Stability Constants of the Binary Complexes of Co(II), Ni(II), Cu(II) & Zn(II) with Thiamine & Ternary Complexes with Thiamine as Primary Ligand & Thymine or Uracil as Secondary Ligand

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Stability constants of the 1 : 1 and 1 : 2 metal-thiamine (vitamin B_1) complexes and 1 : 1 : 1 metal-thiamine-thymine/uracil mixed ligand complexes have been determined in aqueous medium by potentiometric method at $35° \pm 0.1°C$ and $\mu = 0.10 \, M$ (KNO$_3$). The $\Delta \log K$ values for 1 : 2 metal-thiamine systems are positive whereas values for 1 : 1 : 1 metal-thiamine-thymine or -uracil systems are negative. So the $\Delta \log K$ values reveal that mixed ligand complexes are less stable than the binary (1 : 1) complexes.

Thiamine is present in all living organisms and is essential to life. Co-carboxylase, which is widely used in medicine, is a diphosphoric acid ester of thiamine. Co-carboxylase appears as a component of the metalloenzymes which catalyze the decarboxylation of α-ketoacids and some other biochemical reactions. In order to understand and simulate these vital processes, it is very important to study the complexing properties of thiamine. Fridman *et al.*[1-3] and Grinberg *et al.*[4] have studied the complexing properties of thiamine with some divalent metal ions. In the present investigation stability constnats of binary metal-thiamine complexes and ternary metal-thiamine-thymine/uracil complexes have been determined potentiometrically.

The experimental techniques employed for potentiometric study were similar to those reported in our earlier paper[5].

A Shimadzu double beam spectrophotometer with matched 1 cm quartz cell was used to recorded the spectra. All the solutions were equilibrated at 35°C, the ionic strength being maintained at 0.10 M using KNO$_3$; pH was maintained at 4.90 by adding NaOH. The compositions of the complexes were determined using mole ratio method[6]. The formation constants were evaluated using Leden's[7] method. The degree of formation is defined as the ratio of overall concentration of metal ion (C_M) to the equilibrium concentration of free metal ion [M],

$$\phi = \frac{C_M}{[M]} = 1 + k_1[L] + k_1 k_2[L]^2$$

The coefficients k_1, k_2 of the variable [L] were obtained by constructing suitable auxiliary functions (ψ_1, ψ_2) and extrapolating these to zero value of the variable.

Thymine and uracil were obtained from M/s Sigma Chemicals, USA. Thiamine hydrochloride was an E. Merck reagent. The metal salt solutions were standardized by titration with disodium salt of EDTA[8]. Carbonate-free NaOH was prepared and standardized by titration with pure potassium hydrogen phthalate.
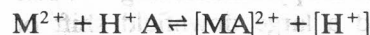
Calculations

The acid dissociation constants of the ligands were calculated by a direct algebraic method[9], using a combination of suitable material balanced equations. The following general expression was derived to calculate the dissociation constants of the ligands.
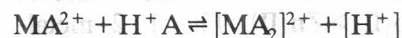
$$K_{na} = \frac{[H^+]\{(a - n + 1)T_L + [H^+] - [OH^-]\}}{T_L - \{(a - n + 1)T_L + [H^+] - [OH^-]\}} \quad \cdots (1)$$

where a = mol of base added per mol of ligand and T_L = total concentration of the ligand species.

For the calculation of stability constants of 1 : 1 and 1 : 2 metal-thiamine complexes, Eqs (2) and (3) respectively were used.

$$M^{2+} + H^+A \rightleftharpoons [MA]^{2+} + [H^+]$$

$$K_{MA}^M = \frac{[MA]^{2+}}{[M]^{2+}[A]} \quad \cdots (2)$$

$$MA^{2+} + H^+A \rightleftharpoons [MA_2]^{2+} + [H^+]$$

$$K_{MA_2}^{MA} = \frac{[MA_2]^{2+}}{[MA]^{2+}[A]} \quad \cdots (3)$$

For the calculation of stability constants of 1 : 1 : 1 ternary complexes (metal-thiamine hydrochloride-L), Eq. (4) was used.

$$K_{MAL}^{MA} = \frac{[MAL]^+}{[MA]^{2+}[L]^-} \quad \cdots (4)$$

where H^+A = thiamine hydrochloride and HL = thymine or uracil.

