



Synthesis and spectroscopic studies of mixed ligand complexes of transition and inner transition metals with a substituted benzimidazole derivative and RNA bases

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ABSTRACT

Few mixed ligand complexes of Transition and Inner transition metals have been synthesized by reacting their metal salts with a substituted benzimidazole derivative, Omeprazole and RNA bases, uracil /adenine. All the complexes were synthesized in ethanolic medium and refluxed in reaction medium. The yield percentage ranging from 80-90%. The complexes are coloured solids and of the type $[M(Ome)(Ade)_2 \cdot 2H_2O]SO_4 \cdot xH_2O$ and $[M(Ome)(ura) \cdot 4H_2O]SO_4 \cdot xH_2O$. They are characterized through elemental analyses, conductance measurements, spectroscopy (FT IR, Mass, 1H NMR and U.V). An IR spectrum indicates that all the ligands behave as bidentate ligand. Molar conductance studies indicates electrolytic behavior of these complexes. The metal complexes have been screened for their antifungal activity towards *Aspergillus niger* fungi. The result obtained is compared with that of parent drug. The result reveals that the metal chelates showed resistance as compared with parent drug.

Keywords: Ligand, Omeprazole, Uracil, Adenine and Antifungal activity.

INTRODUCTION

Transition and Inner transition metal complexes are of continuing interest mainly due to their structural and catalytical properties and their applications in diagnostic pharmaceutical and laser technology [1-6]. They have been found to exhibit anticancer and fungicidal properties also [7]. Physiological activity and commercial applications of many Benzimidazole derivatives have received much attention. Benzimidazole and its derivatives have different activities as they can act as bacteriostats or bactericides, fungicides, anticarcinogens etc. The literature reveals that a large number of drugs have been used to synthesize the complexes with many metals with a view to enhance their therapeutic action [8 -12]. Considering the importance of drugs and their complexes it has been desired to synthesize and characterize some mixed ligand complex of Omeprazole and Uracil/Adenine with transition metals [Cu(II), Cr(II), Co(II), Cd(II), Mn (II)] and Inner transition metals [Th (II), Ce(II), Gd(II), Nd(II)]. The chemical name of omeprazole is - (5-methoxy- 2- {{(4-Methoxy-3, 5-dimethy- 1-pyridiny) methyl} sulfinyl}-1H-benzimidazole) [13-14]. It is an anti ulcer drug with the capacity to inhibit gastric H^+ , K^+ , ATPase, the proton transporting enzyme in the parietal cells that secrete HCL in stomach (wolmark et al 1983).

As the interaction of metal ions with nucleobases is of great interest because of their relevance to the essential, medical or toxic bioactivity of metal, where nucleobase molecule can coordinate as exogenous ligands in metalloproteins, function as cofactors in the enzymatic systems and construct important cell structures e.g. RNA. [15]

The RNA bases Uracil and Adenine is selected as the secondary ligand for the formation of ternary complexes. Uracil is 2 Oxy - 4-Oxy pyrimidine [16]. Adenine is a 9H-Purin-6-amine with a variety of roles in biochemistry including cellular respiration, in the form of both the energy-rich adenosine triphosphate (ATP) and the cofactor nicotinamide adenine binucleotide (NAD) and protein synthesis, as a chemical component of DNA and RNA [17].

EXPERIMENTAL SECTION

All the chemicals used throughout the course of experimental were either BDH or E merck quality. Spectroscopic grade solvents were employed for recording the spectra.

(1) ligand-metal ratio

To confirm the ligand-metal ratio, conductometric titrations using monovariation method were carried out at 25⁰ C. 0.01 M solution of Omeprazole drug was prepared in 20:80 mixture of DMF and water. Similarly, a solution of metal salts were prepared in same solvent of 0.02 M concentration. 20 ml of ligand was diluted to 200ml and titrated against metal salt solution using monovariation method. Conductance was recorded after each addition. Graph is plotted between corrected conductance and volume of metal salt added. From the equivalence point in the graph it has been concluded that the complex formation has taken place in the ratio of 1:1:2 (M: L: L₂) and 1:1:1 (M: L: L). Stability constants and free energy changes were also calculated.

