

## Research Article

## Transition Metal Complexes of (z)-4-((1H-indol-3-yl) methyleneamino) benzoic acid: Synthetic, Structural and Antibacterial studies

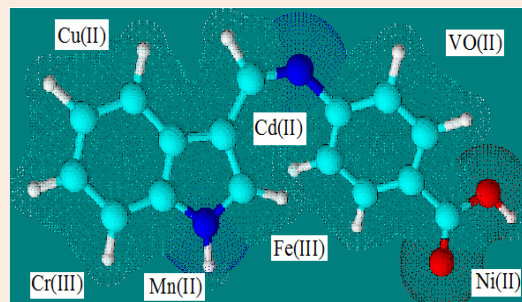
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**Abstract**

Potential azomethine class of ligand(z)-4-((1H-indol-3-yl) methyleneamino)benzoic acid (IMABA) and its VO(II), Cr(III), Mn(II), Fe(III), Ni(II), Cu(II) and Cd(II) complexes were synthesized and characterized by elemental analysis, magnetic, conductance and spectroscopic techniques like UV, IR,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR. Analysis established that the Schiff base is acting as monovalent bidentate ligand. Octahedral geometry was shown by Cr(III), Mn(II), Fe(III), Ni(II), Cu(II), and Cd(II) complexes while VO(II) complex displayed square pyramidal geometry. All the complexes and ligand were assayed for their antibacterial activity against gram positive as well as gram negative bacteria. Among them, VO(II), Fe(III), Ni(II), and Cd(II) complexes showed better activity against all microbes.

**Keywords:** Schiff base, Metal complexes, Antibacterial studies

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**Introduction**

Metal complexes of Schiff bases play an important role in the development of coordination chemistry [1–3]. Schiff base ligands and transition metal complexes derived from them have been found increasing applications in chemical, biological and industrial fields. Transition metal complexes of Schiff bases derived from amino acids are useful in catalysis, organic synthesis and medicine as antibiotics, anti-allergic, and antitumor agents [4]. In the present course of investigation, a novel Schiff base (z)-4-((1H-indol-3-yl) methyleneamino) benzoic acid (IMABA) and its transition metal complexes were synthesized and characterized. Antimicrobial activity of the Schiff base and their metal chelates were examined using plate disc method [5–14].

**Experimental****Preparation of Schiff base and complexes**

An ethanolic solution of 4-aminobenzoic acid (2mM) was mixed with a solution of 3-formylindole (2mM) and refluxed for four hours in a water bath. The resulting solution was concentrated and cooled and the precipitate formed was filtered, washed with ethanol and dried. M.P = 146°C. Complexes of (IMABA) were prepared by mixing ethanolic solutions of metal acetate (2mM), 4-aminobenzoic acid (2mM) and 3-formylindole (2mM). Ferric chloride (2mM) solution was used for the synthesis of Fe(III) complex. The resulting solution was refluxed for 3 hours, concentrated and cooled in an ice bath. The complex formed was filtered, washed with ethanol and dried.

## Physical Measurements

Metal percentage was calculated by standard methods. Magnetic susceptibility measurements were done on Sherwood, UK (Mark 1) magnetic susceptibility balance at room temperature [15–17]. Percentage of carbon, hydrogen and nitrogen content of the Schiff base ligands and their metal complexes were determined by microanalysis using Elementar make Vario EL III model CHN analyzer. Molar conductance studies were conducted in DMSO solvent at a concentration of  $10^{-3}$ M at  $30 \pm 2^\circ\text{C}$ . Cell constant was maintained as 1 in all investigations [18]. Shimadzu FTIR spectrometer and 1800 UV-Visible spectrophotometer were utilized for spectral studies.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR Spectral Studies of ligands and chelates were recorded in DMSO- $d_6$  on a Bruker AVANCE III HD. Mass spectra of the Schiff bases were recorded using QP 2010 model Shimadzu GCMS at a source temperature of  $300^\circ\text{C}$  [19–21]

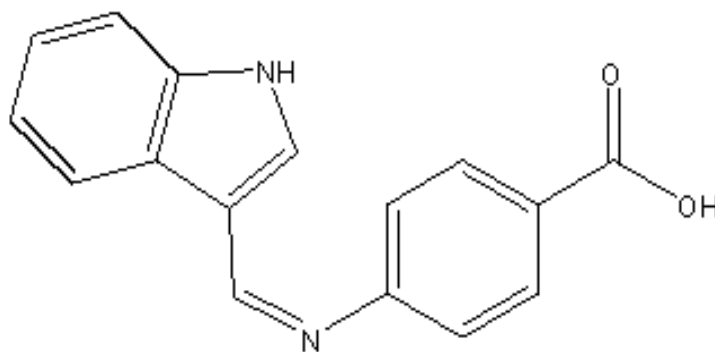
## Antibacterial Studies

The Schiff base and their metal chelates were evaluated for their antibacterial activity against different bacterial strains such as *S. aureus*, *B. subtilis*, *B. thuringiensis*, *E. aerogens*, *E. coli* and *P. vulgaris*, at various concentrations ranging from  $100\text{--}500\mu\text{gdisc}^{-1}$  using plate disc method.

