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Advances in Applied Science Research, 2014, 5(4):171-175

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ISSN: 0976-8610
CODEN (USA): AASRFC

Metal-ligand stability constants of Fe (III), Cd(II), Co(II), Ni(II), Zn(II) metal ion complexes with Lorazepam in aquo-organic media at 0.1 M ionic strength pH metrically

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ABSTRACT

The study of transition metal ion Fe (III), Cd(II), Co(II), Ni(II), Zn(II) and Lorazepam (7-chloro-5-(2-chlorophenyl)-3-hydroxy-1H- 1,4- benzodiazepin-2(3H)-one) as ligand have been studied at 0.1M ionic strength in 60% and 70% EtOH and MeOH water mixture by binary system in pH metry analysis. The data obtained were utilized for the evaluation of dissociation constant and stability constant and compare the valve of Proton ligand stability constant (pK) and Metal ligand stability constant (LogK). These data also used in the prediction of activation parameter ΔG^0, ΔH^0, ΔS^0. *7-chloro-5-(2-chlorophenyl)-3-hydroxy-1H- 1,4- benzodiazepin-2(3H)-one*

Key words: Lorazepam, Ionic strength, pH metry, stability constant, Activation Parameter.

INTRODUCTION

Lorazepam is anxiolytic drugs [1-3].It shows an initial delayed absorption at least for two hours due to its water insolubility. The literature survey reveals that no systematic work has been done on the dissociation constant and stability constant of metal chelate of these drugs [4-6]. Lorazepam is the2'-chloro derivative of Oxazepam to which it is essential identical with regard to short half life of 2 to 6 hours and pharmacological active. The present study describes the result of the proton ligand, metal ligand stability constant of transition metal ion with drug Lorazepam by potentiometer method at ionic strength 0.1 M in aquo-organic media. It was therefore, decided to study in detail, complexation of these chelating reagent in aquo -organic media with reference to various effects. The potentiometric data was utilized for the evaluation of Proton ligand stability constant, metal ligand stability constant at various experimental conditions by adopting Irving-Rossotti Method [7]. Shukla J.P and Coverker [8] investigates metal ligand stability constant of Fe (III) metal ion complexes with some substituted diketones and pyrazoles at 0.1 M ionic strength. Many other researchers have studied the metal ligend stability constant of some transition metal ions with the some substitute's synthesized ligands [9-15].

MATERIALS AND METHODS

Experimental:
The chemicals used were Analar grade (India make). Metal ion Concentration were determined by using EDTA with suitable indicator and used as chelating reagent. Eleco -120 model instrument with accuracy in 0.01 units with glass and saturated calomel electrode was used for the titrations. It was calibrated with the buffer solution of pH 7.00 and 9.20 at 28 ± 0.1 °C before titrations. Metal solution was prepared in double distilled water. Ligand solution is

prepared in 60% & 70% ethanol, sodium hydroxide & nitrate used were of A.R. Grade. Titrations were carried out in an inert atmosphere by bubbling a constant flow of nitrogen gas. The binary system were studied by following pH metric titration

1) Free acid HNO_3 (0.04 M) = A
2) Free acid HNO_3 (0.04 M) and ligand (20×10^{-4}) = A+R
3) Free acid HNO_3 (0.04 M) and ligand (20×10^{-4}) and metal ion (4×10^{-4} M) =A+R+M

All the titrations were carried out in 60 % & 70% ethanol-water mixture by addition of sodium hydroxide. The graph of volume of alkali (NaOH) against pH was plotted. The ionic strength of all the solution was maintained constant (0.1 M) by adding appropriate amount of $NaClO_4$ solution at 298K. The total volume of the test solution was made up to 50 ml. The calculations show that the complexes are formed at a lower pH & are stable even at higher pH value.

Table 1. pH Titration of Lorazepam in the presence of Metal ion(III),Cd(II),Co(II),Ni(II),Zn(II) 70 % EtOH –Water Medium

