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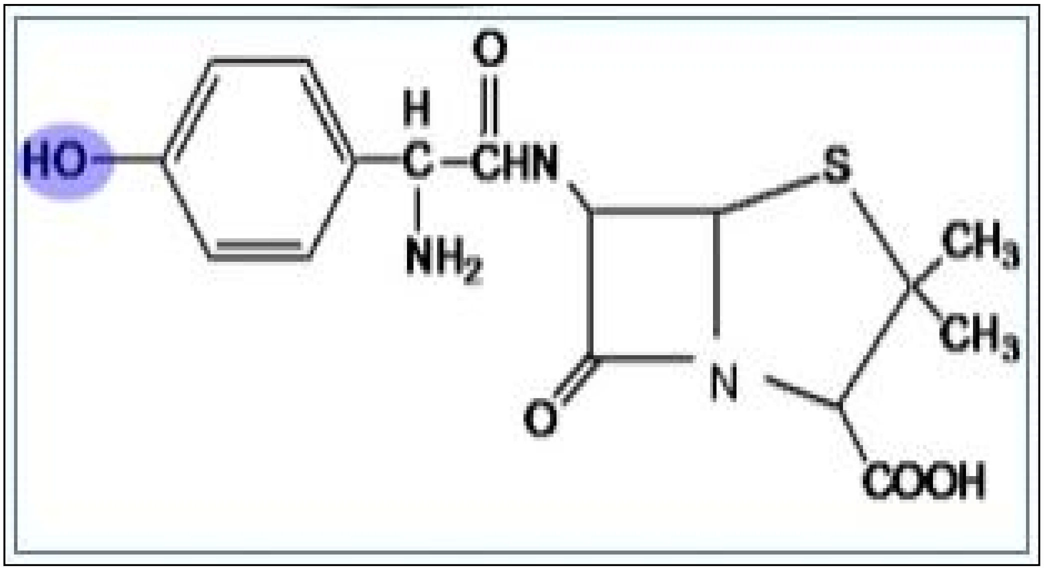
"TO STUDY THE STABILITY CONSTANTS OF SM (III), GD (III) AND DY (III) CHELATE WITH SOME HETEROCYCLIC DRUGS LIKE AMOXICILLIN, LOPERAMIDE AND LORAZEPAM."



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ABSTRACT

The interaction of Sm(III), Gd(III) and Dy(III) metalions with Amoxicillin(Ligand-1), Loperamide (Ligand-2) and Lorazepam(Ligand-3) have been investigated by pH-metric technique at 0.1 M ionic strength at 29^0 C ($\pm0.1^0$C) in 70 % Ethanol-Water mixture. The data obtained were used to estimate the values of proton-Ligand stability constants (pk) and metal–Ligand stability constants (log K) . It is observed that Sm(III), Gd(III) and Dy(III) metalions formed 1: 1 and 1: 2 complexes with all the ligands.

Keywords:

Stability constant,heterocyclic drugs, chelates, ligands, half integral, point wise etc.

INTRODUCTION :

Metal complex formation may be due to displacement of a proton from the ligand causing a drop in the pH-value of the solution. pH- metric studies of metal complexes of a large variety of polycarboxylic acids,Phenols, oximines, carboxylic acids etc have been carried out by many workers[1]. Irving and Rosotti[2] have been given a method for calculation of stability constants of complexes by pH metry.Stability constants of complexes of Th(IV) with some substituted pyrazolines have been studied by Narwade *et.al* [3] potentiometrically. Mahajan *et.al* [4] have been studied Cu(II) complexes with sulphonic acid potentiometrically .Meshram *et .al* [5] have studied the stability constants of complexes of Pr (III), Nd (III) and Sm (III) with some substituted pyrazolines pH-metrically.

Reseantly Shivaji Jadhav *et.al*[6] studied the stability constant of metal-ligand equilibria with special reference to Schiff base and transition elements. Arvind Sing *et.al*[7]. also studied the stability constant of Fe(III) and Mn(II) with chloramphenicol by paper electrophoretic technique.Meshram *et.al*[8]. also studied the Metal-Ligand stability constant of Co(II), Ni(II), Cu(II) metalion complexes with substituted ketones and simple ketones at 0.1 M ionic strength pH metrically.

The study of stability constants of Sm (III), Gd (III) and Dy (III) complexes with substituted heterocyclic drugs are still lacking. It was therefore thought of interest to study the chelating properties of some substituted drugs under suitable conditions potentiometrically.

