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Research Paper

Chelating Competency and Antibacterial Properties of (E)-2-((1H-indol-3-yl)metheneamino)-5-bromobenzoic acid and its Metal Chelates

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Abstract: Heterocyclic compound (E)-2-((1H-indol-3-yl)metheneamino)-5-bromobenzoic acid (IMABBA) and its Mn(II), Ni(II) and Cu(II) complexes were synthesized and characterized by spectral, elemental, magnetic and conductance measurements. Investigations showed that IMABBA behaved as bidentate ligand during chelation. The octahedral geometry of the chelate was confirmed by magnetic and optical spectral studies. The antibacterial studies of the ligand and metal chelates were evaluated and reported.

Keywords: Antibacterial studies, Complexes, 3-Formylindole, Schiff bases.

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Introduction

The compounds which possess azomethine linkage or Schiff bases are well-known for their chelating competency. Such molecules and their metal chelates are having wide variety of applications in the pharmaceutical, catalysis, analytical and corrosion field^[1-15]. Transition metal complexes of Schiff bases derived from aminoacids are useful in organic synthesis and medicine as antibiotics, anti-allergic and antitumor agents^[16]. In the present investigation, a novel Schiff base (E)-2-((1H-indol-3-yl)metheneamino)-5-bromobenzoic acid and its metal complexes were synthesized and characterised. The antimicrobial activity of Schiff base (IMABBA) and their metal chelates were examined by disc diffusion method.

Material and Methods

1H-indol-3-carbaldehyde and 2-amino-5-bromobenzoic acid were purchased from E. Merck. Analar grade metal acetates from Qualigens were used as source of metal for synthesis of the complexes. Shimadzu model FT-IR Spectrometer (Model: IR affinity) and Shimadzu UV-visible-1800 spectrophotometer were used for recording infrared and electronic spectra. Mass spectrum of the compound was recorded using QP 2010 model Shimadzu GCMS. NMR spectral studies were carried out. IMABBA was synthesized by condensing equimolar mixture of 3-Formylindole and 2-amino-5-bromobenzoic acid in ethanol

medium. The reaction mixture was refluxed for five hours, concentrated by evaporation and allowed to cool slowly. The precipitated brown coloured crystals was filtered, washed with ethanol and dried. The Schiff base IMABBA (2mmol) in ethanol was heated to reflux, To the hot refluxing solution, metallic acetates in ethanol medium (2mmol) was added and the resulting mixture was refluxed for 3 hours, evaporated, cooled and the chelates separated was filtered and dried.

Results and Discussion

Characterization of ligand: Elemental analysis data were quite in agreement with molecular formula C₁₆H₁₁N₂O₂Br. In the mass spectrum of IMABBA, the molecular ion peak was absent, and the base peak observed at m/z 144. The signal appeared at δ 12.16 in ¹H_{nmr} spectrum was due to the carboxylic acid proton and the proton present in the azomethine moiety showed its characteristic signal at δ 9.91. A broad signal appeared at δ 6.93 was assignable to the NH proton of the indole moiety. The signals appeared in ¹³Cnmr spectrum of IMABBA were assigned for sixteen different carbon atoms. The signal of the azomethine carbon appeared at 133.57ppm. A peak obtained in the downfield region of the spectrum at 185.95ppm was due to the carboxylic acid carbon.

In the IR spectrum of the ligand, the significant absorption frequencies appeared at 1610cm^{-1} and 1446cm^{-1} can be attributed to the stretching frequencies of the carbonyl bond of the carboxylic acid group. An intense IR peak appeared at 1570cm^{-1} can be assigned to the C=N stretching vibration. The two weak bands due to the electronic transitions in the molecules were observed at 27548cm^{-1} and 37735cm^{-1} which were attributed to transitions to $n \rightarrow \pi^*$ and $n \rightarrow \sigma^*$ respectively. The intense peak observed at 28571cm^{-1} can be assigned to $\pi \rightarrow \pi^*$ transition. The structure of the ligand (IMABBA) was shown in figure 1.

