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Potentiometric Study of Binary and Ternary Complexes of Some Bivalent Transition Metal Ions with Some Pharmaceutical Compounds

A.B. PATIL* and T.H. MHASKE†
Department of Chemistry, P.N. College, Pusad-445 216, India

To explore the complexing tendency of some 3d metal ions the binary and ternary complexation tendencies of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) were studied by the pH-metric technique at the ionic strength 0.1 M (KNO_3) and the temperature 29 ± 0.5°C in aqueous medium. The metal-ligand stability constants of binary complexes were evaluated using Irving-Rossotti titration technique and the metal-ligand stability constants using primary ligands nitrilotriacetic acid (NTA) and iminodiacetic acid (IMDA) and the drugs pyridoxine hydrochloride (PHC) and ethambutol hydrochloride (EHC) as secondary ligands were evaluated at the same conditions using modified form of Irving-Rossotti technique.

Key words: Potentiometric, binary, ternary, transition metal, drug, complexes.

INTRODUCTION

Recently there has been considerable interest in the study of binary, ternary and quaternary complexes by pH-metric method[1–4]. The ligand pyridoxine hydrochloride (PHC) is a vitamin. It plays a part in protein metabolism, the synthesis of fat from protein, haemopoiesis and the nutrition of the skin[5–7]. The ligand ethambutol hydrochloride (EHC) is used in the treatment of mycobacterial infections, particularly tuberculosis[5–7].

The mixed ligand complexes of transition metals are comparatively less studied than inner transition elements. Ternary complexes of Ni(II) with glycylglycine and glycinamide as primary ligands and imidazole, histamine and L-histidine as secondary ligands have been investigated by Nair and Neelkantan[8]. Nair *et al.*[9] have studied the ternary complexes of Ni(II) using histamine and L-histidine as primary ligands and some amino acids, diamines and diamino carboxylic acid as secondary ligands pH-metrically. Stability constants of ternary complexes of Zn(II) and Cd(II) containing catechol and amino acids or dipeptides have been determined potentiometrically by Vaidyan *et al.*[10]. Nair *et al.*[11] have studied the ternary complexes of Ni(II) and Cu(II) with nicotinic acid as primary ligand and imidazole, benzimidazole, histamine and L-histidine as secondary ligands potentiometrically. The study of stability constants of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) with nitrilotriacetic acid (NTA) and iminodiacetic acid (IMDA) as primary ligands and pyridoxine hydrochloride (PHC) and ethambutol

†Department of Chemistry, Govt. V.M.V., Amravati-444 604, India.

hydrochloride (EHC) as secondary ligands are not reported in literature. It was therefore of interest to study the stability constants of binary and ternary complexes of these metal ions with these medicinal compounds at 29 ± 0.5°C and at $\mu = 0.1$ M KNO_3 employing modified form of Irving-Rossotti pH-metric titration technique[12] in aqueous medium.

EXPERIMENTAL

The ligand PHC was obtained from LOBA Chemie and the EHC was of Cadila Pharmaceuticals Ltd. The ligands were used as such. Carbonate-free sodium hydroxide solution was prepared by standard method[13]. All other solutions were prepared in doubly distilled water.

The pH-metric measurements were carried out by using Elico digital pH-meter model L-120 with glass-calomel electrode with an accuracy of ± 0.01 of pH unit at 29 ± 0.5°C. The pH-meter was standardized against 0.05 M potassium hydrogen phthalate solution in acid medium and 0.01 M borax solution in alkaline medium.

For the determination of proton-ligand stability constant of the secondary ligands and metal-ligand stability constants of the binary and ternary complexes, the following sets of solutions were prepared and titrated against standard alkali solution.

Binary Systems

(i) 9.4×10^{-3} M HNO_3.
(ii) 9.4×10^{-3} M HNO_3 + 5.0×10^{-3} M secondary ligand.
(iii) 9.4×10^{-3} M HNO_3 + 5.0×10^{-3} M secondary ligand + 1.0×10^{-3} M metal ion.

