Synthesis, Characterization and Biological Evaluation of Mononuclear Co(II), Ni(II), Cu(II) and Pd(II) Complexes with New N_2O_2 Schiff Base Ligands

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New tetradentate N_2O_2 donor Schiff bases and their mononuclear Co(II), Ni(II), Cu(II), and Pd(II) complexes were synthesized and characterized extensively by IR, ^{1}H-, ^{13}C-NMR, mass, ESR, conductivity measurements, elemental and thermal analysis. Specifically the magnetic and electronic spectral measurements demonstrate the octahedral structures of cobalt(II), nickel(II) complexes and square planar geometries of copper(II), palladium(II) complexes. All the ligands and complexes were screened for their *in vitro* antibacterial activity against two Gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus*) and two Gram-negative bacteria (*Escherichia coli*, *Klebsiella pneumonia*). In this study, Pd(II) complexes exhibited potent antibacterial activity against *B. subtilis*, *S. aureus* whereas other metal complexes also exerted good activity towards all tested strains even than standard drugs streptomycin and ampicillin.

Key words Schiff base; metal complex; antibacterial activity

Schiff bases have a variety of applications in biological, clinical, and pharmacological areas. The synthesis and application of Schiff bases and their coordination compounds have been highly considered in inorganic, organic and biological fields, since their structural properties similar to some of the biological systems.[1—6] Additionally, tetradentate Schiff bases composed of N_2O_2 donor atoms set have been recognized as a kind of important chelating ligands for designing medicinally and catalytically useful metal complexes.[7—9] The flexible coordination behavior of these types of chelating ligands could also be useful to generate interesting dimeric and polymeric structures as synthones for supramolecular chemistry.[10,11] Usually, the N, O donor heterodentate Schiff bases can be derived by condensing the aldehydes/ketones with various amines or amino acids.[12,13] N_2O_2 Schiff base ligands derived from salicylald ehyde and diamine have been known.[14,15] Dialdehydes and diketones with amines and amino acids have also been utilized to obtain a variety of N_2O_2 Schiff base ligands.[16]

Amino acids plays an important role in many physiological activities of the human body and also helpful in understanding biological functions of macromolecules such as proteins.[17] In particular, tryptophan (Trp)/histidine (His) analogues as promising candidates for novel antimicrobial therapeutics. In the recent years, a series of synthetic peptide analogues based on Trp-His and His-Arg (antimicrobial peptides) structural frameworks have been prepared and found to be active against several Gram-positive and Gram-negative bacterial strains as well as against fungal strains.[18] Furthermore, it is well known that the human body contains essential metaloelements which play important roles and interact with many biological molecules to fully understand the physiological functions by studying their chemistry coordination and behavior.[17,18] In the present studies we have introduced an azomethine (Schiff base) linkage to tryptophan/histidine, which may permit a variety in their coordination behaviour and complexation role.

In previous studies, we have described the synthesis, catalytic and biological applications of Schiff bases and their metal complexes derived from *o*-phthalaldehyde (OPA) with various amines.[19—27] In this respect, we have also developed some useful macrocyclic Schiff bases and their metal complexes. Results from these studies have also shown that complexation of metals with Schiff base ligands serves to improve their antimicrobial activity. There are few other research groups also reported the importance of Schiff base chemistry of the combination of *o*-phthalaldehyde with amines.[28,29] However, a careful literature survey reveals that Schiff bases from the combination of amino acids and *o*-phthalaldehyde and their coordination behavior towards the transition elements have yet not been studied. The combination of dialdehyde *i.e. o*-phthalaldehyde and aminoacids is expected to provide a new class of tetradentate N_2O_2 donor ligands to design new coordination compounds with improved catalytic and biological activities. The present manuscript describes the synthesis, characterization and antibacterial activities of cobalt(II), nickel(II), copper(II), and palladium(II) complexes with the tetradentate N_2O_2 Schiff bases derived using *o*-phthalaldehyde, aminoacids *i.e.*, L-tryptophan and L-histidine. The ligands synthesized in this work can behave as dianionic tetra dentate donor groups. All the metal complexes have shown moderate to good antibacterial activity against Gram-positive and Gram-negative bacteria.