## Results and Discussions

### Characterization of Ligand

Elemental analysis, Found C%(72.96), N%(10.10), H%(4.03); Calc: C%(72.72), N%(10.6), H%(4.54). In the HRMS of the ligand the loss of benzoic acid part from the molecular ion gave a cation at  $m/z$  144(100%) as a base peak. Other prominent peaks shown in the mass spectrum at  $m/z$  116, 145 and 146 can be assigned due to the fragment ions  $[\text{C}_8\text{H}_6\text{N}]^+$ ,  $[\text{C}_9\text{H}_7\text{NO}]^+$  and  $[\text{C}_9\text{H}_{10}\text{N}_2]^+$  respectively. The  $^1\text{H}$  NMR (DMSO- $d_6$ ) signal for proton of the carboxylic acid appeared as a singlet at  $\delta$  12.15. Also the azomethine proton, showed its own singlet signal at  $\delta$  9.94. The aromatic protons of both indole and benzene rings resonated in the region  $\delta$  6.54–8.28. The  $^{13}\text{C}$  NMR spectrum in DMSO- $d_6$  showed the carboxylic acid carbon signal at 185.08ppm. A peak at 131.27ppm can be assigned to the azomethine carbon. The aromatic carbon signals were appeared in the  $^{13}\text{C}$  NMR spectrum in the region 110–170ppm. The IR spectrum showed the characteristic C=N stretching vibration in the region of  $1559\text{cm}^{-1}$ . The absorption of stretching vibration of –OH group of the carboxylic acid part appeared as a scalloped band in the region  $3000\text{cm}^{-1}$ . The asymmetric and symmetric stretching vibrations of the carboxylate group were observed at  $1665\text{cm}^{-1}$  and  $1448\text{cm}^{-1}$  respectively. In the electronic spectrum, the absorption bands because of the  $n \rightarrow \sigma^*$ ,  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions, were observed at 38600, 34800 and  $32300\text{cm}^{-1}$  respectively. On the basis of the above results, structure of the ligand IMABA was confirmed and shown in **Figure 1**.



**Figure 1** Molecular Structure of IMABA

**Table 1** Microanalytical, magnetic and conductance data of IMABA and its complexes

Complex	Colour, Yield (%), M.P ( $^{\circ}$ C)	Metal % Found (*)	C % Found (*)	H % Found (*)	N % Found (*)	$\mu_{\text{eff}}$ (BM)	Molar conductance ( $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$ )
IMABA (LH)	Yellow, 80, 146	-	72.96 (72.72)	4.03 (4.54)	10.10 (10.60)	-	-
[(VO)L(Ac)(H <sub>2</sub> O)]	Brown, 72, 240	11.93 (12.53)	53.43 (53.07)	3.62 (3.93)	6.89 (6.88)	1.15	24
[Cr LAc <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]	Grey, 75, 259	13.30 (11.09)	50.93 (51.17)	4.27 (4.47)	6.09 (5.97)	2.94	4
[MnLAc(H <sub>2</sub> O) <sub>3</sub> ]	Brown, 75, 350	12.80 (12.76)	50.68 (50.10)	4.45 (4.64)	6.12 (6.50)	4.92	16
[FeLCl <sub>2</sub> (H <sub>2</sub> O)] <sub>2</sub>	Yellow, 76, 230	13.40 (13.68)	47.67 (47.05)	3.26 (3.18)	6.47 (6.86)	3.74	10
[NiLAc(H <sub>2</sub> O) <sub>3</sub> ]	Grey, 78, 260	13.28 (13.56)	48.76 (49.65)	4.17 (4.60)	6.21 (6.43)	4.15	8
[CuLAc(H <sub>2</sub> O) <sub>3</sub> ]	Green, 69, 230	14.00 (14.44)	49.66 (49.09)	4.37 (4.54)	6.79 (6.36)	2.1	18
[CdL <sub>2</sub> ]	Yellow, 71, 230	17.58 (17.55)	59.67 (60.18)	3.11 (3.44)	8.21 (8.77)	D	15

\*Calculated values

### Characterization of Complexes

All the complexes are found to be amorphous solids and stable to light and air. The analytical data and the physical characteristics of VO(II), Cr(III), Mn(II), Fe(III), Ni(II), Cu(II) and Cd(II) complexes are given in **Table 1**.