Volume of NaOH	pH Of Solution 70%						
	HNO_3 (A)	HNO_3+R	HNO_3+R+ Fe(III)	HNO_3+R+ Cd(II)	HNO_3+R+ Co(II)	HNO_3+R +Ni(II)	HNO_3+R+ Zn(II)
0	2.29	2.28	2.26	2.25	2.25	2.26	2.2
0.6	2.34	2.32	2.3	2.29	2.3	2.29	2.29
1.2	2.41	2.39	2.37	2.36	2.38	2.39	2.28
1.8	2.48	2.46	2.46	2.44	2.46	2.44	2.35
2.4	2.57	2.56	2.55	2.51	2.56	2.54	2.44
2.8	2.66	2.62	2.62	2.62	2.66	2.61	2.55
3.2	2.78	2.73	2.72	2.7	2.73	2.63	2.64
3.6	2.9	2.85	2.82	2.85	2.88	2.7	2.76
4	3.09	3	2.92	3	3.07	3	2.94
4.1	3.2	3.08	3.04	3.08	3.11	3.06	3.01
4.2	3.24	3.15	3.11	3.15	3.2	3.12	3.04
4.25	3.27	3.17	3.14	3.17	3.26	3.17	3.11
4.3	3.31	3.22	3.18	3.27	3.3	3.2	3.15
4.35	3.4	3.26	3.23	3.32	3.33	3.27	3.2
4.4	3.45	3.3	3.27	3.35	3.4	3.32	3.25
4.45	3.53	3.36	3.33	3.45	3.43	3.36	3.33
4.5	3.61	3.4	3.37	3.5	3.5	3.40	3.4
4.55	3.7	3.48	3.4	3.58	3.6	3.45	3.44
4.6	3.86	3.55	3.46	3.65	3.7	3.48	3.55
4.65	4.02	3.65	3.55	3.72	3.8	3.60	3.64
4.7	4.56	3.76	3.63	3.9	3.97	3.66	3.76
4.75	6.7	3.85	3.73	4.14	4.25	3.70	4
4.8	7.3	4.05	3.86	4.52	4.8	3.80	4.33
4.85	7.8	4.4	4.02	6.2	6.9	4.10	5.9
4.9	10.38	5.6	4.28	6.93	7.62	4.21	6.8
4.95	11.1	7.66	4.85	7.2	7.65	5.20	7
5	11.65	10.4	7.05	7.25		7.20	7.25
5.05	12.05	11.11	7.5				