Metal-thiamine hydrochloride (1 : 1) systems

The titration curve of M(II)-thiamine hydrochloride [M(II) = Cu(II), Zn(II), Ni(II) and Co(II)]

showed a sharp inflection at $a = 1$. The formation of a 1:1 complex was assumed before the inflection point and the corresponding formation constants were calculated in the region of titration curve with $a = 0.3$ to 0.7. The stabilities of metal-thiamine hydrochloride were found to decrease in the order: $Cu(II) > Ni(II) > Co(II) > Zn(II)$. The results are presented in Table 1.

Metal-thiamine hydrochloride (1:2) systems

For all the metal ions studied, viz., $Cu(II)$, $Zn(II)$, $Ni(II)$ and $Co(II)$, inflection was obtained at $m = 2$ (mol of base added per mole of metal ion). The stability constants $K_{MA_2}^{MA}$ were, however, calculated before $m = 2$ and the results are presented in Table 2.

Metal-thiamine hydrochloride-thymine or uracil (1:1:1) systems

The titration curves fo $Cu(II)$-thiamine hydrochloride-thymine or uracil systems showed a sharp inflection at $m = 1$. Similar titration curves were obtained for other metal ions, $Zn(II)$, $Ni(II)$ and $Co(II)$. The titration curves indicate the stepwise complex formation of thiamine and thymine or thiamine and uracil. Complex formation of thiamine (vit. B_1) takes place before the inflection point and with thymine or uracil it takes place after the inflection point. The stability constants K_{MAL}^{MA} have been calculated in the buffer region with $m = 1.3$ to 1.7. The results are presented in Table 2.

Thiamine hydrochloride ($pK_a = 4.97$) binds with metal ion through N^1 of the pyrimidine ring[10-13]. The NMR spectra showed a large downfield shift of C_6-H, which is adjacent to N^1 of the pyrimidine ring supporting the involvement of N^1 in coordination[14]. The stabilities of the (1:1) metal-thiamine hydrochloride complexes are in the order: $Cu(II) > Ni(II) > Co(II) > Zn(II)$. The 1:2 metal-thiamine hydrochloride systems are more stable than the corresponding 1:1 systems contrary to statistical considerations. The higher stabilities of the ternary systems as compared with those of the binary ones may be due to the stacking interaction of the ligands. The stacking is more pronounced at lower pH values than the neutral pH[15]. That is why the $\Delta \log K$ values for 1:2 metal-thiamine hydrochloride systems and metal-adenine-cytosine systems[16] are positive whereas for the metal-thymine or uracil (1:2) systems[5,17] the $\Delta \log K$ values are negative (Table 3).

The stability constants for 1:1:1 system of metal-thiamine hydrochloride-thymine or uracil decrease in the order: $Cu(II) > Zn(II) > Ni(II) > Co(II)$. For the two ternary 1:1:1 systems the $\Delta \log K$ va-

Table 1—Stability Constants of (1:1) Metal-Ligand Systems

[Temp. $35° \pm 1°C$; $\mu = 0.10$ M (KNO$_3$)]

Metal ion	Metal-thiamine hydrochloride (1:1)	Metal-thymine (1:1)	Metal-uracil (1:1)
Cu(II)	2.69 (2.78)	6.61	6.04
Zn(II)	2.30	5.23	4.98
Ni(II)	2.52	4.24	3.89
Co(II)	2.36 (2.31)	4.10	3.83

Values are accurate upto ± 0.04; values in the parentheses are calculated spectrophotometrically.

