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Physics

STUDY OF TERNARY COMPLEXES OF RABEPRAZOLE

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ABSTRACT Rabeprazole chemically known as (RS)-2- [(4,(3-methoxypropoxy)3methypyridin-2-yl]-Methylsufinyl)1H -benzo(d) imidazole which is an antiulcertive drug. Rabeprazole is a weak base and it can form several complexes with inner Transition metals ions. Present research work has been focussed on the Spectrophotometric study developed for the determination of interaction of Ce(III), Sm(III), Gd(III), Yb(III) with Pantoprazole having a structure which are able to act as a chelating agent. The reaction of this drug with selected metals chloride hydrated was investigated, structure of complexes are determined with the study of UV, IR, NMR, MASS.Magnetic Susceptibility & Antibacterial study also reveals the activity of complexes.

KEYWORDS : : Antibacterial Study, Rabeprazole (RABE) Proton Pump Inhibitors (PPI)

Introduction

Metal complexes play an important role in biological activity of drug. Physic-chemical helpful in biological activity. Physiological activity and commercial applications of many benzimidazole derivatives have received much attention. Benimidazole and its derivatives have different activities as they can act as becteriostatas or bactericides, fungicides, anticarcinogens. Etc (1-5). This ring system is present in numerous antiparasitic, atiheliminits and anti-inflammatory drugs (6) for example, Rabeprazole, Omeperozole, Pantoprazole and pyridine are the best selling antiulcer drugs are more potent than the parent drug. Rabeprazole (RAB) is a very common PPIs (8) have demonstrated gastic acid suppression superior to that of histamine H2 receptor blockers. 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 (9). Considering the importance of drugs and their complexes it have been desired to synthesize and characterize some inner transition metal. Complexes of Rabeprazole with inner transition metals like Ce, Sm, Gd, Yb transition metal complexes are of continuing interest mainly due to their structural and catalytical properties and their application in diagnostic pharmaceutical and laser technology. Fig-1.

Key Words: Antibacterial Study, Rabeprazole (RABE), Proton Pump Inhibitors (PPI).

Result and Discussion

The reaction of the transition and inner transition metal ions with the ligand DNA bases and Rabeprazole afforded in good yield of stable solid compound. The characterization of their molecular structure was made by elemental analyses conductivity and NMR and IR spectroscopy. The fragmentation pattern of the complexes were studies with the aim of mass spectroscopy. The compounds prepare are of coloured, soluble in ethanol,. 1,4 diozane, DMSO, DMF and insoluble in water. All the studies ternary complexes shows 1:1:1 metal to ligand composition. It is indicated from elemental analyser and exhibit corresponding conductivities suggesting 1:1 electrolytic behavior. The result shows that ligand and lanthanide complexes have inhibitory action against the bacteria. The result indicates that the complex are more active than free ligand. Increased activity of the complexes can be explained on the basis of chelation theory.

Experimental:

All the chemicals used throughout the course of experimental were either BDH or E merck quality. Spectroscoic grade solvents were employed for recording the spectra. The ligand as well as metal complexes were analyzed by standard methods.

Elemental analysis of C,H,N was performed on a carlo erba mod 1108 elemental analyzer. The IR spectra was recorded on varian 1000 FTIR using KBR pallets. The NMR spectra was recorded on bruker DRX -300. 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. The melting point was recorded on labotech instrument.

Preparation of the complexes.

The solid complexes were prepared by mixing the aqueous solution of ligand in molar ratio 1:1:1. The resulting mixtures were than 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. The yield of the products was about 80% (Table-1).

I R Spectra

The relevant vibration bands of the free ligand and the complexes in the region 4000-400 Cm-1 are given table-2.

In case of ternary complex Rabeprazole and Cytosine with metals, all the complexes showed frequency of aromatic secondary amine (N-H) starching occurs at ~3402 cm-1 . Showing that N-H starching shift to lower frequency at ~10/20 cm-1 . N-H starching show involvement for complex formation. Whereas sulfoxide (S=O) starching occur at 1112 cm-1 to higher frequency at ~30/40 cm-1 showing its involvement in complex formation and Aromatic tert. amine (C-N) occur at 1449 cm-1. The shifty of C-N band appears at difference region indicating its bonding with metal In free cytosine molecule the C-N ring band is show in 1298 cm-1 shift to lower frequency on coordination and also change in C=O is at 1630 cm-1 hence these complex cytosine also act as a bidented ligand coordination through nitrogen at N(3)and the C=O

Mass Spectra and Elemental Analysis.

The mass spectra of the complexes shown the molecular ion peaks, supporting the structure of the complexes. The molecular weight and the elemental analysis of all the complexes is reported Table (4).

Electronic spectra

Typical spectral data for the solution of the present inner transition metal complexes of Rabeprazole and Cytosine have been investigated in alcohol some red shift or nephelauxetic effect is observed in the alcohol solution of these complexes. This red shift is usually accreted as evidence of a higher degree of covalence than the presence of aqua compound. In all the complexes marked enhancement in the intensity of the bond has been observed .The red shift of the hyper sensitivity bands has been utilized to calculated the nephelauxetic effect (β) (Table-3).