Characterization of Complexes: All the metal chelates were coloured and non hygroscopic. They are stable in air and light and are insoluble in water and ethanol. They exhibited comparatively appreciable solubilities in aprotic polar solvents such as DMSO and DMF. All chelates exhibited higher melting points than their parent Schiff base. All the complexes exhibited 1:1 stoichiometry between the ligand and the metal ion and can be assigned the general formula $[\text{MLAc}(\text{H}_2\text{O})_3]$ where $\text{M} = \text{Mn}(\text{II}), \text{Ni}(\text{II})$ and $\text{Cu}(\text{II})$. The octahedral geometry was assigned to the metal chelates and given in figure 2. The elemental analysis, molar conductance and magnetic moment data of the complexes are presented in table 1.

Molar conductance: Molar conductance values of complexes in DMSO at a concentration of 10^{-3}M at room temperature were in the range $4\text{--}18\ \text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$. These low values of molar conductance was a clear evidence for the absence of any ionic species outside the coordination sphere and thus all metal chelates were assumed to be acting as non-electrolytic compounds in DMSO.

Magnetic moment measurements: Mn(II) complex showed an effective magnetic moment of 6.1BM, which is nearer to the spin only value. Nickel complex exhibited a μ_{eff} of 2.58BM which was close to the calculated value (2.8BM) using spin only formula. This is an indication for the octahedral geometry of this complex^[17]. The effective magnetic moment value of Cu(II) chelate was 2.0BM, which is in agreement with the value found for octahedral copper complexes^[18,19].

Spectroscopic measurements: Characteristic infrared bands of the ligand and complexes are given in table 2. The coordination site of the Schiff base IMABBA is through the carboxylate moiety, due to this all the symmetric and asymmetric stretching vibrations of the carboxylate group in metal chelates changed into the lower frequency regions ($\sim 20\text{cm}^{-1}$) compared to the stretching frequencies of the free ligand. The metal chelates exhibited their characteristic stretching frequency for C=N group in the region $1540\text{--}1550\text{cm}^{-1}$ which falls in the lower region compared to the azomethine stretching frequency of the free Schiff base (1570cm^{-1}), which support the argument that one of the coordination sites of the bidentate Schiff base ligand is the azomethine nitrogen^[20]. Additional broad bands appeared

in the IR spectra of the chelates between $3260\text{--}3300\text{cm}^{-1}$ which is a strong indication of the presence of water molecules in the coordination sphere^[66]. IR spectrum of the metal chelates at $\sim 510\text{cm}^{-1}$ and $640\text{--}670\text{cm}^{-1}$ can be regarded as the presence of newly formed metal-nitrogen and metal-oxygen coordinate bonds respectively^[21].

In the octahedral environment, Mn(II) complex gave spin-forbidden as well as parity forbidden bands in its electronic spectrum. The three significant bands observed in the regions 13600cm^{-1} , 20030cm^{-1} and 24640cm^{-1} , have been assigned to ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{1\text{g}}(\text{G})$, ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{2\text{g}}(\text{G})$ and ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{1\text{g}}(\text{P})$ transitions respectively^[21]. The electronic transitions in the Ni(II) complex gave three intense bands at 14200 , 18864 and 24243cm^{-1} , which can be assigned to ${}^3\text{A}_{2\text{g}}(\text{F}) \rightarrow {}^3\text{T}_{2\text{g}}$, ${}^3\text{A}_{2\text{g}}(\text{F}) \rightarrow {}^3\text{T}_{1\text{g}}(\text{F})$ and ${}^3\text{A}_{2\text{g}}(\text{F}) \rightarrow {}^3\text{T}_{1\text{g}}(\text{P})$ transitions respectively^[22]. In the octahedral field, Cu(II) chelate is expected to display a band in the electronic spectrum which can be assigned due to ${}^2\text{E}_{\text{g}} \rightarrow {}^2\text{T}_{\text{g}}$ electronic transition. A band with high molar extinction coefficient was observed at 27640cm^{-1} , is assignable to the Laporte forbidden ligand to metal charge transfer band.

