Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(4):1965-1968

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Potentiometric Studies of Ternary Complexes of Zinc with Vitamins and Medicinally important drugs

D. M. Janrao*[1], R. P. Shimpi[2] and R. B. Fadat[2]

[1]*Dept. of Chemistry, J. E. S. College, Jalna, India*
[2]*Dept. of Chemistry, Badrinarayan Barwale College, Jalna, India*

ABSTRACT

The proton ligand stability constants and stability constants of simple and mixed ligand complexes of zinc with pyridoxine, nicotinic acid, tetracycline, gentamycin, benzyl penicillin, ampicillin, streptomycin and ranitidine have been studied potentiometrically at 25±0.5°C and μ=0.1M(KNO_3) in aqueous medium. Zinc forms 1:1 and 1:2 complexes with all the chelating agents except for nicotinic acid-ranitidine, nicotinic acid-ampicillin and nicotinic acid-gentamycin 1:2 complex species does not exist in the solution. The mixed ligand chelates are shown to have formed in simultaneous equilibria. The higher values of stability constants of mixed ligand chelates than the sum of individual log stability constants of the first and second ligand are discussed.

Key words: Stability constants, binary, ternary, pH-metry, complexes, Zn (II).

INTRODUCTION

Recently there has been considerable interest in the study of binary, ternary and quaternary complexes by pH-metric method [1-4]. The metal ions in presence of organic and inorganic ligands, amino acids, peptides, proteins, vitamins and enzymes are playing a major role in the field of analytical Chemistry [5-7],Catalysis [6-8], biology [4,6], medicine [9-12] chemical protection of radiation [13-14] in the study of metalloprotiens and metalloenzymes [15,16]. Marcus and Elizer [1], Beck [2], Schaap and Mc McMaster's [3] have established the theoretical principles and essential mathematics involved in the mixed ligand complexes. An excellent account of the biological importance of mixed ligand complexes has been given by Sigel [4]. The mixed ligand complexes have been studied extensively because of their potential role in biological processes and can manifest themselves as enzyme-metal ion substrate complexes [17-23]. Some Platinum (II) complexes have been shown in last two decades to have anti-carcinogenic properties [24]. Similarly few Palladium (II) complexes were also shown to have inhibitory effects on some cell divisions and these are also shown to be nontoxic. The study of proton-ligands and metal-ligands of dicarboxylic acids and amino acids with some transition and inner transition metals have been reported [25]. Formation constants & thermodynamic parameters of bivalent metal ion complexes with 3-amono 5-methyl isoxazole Schiff bases have been reported [26]. The mixed ligand complexes of transition metal metals are comparatively less studied than inner transition elements [27].

The vitamins, antibiotics and drugs have a significant biological and medicinal importance. In view of the growing interest in the ternary complexes, it is thought worthwhile to study the ternary complexes of number of vitamins and antibiotics with transitions metal zinc (II).

EXPERIMENTAL SECTION

The ligands tetracycline, benzyl penicillin, ampicillin, streptomycin, gentamycin, ranitidine, pyridoxine and icotinic acid were of Himedia AR grade and were used as such. Zinc nitrate BDH AR grade, Potassium hydroxide Himedia AR grade, Potassiun nitrate of s.d.Fine AR grade, nitric acid of Qualigens AR grade. All solutions were prepared in air free conductivity water.

The pH-metric measurements were carried out by using Elico digital pH meter model L-120 with combined glass electrode with an accuracy of ± 0.01 of pH units at 25°C. The pH meter was standardized at different regions of pH (4.00 and 9.18) using standard buffer BDH solutions. The ionic strength was maintained at μ = 0.1M (KNO_3). The pH's was plotted against moles of base added per mole of metal ion/ligand.

