



SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES OF SOME MIXED LIGAND TERNARY METAL COMPLEXES

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ABSTRACT

Mixed-ligand ternary complexes of metal ions such as Cu^{2+} , Zn^{2+} , and Ni^{2+} containing benzimidazole or 2-methyl benzimidazole and amino acids (aspartic acid and glutamic acid) have been synthesized and characterized by elemental analysis, IR, UV-Visible spectral studies and molar conductivity measurement. The synthesized ternary complexes were also tested for their antibacterial activities, and the order of the metal complexes in terms of their antibacterial activities was found to be $\text{Cu}^{2+} > \text{Zn}^{2+} > \text{Ni}^{2+}$.

Key words: Benzimidazole, Amino acids, Ternary metal complexes.

INTRODUCTION

Imidazole is an important ligand of biological interest¹. It occurs in the side chain of the amino acid histidine. Histidine as a ligand also plays an important role in biological systems, and is found to be present in many proteins, enzymes and metalloenzymes, where the imidazole moiety of the histidyl residue forms all or a part of the binding sites of many transition metal ions like Cu^{2+} , Zn^{2+} , Fe^{2+} , Co^{2+} etc.²⁻⁴ The importance of metal imidazole complexes and its derivatives in biological fields is well known in literature⁵⁻⁹, however literature survey reveals that limited work has been done on two very important derivatives of imidazole viz, benzimidazole and 2-methyl benzimidazole^{10,11}. The importance of benzimidazole reflects from the fact that it is a part of the nucleotide portion of vitamin B₁₂, where it plays a vital role in the structure and functioning of the coenzyme. In the recent years, benzimidazole has also gained medical importance¹², and it is used as an antibacterial, antifungal, and antihelminthic agent. The metal chelates of a number of drugs have been found to be more potent than the parent drugs themselves^{13,14}. Keeping the above facts in

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view, this paper presents the synthesis, characterization and antibacterial activities of some ternary metal complexes of benzimidazole and 2-methyl benzimidazole with amino acids (aspartic and glutamic). The metal ions used in these investigations were Cu^{2+} , Zn^{2+} , and Ni^{2+} .

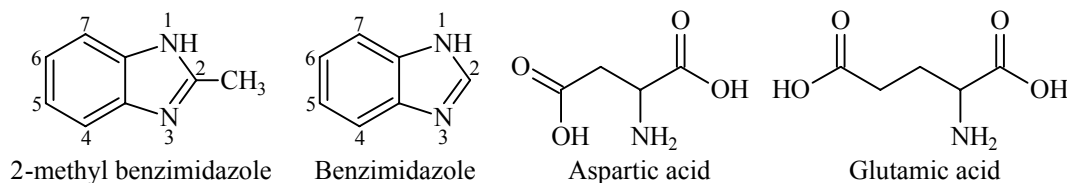


Fig. 1: The structure of the ligands used to prepare ternary complexes

EXPERIMENTAL

Material and method

Benzimidazole, 2-methyl benzimidazole, aspartic and glutamic acids, were obtained from Merck India. All ligands used were of reagent grade. The metal salts (as nitrates) were provided by BDH. All other chemicals used were analytical grade (BDH) products. The infrared spectra in the $4000\text{-}400\text{ cm}^{-1}$ range, and the C, H, and N contents of the isolated complexes were determined at IITR Roorkee (Uttarakhand). Molar conductances of the synthesized ternary metal complexes in DMSO was measured using Systronics digital conductivity meter while as the thermogravimetric analysis was carried out using Perkin Elmer STA 6000 analyser. The optical absorption spectrum for different mixed-ligand ternary metal complexes ($2 \times 10^{-4}\text{ M}$) in DMSO was recorded on a Shimadzu UV-160 spectrophotometer. The spectra's of these solutions in one cm quartz cells was recorded in the wave length region of 220-800 nm. The extinction coefficients for complexes were also calculated at the respective absorbance maxima.

Synthesis of mixed-ligand complexes

A 2.5 mmol solution of benzimidazole or 2-methyl benzimidazole in 20 mL ethanol-water (60 : 40) mixture was prepared and then mixed with 2.5 mmol of aspartic or glutamic acid, dissolved in 20 mL of distilled water. To the resulting solution, 20 mL of (2.5 mmol) metal salt solution (Cu^{2+} , Zn^{2+} , and Ni^{2+} nitrates dissolved in distilled water) was then slowly added with continuous stirring. The pH of the reaction mixture was adjusted at 6-7 by means of an aqueous solution of 0.014 M sodium hydroxide. Constant stirring for about 6 h at 70°C yielded solid precipitate of ternary metal complexes. The precipitate so obtained was filtered, washed several times with water and finally with absolute ethanol and then oven dried at 45°C for 4 hours.