Table 2—Stability Constants of (1:1:1) System

[Temp. $35° \pm 1°C$; $\mu = 0.10$ M (KNO$_3$)]

Metal ion	Metal-thiamine hydrochloride (1:2)	Metal-T. HCl thymine (1:1:1)	Metal-T. HCl uracil (1:1:1)
Cu(II)	4.30 (4.39)	6.21	5.67
Zn(II)	4.10	4.97	4.35
Ni(II)	4.22	3.75	3.28
Co(II)	4.19 (4.10)	3.68	3.17

Values are accurate upto ± 0.05; values in the parentheses are calculated spectrophotometrically.

Table 3—$\Delta \log K$ Values of Various Systems

Metal ion	M(II)-thiamine HCL (1:2)	M(II)-thiamine HCl-thymine (1:1:1)	M(II)-thiamine HCl-Uracil (1:1:1)
Cu(II)	+ 1.61	− 0.40	− 0.37
Zn(II)	+ 1.8	− 0.26	− 0.63
Ni(II)	+ 1.7	− 0.49	− 0.61
Co(II)	+ 1.83	− 0.42	− 0.66

lues are negative indicating that these systems are less stable than the binary 1:1 systems. This is in accordance with the statistical considerations. If the secondary ligand is negatively charged aromatic ligand like pyrocatechol[18], the ternary systems are more stable than the binary ones. In contrast, the stability constants of the mixed ligand complexes containing neutral donors [thymine ($pK_a = 9.51$) or uracil ($pK_a = 9.29$)] as the secondary ligands are in accord with the statistical considerations[5,17,19] where the statistical steric and electrostatic factors lead to lower stability constants for the 1:1:1 metal-ligand complexes as compared with those for the binary systems. A similar trend was observed in metal-bipyridyl-cytosine or thymine or uracil and metal-o-phenanthroline-cytosine or thymine or uracil[5,16,17] systems.

References

1 Fridman Ya D, Levina M G, Sarbae D S, Tsoi E P & Moldogazieva A V, *Chem Abstr*, **88** (1978) 15256d.

2 Fridman Ya D & Gorokhov S D, *Chem Abstr*, **95** (1981) 128194v.

3 Fridman Ya D, Gorokhov S D & Zainutdinova A, *Chem Abstr*, **95** (1981) 214274c.

4 Grinberg A A & Khakinov Kh Kh, *Chem Abstr*, **6** (1961) 71.

5 Taqui Khan M M & Satyanarayana S, *Indian J Chem*, **21A** (1982) 913.

6 Yoe J H & Jones A L, *Indian Engng Chem Analyt Edn*, **16** (1944) 111.

7 Leden I, *Z phys Chem*, **A188** (1941) 160.

8 Schwarzenbach G, *Complexometric titrations* (Interscience, New York) 1957, 77.

9 Taqui Khan M M & Martell A E, *J phys Chem*, **66** (1962) 10.

10 Taqui Khan M M & Amarababu M, *J inorg nucl Chem*, **103** (1981) 76.

11 Gallo A A, Hansen I L, Sable H Z & Swift T J, *J biol chem*, **241** (1972) 247.

12 Kartz H B & Kustin K, *Biochim Biophys Acta*, **313** (1973) 235.

13 Gary J & Adeyemo A, *Inorg chim Acta*, **55** (1981) 93.

14 Hadjiliadis I N, Markopoulos J, Pneumtikakis G, KJatakis D & Theophanides T, *Inorg chim Acta*, **25** (1977) 21.

15 Gilligan T J & Schwarz G, *Biophys Chem*, **4** (1976) 55.

16 Taqui Khan M M & Jyothi M S, *J inorg nucl chem*, **40** (1978) 1731.

17 Taqui Khan M M & Satyanarayana S, *Indian J Chem*, **21A** (1982) 913.

18 Heurex G A L & Martell A E, *J inorg nucl Chem*, **28** (1966) 481.

19 Sigel H, *Metal ions in biological systems*, Vol 2, (Marcel Decker, New York) 1973.