Calculations

The acid dissociation constants of the ligands and stability constants of the simple metal complexes were calculated by the method of Irving and Rosotti [28,29]. The accurate values of log K_1 and log K_2 were calculated by the method of least squares and are compared with the literature values. These are presented in table 1. The formation constants for the determination of stability constants, the concentration of total(first and second) free ligand and the value of X were calculated by the following expression obtained by modification of Thompson and Loraa's method [30] and Ramamoorthy and Santappa's method [31,32]

RESULTS AND DISCUSSION

Table No 1.Dissociation constants of the ligands and stability constants of Zinc complexes of binary and ternary systems

μ = 0.1M (KNO_3) T=298°K

Sr.No.	Name of ligand	pK_1	pK_2	$logK_1$	$logK_2$
01	Pyridoxine V_1	4.94(4.95)	8.98(8.97)	5.3217	2.2923
02	Nicotinic acid V_2	4.90(4.85)	----------	6.4790	----------
03	Tetracyclin R_1	3.33(3.35)	7.31(7.29)	5.2847	2.4615
04	Penicillin benzyl R_2	2.82(2.75)	----------	3.2003	----------
05	Ampicillin R_3	6.84(6.80)	----------	10.3476	----------
06	Streptomycin R_4	8.01(8.0)	----------	3.0881	----------
07	Gentamycin R_5	5.88	7.67	1.4480	1.2358
08	Ranitidine R_6	1.78(1.77)	1.88(1.89)	2.2985	0.8739

$$X = 1 + \frac{2\,[H^+]^2}{K_1 K_2 + K'_1 K'_2} + \frac{[H^+]}{K_2 + K'_2}$$

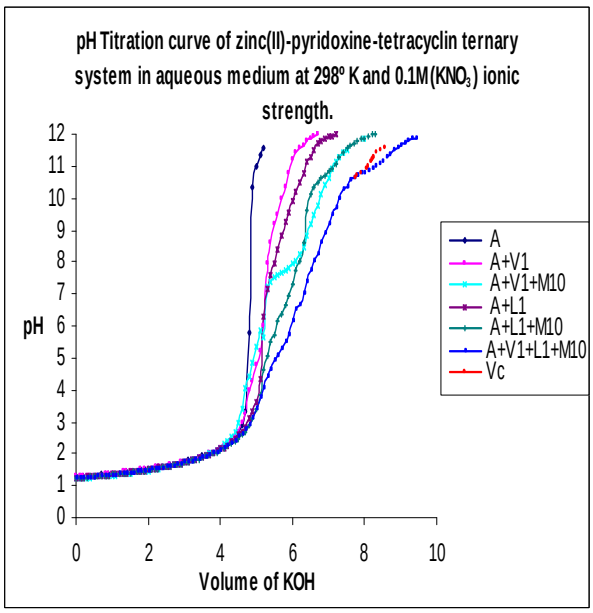
And

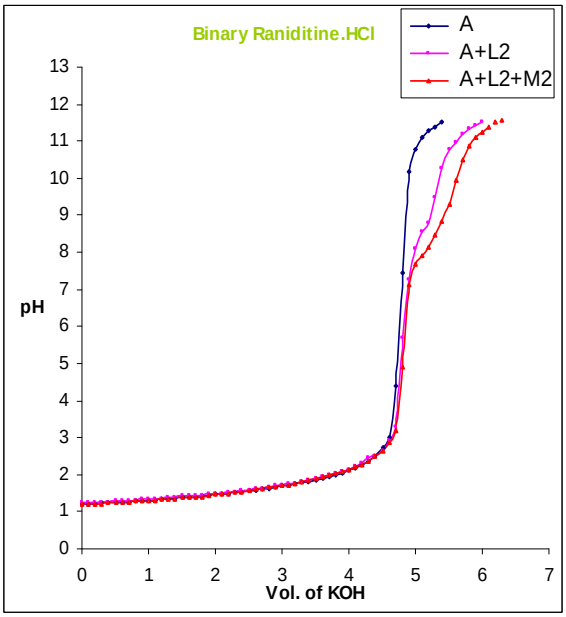
$$A = \frac{2T_L + 2T_A - T_{OH} - [H^+]}{\frac{4\,[H^+]^2}{(K_1 K_2) + (K'_1 K'_2)} + \frac{[H^+]}{(K_2 + K'_2)}}$$

Where T_L and T_A represent the concentrations of first and second ligand, T_{OH} = [KOH],