Ternary Systems

(i) 9.4×10^{-3} M HNO_3.
(ii) 9.4×10^{-3} M HNO_3 + 1.0×10^{-3} M secondary ligand.
(iii) 9.4×10^{-3} M HNO_3 + 1.0×10^{-3} M primary ligand + 1.0×10^{-3} M metal ion.
(iv) 9.4×10^{-3} M HNO_3 + 1.0×10^{-3} M primary ligand + 1.0×10^{-3} M metal ion + 1.0×10^{-3} M secondary ligand.

The ionic strength was maintained constant (0.1 M) by adding required volume of 1 M KNO_3. The ratio of metal (M) : secondary ligand (L) was maintained at 1 : 5 in each of the binary systems and the ratio of metal (M) : primary ligand (A) : secondary ligand (L) was maintained at 1 : 1 : 1 in each of the ternary systems.

RESULTS AND DISCUSSION

Proton-Ligand Stability Constants: The plots of volume of alkali (NaOH) against pH-meter readings were used to evaluate the proton-ligand stability constants of PHC and EHC. The deviation between free acid titration curve and secondary ligand titration curve was used to evaluate the formation functions

$\bar{\eta}_A$. The proton-ligand formation curves were then obtained by plotting the values of $\bar{\eta}_A$ *vs.* pH-meter readings. From the graphs the values of log K_1^H and log K_2^H were evaluated by half integral method (method A) and pointwise calculation method (method B) and presented in Table-1.

TABLE-1
PROTON-LIGAND STABILITY CONSTANTS

Ligands	log K_1^H		log K_2^H		log β^H	
	Method		Method		Method	
	A	B	A	B	A	B
PHC	9.05	9.03	4.95	4.92	14.00	13.95
EHC	9.45	9.40	6.52	6.54	15.97	15.94

Metal-Ligand Stability Constants of Binary Complexes

The metal-ligand stability constants of binary complexes were evaluated assuming that the formation of hydrolysed products, polynuclear complexes, hydrogen and hydroxyl bearing complexes were absent. An examination of titration curves indicates that complex formation has taken place in the solution on the following grounds:

1. The metal titration curves showed displacement with respect to the ligand titration curves along the volume axis. This indicated the affinity of ligand with metal ions which released protons and produced the volume difference $(V_3 - V_2)$.
2. The colour change of the ligand in presence of metal ions appeared showing the formation of new species.
3. The hydrolysis of the metal ions was suppressed due to complex formation and the precipitation did not appear during the titrations.

From the ligand and metal titration curves the values of $\bar{\eta}$ and from that the values of pL were obtained. The formation curves obtained were used to evaluate the metal-ligand stability constants by methods (A) and (B) and presented in Table-2.

The variation of $\bar{\eta}$ was found to be 0 to 2 which indicated that the composition of complexes was 1 :2 in solution. From Table 2, it is obvious that the metal-ligand stability constants of EHC were greater than with respect to PHC in every metal.

The Irving-Williams order[14, 15] of stability constants was followed by both ligands.

Metal-Ligand Stability Constants of Ternary Complexes

The metal-ligand stability constants of the ternary complexes were evaluated assuming that the formation of hydroxy products, polynuclear complexes, hydrogen and hydroxyl bearing complexes was absent. An examination of the titration curves indicated that ternary complex formation had taken place in solution on the following grounds:

TABLE- 2
METAL-LIGAND STABILITY CONSTANTS OF BINARY COMPLEXES

Ligands	log K_1		log K_2		log β	
	Method		Method		Method	
	A	B	A	B	A	B
[Mn(II)-PHC]	2.62	2.62	—	—	—	—
[Co(II)-PHC]	2.92	2.96	2.75	2.75	5.67	5.71
[Ni(II)-PHC]	3.39	3.49	2.81	2.82	6.20	6.31
[Cu(II)-PHC]	5.08	5.06	4.62	4.63	9.70	9.69
[Zn(II)-PHC]	3.88	3.87	3.52	3.50	7.40	7.37
[Mn(II)-EHC]	4.18	4.17	3.28	3.30	7.46	7.37
[Co(II)-EHC]	5.65	5.67	3.68	3.65	9.33	9.32
[Ni(II)-EHC]	6.62	6.62	3.80	3.83	10.42	10.45
[Cu(II)-EHC]	6.92	6.93	4.74	4.71	10.66	11.64
Zn(II)-EHC]	5.79	5.83	3.57	3.61	9.36	9.44