RESULTS AND DISCUSSION

The elemental analysis data along with some other physical properties of the synthesized ternary metal complexes is given in Table 1. The analytical data indicates that the metal : L₁ : L₂ where L₁ = benzimidazole or 2-methyl benzimidazole L₂ = aspartic or glutamic acid is present in the 1 : 1 : 1 stoichiometric ratio, for the isolated ternary metal complexes. The isolated complexes are fairly stable at normal conditions of temperature and pressure and are insoluble in water and as well as in most common organic solvents. However, they show partial solubility in DMF and DMSO giving rise to non conducting solutions¹⁵.

Table 1: Elemental analysis, color and decomposition points of the ternary metal complexes

S. No.	Complex	Color	m.p. (°C) (Decomp.)	Found (Calcd.) (%)			Yield (%)
				C	H	N	
1	Cu(BEN)(AA).2H ₂ O	Blue	> 300	37.78 (37.86)	4.23 (4.33)	12.11 (12.05)	71
2	Cu(BEN)(GA).2H ₂ O	Blue	> 300	39.67 (39.72)	4.96 (4.73)	11.87 (11.58)	76
3	Zn(BEN)(GA).H ₂ O	Pale white	255-260	41.87 (41.54)	4.21 (4.34)	11.95 (12.20)	57
4	Zn(BEN)(AA).H ₂ O	Pale white	243-250	40.01 (39.72)	3.33 (3.89)	12.85 (12.62)	59
5	Ni(MBEN)(AA).2H ₂ O	Dull Green	> 300	40.67 (40.25)	4.25 (4.78)	11.76 (11.74)	69
6	Ni(MBEN)(GA).2H ₂ O	Dull Green	> 300	42.05 (41.97)	4.98 (5.13)	11.18 (11.29)	70

(Where BEN = benzimidazole, MBEN = 2-methyl benzimidazole, AA = Aspartic acid and GA = Glutamic acid)

IR spectra

The most important IR bands of the prepared ternary complexes are given in Table 2. The IR spectrum of the free primary ligands i.e benzimidazole or 2-methyl benzimidazole display a strong band in the 3079-3104 cm⁻¹ range, which is ascribed to the stretching vibrations of N-H of the pyrrolic nitrogen atom. The position of this band shows no significant change in the ir spectra of the various isolated complexes, suggesting the non-

involvement of this group in coordination bonding. Moreover the stretching vibrations of the azomethine C=N group appearing in the range of 1500-1560 cm^{-1} in the IR spectra of both benzimidazole ligands are shifted to lower frequencies in the IR spectra of the ternary complexes, suggesting that this group of the heterocyclic ring is involved in the bond formation with the concerned metal ion, the IR spectra of free amino acids exhibit prominent bands mainly in three regions, first in the 3230-3200 cm^{-1} range ascribed to the asymmetric stretching vibrations of NH_3^+ group second in the 1716-1570 cm^{-1} range and third in the 1415-1425 cm^{-1} range attributable to the asymmetric and symmetric stretching vibrations of COO^- group, where amino acids exist as zwitter ions. The bands which correspond to $\nu_{\text{asym}} \text{NH}_3^+$ however show a shift to higher frequencies and lower intensity in the IR spectra of complexes (Fig. 2), suggesting a probable interaction of this group with the metal ion, where NH_3^+ group of the free amino acid gets deprotonated and binds to metal ions through the neutral NH_2 group upon coordinate bond formation. Further the bands in the lower range due to the vibrations of the amino acid carboxylic group show a marked shift towards lower frequencies in the spectra of complexes, moreover $\Delta\nu = \nu_{\text{asym}}(\text{COO}) - \nu_{\text{sym}}(\text{COO})$ values (Table 2) give evidences about the involvement of this group in the coordination. Besides the appearance of broad bands in the 3550-3490 cm^{-1} reveal the presence of hydrated and/or coordinated water molecules in the prepared ternary metal complexes¹⁶.