(2) Preparation of the complexes

For the formation of mixed ligand complexes Transition and Inner transition metals are used with primary ligand Omeprazole and secondary ligands uracil/adenine. The solid complexes were prepared by mixing the aqueous solution of metal salts with ethanolic solution of ligand in molar ratio 1:1. The resulting mixtures were then refluxed for 4-5 hours to give the precipitate. After cooling at room temperature the solid complexes were filtered as fine precipitates. These precipitates were washed twice with water. Then they were dried and stored in a desiccators containing dry calcium chloride.

(3) Physical measurement

Conductance measurement was done in DMF. The melting point was recorded on labotech instrument. The Mass spectra was done on a jeol SX-102 spectrophotometer using argon as the FAB gas. Elico, SL191 double beam uv-vis spectrophotometer is used for recording u.v-vis spectra. Elemental analysis was performed on a Carlo erba mod 1108 elemental analyzer. The FTIR spectrum was recorded on varian 1000 FTIR using KBR Pallets. The ¹HNMR spectra was recorded on bruker DRX-300. The antifungal activity is studied by paper disk method and data was recorded after 48 hours of incubation.

RESULTS AND DISCUSSION

The reaction of the Transition and Inner transition metal ions with Omeprazole and Uracil/Adenine afforded in good yield (80-90%) of stable solid compound. The characterization of their molecular structure was made by elemental analysers conductivity and spectroscopy studies. The compounds prepared were of blue /brown colour, soluble in ethanol, 1, 4 dioxane, DMSO, DMF and insoluble in water.

The analytical data including yield percentage of the complexes are recorded in table 1.

TABLE – 1: Analytical and Physical Characteristic of mixed ligand complex.

Sr. no.	Complexes	Yield(%)	Colour	Melting point(°C)	Solubility	Molar Conductance (Λ ^s cm ² mol ⁻¹)
1	[Cu(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	90	Blue	250	Freely soluble in DMF, DMSO, Ethanol. Insoluble in cold water, HCl.	19.12
2	[Cr(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	85	Brown	270	Freely soluble in DMF, Ethanol. Insoluble in cold water, NaOH, HCl.	20.9
3	[Mn(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	81	Light Brown	260	Freely soluble in DMF, DMSO, Ethanol. Insoluble in cold water, NaOH, HCl.	12.32
4	[Cd(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	86	Dark Brown	240	Freely soluble in DMSO, Ethanol. Insoluble in cold water, HCl.	12.01
5	[Co(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	82	Brown	280	Freely soluble in DMF, DMSO, Ethanol. Insoluble in cold water, NaOH, HCl.	23.9
6	[Th(Ome)(Ura).4H ₂ O]SO ₄ .XH ₂ O	90	Light Brown	316	Freely soluble in DMF, Ethanol, 1,4 Dioxane, Nitric acid, cold water and partially in hot water.	88.8
7	[Ce(Ome)(Ura).4H ₂ O]SO ₄ .XH ₂ O	92	Brick red	316	Freely soluble in DMF, DMSO, Ethanol, 1,4 Dioxane, Nitric acid, cold water and partially in hot water	86.5
8	[Gd(Ome)(Ura).4H ₂ O]SO ₄ .XH ₂ O	86	Light Brown	302	Freely soluble in DMF, DMSO, Ethanol, 1,4 Dioxane, Nitric acid, cold water and partially in hot water.	84.2

IR SPECTRA

The relevant vibration bands of the free ligands and the complexes are in the region 4000-400 cm^{-1} , [18 -20]. The characteristics frequencies of the ligands and mixed ligand complexes of the metals are given in table 2.

In case of Omeprazole molecule the N-H (aromatic sec. amine) stretching occurs at 3050 cm^{-1} , where as sulfoxide (S=O) stretching occurs at 1076 cm^{-1} . The aromatic tertiary amine (C=N) occurs at 1660 cm^{-1} in Omeprazole [21]. In free uracil molecule the N-H and CO frequency is located in 1800- 1300 cm^{-1} region. The bending vibration of N(1)-H is at 1567 cm^{-1} where as N(3)-H vibration is at 1408 cm^{-1} . The position and intensity of the bands assignable to the 2-keto group is at 1750 cm^{-1} [22]. In free ligand Adenine molecule the (N-H) and (C-N) frequency is located in 1300-1600 cm^{-1} region. The bending vibration of N (9)-H is at 1418 cm^{-1} and (C-N) band is at 1366 cm^{-1} .