METHODOLOGY :

Metal nitrates (BDH) were dissolved in perchloric acid and their concentrations were estimated by standard methods[9].Hetrocyclic drugs are insoluble in water and hence 70 % Ethanol-water (*v*|*v*) was used as a solvent. Ethanol was purified by standard method[10] and its purity was checked. pH-measurements were carried out with ELICO pH-meter (accuracy ± 0.05 unit) using glass and calomel electrodes at 29^{0}C (± 0.1^{0}C) The β-values (pH- meter readings in 70 % Ethanol-water mixture) were converted to (H^+) values by applying the corrections proposed by Van Uitert and Hass[11].The overall 0.1 M ionic strength of solution was calculated by the expression

$$\mu = \frac{1}{2}\sum_{i=1} CiZi^2$$

The contribution of the other ions in addition to Na^+ and ClO_4^- was also taken into considerations.

Experimental :

Proton- Ligand stability constants :

Used heterocyclic drugs may be considered as monobasic acids having one replaceable H^+ ion from OH group and can therefore be represented as HL ie.

$$HL \rightleftharpoons H^+ + L^-$$

The titration data were used to construct the curves between volume of NaOH Vs pH.

It was observed from the titration curves that the ligand curves start devating from the free acid curves at about pH 3.25 for ligand-1, about pH 4.35 for ligand-2 and for ligand-3 pH 4.25. The deviation increased continuously upto pH 11.5 to 12.5 . It indicate that OH group starts to dissociate at 3.50 and complete its dissociation at about pH 11.5

The average number of protons associated with the ligand ($\bar{n}A$) was determined from ligand titration curves employing the equation of Irving and Rossotti[12].The pk values were estimated from formation curve (nAVs pH) by-noting the pH at which nA =0.5. The accurate values of pk were estimated by pointwise calculation which are presented in Table-I.

Table-I
Determination of proton- ligand stability constant (pK)
of some substituted hetrocyclic drugs at 0.1M ionic strength.

System	Constants pK	
	Half integral	Point wise
ligand-1	11.15	11.20(±0.05)
ligand-2	11.85	11.90(±0.05)
ligand-3	11.95	12.00(±0.05)

METAL-LIGAND STABILITY CONSTANTS.

Metal ligand stability constants of Sm(III),Gd(III) and Dy(III) complexes with some substituted hetrocyclic drugs were determined by employing Bjerrum-Calvin pH -titration technique adopted by Irving and Rossotti.

The formation of chelates between Sm (III),Gd (III) and Dy(III) and the substituted hetrocyclic drugs was indicated by

i)The significant departure, starting from pH 3.00 for Sm(III), pH 2.65 for Gd(III) and pH 2.85 for Dy(III) complex system.
ii)The change in colour from brown to dark yellow and then faint yellow as pH raised from pH 3.00 to pH 11.50.

The log K values were directly read from the formation curves ($\bar{n}$Vs pL) using half integral method.

The most accurate log K values were calculated by pointwise calculation methods are presented in Table-II for all the system.

Table -II
Metal-ligand stability constants (log K) of Sm (III),Gd (III) and Dy(III)
Complexes with substituted hetrocyclic drugs at 0.1 M ionic strength.

System	Constants	
	Log K_1	Log K_2
Sm (III) ligand-1	10.65	10.05
Sm (III) ligand-2	11.15	10.25
Sm (III) ligand-3	11.95	10.97
Gd (III) ligand-1	10.05	8.91
Gd (III) ligand-2	11.00	9.12
Gd (III) ligand-3	11.90	10.42
Dy (III) ligand-1	10.55	7.97
Dy (III) ligand-2	10.95	9.14
Dy (III) ligand-3	12.15	11.92

RESULT AND DISCUSSION :

Table III
Metal-ligand stability constant at 0.1 M ionic strength :

System	Constants	
	Log K_1- log K_2	Log K_1/Log K_2
Sm (III) ligand-1	0.6	1.05
Sm (III) ligand-2	0.9	1.08
Sm (III) ligand-3	0.98	1.08
Gd (III) ligand-1	1.14	1.12
Gd (III) ligand-2	1.88	1.20
Gd (III) ligand-3	1.48	1.14
Dy (III) ligand-1	2.58	1.32
Dy (III) ligand-2	1.81	1.19
Dy (III) ligand-3	0.23	1.01

The result shows that the ratio log K_1/ log K_2 is positive in all cases. This implies that there is little or no steric hindrance to the addition of second ligand molecule.

Validity of log K = a pK+ b relation :

The linear relationship log K = a pK+ b has been found out by some workers[13] to hold for transition metal complex of series of closed related ligands.

The stability of the metal complexes of substituted heterocyclic drugs are Sm(III)<Gd(III)<Dy(III).

The plot of logK_1/log K_2 Vs pK shows satisfactory linear relationship giving slope values of 1.00 & 1.05 respectively.The partial free energies of metal - ligand & proton-ligand complexes exactly compensate each other, when log K Vs pK plot is linear with a slope of unity.

Such results are also found by Narwade *et.al.*[3] and Meshram *et.al.*[5]

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