

Potentiometric study of the transition metal (II) ion complexes with drug diazepam[7- chloro-1-methyl-5-phenyl-3H-1,4- benzodiazepine -2- one]

NEERAJ SHARMA

Biotech Department, G.L.A. Institute of Professional Studies, Mathura (India).

(Received: February 02, 2009; Accepted: March 25, 2009)

ABSTRACT

The potentiometer studies have been carried out on metal complexes of Co (II) ; Mn (II) ; Cu (II); & Zn (II) with drug diazepam [7- chloro -1- methyl -5- phenyl -3H-1,4- benzodiazepine -2- one]. The proton ligand dissociation constant of the ligand & the formation constants of their metal complexes have been determined by Albert Serjent method at $25 \pm 1^\circ\text{C}$ & an ionic strength 0.1 M KNO_3 in 50 : 50 % (v / v) ethanol – water medium. From the variation of pK values with temperature the values of ΔG , ΔH & ΔS were also evaluated in aqueous medium at 25°C .

Key words: Potentiometer, complexes, diazepam.

INTRODUCTION

Derivatives of 1, 4- benzodiazepine are used in medicine as tranquilizer & sedative hypnotic agents¹⁻³. The survey of the literature ⁴⁻⁶ reveals that a little work has been done on the synthesis & physicochemical studies of transition metal complexes of drug diazepam. But, no attempts have been made, to determine the formation constants of metal complexes derived from 1,4 – benzodiazepines. Few reference ⁷ have suggested by the help of X – ray study of 1,4 – benzodiazepine (Parazepam) act as an anionic bidentate ligand , being Coordinated to the metal centre through the N (4) atom & the ortho carbon atom phenyl ring. The present study describes the result of formation constants of transition metal ion with drug diazepam by potentiometer method at a fixed ionic strength $\mu = 0.1 \text{ M KNO}_3$ & temperature $25 \pm 1^\circ\text{C}$, in aqueous medium.

EXPERIMENTAL

All the chemicals used were of A R grade. The complexes were prepared by mixing the molar solutions of respective metal nitrates & ligand with molar ratio 1 : 1 at pH 6 to 7. The product were crystallized from ethanol & their purity checked by TLC. The metal nitrates were dissolved in double distilled water & standardized ⁸. The stiochiometric ratio was confirmed by Fengers method ⁹.

An Elico LI -120 pH meter in conjunction with a combined electrode was used. The Albert – Serjent method ¹⁰ was used to obtain pK & log K values. The measurements were made at $25 \pm 1^\circ\text{C}$ & $\mu = 0.1 \text{ M KNO}_3$ in 50 / 50 % (v/v) ethanol – water medium.

The following sets of the systems were titrated at $25 \pm 1^\circ\text{C}$ & ionic strength $\mu = 0.1 \text{ M KNO}_3$,

the total volume (50 ml) being kept constant at the beginning of the titrations. The pH observed during the titrations were plotted against moles of alkali (m) added per mole of metal ion or ligand in figs.

Systems – M^{+2} – DZ -

- 10 ml, 0.025 M Metal solution + 5 ml 0.1 M [Curve a figs respectively metal] KNO_3 + 35 ml distilled water]
- 10 ml, 0.025 ml ligand + 5 ml 0.1 M KNO_3 [curve b figs]
- 10 ml, 0.05 M metal solution + 10ml, 0.05 M ligand (DZ) solution+ 5 ml 0.1M KNO_3 + 25 ml distilled water [Curve c figs]

RESULTS AND DISCUSSION

The formation constants of the complexes formed due to interaction of divalent transition (II) metal & ions with drug diazepam were calculated by measuring the magnitude of the lone pair of electron liberated during the titration of the ligand in absence & in presence of metal against standard (0.1M) solution. The ligand & metal ligand stability

constants values & thermodynamics parameters of complexes have been presented in the accompanying table.