Experimental

All the chemicals used in this work were of analar grade. Solvents were purified and dried before use according to the standard procedures. The metal contents were determined by complexometric titration with ethylenediaminetetraacetic acid (EDTA) for cobalt. Nickel and palladium were determined by gravimetric procedure using dimethylglyoxime as precipitating agent and copper was determined by iodometric procedure. Elemental analysis (C, H, and N) was obtained using Perkin-Elmer elemental analyzer. The infrared spectra were recorded in KBr/Nujol on Perkin- Elmer-283 spectrophotometer in the range of 4000—200 cm^{-1} and electronic spectra in MeOH were obtained using Shimadzu UV-265 Spectrometer. ^{1}H- and ^{13}C-NMR spectra in dimethyl sulfoxide (DMSO) were recorded on a Brucker

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Table 1. Analytical and Physical Data of the Ligands and Complexes

S. No.	Complexes/Formulae	Color	Found (Calcd %)				mp (°C)/ Decomp. Temp.	$^{\Lambda}M^{\alpha}$ (BM)	μ_{eff}	Yield (%)
			M	C	H	N				
1	CEIMAP	Pale	—	71.08	5.14	11.01	188—190	—	—	75
	$C_{30}H_{26}N_4O_4$	Yellow		(71.12)	(5.17)	(11.06)				
2	CIMPAP	Yellow	—	58.10	4.88	20.52	180—182	—	—	78
	$C_{20}H_{20}N_6O_4$			(58.12)	(4.94)	(20.58)				
3	$[Co(CEIMAP)(H_2O)_2]2H_2O$	Pink	9.30	56.68	5.10	8.63	250—252	9	4.96	80
	$C_{30}H_{32}N_4O_8Co$		(9.27)	(56.70)	(5.08)	(8.82)				
4	$[Co(CIMPAP)(H_2O)_2]2H_2O$	Pale	10.36	46.50	5.58	14.70	243—245	12	5.13	78
	$C_{20}H_{26}N_6O_8Co$	Pink	(10.39)	(46.56)	(5.68)	(14.81)				
5	$[Ni(CEIMAP)(H_2O)_2]2H_2O$	Light	9.20	56.73	5.05	8.78	235—237	15	3.09	82
	$C_{30}H_{32}N_4O_8Ni$	Green	(9.27)	(56.70)	(5.08)	(8.82)				
8	$[Ni(CIMPAP)(H_2O)_2]2H_2O$	Green	10.35	46.50	5.60	14.73	220—223	17	3.26	84
	$C_{20}H_{26}N_6O_8Ni$		(10.39)	(46.56)	(5.68)	(14.84)				
7	$[Cu(CEIMAP)]2H_2O$	Light	10.58	59.66	4.70	9.30	248—250	10	1.93	76
	$C_{30}H_{30}N_4O_6Cu$	Green	(10.52)	(59.64)	(4.67)	(9.27)				
8	$[Cu(CIMPAP)]2H_2O$	Green	12.58	46.45	4.40	16.65	234—236	14	1.92	75
	$C_{20}H_{22}N_6O_6Cu$		(12.56)	(46.48)	(4.38)	(16.61)				
9	[Pd(CEIMAP)]	Reddish	17.44	58.40	3.98	9.20	255—256	13	—	78
	$C_{30}H_{24}N_4O_4Pd$	Brown	(17.42)	(58.92)	(3.96)	(9.17)				
10	[Pd(CIMPAP]	Reddish	20.80	46.88	3.60	16.42	240—242	17	—	85
	$C_{20}H_{18}N_6O_4Pd$	Brown	(20.75)	(46.84)	(3.54)	(16.39)				

WH 300 (200 MHz) and Varian Gemini (200 MHz) spectrometers using tetramethylsilane (TMS) as an internal reference. An ion trap mass spectrometer (Agilent Series LC/MSD Trap SL) equipped with an electrospray ionization (ESI) source was used for MS analyses (Agilent, Palo Alto, CA, U.S.A.). Conductance measurements were carried out at room temperature on freshly prepared 10^{-3} M EtOH solutions using a Coronation digital conductivity meter. The magnetic studies were carried out at room temperature on a Gouy balance calibrated with Hg [$Co(SCN)_4$]. The ESR spectra of Cu(II) complex are recorded at room temperature and liquid nitrogen temperature (LNT). The thermogravimetric-differential thermogravimetric (TG-DTG) thermograms of the complexes were recorded on Mettler Toledo star system. The antibacterial activity of the compounds was determined by the cup plate method and the minimum inhibitory concentration by liquid dilution method.