1HNMR Spectra

To confirm the coordination of the ligand to the metal ions the complexes, 1HNMR spectra was recorded for the ligand and its inner transition metal complexes in DMSO as solvent. The important chemical shifts for the protons of ligand and the complexes are given in the table (5). The NMR data indicates that the important chemical shift for the ligand have changed by coordination. In Rabeprazole complexes there is no appreciable charge in the signals of H. thus NMR studies confirms the structure of metal complexes nor involve mithylene methoxy and arometice pyridine proton. The cytosine show 9.9 N(1)-H. The integrated proton ratio also corresponds to the proposed structure. (Table no.5).

Antibacterial activity

The Antibacterial activity of the ligand, metal salt and the

corresponding complexes were assayed simultaneously against Pseudomonas Aeruginosa (PA) by paper disk method at room temperature. The Zone inhibition against microorganisms were in mm. The result show that the ligand and inner transition metal complexes have inhibitory action against the bacteria .The result indicate that the complexes are more active than the free ligand .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 cheleate (Table no.6).

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Table - 1 Physical characteristics of Mixed Ligand Complexes of RABE & CYTO

S.No	Compl exes	Colou r	Meltin g point ( )	yield	Solubility	Mass magnetic Susceptib ility (10-6 cgs)	Am (ohm-1 cm2 mol-1)
1	Ce –RAB -CYT O	Black	310	90	Freely soluble in DMF, DMSO, Ethanol 1,1,4 Dioxane, Nitric acid, Insoluble n could water NaOH and partially in hot water. Insoluble in acetone, methanol	-0.14 (diamagn etic)	44.28
2	Sm- RABE -CYT O	Black	312	88	Freely soluble in DMF, DMSO, Ethanol 1,1,4 Dioxane, Nitric acid, Insoluble n could water NaOH and partially in hot water. Insoluble in acetone, methanol	-0.34 (diamagn etic)	39.27
3	Gd- RABE -CYT O	brown	315	81	Freely soluble in DMF, DMSO, Ethanol 1,1,4 Dioxane, Nitric acid, Insoluble n could water NaOH and partially in hot water. Insoluble in acetone, methanol	-0.19 (diamagn etic)	37.07
4	Yb- RABE -CYT O	Black	317	87	Freely soluble in DMF, DMSO, Ethanol 1,1,4 Dioxane, Nitric acid, Insoluble n could water NaOH and partially in hot water. Insoluble in acetone, methano	-0.35 (diamagn etic)	41.08

Table -2 IR Frequencies (CM-1) of RAB-CYTO & their Ternary Complexes (cm1)

S. No	Comple x	Aromatic Sec. Amine N-H Stretches	Aromatic Tert. Amine C-N	S=O Stretchin g	C-N Ring	C=O Aromat ic	C- H Alipha tic Stretch ing
1	Rabepra zole	3413	1460	1090	-	-	2933
2	Cytosine	-	-	-	1276	1700	-
3	Ce- RABE- CYTO	3402	1449	1112	1298	1630	2931
4	Sm- RABE- CYTO	3413	1461	1095	1262	1630	2931
5	Gd- RABE- CYTO	3347	1445	1085	1201	1650	2901
6	Yb- RABE- CYTO	3347	1460	1087	1295	1645	2900

Table no. 3 Electronic spectral data and related bonding parameter of Ternary Complexes

S.no.	Ligan d	Max (nm)	ABS	Wave no. (Cm-1)	ε max (Lmol -1 cm-1)	Assignm ent	Lanthani de salts (cm-1)	Comple x band (Cm-1)	ß
1	Ce- RABE -CYT O	292	0.90 0	34246	0900	→π*	32894 40485	34246 -	1.04 1 -
2	Sm- RABE -CYT O	292 216	0.85 2 1.23 5	34246 46296	0852 1235	π →π* n →π*	26737 27700	34246 46296	1.28 0 1.67 0
3	Ce- PAN- URA	288 218	1.47 2 1.51 7	34722 45871	1472 1517	π →π* n →π*	32894 40485	34722 45871	1.05 5 1.13 3
4	Sm- PAN- URA	287 221	1.57 7 1.43 5	34843 45248	1577 1435	π →π* n →π*	26737 27700	34843 45248	1.30 3 1.63 3

Table no. -4 Mass & Elemental Analysis of Mixed ligand Complexes of RABE, CYTO /URA

S. No	Comple x	Structur e	Calculat ed Mass	Spectru m Mass	Stable	%C exp. (Theor.)	%H exp. (The or.)	%N exp. (Theo r.)	%S exp. (Th eor.)
1	Rabepr azole	-	359.44	359.44	Stable	60.14	5.88	11.41	8.91
2	Cytosin e	-	111.10	111.10	Stable	43.23	4.53	37.81	-
3	Ce- RABE- CYTO	1:1:1.H 2O	732	769	Stable	40.35 (40.46)	3.91 (4.0 1)	12.77 (12.8 6)	4.37 4.16
4	Sm- RABE- CYTO	1:1:1.H 2O	727	767	Stable	39.73 (39.85)	3.87 (3.9 5)	12.49 (12.6 7)	4.40 4.17
5	Gd- RABE- CYTO	1:1:1.6 H2O	842	845	Stable	39.29 (39.43)	3.79 (3.9 1)	12.39 (12.5 4)	3.80 3.78
6	Yb- RABE- CYTO	1:1:1.H 2O	867	845	Stable	38.46 (38.51)	3.17 (3.2 3)	12.01 (12.2 5)	3.69 3.78