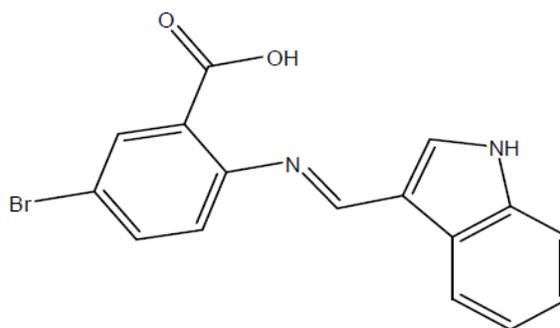


Figure 1: Structure of IMABBA

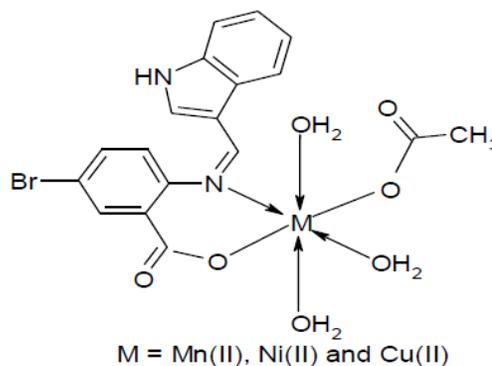


Figure 2: Structure of metal complexes of IMABBA

In the ^1H NMR spectra of all the metal complexes, the signal due to the carboxylic acid proton was absent, showing that one of the linkages by the ligand to the metal ion is through the carboxylate part of the Schiff base, after deprotonation. Also a shift for the azomethine proton peak to the downfield regions, suggests that second coordinating

moiety of the ligand is the azomethine nitrogen. In the ^{13}C NMR spectra of all complexes, the peak due to the azomethine carbon atom in the metal chelates are shifted to downfield region which is an indication of the coordination through the C=N moiety.

Table 1: Microanalytical, magnetic and conductance data of transition metal complexes of (E)-2-((1H-indol-3 yl) metheneamino)-5-bromobenzoic acid (IMABBA)

Complex	Colour M.P($^{\circ}\text{C}$)	Metal % Found (Calcd.)	C % Found (Calcd.)	H % Found (Calcd.)	N % Found (Calcd.)	Br % Found (Calcd.)	μ_{eff} (BM)	Ω	Geometry
IMABBA (LH)	Yellow 155	-	52.30 (56.14)	3.88 (3.21)	8.66 (8.18)	23.54 (23.09)	-		-
[MnLAc(H ₂ O) ₃]	Grey 240	10.65 (10.81)	44.23 (44.44)	3.34 (3.73)	5.21 (5.50)	15.43 (15.52)	6.1	18	Octahedral
[NiLAc(H ₂ O) ₃]	Grey 278	11.85 (11.50)	42.47 (42.10)	3.19 (3.70)	5.51 (5.46)	15.14 (15.39)	2.58	4	Octahedral
[CuLAc(H ₂ O) ₃]	Green 340	12.37 (12.36)	41.28 (41.60)	2.01 (2.89)	5.02 (5.40)	15.78 (15.25)	2.00	15	Octahedral

*Calcd: Calculated value, Ω : Molar conductance in $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$

Table 2: Characteristic infrared absorption frequencies of IMABBA and its transition metal complexes

Compound	$\gamma_{\text{H}_2\text{O}}$	γ_{COO} (asym)	$\gamma_{\text{C=N}}$	γ_{COO} (sym)	$\gamma_{\text{C-OO}}$	In plane bending	Out of plane bending	$\gamma_{\text{M-O}}$	$\gamma_{\text{M-N}}$
IMABBA (LH)	-	1610	1570	1446	1236	1128	790, 759	-	-
[MnLAc(H ₂ O) ₃]	3305	1583	1541	1423	1242	1004	821, 758	640	505
[NiLAc(H ₂ O) ₃]	3317	1585	1548	1417	1375	1055	827, 731	677	512
[CuLAc(H ₂ O) ₃]	3267	1597	1554	1417	1371	1091	817, 727	675	520

