



STUDIES THE EFFECT OF DIELECTRIC CONSTANT OF MEDIUM ON STABILITY CONSTANTS OF ETODOLAC AND ITS COMPLEXES WITH FE(II) ION

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ABSTRACT

The solution studies of binary complex of etodolac with Fe(II) ion have been performed. The protonation constant of cortisone and the stability constant of complexes with Fe(II) ion at 303K were investigated. The ionic strength is constant maintained 0.1M by adding KNO₃. The pK and logK values of the complexes were determined in 10% to 50% dioxane –Water medium by the pH metric method. The pK and logK values of the complexes increased as ethanol content increased.

KEYWORD: Etodolac, Stability constant, Protonation constant, Dielectric constant.

INTRODUCTION

The substituted heterocyclic drug Etodolac(RS)-2-(1,8-Diethyl-4,9-dihydro-3H-pyran[3,4-b]indol-1-yl)acetic acid is non steroidal anti-inflammatory drug.^[1] The R-enantiomer of etodolac is inactive against COX enzymes, but inhibits beta-catenin levels in hepatoma cells.^[2] The lanthanide compounds have a remarkable importance in daily life^[3,4]. The influence of dielectric constant on complex equilibrium between substituted pyrazilines and lanthanide metal ions in dioxane-water system have been studied.^[5] The stability constant of lanthanides and Iminodiacetic acid in water and dioxane-water mixture have been studied by potentiometric method at constant ionic strength.^[6] The dissociation constant of Succinic acid, Azelic acid, Acetic acid in methanol-water, Ethanol-water, dioxane-water system at different dielectric constant have been studied.^[7] The stability constant of 4-Amino, 3-Naphthol Sulphonic acid with Cu(II) metal ions in different dielectric constant of medium using ethanol-water system by pH metry was studied.^[8] Reddy^[9] et.al. have showed the effect of dielectric constant on the stability constant of Co(II) and Ni(II) with two mercaptoethyl benzimidazole, glycine, ethylene diamine and salicylic acid in various properties of ethanol-water mixtures at 30°C and ionic strength is 0.1M.

The present paper describes the complexation of Cu(II) with Etodolac in 0.1M ionic strength. The present work includes the determination of pK and logK values at various percentage of dioxane-water medium.

Experimental

The pH measurements were carried out with equip-tronic EQ-610 pH meter (accuracy ± 0.01 units) using combine glass electrode at 208 K. ferrous sulphate (99.9% Pure) was used. All chemical reagent used in this work are A.R. grade. The solution of drug was prepared in dioxane-water. The pH metric readings in different percentage (10%, 20%, 30%, 40%, 50%) of dioxane–water mixture were converted to [H⁺] value by applying the correction proposed by Van Uitert Haas. The overall ionic strength of solution was constant maintained by adding KNO₃. All the solutions were titrated with standard carbonate free NaOH (0.2N) solution at constant ionic strength. The titration was carried out in different percentage (10%,20%,30%,40%,50%) of dioxane–water medium. The values of dielectric constant of different percentage of dioxane-water taken from literature.^[10] The experimental procedure involved pH metric titrations of solutions of –

- 1) Free HClO₄ (A)
- 2) Free HClO₄ + Ligand (A+L)
- 3) Free HClO₄ + Ligand +Metal ion (A+L+M)

Data obtained from each titration was plotted as pH Vs volume of NaOH added and corresponding volume at successive pH for each set was determined and calculated.

RESULT AND DISCUSSION

The proton-ligand and meta-ligand stability constant of cortisone and its complexes with Fe(II) metal ions are given in table -1. It could be seen that pK and logK values increased with increase in the percentage of dioxane with decrease in dielectric constant of medium,

this is due to the interaction between lanthanide ions and ligand is mainly electrostatic, as well as because of the effect of bulk solvent. The lowering of dielectric constant would increase the electrostatic force of attraction between metal ion and negatively charged ligand to form complex. The values of pK calculated by point wise calculation method. The metal-ligand stability constants were determined by half integral method. Higher values

of $\log K_1$ and $\log K_2$ showed that ligands are stronger chelating agents. The dielectric constant of medium strongly affected on proton-ligand and metal-ligand stability constants because of the fact that at least one of the constituent is charged and other is either charged or has dipole moment. The plots of $\log K_1$ and $\log K_2$ Vs $1/D$ for the entire system exhibit a linear relationship.

Table-1 pK and LogK values of cortisone and its complexes with Fe(III) in different percentage of Dioxane-water mixtures at 0.01 ionic strength.

% Dioxane	Dielectric constant (D)	1/D	Mole-fraction	Etodolac	Etodolac + Fe(II)	
				pK	LogK ₁	LogK ₂
10	70.33	0.01422	0.02279	6.1245	6.35	4.35
20	61.86	0.01617	0.04985	7.1976	6.97	4.79
30	53.28	0.0187	0.08252	7.7896	7.46	5.05
40	44.54	0.02245	0.12270	8.1546	7.95	5.48
50	35.84	0.02789	0.17350	8.9742	8.48	5.95

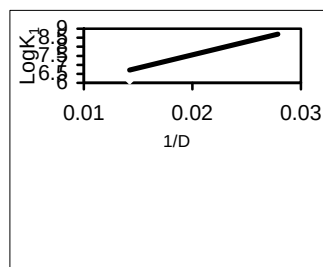


Fig.1-Plots of LogK₁ Vs 1/D

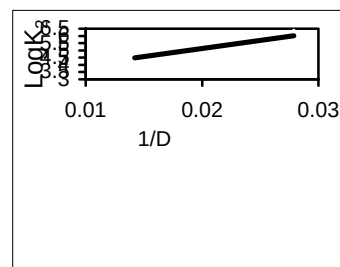


Fig.2-Plots of LogK₂ Vs 1/D

CONCLUSION

The proton-ligand and metal-ligand stability constant of complexes increased with increased percentage of ethanol. As the values of dielectric constant of medium decreases, the values of proton-ligand and metal-ligand stability constant of complexes increases. The dielectric constant of medium decreased, as expected from the electrostatic nature of interaction between metal ions and ligands.

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