Synthesis of Schiff Bases. 2-{[(*E*)-1-[2-({[1-Carboxy-2-(1*H*-3-indolyl) ethyl]imino}methyl)phenyl]methylidine}amino)-3-indolyl)propanoicacid (CEIMAP) (L_1) KOH (0.32 g) was dissolved in methanol and methanolic solution of L-tryptophan (0.02 mol) was added to it. The mixture was stirred magnetically at room temperature for 1 h. When the mixture became homogeneous, a solution of *o*-phthalaldehyde (0.01 mol, 1.32 g) in methanol (20 ml) was added. After 2 h yellow crystals were appeared. The crystals were filtered and washed with ethanol and recrystallized from hot methanol. The crystals were suction filtered washed with diethyl ether and dried in vacuum. The product was found to be TLC pure in 7 : 3 mixtures of methanol and chloroform.

2-({(*E*)-1-[2-({[1-Carboxy-2-(1*H*-5-imidazolyl)(ethyl]imino}methyl) phenyl]methylidine}amino)-3-1*H*-5-imidazolyl)propanoicacid (CIMPAP) (L_2) L(+) histidine (0.02 mol) dissolved in MeOH (10 ml) was added slowly with constant stirring to an alcoholic solution (20 ml) containing KOH. The solution was stirred for 1 h and filtered. To the filtrate *o*-phthalaldehyde (1.32 g, 0.01 mol) dissolved in MeOH (20 ml) was added drop wise with constant stirring. The resulting yellowish solution was evaporated under reduced pressure and kept at room temperature for 1 d. The yellow precipitate was filtered, washed with cold alcohol and ether then crystallized twice from methanol. The crystals were suction filtered, washed with diethyl ether and dried in vacuum. The product was found to be TLC pure in 6 : 4 mixtures of ethyl acetate and *n*-hexane, tested in perpendicular directions.

General Procedure for Synthesis of Metal Complexes A solution of cobalt(II) acetate, nickel(II) acetate, copper(II) acetate and palladium(II) chloride (0.002—0.005 mol) in methanol (25 ml) was added drop wise to a methanolic solution (30 ml) of Schiff base (0.002—0.005 mol) and stirred at room temperature with constant stirring. The resulting mixture was allowed to reflux on a water bath for 2 h until a solid is separated out. The precipitates were suction filtered, purified by repeated washing with chloroform and methanol and dried in vacuum desiccators (yield=75—85%).

Results and Discussion

The analytical data and the physical properties of the complexes are listed in Table 1. The complexes can be represented by the formula [ML $(H_2O)_2$]$2H_2O$ where [M=Co(II), Ni(II)], [ML]×H_2O where [M=Cu(II) and Pd(II)] and [L=L_1, L_2]. In addition, all these compounds (except Pd(II) complex) showed a single peak in ESI-MS suggesting the purity of the ligands and their metal complexes. The MS data is in good agreement with the proposed molecular formulae. The low molar conductance values of all the complexes in dichloromethane measured at 10^{-3} M concentration are in the range of 9—17 indicate that all the complexes behave as non-electrolytes.[30] The general strategy for the synthesis of Schiff base ligands and their metal complexes is illustrated in Chart 1.

Infrared Spectra The infrared frequencies of the Schiff base ligand and its Co(II), Ni(II),Cu(II) and Pd(II) complexes are given in Table 2. All the complexes exhibit broad bands in the 3440—3590 cm^{-1} range and this may be attributed to the presence of coordinated or lattice water molecules. A strong IR absorption band observed in the free Schiff base around 1615—1630 cm^{-1}, assignable to the ν(C=N) stretching vibration, was shifted to lower wave numbers by 15—20 cm^{-1} upon coordination. This feature indicates that the imino nitrogen is coordinated to the metal ion. Further, the $\nu_{asym}(COO^-)$ absorption of ligands was shifted to higher frequency in the 1575—1590 cm^{-1} range and the $\nu_{sym}(COO^-)$ was shifted to lower frequency in the 1340—1386 cm^{-1} range in the respective spectra of complexes. The shift observed for both $\nu_{asym}(COO^-)$ and $\nu_{sym}(COO^-)$ visualizes the coordination of carboxyl oxygen to the metal ions along with imino nitrogen atom.[31] In the low frequency regions, bands detected around 520—535 cm^{-1} ranges are assigned to M–N (imino nitrogen) and the bands at 420—460 cm^{-1} ranges are assigned to M–O (carboxylato oxygen atom).[20—27,32]