In case of ternary complexes of M-OME-URA, all the complexes showed frequency of (N-H) at ~3050 cm^{-1} showing that there is no involvement (N-H) group in complex formation, where as sulfoxide stretching shifts to lower frequencies at ~ 50/60 cm^{-1} due to coordination of the sulfonyl oxygen with lanthanides in all the complexes. The frequency of (C=N) bands appears at different region lowered by ~ 40 cm^{-1} indicating the coordination of nitrogen atom of (C=N) with metal. Thus, Omeprazole molecule chelates with metal ions using its (C=N) group and (S=O) group, acting as bidentate ligand. The position and intensity of the bands assignable to the 2 keto group of uracil in the complexes change appreciably with respect to free uracil molecule. The bending frequency of Uracil due to N(1)-H remains almost unchanged both in intensity and position while the vibration bands due to N(3)-H at 1408 cm^{-1} disappears completely in all the complexes and Thus, in the complexes uracil acts as a chelating ligand binding through its C (2) =O and N (3). In case of ternary complexes of M-OME-ADE there is a considerable shifts in the frequencies of (S=O) and (C=N) of Omeprazole ligand and also in N(9)-H and C-N band of adenine molecule. Thus, in the complexes adenine acts as a chelating ligand binding through its N(9)-H and C-N.

Additional bands in the complexes in the region 725- 765 cm^{-1} compared with IR spectra of free ligand have tentatively been assigned to M-O frequency and new band appeared at 1380-1390 cm^{-1} in complexes might be due to chelate ring formation in the complex. The appearance of strong band at ~820 cm^{-1} and ~ 3380 cm^{-1} in the spectra of all the mixed ligand complexes indicates the presence of coordinated water.

Table 2: IR BANDS OF MIXED LIGAND COMPLEXES OF OMEPRAZOLE & URA/ADE

Sr. No.	Ligand and Metal complexes	ν (S=O) cm^{-1}	ν (C=N) cm^{-1}		ν (N-H) cm^{-1}	ν (CN) cm^{-1}	ν N(3)-H) cm^{-1}	ν C(2)=O) cm^{-1}	ν (M-O) cm^{-1}	ν (Coordinated H ₂ O) cm^{-1}	
			Stretching	Bending						Stretching	Bending
1	Omeprazole	1076	1660	547	-	-	-	-	-	-	-
2	Uracil	-	-	-	-	-	1408	1750	-	-	-
3	Adenine	-	-	-	1418	1336	-	-	-	-	-
4	[Cu(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	1120	1581	540	1408	1321	-	-	787	33480	844
5	[Cr(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	1038	1602	552	1415	1352	-	-	723	3211	586
6	[Co(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	1058	1582	562	1400	1314	-	-	757	3252	862
7	[Cd(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	1123	1590	550	1401	1338	-	-	733	3399	842
8	[Mn(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	1125, 1023	1600	542	1410	1367	-	-	796	3117	873
4	[Th(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	1032	1637	529	-	-	Dis	1637	760	3428	824
5	[Ce(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	1020(w)	1638(s)	525	-	-	Dis	1638(s)	730	3450	821
6	[Gd(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	1050(s)	1636(s)	550	-	-	Dis	1636(s)	780	3390	815

¹H NMR SPECTRA

To confirm the coordination of the ligands to the metal ion the complexes, ¹H NMR spectra was recorded for the ligands and its Transition and Inner transition metal complexes. The important chemical shifts for the ligands and the complexes are given in the table 3.

The ¹H NMR spectra of the ligand has the expected characteristic signals. The CH₃ proton shows singlet at δ 2.16 and O-CH₃ proton at δ 3.69 ppm the peak observed at δ 4.71 is attributed to CH₂ protons. In addition multiplet peak at δ 6.8-8.2 may be due to aromatic protons and peak at δ 13.2 is observed due to NH proton of benzimidazole ring.

