



Studies the effect of ionic strength of medium on the thermodynamic parameters of etodolac with Cu (II), Zn (II) complexes

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Abstract

The metal-ligand and proton–ligand stability constant of Cu(II) and Zn(II) with substituted heterocyclic drug (Etodolac) were determined at various ionic strength by pH metric titration. NaClO₄ was used to maintain ionic strength of solution. The results obtained were, extrapolated to the zero ionic strength using an equation with one individual parameter. The thermodynamic stability constant of the complexes were also calculated.

Key word: Ionic strength, Stability constant, substituted heterocyclic drug.

I. Introduction

The substituted heterocyclic drug Etodolac(*RS*)-2-(1,8-Diethyl-4,9-dihydro-3*H*-pyrano[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]. It forms complex with Cu(II) and Zn(II). Th. SarodaDevi[3]*et.al.* have studied the stability constant of Co (III) with 1-Amidino-0-methylurea as primary ligand at different ionic strength. Agrawal[4]*et.al.* have studied the influence of ionic strength of medium on complex equilibria. Meshram[5]*et.al.* have studied the association and dissociation constant of Pr(III) complexes with 3-(2-hydroxy-3-Iodo-5-methyl phenyl)1,5 diphenyl pyrazoline at different ionic strength. Khorrami[6]*et.al.* have studied the stability constant of vanadium with glycine at various ionic strength by potentiometric titration technique. Majlesi[7]*et.al.* have determined the stability constant of Mo (IV) with Iminodiacetic acid at different ionic strength maintain by using sodium per chlorate. Sharma[8]*et.al.* have studied the effect of ionic strength and solvent effect on thermodynamic parameters. They have also studied the mechanism of protonation and complex formation of binary complexes of La (III), Ce (III), Pr (III) and Nd(III) with amino pyridines.

After review of literature survey, the detail study of complex under identical set of experimental condition is still lacking. It was thought of interest to study the effect of ionic strength on thermodynamic parameters of complexes of substituted heterocyclic drug with Cu (II) and Zn(II) in 50% ethanol-water mixture by pH metrically.

II. Experimental

The pH measurements were carried out with equip-tronic EQ-610 pH meter (accuracy ± 0.01 units) using combine glass electrode at 298 K. Pure rare earth nitrates (99.9% Pure) were used. Metal ion solutions were prepared in triply distill water and concentration was estimated by standard method. The solution of drugs was prepared in solvent. The pH metric readings in 70% ethanol –water mixture were converted to [H⁺] value by applying the correction proposed by Van Uitert Haas. The ethanol was purified by the method described by Vogel[9]. The overall ionic strength of solution was constant maintains by adding NaClO₄. All the solutions were titrated with standard carbonate free NaOH (0.2N)

solution at different ionic strength. The titration was carried out at ionic strength by adding NaClO₄(0.02, 0.04, 0.06, 0.08, 0.1M).

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 is plotted as pH Vs volume of NaOH added and corresponding volume at successive pH for each set is determined and calculated.

III. Result and Discussion

In the present investigation the dependence of proton-ligand stability constant and metal-ligand stability constant on ionic strength of medium was examined by taking fix concentration of metal nitrates and ligand solution during pH metric titration. The system has been studied at 0.02, 0.04, 0.06, 0.08, 0.1M ionic strength by varying the concentration of sodium perchlorate. The total ionic strength of medium is calculated by equation.

$$\mu = \frac{1}{2} \sum C_i Z_i^2$$

C_i, Z_i are the concentration and valency of ith ion respectively. The values of proton–ligand and metal ligand constant of Cu(II) and Zn(II) complexes at different ionic strength 0.02,0.04,0.06, 0.08 and 0.1M determined. These values determined by using Irving-Rossotties method. From table-1, it was seen that the values of proton–ligand stability constant (pK) decreases with increasing ionic strength of medium. The metal-ligand stability constant (logK) also decrease with increasing ionic strength. For determination of stability constant at zero ionic strength the Bronsted equation is used.

$$\text{LogK} = \text{logK}^0 + 2A Z_+ Z_- \sqrt{\mu} \text{ ----- (5)}$$

$$\text{PK} = \text{PK}^0 - 2AZ_+ Z_- \sqrt{\mu} \text{ ----- (6)}$$

Where K⁰ is the formation constant at zero ionic strength, pK⁰ is proton-ligand stability constant at zero ionic strength, ‘A’ is the Debye-Huckel constant, 2 is the difference in square of the changes of product and reactant ion.

The pK⁰ and logK⁰ values were calculated by plotting the graph of pK, logK₁, logK₂ versus $\sqrt{\mu}$
 Influence of ionic strength of medium---Cu (II), Zn (II) complexes.