Plot of pH vs. Volume of NaOH showing in fig. 1-5

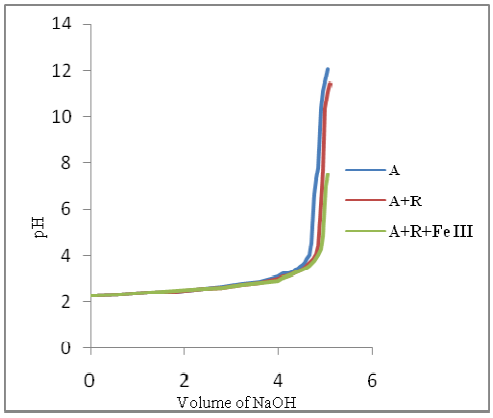

Fig. 1

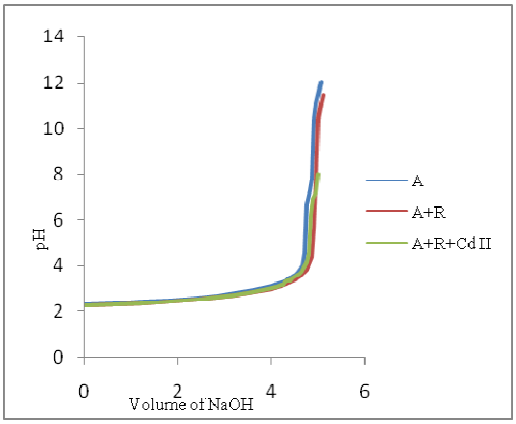

Fig.2

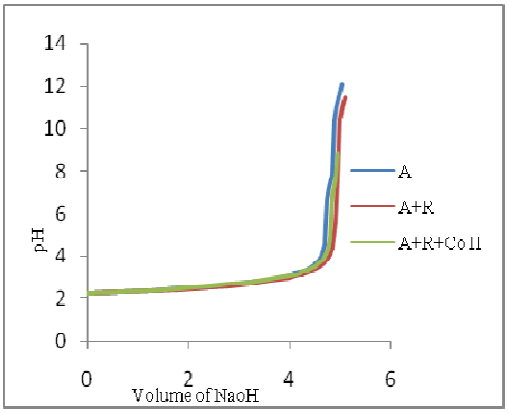

Fig. 3

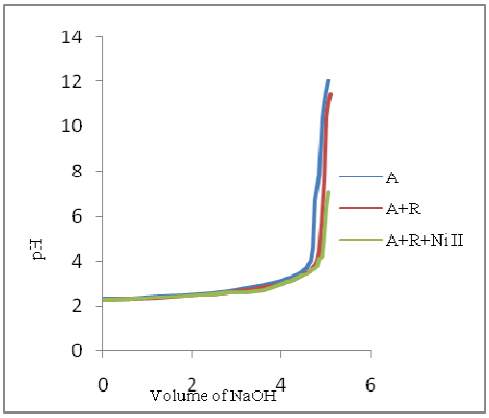

Fig. 4

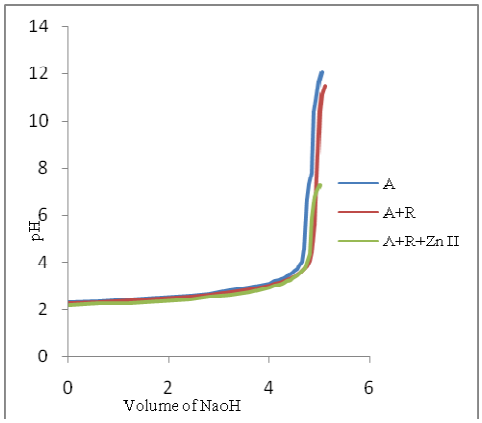

Fig. 4

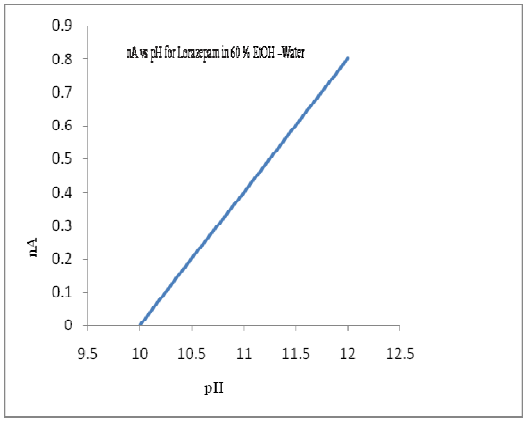

Fig.5

Table 2. pK and Log K of Metal chelate of Lorazepam in 70% EtOH –Water Medium At different ionic strength

% (v/v)	Ionic Strength		
	0.1M	**0.25M**	**0.5M**
pK1	2.84	2.70	2.64
pK2	11.70	11.50	11.46
Fe(III)	11.32 11.18	11.00 11.01	10.96 10.88
CdII)	11.40 8.80	11.52 -	11.12 8.52
Co(II)	11.40 7.80	10.38	10.11 -
Ni(II)	10.15 -	10.00 2.65	10.00 8.20
Zn(II)	10.56 4.61	10.44 4.50	10.24 4.36

Table 3: Stepwise stability constant Lorazepam in 70 % EtOH at 298 k at 0.1 M ionic strength

% →	60%	
Metal ↓	Log K_1	Log K_2
Fe(III)	11.26	11.13
CdII)	11.34	8.77
Co(II)	11.31	11.05
Ni(II)	10.46	-
Zn(II)	-	4.50

Table 4: Activation Parameter of Lorazepam in 70 % EtOH at 298 k at 0.1 M ionic strength

1:1	$-\Delta G^0$	$-\Delta H^0$	$-\Delta S^0$
Fe(III)	60.48	3.69	0.190
CdII)	60.93	3.16	0.193
Co(II)	61.62	2.53	0.198
Ni(II)	62.76	3.23	0.197
Zn(II)	63.62	2.70	0.200

RESULTS AND DISCUSSION

Proton-ligand stability constants:

The metal-ligand study of Lorazepam [7-chloro-5-(2-chlorophenyl)-3-hydroxy-1H- 1,4- benzodiazepin-2(3H)-one)ware studied in Ethanol- water media in presence of Fe(III),Cd(II), Co(II), Ni(II), Zn(II) metal ions by pH metric measurements at various temperature at 0.1 M ionic strength .The Lorazepam [7-chloro-5-(2-chlorophenyl)-3-hydroxy-1H- 1,4- benzodiazepin-2(3H)-one was monobasic acids having only one dissociable H+ ion from OH group. It can therefore, be represented as HL

$$HL \underset{}{\overset{k_1}{\rightleftharpoons}} H^+ + L^-$$

Proton ligand stability constant kiH is represented as;

$$Ki^{H} = \frac{aH;L}{aHi-1+L^{a}H}$$

The proton-ligand formation number (nA) were calculated by Irving and Rossetti expression.

$$\bar{n}_A = \gamma - \frac{(V_2 - V_1) \times (E^0 + N)}{(V^0 + V_1) T_L^0}$$

Where,

V^0 = Initial volume of solution

E^0 = Initial concentration of free acid

TL^0 = Concentration of ligand
γ = Number of replaceable protons
N = Avogadro's number
$(V_2 - V_1)$ = Volume of alkali N, consumed by acid and ligand on the given.

The values of the change in free ΔG^0, ΔH^0 , ΔS^0.can be calculated by following equation.

$$\Delta G = -2.303 RT \log K$$

The observed pK and Log K for Lorazepam in EtOH –Water Medium are shown in Table 3. It would be seen from above Table 4 that the stability constant increase with increase in percentage of the solvents, and also decrease with increase in ionic strength. It could be seen from table 5 ΔG and ΔH were found to be highly negative, while ΔS valve were to be positive .Science the Log K are found to be very high, there must be strong interaction between the metal ion and the chelating reagents. The positive entropy valve were accounted towards the interaction with positive and negative ions.

$$\Delta H = 2.303\ \Delta T \log K$$

CONCLUSION

The value pK and log K for Lorazepam in aqua organic media shows variable. The stability constant increases with increasing percentage of the solvent. The negative value of ΔG indicates that reaction tends to proceed spontaneously. The negative value of ΔH shows the reaction is exothermic in nature.

Acknowledgements
We are very much thankful to Late Dr .V.G.Dongra Professor, Department of Chemistry, Mumbai University, Mumbai and Late Dr .V. W.Kamble, Deputy Director , Forensic Lab , Aurangabad for his valuable guidance and supports for research work .

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