. In case of ternary complexes of Omeprazole- Uracil/Adenine, the chemical shifts occurs at low field i.e deshielding of proton occurs in methylene group proving the involvement of electron of S=O in bonding. Signals observed in the complexes at region of δ 8.18- 8 due to the azomethine proton are either remained unaffected or shifted slightly to higher field with reference to those of the parent ligand and the position of signal due to NH proton remain unaffected in the complexes. Rest of the chemical shift is more or less same in the ligands and their complexes. Pure Uracil/Adenine shows the chemical shifts at δ 10.7 ppm in N-H but in few complexes this have been disappeared

showing that there is deprotonation of hydrogen in Uracil/Adenine molecule and the new bond of M-N have been made in complexes These observations support the assigned structure to the complex

TABLE – 3: ¹H NMR SIGNALS OF MIXED LIGAND COMPLEXES OF OMEPRAZOLE AND URA/ADE

Sr. No	Kind of Proton	Atom no.	Omeprazole	[Cr(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	[Mn(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	[Th(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	[Ce(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	[Gd(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O
1	Aromatic Benzimidazole	6,7,9	6.8 -7.9	6.6-7.8	6.4-7.9	6.84-7.90	6.88-7.90	6.91-7.86
2 (a)	Aromatic Pyridine	17	8.22	8.2	8.24	8.25	8.27	8.2
3	Methylene -CH ₂ -	14	4.71-4.75	4.6	4.2	4.2(weak)	4.0-4.2(weak)	4.2(weak)
4 (a)	Methoxy O-CH ₃	13	3.69	3.2	3.1	3.1/3.2(s)	3.2-3.4	3.3-3.4
(b)	O-CH ₃	23	3.81	3.8	3.5	3.82	3.7(sharp)	3.7/3.8
5 (a)	Methyl -CH ₃ -	24	2.16	2.2	2	2.14	2.1	2.1
(b)	Methyl -CH ₃ -	21	2.5	2.5	2.5	2.48	2.52	2.58
6	Adenine	9	-	-	-	-	-	-
7	Uracil	1	-	-	-	12.68	12.8	-

MASS SPECTRA

In the present investigations, the mass spectrum of the Omeprazole shows the formation of molecular ion peak at M/Z 344 corresponds to the total molecular weight of the ligand. The mass spectra of the cerium and thorium shows the molecular ion peaks at M/Z 669 and 761 respectively supporting the composition of the complexes. Cu(II), Cr(II), Co(II), Cd(II) and Mn(II) shows the molecular ion peak at M/Z 680, M/Z 807, M/Z 693, M/Z 689 respectively supporting the composition of the complexes. Data on the molecular weight of complexes are present in table along with the values calculated on the basis of established molecular formulae of the complexes as shown in table 4.

TABLE: 4(a): Molecular Mass & Elemental Analysis of Mixed Ligand Complexes of Omeprazole & Adenine

Sr. no	Name of complex	structure	cal. Mass	spec. mass	Base peak	C	H	N	O	Metal (%)
1	[Cu(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	1:1:2:2H ₂ O	680	685	360	42.5	16.7	16.47	4.7	19.63
2	[Cr(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	1:1:2:2H ₂ O	807	811	406	35.8	14.12	13.3	13.87	3.9
3	[Co(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	1:1:2:2H ₂ O	693	685	360	41.7	16.4	16.1	4.6	21.2
4	[Mn(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .XH ₂ O	1:1:2:2H ₂ O	689	685	360	41.9	16.5	16.25	4.65	20.7

TABLE : 4(b) Molecular Mass & Elemental Analysis of Mixed Ligand Complexes of Omeprazole & Uracil

S.No.	complex	structure	cal. Mass	spec. mass	Found Mass (Calculated Mass %)					
					C	H	N	O	S	Metal
1	[Th(Ome)(Ura).4H ₂ O]SO ₄ .XH ₂ O	1:1:1.4H ₂ O	761	762	33.07 (33.11)	3.01 (4.07)	9.18 (9.19)	18.89 (18.92)	4.19 (4.2)	31.66 (30.51)
2	[Ce(Ome)(Ura).4H ₂ O]SO ₄ .XH ₂ O	1:1:1.4H ₂ O	669	661	38.12 (37.66)	4.68 (4.63)	10.59 (10.46)	21.78 (21.52)	4.84 (4.78)	19.99 (20.95)
3	[Gd(Ome)(Ura).4H ₂ O]SO ₄ .XH ₂ O	1:1:1.4 H ₂ O	668	661	38.12 (37.72)	4.38 (4.34)	10.59 (10.47)	19.36 (19.16)	4.84 (4.79)	22.71 (23.53)

ELECTRONIC SPECTRA

Typical spectral data of the metal salts, ligands and ternary complexes of Transition and Inner transition metal complexes have been investigated in alcohol and shown in table 5.