The room temperature magnetic moments and molar conductance value of the complexes are also represented in this table. From the elemental analysis, these complexes are given the general formula [ML(Ac)(H<sub>2</sub>O)<sub>3</sub>] for Mn(II), Ni(II) and Cu(II) complexes, while the other complexes possess the formula [VOL(Ac)(H<sub>2</sub>O)], [CrL(Ac)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>], [FeL(Cl)<sub>2</sub>(H<sub>2</sub>O)]<sub>2</sub> and [CdL<sub>2</sub>]. In all complexes, except cadmium complex, there exist 1:1 stoichiometry between the metal and the ligand.

### Molar conductance

Molar conductance values of the complexes in DMSO at a concentration of  $10^{-3}\text{M}$  at room temperature were in the range of  $4\text{--}24\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ , which establish the non electrolytic behaviour of the chelates.

### Magnetic moment measurements

Manganese complex showed a magnetic moment value of 4.92 BM, which suggests the distorted octahedral geometry.  $\mu_{\text{eff}}$  for Cu(II) complex was 2.1BM, which is slightly higher than the spin only value (1.8BM). This accounts for the slight orbital contribution to the spin only value and the absence of spin-spin interactions. Therefore a tetragonally distorted octahedral geometry is suggested for this complex. Fe(III) complex exhibits low magnetic moment (3.74BM) than the value expected for the high spin  $\text{Fe}^{3+}$  complexes. The very low effective magnetic moment is the indication of the presence of antiferromagnetic exchange in the complex. Hence a dimeric octahedral geometry was assigned to this chelate. The cadmium complex was found to be diamagnetic in nature and hence a tetrahedral structure is proposed to it. The  $\mu_{\text{eff}}$  shown by VO(II) complex is 1.15BM, suggests the square pyramidal geometry to the chelate. Octahedral geometry is suggested to Cr(III) complex of IMABA, since it exhibited a magnetic moment value of 2.94BM.

### Infrared spectra

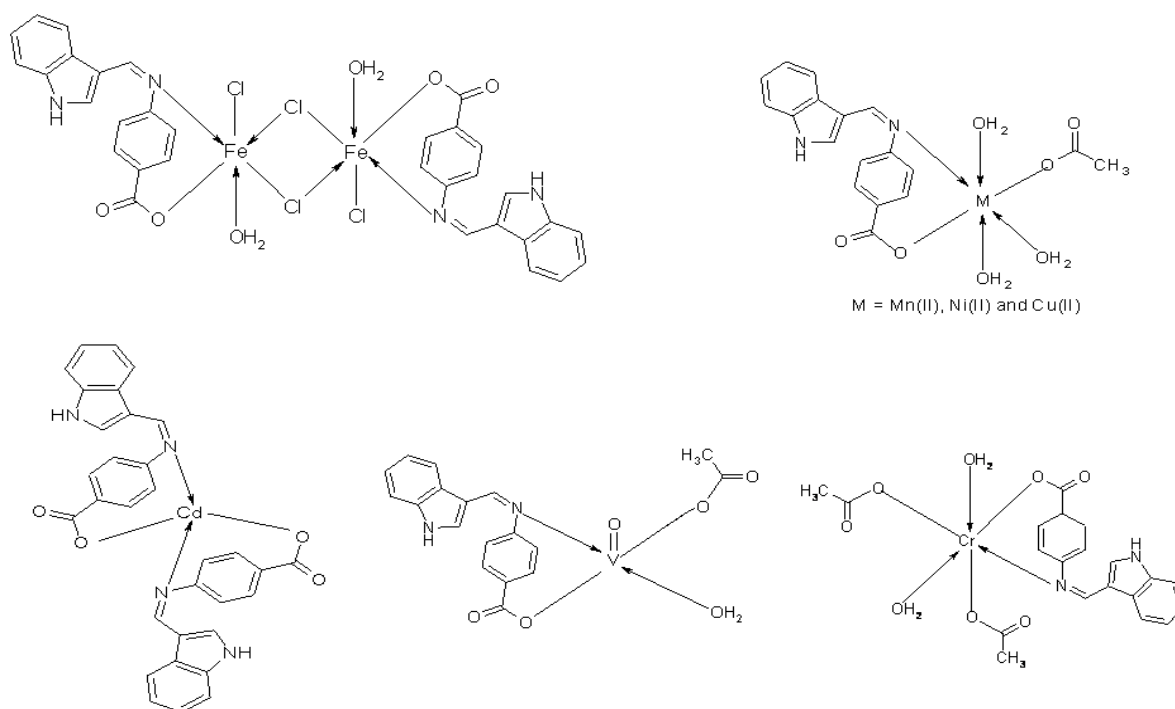
A shift of  $\gamma_{C=O}$  to the lower frequencies in the IR spectra of complexes depicts the chelation of the ligand to metal ion through the carboxylate oxygen.  $\gamma_{C=N}$  also undergoes shift to lower frequencies which shows the coordination of nitrogen atom of the azomethine linkage to the metal atom, during complexation [22]. In all the complexes, the symmetric and asymmetric stretching vibrations of the carboxylate group occur at  $\sim 1430$  and  $\sim 1630\text{cm}^{-1}$  respectively, showing a difference of about  $200\text{cm}^{-1}$ . Therefore in all the present chelates, the carboxylate group exists as a monodentate moiety [23]. The presence of coordinated water molecules in the complexes except  $[\text{CdL}_2]$  is confirmed by the observation of broad band around  $3300\text{--}3400\text{cm}^{-1}$ . Conclusive evidence regarding the bonding of nitrogen and oxygen with the metal ion were provided by the occurrence of  $\gamma_{M-N}$  and  $\gamma_{M-O}$  bands in the regions  $502\text{--}531\text{cm}^{-1}$  and  $609\text{--}677\text{cm}^{-1}$  respectively. (**Table 2**)