K_1K_2 and $K'_1K'_2$ are the first and second dissociation constants of the two ligands. The value of stability constants of the mixed complexes is given by

$$\log K_{MLA} = \frac{[T_M - \frac{1}{2} A - X]}{\frac{1}{2}\,[A]^3\,X}$$





It is observed that ampicillin have highest value of logKs 10.35. This might be due to strong basicity and greater number of chelate rings. The logKs for tetracyclin 7.74 and pyridoxine hydrochloride 7.61 are found to be nearly the same. In case of Nicotinic acid only $logK_1$ is obtained which is found to be 6.48. Similarly for penicillin benzyl, ampicillin, and streptomycin only $logK_1$ values are obtained. This shows that 1:1 species are exist in the solutions for these ligands with Zn (II) ion. In case of pyridoxine hydrochloride and tetracyclin, gentamycin and ranitidine 1:1 as well as 1:2 species may exist in the solution. The lowest values for logKs are found gentamycin, streptomycin and ranitidine. These might be due to steric hindrance.

The metal-ligand stability constants for the selected ligands with Zn (II) ion follow the following order

Ampicillin > Tetracyclin > Pyridoxine > Nicotinic acid > Penicillin Benzyl > Streptomycin > Ranitidine > Gentamycin.

In all the systems mentioned above, the $logK_{MLA}$ was found to be positive. However in case of Zn (II)-Nicotinic acid-Ranitidine system there was no separation of the mixed-ligand curve from the binary curves indicating the absence of 1:1:1 species. Again in case of Zn(II)-Nicotinic acid-Ampicillin and Zn(II)-Nicotinic acid-Gentamycin the composite curve falls to the right hand side of the experimental curve; this shows that in these cases mixed-complex species does not exist in the solution. The $logK_{MLA}$ value for some of the systems comes out to higher such as Zn (II)-pyridoxine-ampicillin ($logK_{MLA}$ = 46.97); Zn (II)-pyridoxine-streptomycin ($logK_{MLA}$ = 37.74). Similarly higher values of stability constants was found for N-(phosphono-methyl) glycine (PGM) with some metal ion such as Al^{+3} and Fe^{+3} i.e. 22.1 and 23 respectively [33-34].

All systems show positive values of $\Delta logK_{MLA}$. This indicates that ternary complexes are more stable than binary complexes.

Table No.2 Ternary complex of Zn (II) in presence of Drugs and Vitamins

Sr.No.	Systems	pH of separation	pH of hydrolysis	$logK_{MLA}$	$\Delta logK_{MLA}$
01	Zn(II)-Pyridoxine-tetracyclin	3.7	7.40	18.2041	+7.5977
02	Zn(II)-Pyridoxine- Penicillin benzyl	5.5	7.01	9.0489	+0.5269
03	Zn(II)-Pyridoxine- Ampicillin	5.1	7.74	46.9756	+31.3063
04	Zn(II)-Pyridoxine- Streptomycin	4.3	7.76	37.7406	+29.3308
05	Zn(II)-Pyridoxine- Gentamycin	4.4	7.22	33.0246	+26.2549
06	Zn(II)-Pyridoxine- Ranitidine	7.9	7.48	9.8119	+2.1917
07	Zn(II)- Nicotinic acid -tetracyclin	4.1	5.70	28.4970	+16.7333
08	Zn(II)- Nicotinic acid - Penicillin benzyl	3.7	7.41	10.8823	+1.2030
09	Zn(II)- Nicotinic acid - Ampicillin	4.3	7.42	--	--
10	Zn(II)- Nicotinic acid - Streptomycin	3.2	7.76	28.5746	+19.0075
11	Zn(II)- Nicotinic acid - Gentamycin	6.4	7.33	--	--
12	Zn(II)- Nicotinic acid - Ranitidine	7.3	7.04	--	--

