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Evaluation of stability constants of promazine(PMZ) with Fe (III), Cd (II), Pb (II), Cu (II) and Zn(II) complexes by pH metric method

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ABSTRACT

A potentiometric titration technique has been used to determine the stability constants of complexes of promazine in aqueous medium. The proton-ligand and metal-ligand stability constants of Fe (III), Cd (II), Pb (II), Cu (II) and Zn(II) metal ions with PMZ have been performed at different temperatures 298 ^{0} K and 308 ^{0}K at 0.1M ionic strength. The Metal ligand stability constants are determined by different Computational Methods. The thermodynamic parameters (ΔG, ΔH and ΔS) and the thermodynamic stability constants for all of the investigated complexes were determined potentiometrically.

Keywords: Metal complexes, Promazine, Stability constant, Thermodynamic Parameters

INTRODUCTION

Phenothiazine drugs are compounds with a well known neuroleptic activity [1]. All the phenothiazines possessing the antipsychotic activity have a three-carbon chain between the nitrogen atoms of the middle ring and three carbons the side chain. As a result of exhaustive screening, phenothiazine derivatives are now known to have tranquilizers [2], antimalarial [3], antipsychotropic [4], antimicrobial [5-8], antitubercular [9-13], antitumor [14-16], antihistamine [17] and analgesic [18] properties.

Metal complexes are widely used in various fields such as biological processes, pharmaceuticals, analytical processes, separations techniques, etc. Metal complexes play a vital role in nature, they have been extensively used in clinical applications as enzyme inhibitors [19], anti-bacterial [20, 21], antiviral [22-24] and as anti-cancerous [25-27].

Different kinds of metals have been employed in these complexes including platinum, gold, vanadium, iron, molybdenum, cobalt, tin, gallium, copper and many others [24].Metal complexes of adenine (A) have been shown to possess anticancer activity [28-31]

The present work describes the interaction between Fe (III), Cd (II), Pb (II), Cu (II) and Zn (II) metal ions with Promazine hydrochloride (PMZ) as ligand in aqueous medium has been determined by pH-Meter. The thermodynamic parameters (ΔG, ΔH and ΔS) and the thermodynamic stability constants were determined in aqueous medium at different temperatures 298 ^{0} K and 308 ^{0}K at 0.1M ionic strength by the Calvin Bjerrum titration technique adopted by Irvin and Rossetti. The Metal ligand stability constants is determine different Computational Methods like Half integral method [32]/ Interpolation at half n values [34], Least square method [33], Linear plot method [32] and Point wise calculation method [35].

MATERIALS AND METHODS

All chemicals were purchased from Aldrich and S.d. Fine Ltd,Mumbai (India), and were used without further purification. The solutions of reagents were prepared in double glass distilled water having pH about 6.98 to 7.00. The metal ion concentrations were determined by using sodium salts of ethylene diamine tetra acetic acid (EDTA) and suitable indicators. The molarity of KOH solution was determined by titrating with known weight of oxalic acid and also with potassium phthalate by using phenolphthalein indicator**.** In all the systems studied, the metal ion concentration was kept at $4x10^{-4}$ M (i.e. 2 ml of 0.01M in 50 ml total volume). Similarly, the ligand concentration was kept at $2x10^{-3}$ M in all titrations.

The pH measurements were made using a digital pH meter model L-120 with combined glass electrode (reading accuracy ± 0.001 pH units). The instrument was standardized at different regions of pH using standards buffer (BDH) solutions and was checked by titrating 0.40M nitric acid against potassium hydroxide. The temperature of experimental solution was always maintained during the progress of the titration. The thermostat model Hakkin-1101 was used to maintain the temperature. The reaction mixture (50ml) was taken in cell having an outer thermostatic jacket for circulating water at a constant temperature. The activated combined glass electrode was dipped into the reaction mixture and pre-purified nitrogen gas was bubbled through it during the progress of pH titration. The reaction mixture was continuously stirred with the help of a magnetic stirrer (REMI 1 MLH) to maintain the homogeneity of the reaction mixture**.**

The following three set of solutions were titrated separately against standard carbonate free KOH solution.

1. Free acid titration (A): HNO_3 ($2x10^{-2}$ M)
2. Free acid + ligand titration (A +R): A ($2x10^{-2}$ M) + R ($2x10^{-3}$ M)
3. Free acid + ligand + metal titration (A +R+M): A ($2x10^{-2}$ M)+R($2x10^{-3}$ M)+ M($4x10^{-3}$ M).

The pH meter reading were taken after fixed interval until stable reading was obtained and then curves of pH verses ml of alkali were plotted (Fig.1). The proton-ligand and metal-ligand binary formation constants were determined by Irving-Rossotti method [36].