Table - 5 Proton -1H NMR Data of Ligand and their metal complexes (Ternary Complexes)

S.	Assignment of Proton type	Position of proton	Chemical shift: (δ) ppm				
			RABE	Ce-RABE-CYTO	Sm --RABE-CYTO	Gd-RABE-CYTO	Yb – RABE-CYTO
1	Methylene - CH2	2	4.7	4.7(Weak)	4.78 (Weak)	4.7	4.7
2	Methyl-CH3	3	2.2	2.3	2.3-2.5	2.3	2.4
3	Methoxy -O-CH3	4	3.3	3.4	3.5	3.6	3.5
4	CH2-O-CH3	4	4.1	4.3	4.4	4.5	4.5
5	Aromatic pyridine	5	6.6	6.0	6.1	6.0	6.0
6	Aromatic Pyriding	6	8.2	8.3	8.9	8.9	8.3
7	Aromatic Benzimidazole	5,6,7,8	7.1-7.5	7.3-7.7	7.1-7.5	7.1-7.7	7.1-7.5
8	Cytosine N(1)-H	1	10.7	-	-	-	-

Table - 6 Sensitivity Test of Pantoprazole & its Ternary Complexes against Pseudomonas aeruginosa

Complex	Zone of inhibition (mm)			
	25 µg/ml	50 µg/ml	75 µg/ml	100 µg/ml
Ce-RABE-CYTO	0	0	10	12
Se-RABE-CYTO	10	10	10	10
Gd-RABE-CYTO	0	0	11	10
Yb-RABE-CYTO	10	10	0	10

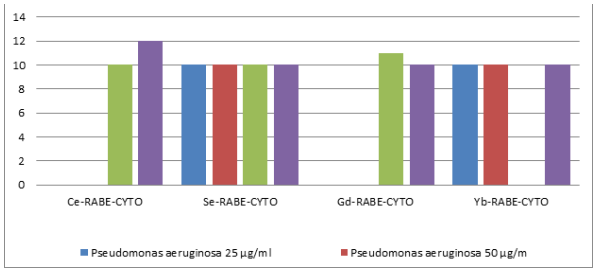

Figure: 1 Sensitivity Test of Pantoprazole & its Ternary Complexes against Pseudomonas aeruginosa

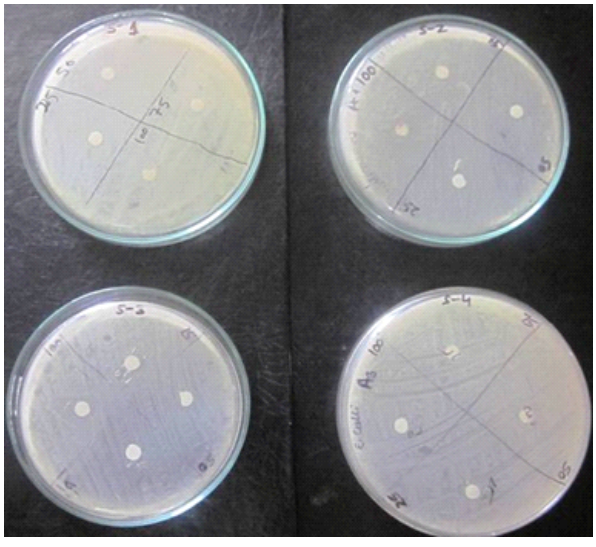

Figure: 2

Effect of 1. Ce- RAB-CYTO 2. Sm- RAB-CYTO 3. Gd- RAB-CYTO 4. Yb- RAB-CYTO on Pseudomonas Aeruginosa

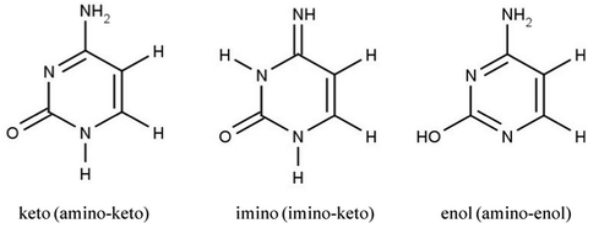

Figure: 3 The pyrimidine-Cytosine and Uracil

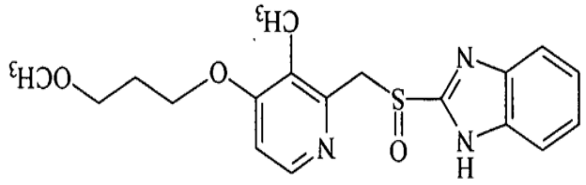

Figure 4: Rabeprazole
Molecular formula : $C_{18}H_{21}N_3O_3S$

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