Table 2: Important infrared bands (cm^{-1}) of the various synthesized ternary metal complexes

Complex	ν (OH)	ν (NH_2)	ν (NH)	ν_{asym} (COO)	ν_{sym} (COO)	$\Delta\nu$	ν (M.N)
Cu(BEN)(AA).2H ₂ O	3529	3315	3100	1593	1410	183	540
Cu(BEN)(GA).2H ₂ O	3540	3326	3091	1597	1406	191	544
Zn(BEN)(GA).H ₂ O	3507	3294	3105	1614	1397	217	543
Zn(BEN)(AA).H ₂ O	3512	3305	3110	1610	1400	210	541
Ni(MBEN)(AA).2H ₂ O	3499	3330	3085	1588	1417	171	544
Ni(MBEN)(GA).2H ₂ O	3509	3345	3095	1590	1420	170	541

(Where BEN = Benzimidazole, MBEN = 2-Methyl benzimidazole,
AA = Aspartic acid and GA = Glutamic acid)

Electronic spectra

The electronic spectra corresponding to the ternary metal complex are as given in the Table 3. The spectra of all the metal complexes show well defined, high molar extinction

coefficient band in the 390-456 nm region. This band can be ascribed to the intermolecular ligand to metal charge transfer (L-M CT transitions)¹⁷. In addition to the L-M CT transitions the electronic spectra of Ni²⁺ complex displays distinct bands in the 580-633 nm region and a weak shoulder band in 375-400 nm region. The bands were assigned to ³A_{2g} → ³T_{1g}(F) and ³A_{2g} → ³T_{1g}(P) transitions respectively, which correspond in an octahedral structure for Ni²⁺ complex¹⁸. The electronic spectra of Cu²⁺ complex is marked by the presence of a broad band in the region 610-665 nm followed by a shoulder band in the near infrared region and based on the previously published reports, these bands could be assigned to three transitions, which are similar in energy viz ²B_{1g} → ²A_{1g}, ²B_{1g} → ²B_{2g} and ²B_{1g} → ²E_g giving rise to a single broad band^{19,20}. This is in accordance with the distorted octahedral structure shown by Cu²⁺ complexes due to dynamic Jahn-Teller distortion. The Zn²⁺ complexes show only a single well defined band in the 400 nm region, which is the result of intermolecular ligand to metal charge transfer transitions.

Table 3: Electronic absorption spectral data of the mixed metal complexes

Complex	λ_{\max} (nm)	λ_{\max} (mol ⁻¹ cm ⁻¹ L)	Band assignment
Cu(BEN)(AA).2H ₂ O	435	2398.8	ligand to metal charge transfer
	625	48.7	² B _{1g} → ² A _{1g} , ² B _{1g} → ² B _{2g} and ² B _{1g} → ² E _g
Cu(BEN)(GA).2H ₂ O	428	2423.0	ligand to metal charge transfer
	610	46.6	² B _{1g} → ² A _{1g} , ² B _{1g} → ² B _{2g} and ² B _{1g} → ² E _g
Zn(BEN)(GA).H ₂ O	400	2650.6	ligand to metal charge transfer
Zn(BEN)(AA).H ₂ O	400	2645.9	ligand to metal charge transfer
Ni(MBEN)(AA).2H ₂ O	440	2411.4	ligand to metal charge transfer
	633	23.56	³ A _{2g} → ³ T _{1g} (F)
	375	35.98	³ A _{2g} → ³ T _{1g} (P)
Ni(MBEN)(GA).2H ₂ O	430	2458.0	ligand to metal charge transfer
	645	27.13	³ A _{2g} → ³ T _{1g} (F)
	390	40.00	³ A _{2g} → ³ T _{1g} (P)

In order to get more information regarding the structure of the different synthesized ternary complexes their thermal analyses was also conducted. By and large, the TG curves show a weight loss step in the 65-115°C. The mass loss is consistent with the removal of one hydrated or coordinated water molecule, however the metal complexes Cu (BEN) (AA), Cu (BEN) (GA), Ni (MBEN) (GA), Ni (MBEN) (AA) where BEN = benzimidazole, MBEN = 2-methyl benzimidazole, AA = Aspartic acid and GA = Glutamic acid also show

another weight loss step in the 130-250°C due to elimination of another coordinated water molecule. This is in agreement with the IR and elemental analysis studies. The complexes also show a steep mass loss at high temperatures in the 300-750°C which corresponds to the decomposition of the ternary metal complexes.

