllus niger, Trichophyton* sp., and *Candida albicans*, respectively. In case of *Mucor* sp., *Trichophyton* sp. and *Fusarium* sp. the highest inhibition zone *i.e.* 23, 25, 25 mm were found in Zn(II) complex. The Co(II) complex show highest zone of inhibition 24 mm against *Trichophyton* sp. The complexes of Mn(II), Ni(II) and Zn(II) show same inhibition zone (21 mm) when treated against *Aspergilllus flavus*.

The results of the investigation revealed that antimicrobial activity of the H_4L compound increases after metal chelation, because chelation reduces the polarity of the central metal ion by partial sharing positive charge with the donor groups [39]. This process increases the lipophilic nature of the central metal ion [40], which in turn favors its permeation to the lipid layer of the membrane. Other factors *viz.* stability constant, molar conductivity, solubility, and magnetic moment are also responsible for increasing the antimicrobial activity of the complexes [41].

5. Conclusion

Metal complexes were prepared by the reaction of H_4L and metal salts in 1 : 2 molar ratio and structures were proposed from analytical and spectral data. All the binuclear metal complexes show better antimicrobial activity than the ligand against all the pathogens.

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