The pK1 & pK2 values (4.31 & 9.40) of ligand which represent the donation of lone pair of electron of N (1) & N (4) atom were determined. The ligand has Cl atom at 3-position to azomethine nitrogen & it does not display pK value. The absence of pK value may be due to strong electron withdrawing effect of Cl atom present in the ligand. The electron density on the azomethine nitrogen is almost totally withdrawn by the chlorine resulting in the generation of positive charge on the azomethine nitrogen. Hence donation of lone pair of electron of azomethine nitrogen does not take place resulting in the absence of pK1 value. In ligand having methyl group at N(1) position to N- CH_3 group, there is +I effect hence azomethine nitrogen is more basic ¹¹.

The calculations show that the complexes are formed at a lower pH & are stable even at a higher pH value. The values of the change in free energy (ΔG), enthalpy (ΔH) & entropy (ΔS) have

Table 1: Stability constant & thermodynamic parameters of metal ligand complexes at different temperatures ($\mu= 0.1$ M KNO_3)

System	Temp. °C	Stability Constant	ΔG (K.cal mol ⁻¹)	ΔH (K.cal mol ⁻¹) (25/35)	ΔS Cal mol ⁻¹ at 25°C
LigandDiazepam (DZ)	2535	3.37 3.78	4.5965.426	17.2200	73.208
Co -DZ	25	5.56	7.582	13.440	70.544
	35	5.88	8.019		
Mn- DZ	25	5.87	8.005	15.960	80.419
	35	6.25	8.428		
Cu -DZ	25	5.09	6.941	13.860	69.802
	35	5.42	7.526		
Zn- DZ	25	5.82	7.937	15.540	78.782
	35	6.16	8.814		
Fe - DZ	25	4.45	6.068	12.600	62.644
	35	4.75	6.526		
Cr- DZ	25	5.58	7.609	10.920	62.177
	35	5.84	8.175		

been calculated at 25 °C temperature by using the following equations.

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

Where,

K = formation constant of the complex

T = absolute temperature

R = gas constant

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

or

$$\frac{\Delta H}{T_1 - T_2} = 2.303 R \log \left(\frac{K_2}{K_1} \right)$$

$$\Delta S = \frac{\Delta H - \Delta G}{T}$$

The stability constants of the metal ions follow the order $\text{Co} < \text{Zn} < \text{Mn} < \text{Cu}$. It is clear from the log K values that there is decrease in these values for the metal complexes compared to the ligand. The negative values of ΔG indicate that the reaction tends to proceed spontaneously. The values of ΔG is less negative at higher temperature confirm ΔS is more negative at higher temperature confirm that the complexes are not stable at higher temperature¹². The negative values of ΔH show that the reaction are exothermic in nature.

REFERENCES

1. C. Preti, and G.Tosi, *J. Coord. Chem.*, **6**: 81 (1976).
2. C. Preti and G. Tosi, *Transition Met. Chem.*, **3**: 246 (1978).
3. G. Minghetti, M. L. Gandu, C. Foddai, M. A. Cinellu, F. Demartin and M. Manassero, *Inorg. Chim. Acta*, **86**: 93 (1984).
4. M. A. Cinellu, S. Stoccoro, D. Minghetti and F. Demartin, *Inorg., Chim. Acta*, **168**: 33 (1990).
5. O. Cazar, L. David, V. Chis, E. forisz and C. Cosma, *J. Anal. Chim.*, **335**: 701 (1996).
6. A. Ouchi, T. Takeuchi, M. Nakatani and Y. Yakanashi, *Bull Chem. Soc.*, **44**: 434 (1971).
7. M. A. Cinellu, S. Gladiali, G. Minghetti and S. Stoccoro, *J. Orga. Chemistry*, **401**: 371-384 (1991).
8. A. I. Vogel, "A text book of quantitative chemical analysis," 5th ed., Longman, London. (1961).
9. P. Job, *Ann.*, **9**: 113 (1928).
10. S. Glasstone, "An introduction to electrochemistry", East- West press, New Delhi, 433 (1974).
11. R. K. Pardeshi, N. G. Palaskar and T. K. Chondhekar, *J. Indian Chem. Soc.*, **79**: 958-959 (2002).
12. F. Khan and A. V. Mahojani, *J. Indian chem. Soc.*, **61**: 165 (1984).