Table- 1. Proton–ligand (pK) and metal-ligand stability constant (LogK) values for Cu (II) and Zn (II) with streptomycinat various ionic strength (μ)

μ	$\sqrt{\mu}$	$\sqrt{\mu}/1+\sqrt{\mu}$	$[\sqrt{\mu}/1+\sqrt{\mu}] - 0.3\sqrt{\mu}$	LogK ₁	LogK ₂	pK
Cu(II) + Etodolac						
0.02	0.1414	0.1239	0.0815	6.95	3.35	7.4735
0.04	0.2000	0.1667	0.1067	5.70	2.90	6.1912
0.06	0.2450	0.1968	0.1233	4.45	2.55	5.9805
0.08	0.2828	0.2205	0.1356	3.30	2.10	5.0879
Zn (II) + Etodolac						
0.02	0.1414	0.1239	0.0815	6.85	4.35	7.2837
0.04	0.2000	0.1667	0.1067	5.70	4.05	7.1011
0.06	0.2450	0.1968	0.1233	5.50	3.78	6.8515
0.08	0.2828	0.2205	0.1356	4.95	3.60	6.3688

Table 1. Thermodynamic stability constant (pK₀ and Log K₀) values for Ce (III) and Gd (III) with streptomycin.

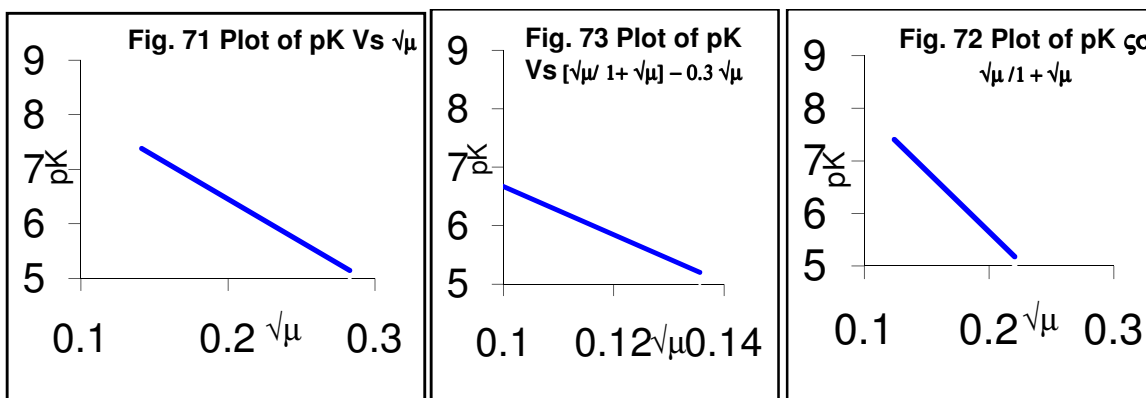
Systems	LogK	LogK ₁ Vs √μ	LogK ₁ Vs √μ/1+√μ	LogK ₂ Vs [√μ/1+√μ] - 0.3√μ	LogK ₂ Vs √μ	LogK ₂ Vs √μ/1+√μ	LogK ₂ Vs [√μ/1+√μ]- 0.3√μ
Etodolac+ Cu (II)	LogK ₁ ⁰	10.70	12.54	11.74			
	Log K ₂ ⁰	--	--	--	4.606	5.223	5.553
Etodolac+ Zn(II)	LogK ₁ ⁰	8.824	9.491	9.066	--	--	--
	Log K ₂ ⁰	--	--	--	5.12	5.504	5.333

Table 2. Proton-ligand stability constant at zero ionic strength (pK⁰) values

System	pK Vs √μ	pK Vs √μ / 1+ √μ	pK Vs [√μ/ 1+ √μ] - 0.3 √μ
pK⁰			
Etodolac	9.612	10.770	10.260

Table 3. Values of ΔZ² determined from different plots

System	pK Vs √μ		pK Vs √μ/ 1+ √μ		pK Vs [√μ/ 1+ √μ] -0.3√μ	
	Slope	ΔZ ²	Slope	ΔZ ²	Slope	ΔZ ²
Etodolac	-15.77	-30.55	-41.11	-79.66	-23.08	-44.72



From table 2, it was seen that the good agreement among thermodynamic constant obtained from different plots. The plots pK, logK₁, logK₂ versus gives straight line over the entire range of ionic strength for both systems. It shows that the bronsted relationship is valid for dissociation equilibrium. FazlurRahman[10] *et. al.* have determined similar results of stability constant of different metal complexes with substituted acetophenone oxime at 0.1, 0.05, and 0.01M ionic strength in 50% dioxane. The values of ΔZ² were calculated from the slope of plots PKVs, LogK₁ Vs, LogK₂ Vs. The value of 'A' was taken equal to 0.5161[11] The value of ΔZ² given in table 3. The observed value of ΔZ² is

different than the expected value. These values do not give conclusive evidence regarding the magnitude of the charge of reacting species. This discrepancy may be due to the limited applicability of Bronsted equation. Narwade [12], Meshram [4], Nehete [13] also recorded same discrepancy.

IV. Conclusion

The calculated values of stability constant at various ionic strength are high. From data the conclusion is, the complexes of Etodolac with Cu (II) and Zn (II) is quite stable at over all range of ionic strength. The values of thermodynamic parameters are nearly same from all plots was good agreement of results.

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