Studies on formation constants of some transition metal complexes containing folic acid as a primary ligand and some amino acids as a secondary ligands

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The stability constants (Δ log K) of the ternary complexes of copper(II) and nickel(II) with folic acid (FA) and some amino acids such as tryptophane (tryp), tyrosine (tyr), dipicolinic acid (DPA) and adenosine triphosphate (ATP) have been determined by potentiometric method and their redox behaviour have been examined by cyclic voltammetric method. An astatistical increase in the value of mixed ligand formation constants was observed by small negative or positive value of Δ log K. The potentiometric and the cyclic voltammetric study show the complexes of Ni^{II} are more stable than that of complexes of Cu^{II}.
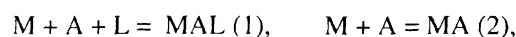
The studies of mixed ligand complexes of the type MAL (where, A = FA) have assumed significant biological effect because folic acid is necessary for the growth of a number of micro-organisms and is effective in the treatment of certain types of anaemia[1]. A knowledge of stability constant gives an idea about the use the metal complexes in different fields[2-5]. Keeping these in mind an attempt has been made to investigate the stability or formation constant of several complexes of different metal ions with mixed ligands. The formation constant (log K_{MAL}^{M}) of the mixed ligand complexes of the type MAL, where M = Cu^{II} or Ni^{II}; A = folic acid and L = tryptophane (tryp)/tyrosine (tyr)/dipicolinic acid (DPA) or adenosine triphosphate (ATP) in 50% aqueous dioxan and 0.2 mol dm^{-3} $NaClO_4$ solution have been determined at (25 ± 1°) using a computer programme. The values of Δ log K are calculated by using the following relation :

$$\Delta \log K = \log K_{MAL}^{MA} - \log K_{ML}^{M},$$

where $\log K_{MAL}^{MA} = \log K_{MAL}^{M} - \log K_{MA}^{M}$.

The terms K_{MAL}^{M}, K_{MA}^{M}, K_{ML}^{M} and K_{MAL}^{MA} are the equilibrium constants for the equations 1, 2, 3 and 4. The equations are as follows :

$$M + A + L = MAL \ (1), \qquad M + A = MA \ (2),$$
$$M + L = ML \ (3), \qquad MA + L = MAL \ (4)$$

The cyclic voltammetric (CV) studies have been employed to confirm the formation and stability of mixed ligand complexes. The obtained results are summerized in Tables 1 and 2.

Table 1. Proton-ligand formation constants of Cu^{II} and Ni^{II} binary complexes in dioxane-water (1 : 1, v/v) medium with I = 0.2 M ($NaClO_4$) at 25 ± 1° with standard deviation in parentheses

Ligand (L)/(A)	$\log K_1^H$	$\log K_2^H$	$\log K_{CuL}^{Cu}$	$\log K_{CuL_2}^{Cu}$	$\log K_{NiL}^{Ni}$	$\log K_{NiL_2}^{Ni}$
Tryptophane	9.44 (+0.02)	11.43 (+0.03)	7.98 (+0.00)	15.36 (+0.01)	5.30 (+0.00)	9.70 (+0.16)
Tyrosine	9.44 (+0.01)	10.48 (+0.02)	7.30 (+0.15)	14.01 (+0.25)	5.15 (+0.04)	9.40 (+0.09)
Dipicolinic acid	4.25 (+0.15)	6.39 (+0.25)	8.89 (+0.20)	16.28 (+0.21)	11.09 (+0.04)	13.12 (+0.02)
Adenosine triphosphate	6.42 (+0.15)	10.48 (+0.21)	8.22 (+0.01)	10.00 (+0.03)	5.81 (+0.09)	8.20 (+0.04)
Folic acid	4.65 (+0.01)	8.75 (+0.01)	9.96 (+0.09)	16.25 (+0.10)	12.70 (+0.06)	18.29 (+0.10)

Table 2. Stability constants of mixed ligand complexes [Cu(FA)(L)] and [Ni(FA)(L)] in dioxane-water (1 : 1, v/v) medium with I = 0.2 M ($NaClO_4$) at 25 ± 1°