REFERENCES

[1] Marcus,Y. and Elizer, I., *Coor. Chem. Review* **(1969)**, 4, 273.
[2] M.T. Beck, The determination of complex equilibria, **(1969)**, 172.
[3] Schaap, W.B. and McMasters, D.L., *J. Am. Chem. Soc.*, **(1961)**, 83, 4699.
[4] Sigel, H., Metal ions in biological systems. Marcel Dekker Inc., New York, 2, 1 **(1973)**; 5, 250 **(1976)**, 6, 1 **(1976)**.
[5] Flaschka, H.A. and Bernard, A.J., *Chelates in analytical Chemistry*, **(1967)**,Vol. I, Marcel Dekker Inc., New York.
[6] Dwyer, F.P. and Mellor, D.P., *Chelating agents and metal chelates, Academic Press*, **(1964)**, New York.
[7] Burger, K., Millor, I.T. and Allen, D.W., *Coordination chemistry : Experimental methods. Butterworths Co. (Publishers) Ltd., London* **(1973)**.
[8] Swift, H.E., Bozik, J.E. and Wu. C.Y., *J. Catalysis* **(1970)**, 17, 331.
[9] Seven, M.J. and Johnson, C.A., Metal binding in medicine. J. B. Lippincot Co., Philadelphia **(1960)**.
[10] Albert, A., The strategy of chemotherapy symposium of the society for general microbiology, (1958),Vol. 8. Cambridge University Press.
[11] Albert, A. Selective toxicity. Methuem, London **(1960)**.
[12] Albert, A., Rubbo, S.D., Goldacre, R.J. and Balfour, B. G., *Brit. J. Exptl. Path.* **(1947)**, 28, 69.
[13] Jones. M.M., Nature **(1960)**,185, 96.
[14] Kallwarf, D.R., Nucleonics, **(1960)**,18, 76.
[15] Bert L. Balee, in *Advances in Protein Chemistry*, Vol. 10 p.317
[16] Boyer, Paul D., Henry Lardy and Karl Myrback, *The enzymes. Second edn. (Completely revised). Academic Press, Inc, New York*, **(1959)**, pp. 391.
[17] Smith, E.L., *Advan. Enzymol*. **(1951)**,12, 191.
[18] Vallee, B.L. and Coleman, J.E., *Compr. Biochem.* **(1964)**, 12, 165.
[19] Malmstrom, B.G. and Rosenberg, A., *Advan. Enzymol*. **(1959)**,21, 131.
[20] Vallee, B.B., *Advan. In Protein Chem.*, **(1955)**,10, 317.
[21] Malmstrom, B.G., *Arch. Biochem. Biophys*. **(1955)**,58, 398.
[22] Hallerman, L. and Stock, E.C., *J. Biol. Chem*. **(1938)**,125, 771.
[23] Mildvan, A.S. and Cohn, M., *J. Biol. Chem*. **(1966)**,241, 1178.
[24] Cleare, M.J., *Cord. Chem. Rev*. **(1974)**, 12, 349.
[25] G.V. Mane et al *J.Chem.Pharm.Res.*,4(2); 1022-1027**,(2012)**.
[26] Shivraj et al *J.Chem.Pharm.Res.*,3(5); 226-233**,(2011)**.
[27] A.B. Patil T.H. Mhaske, *Asian J. Chem.*, Vol. 14,No. 1 p. 125-129 **(2002)**.
[28] Irving, H.M. and Rossotti, H.S., *J. Chem. Soc*., **(1954)**, 2904.
[29] Irving, H.A and Rossotti, H.S., *J. Chem. Soc*., **(1953)**, 3397.
[30] Thompson, L.C. and Loraas, J.A., *Inorg. Chem*. **(1962)**,1, 490.
[31] Santappa, M. and Ramamoorthy, S., *Indian J. Chem.* **(1971)**,9, 381.
[32] Ramamoorthy, S. and Santappa, M., *J. Inorg. Nucl. Chem*. **(1970)**, 32, 1623.
[33] The lower and upper limit of stability constant *"Chemistry of complex Equilibria"* p.24. by M.T. Beck, I. Nagypal.
[34] *Critical Evaluation of Stability Constants of Phosphonic acid Pure Appl. Chem.* **2001**,Vol 73 No 10, pp. 1641-1677. ©2001 IUAC.