The electronic spectra of the Omeprazole displays absorption bands at 219, 301 which is assigned to n-π* and π-π* transition respectively. The electronic spectra of the URA displays absorption bands at 224, 269 which are assigned to n-π* and π-π* transition respectively. The electronic spectra of the complexes are similar to that of the ligand expect for a very slight shift towards lower frequency. This slight shift was attributed to the effects of the crystal field upon the inter electronic repulsion between the 4f electrons.

Some red shift or nephelauxetic effect is observed in the alcohol solutions of these complexes. This red shift is usually accepted as evidence of a higher degree of covalency than the presence of aqua compounds.[23- 24].In all

the complexes, marked enhancement in the intensity of the bond has been observed. This red shift of the hyper sensitive bands has been utilized to calculate the nephelauxetic effect (β) in these chelate complexes. From the β values the covalence factors ($b^{1/2}$), Sinha parameter ($\delta\%$) (metal- ligand covalency percent) and the covalency angular overlap parameter (η) have been calculated using the expressions 25] below

$$b^{1/2} = \frac{1}{2}[(1 - \beta)^{-1/2}],$$

$$\delta(\%) = [(1 - \beta) / \beta] \times 100,$$

$$\eta = [(1 - \beta)^{1/2} / \beta^{1/2}]$$

The positive values for $(1 - \beta)$ and $\delta\%$ in these coordination compounds suggest that the bonding between metal and ligand is covalent compared with the bonding between the metal and an aqua ion. The values of parameter of bonding ($b^{1/2}$) and angular overlap parameter (η) were found to be positive, indicating covalent bonding.

The proposed scheme for the formation of ternary complex is shown in figure 1

TABLE-5 ELECTRONIC SPECTRA OF MIXED LIGAND COMPLEXES OF OMEPRAZOLE AND URA

Sr. No	Name Of Complex	Band position (nm)	Band position(cm^{-1})	B	1 - β	$b^{1/2}$	$\delta\%$	η
1	[Cu(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	296	33780	-	-	-	-	-
		290	34480					
2	[Cr(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	238	42020	0.45	0.55	0.3514	44.3	0.0624
		239	41840	0.45	0.55	0.3522	49.6	0.06249
3	[Co(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	236	42370	0.43	0.57	0.37	56.6	0.0614
		237	42190	0.43	0.57	0.3762	56.6	0.06138
4	[Cd(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	284	35210	-	-	-	-	-
		285	35090					
5	[Mn(Ome)(Ade) ₂ .2H ₂ O]SO ₄ .xH ₂ O	250	40000	0.41	0.59	0.38	59	0.0779
		252	39680	0.41	0.59	0.38	59	0.0779
6	[Th(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	216	46296	0.9722	0.0278	0.08336	2.8594	0.0138
		294	34014	0.785	0.215	0.23184	27.3885	0.10104
7	[Ce(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	220	45455	0.96366	0.03634	0.09532	3.7718	0.018
		295	33898	0.77288	0.02271	0.23829	29.3861	0.10625
8	[Gd(Ome)(Ura).4H ₂ O]SO ₄ .xH ₂ O	223	44843	0.93723	0.06277	0.12526	6.6973	0.06278
		294	34013	0.86054	0.13946	0.18672	16.2061	0.13946