^{1}H-NMR Spectra The NMR spectra of the Schiff base ligands and Pd(II) complexes were shown in Table 3. In the

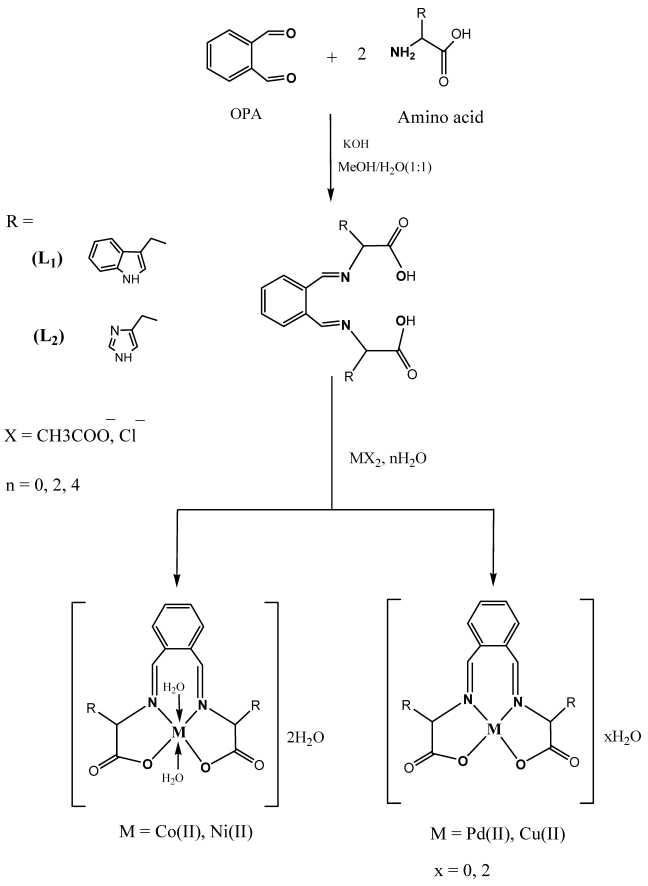


Chart 1. Synthetic Pathways of Schiff Base Ligands and Metal Complexes

free Schiff base spectra the signals were appeared in the range of 8.18—8.20 ppm due to (HC=N) protons.[24] However in the spectra of Pd(II) Schiff base complexes, the signals were observed in the up field regions of 8.28—8.30 ppm supporting the coordination of imino nitrogen atom to Pd(II).[25] While the free ligands NMR spectra have a characteristic NMR signal for carboxyl group proton in the 10.17—10.88 ppm range, the disappearance of this signal in the ^{1}H-NMR spectra of Pd(II) complexes indicating the involvement of carboxylate ion oxygen in chelation through deprotonation. There is no appreciable change in the peak position corresponding to NH and aromatic protons.

^{13}C-NMR Spectra The ^{13}C-NMR signals for the Pd(II) complexes are assigned by the comparison with the spectra of corresponding free Schiff base ligands. A down field shift of CH=N group in the range of 172.6—174.5 ppm and for carboxyl carbon COO^- ion in the range of 192.6—195.0 ppm in the complex NMR spectra indicates that the ligand coordinates through both the nitrogen atom of CH=N and the oxygen of COO^- ion.[19—27]

Electronic Spectra The Co(II) complex exhibited well resolved bands at 1040—1090, 518—540 nm and a strong high energy band at 426—494 nm and are assigned to transitions, $^4T_{2g}\leftarrow{}^4T_{1g}(F)$ (ν_1), $^4A_{2g}\leftarrow{}^4T_{1g}(F)$ (ν_2) and $^4T_{1g}(P)\leftarrow{}^4T_{1g}(F)$ (ν_3) for a high spin octahedral geometry.[19] The magnetic susceptibility measurements for the solid Co(II) complex is also indicative of four unpaired electrons per Co(II) ion suggesting consistency with their octahedral environment. The Co(II) complexes exhibit magnetic moment values of 4.96—5.12 which are well agree with the octahedral range

Table 2. Infrared Spectral Data of the Ligands and Complexes (cm^{-1})