RESULTS AND DISCUSSION

The complexes of Promazine hydrochloride(PMZ) were studied in presence of Fe (III), Cd (II), Pb (II), Cu (II) and Zn (II) in aqueous medium at different temperatures 298 ^{0}K and 308 ^{0}K at 0.1M ionic strength. We have studied the proton ligand stability constants and metal ligand stability constants by the Calvin Bjerrum titration technique adopted by Irvin and Rossotti. The pH metric titration curves and plot of pH Vs nA at different temperature are shown in figure 1 and 2 respectively. The dissociation constant and stability constant of Promazine at different temperatures are summarized in Table 1 and 2.

Table 1: Proton-ligand stability constants of the ligand (PMZ)

Temperatures	pK
298 ^{0}K	9.412
308 ^{0}K	9.306

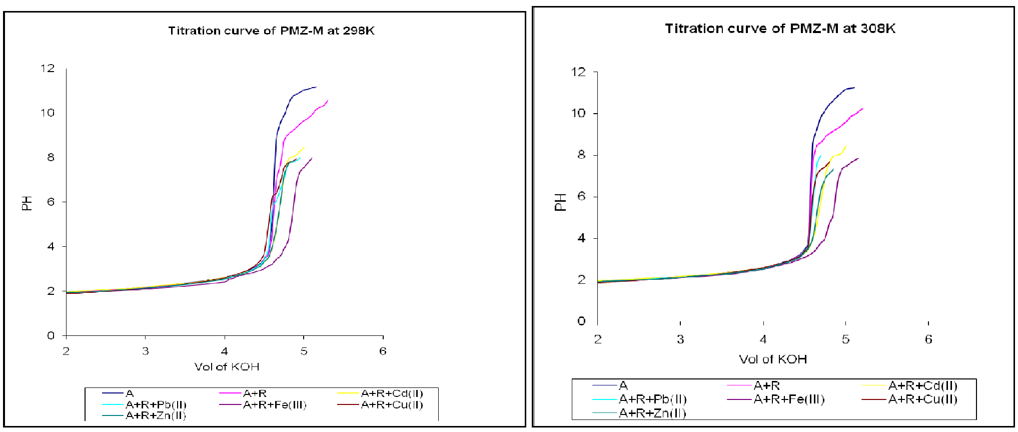

Figure 1: Plot of pH v/s volume of added KOH to Set 1, 2 and 3

Table 2: Metal ligand stability constant of M-(PMZ) at different temperature

System	LogK							
	$298\ ^0K$				$308\ ^0K$			
	Computational Methods				Computational Methods			
	a	b	c	d	a	b	c	d
Cd (II)-PMZ	7.201	7.181	7.188	7.208	7.152	7.139	7.133	7.128
Pb (II))-PMZ	5.798	5.780	5.802	5.810	5.241	5.248	5.250	5.231
Fe (III))-PMZ	9.162	9.170	9.150	9.168	8.861	8.878	8.864	8.838
Cu (II))-PMZ	5.274	5.280	5.284	5.268	5.147	5.156	5.150	5.161
Zn (II))-PMZ	7.328	7.320	7.316	7.330	7.275	7.290	7.280	7.277

(a) Interpolation at half n values, (b) Least square method, (c) Linear plot method , (d) Point wise calculation method

Calvin and Wilson have demonstrated that pH measurements made during titrations with alkali solution of ligand in the presence and absence of metal ion could be employed to calculate the formation functions nA , n and pL and stability constants can be computed. Irving and Rossotti [36], titrated following solutions against standard KOH solution N° keeping total volume V° constant.

The formation functions nA , n and pL can be computed from the following eqations:

$$n\,A = \gamma - \frac{(V_2 - V_1)(N + \varepsilon^0)}{(V_0 + V_1)T^0L} \quad \textbf{(1)}$$

$$n = \frac{(V_3 - V_2)(N + \varepsilon^0)}{(V_0 + V_2)nA\,T^0M} \quad \textbf{(2)}$$

$$PL = \log \left\{ 1 + \frac{\frac{[H^+]}{K_2} + \frac{[H^+]^2}{K_1K_2}}{(T^0L - T^0M)\,\bar{n}} \times \frac{(V_0 + V_3)}{V_0} \right\} \quad \textbf{(3)}$$

Where,
Vo = Initial volume of the solution.
V_1, V_2 and V_3 = volume of alkali required for the (A), (A + R) **and (A + R + M)** titrations respectively for same pH value
T^0L = Initial concentration of ligand.
ε^0 = Initial concentration of acid (HNO3)
γ = Number of replaceable protons.

By the knowledge of nA , n , pH and pL protonation and stepwise stability constants can be computed by different methods such as Half integral method/Interplotation at half n values, Least square method, Linear plot method and Point wise calculation method.