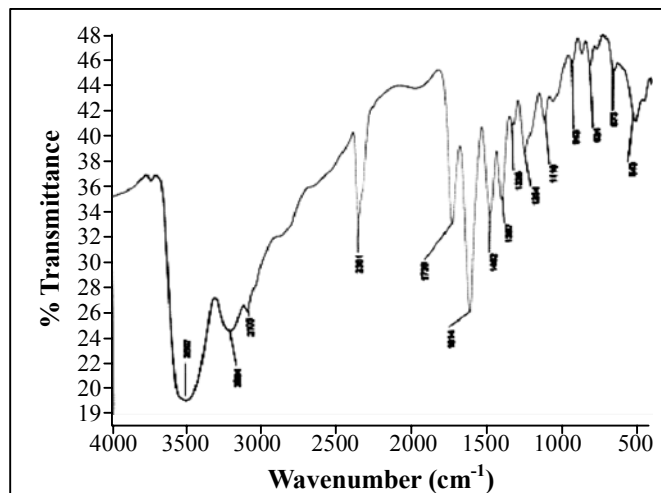


Fig. 2: IR spectrum of Zn(benzimidazole)(glutamic acid).H₂O complex

Antibacterial activity

The antibacterial activity of the metal complexes against *Staphylococcus aureus* (+ve), *Pseudomonas aeruginosa* (-ve) and *Escherichia coli* (-ve) was carried out by measuring the inhibition diameter using agar as the medium by cup-plate method²¹ and the data has been provided in Table 4.

Table 4: Antibacterial activity of the prepared Cu²⁺, Zn²⁺ and Ni²⁺ complexes

S. No.	Complex	Inhibition zone (mm)		
		<i>Staphylococcus aureus</i> (+ve)	<i>Escherichia coli</i> (-ve)	<i>Pseudomonas aeruginosa</i> (-ve)
1	Cu(BEN)(AA).2H ₂ O	22	20	23
2	Cu(BEN)(GA).2H ₂ O	23	22	20
3	Zn(BEN)(GA).H ₂ O	17	19	16
4	Zn(BEN)(AA).H ₂ O	18	15	15

Cont...

S. No.	Complex	Inhibition zone (mm)		
		<i>Staphylococcus aureus</i> (+ve)	<i>Escherichia coli</i> (-ve)	<i>Pseudomonas aeruginosa</i> (-ve)
5	Ni(MBEN)(AA).2H ₂ O	12	12	10
6	Ni(MBEN)(GA).2H ₂ O	13	10	12
7	Streptomycin	27	25	25
8	DMF	0	0	0

As the test solutions were prepared in DMF (1 mg/mL), its zone of inhibition was found to be very small and therefore was taken as zero. From the results, it can be seen that the complexes of Cu²⁺ and Zn²⁺ show moderate activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa* and low activity against *Escherichia coli* while as Ni²⁺ complexes show weak activity against all the microbes when compared with the standard drug streptomycin. Thus the antimicrobial activity follows the order Cu²⁺ > Zn²⁺ > Ni²⁺ complexes.

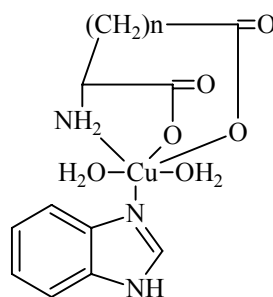


Fig. 3: Suggested structure for Cu(benzimidazole)(aspartic or glutamic acid).2H₂O complex, such that n = 1 for aspartic acid and n = 2 for glutamic acid, respectively

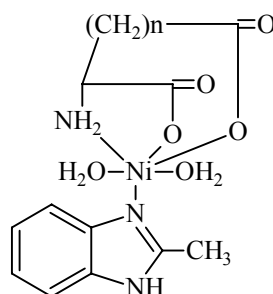


Fig. 4: Suggested structure for Ni (2-methyl benzimidazole)(aspartic or glutamic acid). 2H₂O complex, such that n = 1 for aspartic acid and n = 2 for glutamic acid, respectively

CONCLUSION

On the basis of results obtained from elemental analysis, thermal analysis, IR and electronic spectral studies, it can be concluded that benzimidazole and 2-methyl benzimidazole is coordinated to the metal ion as a monodentate ligand through the heterocyclic nitrogen atom, while as the amino acids are chelated to the central metal ion as a tridentate ligand utilizing the two oxygen atoms of the carboxylate groups and the nitrogen of the amino group. The structures of the complexes under investigation, proposed on the basis of the above experimental evidences, are shown in Figs. 3 and 4.

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