S. No.	Complexes	ν(C=N)	ν(N–H)	ν(C–O) of COOH	ν(COO–) asy/sym	ν(M–H_2O)	ν(M–N)	ν(M–O)
1	CEIMAP	1630	3198	1720	—	—	—	—
2	CIMPAP	1618	2919	1710	—	—	—	—
3	[Co(CEIMAP)(H_2O)$_2$]2H_2O	1615	3398	—	1590, 1376	710	520	460
4	[Co(CIMPAP)(H_2O)$_2$]2H_2O	1600	2919	—	1585, 1340	712	535	450
5	[Ni(CEIMAP)(H_2O)$_2$]2H_2O	1615	3198	—	1584, 1376	710	520	460
6	[Ni(CIMPAP)(H_2O)$_2$]2H_2O	1600	2915	—	1575, 1340	712	535	450
7	[Cu(CEIMAP)]2H_2O	1628	3390	—	1590, 1376	—	535	464
8	[Cu(CIMPAP)]2H_2O	1618	2910	—	1585, 1386	—	528	458
9	[Pd(CEIMAP)]	1630	3394	—	1590, 1376	—	520	460
10	[Pd(CIMPAP]	1618	2916	—	1585, 1340	—	535	420

Table 3. ^{1}H- and ^{13}C-NMR Spectral Data of the Ligands and Complexes

S. No.	Complexes	^{1}H-NMR peak position (δ ppm)	^{13}C-NMR peak position (δ ppm)
1	CEIMAP	10.17 (2H, s, COOH), 9.80 (2H, s, NH), 8.18 (2H, s, CH=N),7.35—7.58 (12H, m,Ar-H), 3.49—3.65 (2H, d, CH), 2.18—2.20 (4H, d, CH_2)	18.8 (2C, CH_2), 69.1 (2C, CH), 117.8, 121.6, 126.8, 130.9, 133.2, 135.6 (22C, Ar-C), 152.6 (2C, CH=N), 176.0 (2C, COOH)
2	CIMPAP	12.20 (2H, d, NH), 10.88 (2H, s, COOH), 8.20 (2H, s, CH=N), 7.37—7.73 (4H, m, Ar-H), 6.98 (4H, s, CH), 3.79 (2H, t, CH), 3.18 (4H, s, CH_2)	19.6 (2C, CH_2), 68.4 (2C, CH), 118.8, 131.4, 134.5, 136.3 (12C, Ar-C), 152.5 (2C, CH=N), 176.1 (2C, COOH)
3	[Pd(CEIMAP)]	9.80 (2H, s, NH), 8.28 (2H, s, CH=N), 7.35—7.58 (12H, m, Ar-H), 3.49—3.60 (2H, d,CH), 2.18—2.20 (4H, d, CH_2)	19.6 (2C, CH_2), 69.8 (2C, CH), 117.2, 121.3, 126.4, 131.2, 132.8, 135.7 (22C, Ar-C), 172.6 (2C, CH=N), 195.0 (2C, COO^-)
4	[Pd(CIMPAP]	11.98 (2H, d, NH), 8.28 (2H, s, CH=N), 7.37—7.73 (4H, m, Ar-H), 6.99 (4H, s, CH), 3.79 (2H, t, CH), 3.20 (4H, s, CH_2)	19.4 (2C, CH_2), 68.2 (2C, CH), 119.0, 131.2, 134.4, 136.4 (12C, Ar-C), 174.5 (2C, CH=N), 192.6 (2C, COO^-)

of 4.3—5.2 BM this further supports the electronic spectral results.

The electronic spectra of the Ni(II) complex showed d–d bands in the regions 995—1072, 640—725 and 360—390 nm and are assigned to $^3T_{2g}(F)\leftarrow{}^3A_{2g}(F)$ $^3T_{1g}(F)\leftarrow{}^3A_{2g}(F)$ and $^3T_{1g}(P)\leftarrow{}^3A_{2g}(F)$ transitions respectively consistent with their octahedral configuration.[21] Ni(II) complexes showed the magnetic moment values of 3.09—3.26 within the range of 2.8—3.5 BM (octahedral range) suggesting consistency with their octahedral environment.