The following thermodynamic parameters: *ΔG°*, *ΔH°* and *ΔS°* were determined for chelate depending on their stability constants [37]. The free energy of formation *(ΔG°*) of a complex is related to its stability constant by the relation [37]:

$$-\Delta G° = 2.303\,RT\log K \quad \textbf{(4)}$$

Where, *R* = universal gas constant, *T* = absolute temperature and log*K* = stability constant of the complex.

$$\Delta H^0 = 2.303\,RT_1T_2 \left\{ \frac{(\log K_2 - \log K_1)}{T_2 - T_1} \right\} \quad \textbf{(5)}$$

$$\Delta S = \frac{\Delta H - \Delta G}{T} \quad \textbf{(6)}$$

Where, $\log K_1$ and $\log K_2$ are the respective stability constants of the complex at the absolute temperatures T and T_2 respectively.

Effect of Temperature:
It is seen from Table 1and Table 2 that stability constants gradually decreases with rise in temperature showing there by that lower temperature favours the formation of stable complexes.

Thermodynamic Parameters:
Thermodynamic functions such as Free energy (ΔG), Entropy (ΔS) and Enthalpy (ΔH) accompanying complexation are determined by equation 3, 4 and 5. The values of these thermodynamic functions are given in Table 3. The negative values of (ΔG) shows that the reaction tends to proceed spontaneously. The negative value of (ΔH) indicate the exothermic nature of reaction process in fair agreement with increasing stability suggesting lower temperature favours the chelation process. The entropy values indicate that complexation is favoured by enthalpy and entropy factors.

Table:3 Thermodynamic activation parameters for the formation of 1:1 complex of PMZ-M

Metal ions	-ΔG KJ/mol	-ΔH KJ/mol	-ΔS KJ/mol
Cd(II)	41.08	8.57	0.109
Pb(II)	33.07	97.47	0.216
Fe(III)	52.26	52.62	0.001
Cu(II)	30.08	22.22	0.026
Zn(II)	41.80	9.27	0.109

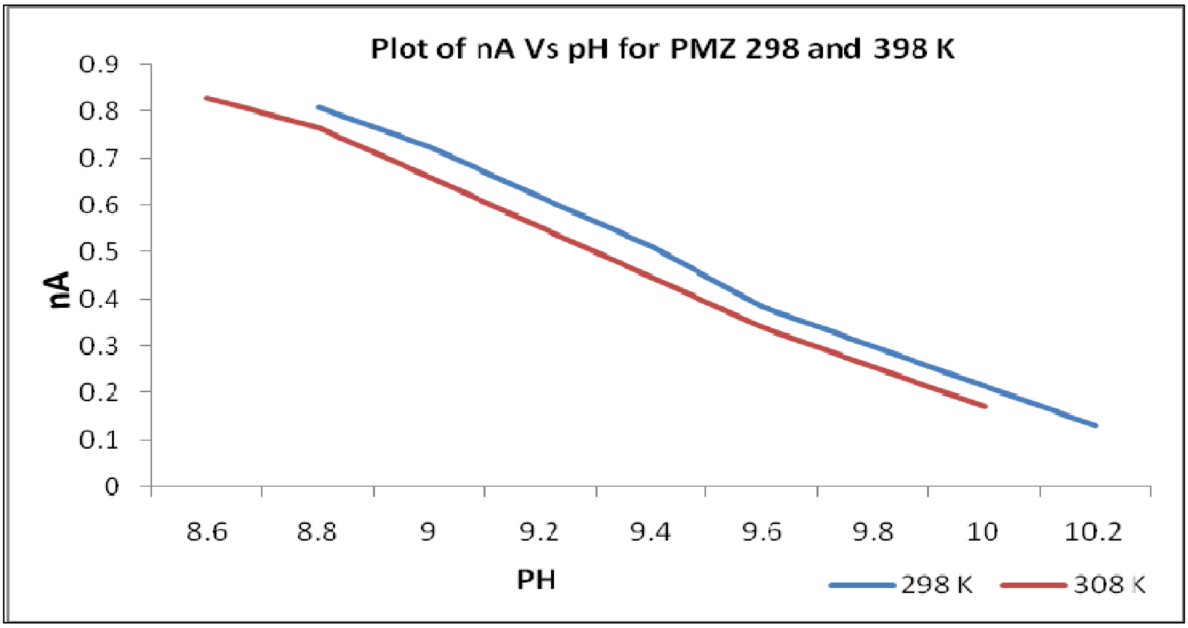

Figure 2: Plot of pH Vs nA at different temperature

CONCLUSION

The results obtained from the potentiometric measurements, the values of pKa were found to decrease with increasing temperature. The values of the thermodynamic functions ΔG, ΔH and ΔS were calculated. The values of stability constants reveal that the stability constants decrease with increasing temperature, along with the pKa value.

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