1. The ternary complex titration curves show displacement with primary complex titration curves. The horizontal distance was measured between acid curves and the secondary ligand curves ($V_2 - V_1$) and subtracted through the horizontal distance between ternary complex curves and primary complex titration curves ($V_4 - V_3$) show a positive difference which proves the earlier release of protons in the formation of ternary complexes.
2. The hydrolysis of metal ions was suppressed and precipitation did not occur.

The values of $\bar{\eta}$ vary from 0 to 1, thus confirming the formation of 1 : 1 : 1 mixed ligand complexes. The values of $\log_{MAL}^{NTA}$ and $\log_{MAL}^{IMDA}$ have been evaluated from the formation curves ($\bar{\eta}$ *vs.* pL). At $\bar{\eta} = 0.5$ in the formation curve, pL = log K. The log K values were also evaluated by pointwise calculation method B. The metal-ligand stability constants of PHC and EHC as secondary ligands and NTA and IMDA as primary ligands are presented in Table-3.

TABLE -3
METAL-LIGAND STABILITY CONSTANTS OF TERNARY COMPLEXES

Systems	Constants (logK)									
	Mn(II)		Co(II)		Ni(II)		Cu(II)		Zn(II)	
	A	B	A	B	A	B	A	B	A	B
[M(II)-NTA-PHC]	4.63	4.64	4.75	4.78	5.00	5.03	5.48	5.51	4.89	4.92
[M(II)-IMDA-PHC]	3.96	3.98	4.62	4.65	5.00	4.99	5.58	5.59	4.12	4.06
[M(II)-NTA-EHC]	4.85	4.88	4.96	5.01	5.40	5.41	5.61	5.59	4.27	4.30
[M(II)-IMDA-EHC]	4.29	4.28	5.51	5.45	6.01	5.98	6.14	6.15	4.51	4.55

The Irving-Williams natural order[14, 15] was observed in case of binary as well as ternary complexes which is

$$Mn(II) < Co(II) < Ni(II) < Cu(II) < Zn(II).$$

The aim of the study was to know whether the effect of binary and ternary complexes as compared to plain drug is different or the same. This part of application is in progress as it is time-consuming.

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REFERENCES

1. A.E. Martell, Stability Constants, Special Publication Nos. 17 and 25, The Chemical Society, London (1964 and 1971).
2. A.E. Martell and R.M. Smith, Critical Stability Constants-1: Amino Acids, New York (1974).
3. H. Sigel, Metal Ions in Biological Systems-2, Marcell-Dekker, Inc., New York (1973).
4. M.T. Beck, Chemistry of Complex Equilibria, Van Nostrand, New York, pp. 174–190 (1970).
5. The Pharmaceutical Codex, 11th Edn., The Pharmaceutical Press, London (1979).
6. Clarke's Isolation and Identification of Drugs, 2nd Edn., The Pharmaceutical Press, London (1986).
7. Remington's Pharmaceutical Science, 17th Edn., Mack Publishing Co., Easton, Pennsylvania (1985).
8. M.S. Nair and M.A. Neelkantan, *Indian J. Chem.*, **34A**, 576 (1995).
9. ———, *Indian J. Chem.*, **37A**, 1084 (1998).
10. Alexander Vaidyan and P. K. Bhattacharya, *Indian J. Chem.*, **33A**, 1003 (1994).
11. M.S. Nair and M.A. Neelkantan, *Indian J. Chem.*, **38A**, 1307 (1999).
12. H. Irving and H.S.Rossotti, *J. Chem. Soc.*, **76**, 2904 (1954).
13. A.I. Vogel, A Text Book of Quantitative Analysis, Longmans, London, p. 241 (1961).
14. H. Irving and R.J.P. Williams, *Nature*, **162**, 746 (1948).
15. ———, *J. Chem. Soc.*, 3192 (1953).

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