The electronic spectra of the Cu(II) complexes showed an intensive band at about 732—676 nm attributed to $^2A_{1g}\leftarrow{}^2B_{1g}$ transition and a broad band around 494—320 nm attributed to $^2E_g\leftarrow{}^2B_{1g}$ transition of square planar environment.[20] The magnetic susceptibility measurements of Cu(II) complexes is 1.92—1.93 BM, which suggests the presence of one unpaired electron with square-planar configuration. Furthermore, the electronic spectra of the Pd(II) complexes exhibit bands in the regions of 690—600, 555—450 and 410—370 nm, but all these three were not observed in most of the complexes. The Pd(II) complexes prepared have been found to show a broad d–d transition band in the region of 480—465 nm assignable to $^1B_{1g}\leftarrow{}^1A_{1g}$ transition typical for the square planar geometry.[25,26] Magnetic susceptibility measurements show these complexes to be diamagnetic, confirmed by sharp signals in the ^{1}H-NMR spectra.

Thermal Analysis The thermograms of all the Co(II), Ni(II) complexes show three stages of decomposition, the first two corresponding to loss of water molecules and the third corresponding to decomposition of the complex with the loss of organic moiety.[19,21] The thermograms of Co(II)/Ni(II) complexes show initial weight loss in the temperature range of 90.4—104 °C also the differential scanning calorimetry (DSC) curve of these complexes show an endothermic peak in the above temperature range further giving evidence for the presence of water molecules. The loss of water molecules in this temperature range indicates that they are present as lattice-held water.[33] The second stage corresponds to the loss of water molecules in the temperature range of 160—195 °C corresponding to the loss of coordinated water molecules. The presence of endothermic peak at 175—200 °C in DSC curve of the complex also further confirms the presence of coordinated water. The third stage weight loss show in the temperature range of 245—275 °C corresponds to the loss of organic moiety.[34] The thermograms of Cu(II) complexes show only two stages of decomposition. The first stage of the thermogram corresponds to the dehydration of water molecules and the second stage for the loss of organic moiety.[20] The thermal data of Pd(II) complexes indicate no coordinated water molecules. The sharp decomposition corresponding to the loss of organic moiety in complexes can be seen in the differential thermal analysis (DTA) curves which contain one short exothermic peak falling in the range of 258—286 °C.[25] The final product of decomposition of all the complexes above 680 °C corresponds to metal oxide.

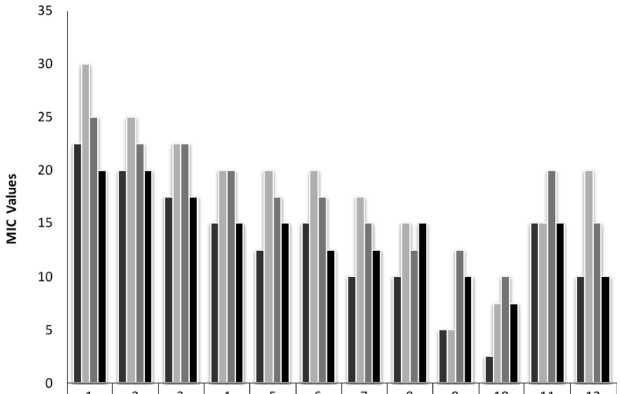
ESR Spectra The trends of ESR spectra of Cu(II) complexes $g_\perp(2.215)>g(2.044)$ observed for [Cu(CEIMAP)] $2H_2O$ and $g_\parallel(2.204)>g_\perp(2.038)$ observed for [Cu(CIMPAP)]$2H_2O$ indicate a d(x^2-y^2) ground state. The $g_\parallel>2.3$ is characteristic of an ionic environment and $g_\parallel<2.3$ of a covalent environment in M–L bonding. In the present complexes $g_\parallel$ indicate a fair degree of covalent character in the Cu–L bonding.[35,36]

Antibacterial Activity Antibacterial activities of Co(II), Ni(II), Cu(II) and Pd(II) complexes were studied along with the metal salts (cobalt(II) acetate, nickel(II) acetate, copper(II) acetate, and palladium(II) chloride), metal free ligands and two existing antibacterial drugs *viz.*, streptomycin and ampicillin. Preliminary screening for all the metal salts, metal free ligands and complexes were performed at the fixed concentration of 1000 μg/ml. Based on the obtained values of the relative zone inhibition,[37—43] of the two ligands such as CEIMAP and CIMPAP and their complexes were found to be very effective (Table 4) than ligand free metal acetates and chlorides. Inhibition was recorded by measuring

Table 4. Zones of Inhibitions of Ligands, Metal Salts, Complexes and Standard Drugs against Four Different Bacteria