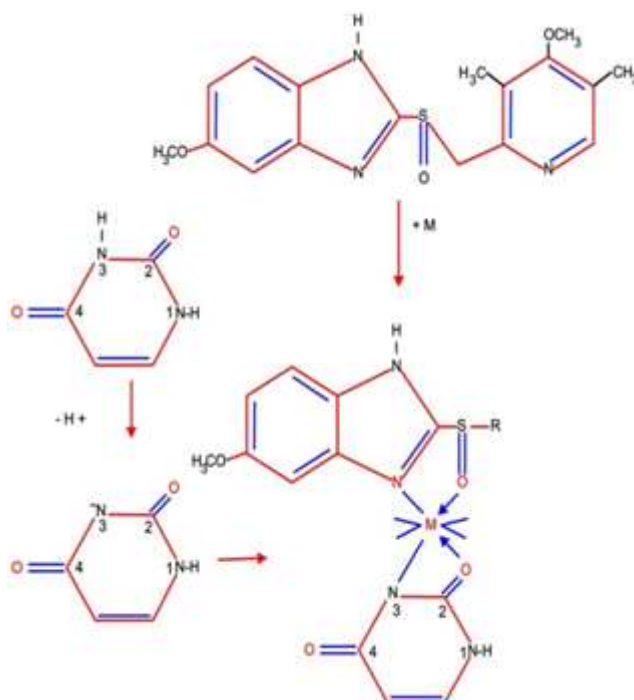


Fig. 1 .Proposed scheme of formation of representative ternary complex (M-OME-URA)

ANTIFUNGAL ACTIVITY

The antifungal activity of the ligand, metal salts and the corresponding complexes were assayed simultaneously against *Aspergillus niger* by paper disk method at room temperature. The pure metal salt, Uracil, Adenine and Omeprazole drug showed activity in *Aspergillus niger*. The zones of inhibition against microorganism were measured (in cm) after 48 hours of incubation as shown in table 6. In *Aspergillus niger* culture the ternary complex of Omeprazole with Cr (II) shows similar inhibitory activity as compared to parent drug Omeprazole Whereas Mn (II), Cu (II), Cd (II) shows higher Antifungal activity.

The ternary complexes of Th with Omeprazole and Uracil showed less inhibition zone but the complexes of Gd and Ce showed higher inhibition zone. The result indicates that the complexes are more active than free ligands. Increased activity of the complexes can be explained on the basis of chelation theory. If the orbital of each metal ion overlaps the ligand orbital increases which enhances the lipophilicity of complexes due to delocalization of electron in the chelate.

TABLE – 6(A) Sensitivity Test of Omeprazole, Adenine & Their Complexes against A. niger Culture

Sr.No.		Inhibition Diameter (cm)			
		Metal ion	Omeprazole	Adenine	M-Omeprazole-Adenine
1	Cu	1.6	0.5	0.8	2.0
2	Co	1.3	0.5	0.8	1.7
3	Cr	1.8	0.5	0.8	1.9
4	Mn	1.4	0.5	0.8	2.0
5	Cd	1.0	0.5	0.8	1.2

TABLE – 6(B) Sensitivity Test of Omeprazole, Uracil & Their Complexes against A. niger Culture

Sr.No.		Inhibition Diameter(cm)			
		Metal ion	Omeprazole	Uracil	M-Omeprazole-Uracil
1	Th	1.1	0.5	0.9	1.2
2	Ce	0.7	0.5	0.9	1
3	Gd	0.8	0.5	0.9	1.3

The characterization of the newly synthesized transition and inner transition metals with Omeprazole and RNA bases was made by stoichiometric analysis, molar conductivity and spectroscopic studies. The electronic spectra data indicates the stereochemistry of the mixed ligand complexes. The I.R. data reveal that both the primary (Omeprazole) as well as secondary (URA) ligand function as bidentate ligands while Omeprazole molecules chelates with the metal ions using its C=N group and S=O group, the uracil acts as a chelating ligand binding through its C (2) =O and N (3) group. The ¹H-NMR spectra of non-equivalent proton of Omeprazole & Uracil in complex exhibit chemical shift towards lower field due to complexation with metals.

The results of the study thus indicate the possibility of formation of metal- bridged drug receptor complex during antiulcer activity of the drug. The complexes may be formulated as [M(Ome)(Ade)₂.2H₂O]SO₄.xH₂O and [M(Ome)(Ura).4H₂O]SO₄.xH₂O.

Acknowledgement

Authors are grateful to Mr. Choudary of Nosch lab, Hyderabad for providing pure powdered Omeprazole. MPCST Bhopal for providing U.V. spectra. Cali lab for IR spectroscopies is also acknowledged. CDRI Lucknow for -mass spectrum, NMR, elemental analysis.

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