### Electronic spectra

Electronic spectrum of the ligand was characterized by three bands in the region  $38600$ ,  $34800\text{cm}^{-1}$  and  $32300\text{cm}^{-1}$  which can be assigned to be  $n \rightarrow \sigma^*$ ,  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions respectively. During complex formation, a red shift is detected for these bands which indicate the involvement of the ligand in coordination.  $\text{VO}^{+2}$  chelate displays an additional band at  $12800\text{cm}^{-1}$  which can be assigned to the transition  ${}^3\text{B}_2 \rightarrow {}^2\text{E}$ , suggesting square pyramidal geometry [24, 25]. The Ni(II) complex exhibits three additional bands in the region  $13200\text{cm}^{-1}$ ,  $17200\text{cm}^{-1}$  and  $23400\text{cm}^{-1}$  attributable to  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})$ ,  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$  and  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$  transitions, which corresponds to octahedral structure [26]. In confirmation to the distorted octahedral structure suggested from magnetic studies, the electronic spectrum of Cu(II) complex exhibits two bands at  $13700\text{cm}^{-1}$  and  $15800\text{cm}^{-1}$ ; the former may be assignable to  ${}^3\text{E}_g \rightarrow {}^3\text{T}_{2g}$  transition [27] and the later may be attributed to L  $\rightarrow$  M charge transfer band, suggesting thereby the octahedral geometry. In Mn(II) complex, central metal atom in the octahedral environment was confirmed by the presence of electronic spectral bands at  $12900$ ,  $14500$  and  $24800\text{cm}^{-1}$ . In agreement with the magnetic moment values, these spectral bands can be assigned to the transitions  ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}(\text{G})$ ,  ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{G})$  and  ${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g(\text{G})$  respectively. An intense band at  $29100\text{cm}^{-1}$  in the electronic spectrum of Fe(III) complex may be attributed to the L  $\rightarrow$  M charge transfer band. Another shoulder peak at  $18900\text{cm}^{-1}$  exhibited by the iron complex may be due to  ${}^5\text{T}_{2g} \rightarrow {}^5\text{E}_g$  transition, confirming its octahedral geometry. Since ground state Fe(III) in high spin [28] complex is  ${}^6\text{A}_1$ , all the d-d transitions are weak and obscured with the intense charge transfer bands. Cr(III) also showed a similar charge transfer band at  $12800\text{cm}^{-1}$ . From the spectroscopic and magnetic studies, geometries can be assigned to the metal complexes of IMABA (**Figure 2**).