S. No.	Ligand/Complexes	Zones of inhibition (mm)			
		Gram+ve bacteria		Gram−ve bacteria	
		a	b	c	d
1	CEIMAP	10	12	08	09
2	CIMPAP	12	14	11	10
3	Cobalt(II) acetate	05	04	02	03
4	$[Co(CEIMAP)(H_2O)_2]2H_2O$	24	22	18	20
5	$[Co(CIMPAP)(H_2O)_2]2H_2O$	27	23	23	20
6	Nickel(II) acetate	04	04	02	03
7	$[Ni(CEIMAP)(H_2O)_2]2H_2O$	30	32	28	25
8	$[Ni(CIMPAP)(H_2O)_2]2H_2O$	34	34	32	30
9	Copper(II) acetate	06	05	04	04
10	$[Cu(CEIMAP)]2H_2O$	36	35	36	32
11	$[Cu(CIMPAP)]2H_2O$	37	36	38	35
12	Palladium(II) chloride	08	08	05	06
13	[Pd(CEIMAP)]	38	38	40	37
14	[Pd(CIMPAP)]	40	39	44	36
15	Streptomycin	10	12	06	06
16	Ampicillin	11	13	08	07

a, *Bacillus subtilis* (MTCC 619); b, *Staphylococcus aureus* (MTCC 96); c, *Escherichia coli* (MTCC 722); d, *Klebsiella pneumoniai* (MTCC 109).



	1	2	3	4	5	6	7	8	9	10	11	12
B.subtilis	22.5	20	17.5	15	12.5	15	10	10	5	2.5	15	10
S.aureus	30	25	22.5	20	20	20	17.5	15	5	7.5	15	20
E. coli	25	22.5	22.5	20	17.5	17.5	15	12.5	12.5	10	20	15
K.pneumonia	20	20	17.5	15	15	12.5	12.5	15	10	7.5	15	10

Fig. 1. Comparison of MIC Values (in μg/ml) of Schiff Bases, Metal Complexes and Standard Drugs against Different Bacteria

* 1, 2=ligands, 3—10=metal complexes, 11, 12=standard drugs (see Table 4).

the diameter of the inhibition zone at the end of 24 h for bacteria. The metal complexes showed more increased activity than corresponding ligands and ligand free metal salts. The minimum inhibitory concentrations (MIC) of all these complexes were also verified by the liquid dilution method in which the effectiveness was observed at lower concentrations.[37—43] The comparison of the MICs (in μg/ml) of all complexes and standard drugs against tested strains are presented in Fig. 1. It was found that Co(II), Ni(II), Cu(II) complexes have good activity against all bacterial strains with MIC value (10—22.5 μg/ml). In particular, Pd(II) complexes showed excellent activity (MIC range 2.5—12.5 μg/ml) against all the bacterial strains even than standard drugs streptomycin and ampicillin. The antibacterial activity of ligands and their complexes is due to the presence of indole and imidazole moieties in them. Furthermore results from these studies have also shown that complexation of metals to CEIMAP or CIMPAP ligands serves to improve the antimicrobial of the ligands (results from Table 4). This higher antibacterial activity of the metal complexes compared to ligands is may be due to the change in structure due to coordination and chelating tends to make metal complexes act as more powerful and potent bactereostatic agents, thus inhibiting the growth of the bacteria. Furthermore, chelation reduces the polarity of the metal ion mainly due to the partial sharing of its positive charge with the donor groups within the chelate ring system. Such chelation increases the lipophilic nature of the central metal atom, which favors its permeation more efficiently through the lipid layer of the microorganism, thus destroying them more forcefully.[23,44]

Conclusion

The combination of *o*-phthalaldehyde and amino acids has been used to develop some new tetradentate N_2O_2 Schiff base ligands and consequently their metal complexes. The tetradentate behavior *i.e.* involvement of both imino nitrogen and carboxy oxygens of these Schiff bases was confirmed by IR and NMR spectroscopic measurements. The octahedral and squareplanar geometries of the complexes were further confirmed by electronic spectroscopic and magnetic measurements data. ESR spectroscopic measurements were monitored to explain the covalent nature of the complexes synthesized. These complexes were found to be effective antibacterial agents than commercial streptomycin and ampicillin drugs. However, the method of action of these compounds is unknown. We assumed yet the potent activity of ligands and their complexes is may be due to the presence of indole and imidazole moieties in them.

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