Thermal analysis: Mn(II), Ni(II) and Cu(II) complexes of the Schiff base, 3FI2A5BBA were subjected to thermal analysis, using the techniques TGA and DTA. All the complexes incurred significant mass loss near 200°C , due to the loss of coordinated water molecules. Mn(II) and Ni(II) complexes exhibited a three stage decomposition pattern while Cu(II) chelate showed two stage decomposition. From the thermal studies it is concluded that the relative thermal stabilities of the chelates decrease in the order $[\text{CuLAc}(\text{H}_2\text{O})_3] > [\text{NiLAc}(\text{H}_2\text{O})_3] > [\text{MnLAc}(\text{H}_2\text{O})_3]$.

Antibacterial studies on the Schiff base, IMABBA and its metal complexes: The Schiff base, 3FI2A5BBA and its transition metal complexes were subjected to antibacterial

activity on six different gram positive and gram negative bacterial strains. The cotton swab method was employed for the development of bacterial culture and the drug inoculation was made by plate disc method. Antibacterial data of these compounds, the Schiff base and its chelates, are depicted in detail in the table 3. Mn(II) complex showed very good activity (12mm) against the growth of *B. subtilis* even at a concentration of $100\mu\text{gdisc}^{-1}$. Compared to the activity of standard antibiotics, this result is highly remarkable. Diameter of zone of inhibition exhibited by the copper complex at a concentration $100\mu\text{gdisc}^{-1}$ is 11mm on bacteria *S. aureus*. At the same concentration Schiff base IMABBA, showed growth inhibition diameter as 2mm, which establishes the role of chelation through azomethine moiety upon antibacterial power of the complex. Antibacterial strength of the Ni(II) complex of the ligand

IMABBA was found to be more or less same with that of the free Schiff base. The inhibitory power of these Schiff bases was found to be increased upon metal chelation owing to the theory of Tweedy^[23]. This may be due to the increased lipophilic nature of the complexes upon chelation. Such increased activity of the metal chelates can be explained the basis of Overtone's concept of cell permeability. The lipid membrane that surrounds the cell will permit the passage of lipid soluble materials. The

polarity of metal ions will be reduced considerably on chelation due to the overlapping of the ligand orbitals and partial sharing of positive charge of the metal ions to the donor group. In this scenario, the delocalization of the π electron over the whole chelate ring will be very high and hence enhances the lipophilicity^[24-26]. This increased lipophilicity causes to increase the penetration of the metal chelates in to lipid membrane and blocks the metal binding sites of the enzymes of microbes.

Table 3: Antibacterial activity of the Schiff base (E)-2-((1H-indol-3-yl)metheneamino)-5-bromobenzoic acid (IMABBA) and its transition metal complexes

Compound	Diameter of zone of inhibition (mm) at different concentrations (μgdisc^{-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>		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
IMABBA	2	9	12	5	7	12	5	6	12	5	7	10	5	9	11	7	8	15
[MnLAc(H ₂ O) ₃]	9	8	10	12	13	14	5	7	10	11	12	13	13	11	12	8	9	10
[NiLAc(H ₂ O) ₃]	2	7	10	4	8	10	4	8	11	7	8	9	8	11	11	8	9	10
[CuLAc(H ₂ O) ₃]	11	14	15	8	13	16	7	12	17	5	10	15	4	6	8	5	11	18

A: 100 μgdisc^{-1} , B: 200 μgdisc^{-1} , C: 500 μgdisc^{-1}

Conclusion

- Novel heterocyclic Schiff base (E)-2-((1H-indol-3-yl)metheneamino)-5-bromobenzoic acid (IMABBA) and its metal chelates were synthesized.
- Structure of the ligand and chelates were established by various analytical methods and it was proved that a 1:1 stoichiometry exist between the ligand and the metal ion. Octahedral geometry was suggested for the chelates.
- The ligand and the complexes were screened for their antibacterial activities.
- Mn(II) complex exhibited pronounced growth inhibition against the growth of *B. subtilis*.

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