**Table 2** Characteristic infrared absorption frequencies of IMABA and its transition metal complexes

Complex	$\gamma_{\text{H}_2\text{O}}$	$\gamma_{\text{COO}}$ (asym)	$\gamma_{\text{C=N}}$	$\gamma_{\text{COO}}$ (sym)	Out of plane bending	$\gamma_{\text{M-O}}$	$\gamma_{\text{M-N}}$
IMABA (LH)	-	1665	1559	1448	758	-	-
$[(\text{VO})\text{L}(\text{Ac})(\text{H}_2\text{O})]$	3406	1651	1502	1406	854, 748	609	527
$[\text{Cr LAc}_2(\text{H}_2\text{O})_2]$	3367	1637	1523	1446	790, 756	638	513
$[\text{MnLAc}(\text{H}_2\text{O})_3]$	3348	1647	1502	1436	790, 759	634	531
$[\text{FeLCl}_2(\text{H}_2\text{O})]_2$	3404	1649	1502	1436	856, 748	657	528
$[\text{NiLAc}(\text{H}_2\text{O})_3]$	3320	1603	1554	1408	788, 754	677	502
$[\text{CuLAc}(\text{H}_2\text{O})_3]$	3251	1614	1539	1402	852, 777	638	511



**Figure 2** Structures of metal complexes of IMABA

## Antibacterial Studies

**Table 3** Antibacterial activity of the Schiff base (IMABA) and its transition metal complexes

Compound	Diameter of zone of inhibition (mm) at different concentrations ( $\mu\text{gdisc}^{-1}$ )																	
	<i>S. aureus</i>			<i>B. subtilis</i>			<i>B. thuringiensis</i>			<i>E. aerogenes</i>			<i>E. coli</i>			<i>P. vulgaris</i>		
	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>
4 IMABA	2	3	7	3	3	6	1	2	4	2	4	6	6	6	4	3	4	5
VO(II) complex	10	12	19	4	12	18	9	15	18	5	11	14	6	10	16	5	14	17
Cr(III) complex	7	6	7	3	4	7	2	5	8	2	2	4	3	3	5	6	6	5
Mn(II) complex	5	6	7	2	4	6	3	5	6	2	4	7	2	4	6	3	3	8
Fe(III) complex	11	13	15	11	14	16	9	13	15	7	10	14	8	12	12	4	10	13
Ni(II) complex	12	13	16	7	11	15	5	10	15	11	14	16	7	11	16	5	9	14
Cu(II) complex	6	6	7	3	2	5	2	3	7	3	6	8	5	4	6	6	7	8
Cd(II) complex	13	20	27	18	19	24	14	17	22	17	19	26	15	20	25	18	19	22

\*C<sub>1</sub>=100  $\mu\text{gdisc}^{-1}$ , C<sub>2</sub>=200  $\mu\text{gdisc}^{-1}$ , C<sub>3</sub>=500  $\mu\text{gdisc}^{-1}$

The *in vitro* cytotoxic data of the Schiff base IMABA and its transition metal complexes upon different bacterial strains at varied concentrations are represented in the **Table 3**. It is obvious from the data that majority of the transition metal complexes of the ligand IMABA showed enhanced antibacterial activity than the parent Schiff base. The activity of Cd(II) complex of IMABA was very high and comparable to the activity of the standard antibiotics especially against *S. aureus*, *B. subtilis*, *E. coli* and *P. vulgaris*. This complex showed considerable antibacterial activity even at low concentrations. The zone of inhibition reaches to approximately 20 mm even at a concentration of 200 $\mu\text{gdisc}^{-1}$ . The Cu(II) and Mn(II) complexes of IMABA showed very little or no activity against the studied bacterial strains. Fe(III) and Ni(II) complexes of IMABA exhibited appreciable activity. The Fe(III) complex showed the diameter of inhibition zone 16mm for the concentration 500 $\mu\text{gdisc}^{-1}$ . A maximum of 19mm diameter of growth inhibition zone was obtained for VO(II) complex of IMABA at 500 $\mu\text{gdisc}^{-1}$  on the *S. aureus*. Comparatively poor activity was noticed for Cr(III) complex.

## Conclusion

1. Novel heterocyclic Schiff base (z)-4-((1H-indol-3-yl) methyleneamino) benzoic acid (IMABA) and its transition metal complexes were synthesized and characterized.
2. Analysis established that the Schiff base acted as monovalent bidentate ligand in all complexes.
3. All complexes, except cadmium complex displayed 1:1 stoichiometry between the metal and the ligand.
4. Octahedral geometry was exhibited by Cr(III), Mn(II), Fe(III), Cu(II) and Ni(II) complexes. Square pyramidal geometry was assigned to VO(II) chelate, while Cd(II) complex showed tetrahedral geometry.
5. The ligand and the complexes were screened for their antibacterial activities.
6. Cd(II) complex exhibited pronounced growth inhibition against the growth of *S. aureus*, *B. subtilis*, *E. coli* and *P. vulgaris*.

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