System	$\log K_{CuAL}^{Cu}$	Δ log K	System	$\log K_{NiAL}^{Ni}$	Δ log K
Cu(FA)(L)			Ni(FA)(L)		
Cu(FA)(tryp)	17.94 (+0.07)	–0.14	Ni(FA)(tryp)	18.00 (+0.00)	+0.10
Cu(FA)(tyr)	17.30 (+0.27)	–0.04	Ni(FA)(tyr)	18.35 (+0.10)	+0.14
Cu(FA)(DPA)	18.60 (+0.16)	–0.25	Ni(FA)(DPA)	18.40 (+0.17)	+0.01
Cu(FA)(ATP)	18.08 (+0.12)	+0.10	Ni(FA)(ATP)	18.70 (+0.15)	+0.20

Results and discussion

It is observed from Table 2 that $\Delta \log K$ values for the Cu(FA)(L), where L = tryp/tyr/DPA are negative, as expected from the statistical considerations. The value of $\Delta \log K$ becomes more negative with increasing charge on the ligand L and size of the chelate ring formed around the metal ion. The order of destabilization may be as follows : DPA > tryp > tyr. This order of destabilization may be explained by considering the number of ring formed in complex compound. The DPA molecule contains two negatively charged $(O^- - O^-)$ carboxylate ions as a result one mole- cule of DPA may form two five membered rings on complexation with Cu^{2+} ion. The possible ring of Cu-FA-DPA complex is shown below :
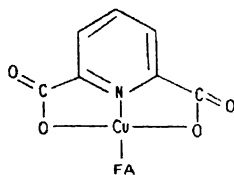
The two negatively charge of DPA molecule destabilizes the ternary complex. This leads to larger negative values of $\Delta \log K$. The tryptophane coordinating complex (Cu-FA-tryp) compound shows lower negative $\Delta \log K$ value as compared to the DPA containing ternary complex (Cu-FA-DPA). This is because Cu-FA-tryp ternary complex may form only one five membered ring as shown below :
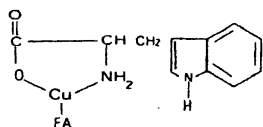
Besides this tryptophane contains $N-O^-$ donor group having one neutral and one negatively charged atom which makes the complex more stable. Tyrosine also composed of $N-O^-$ donor group. Hence Cu-FA-tyr exhibits lower negative $\Delta \log K$ value than that of Cu-FA-DPA ternary complex. Cu-FA-tyr shows higher stability as compared to the Cu-FA-tryp. This may be due to the fact that the ternary complex Cu-FA-tyr contains intramolecular hydrogen bond as shown below :
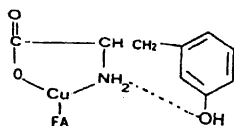
Folic acid has two negative $(O^- - O^-)$ charges. The second negatively charged ligand faces electrostatic repulsion in forming ternary complexes. Hence, the tendency of L^{n-} to get bound to MA will be less than to get bound with charged M^{2+} ion in the formation of binary complex ML, leading to negative $\Delta \log K$. The electrostatic repulsion is more with increasing charge on L^{n-} resulting in more negative $\Delta \log K$ values.

It is also observed from Table 2 that the $\Delta \log K$ value for the complex of Cu(FA)(ATP) is positive. This may be due to intramolecular interligand interaction. FA has a non coordinated side group containing two pyridyl rings. On the other hand, the non coordinated side group of ATP is adenine-ribose. The non-coordination side group (adenine-ribose) of ATP comes over the two pyridyl rings of folic acid and hence non-covalent hydrophobic interaction is possible. This intramolecular interligand interaction stabilizes the ternary complex leading to positive $\Delta \log K$ value.

The $\Delta \log K$ values are smaller for the Cu^{II} complexes as compared to Ni^{II} complexes are due to the presence of tridentate ligand folic acid. The tridentate ligand folic acid, occupy the three equatorial position around the metal ion. Hence in the formation of the ternary complex, the bidentate ligand (L) has to occupy one equatorial and one axial position. Due to Jahn-Teller effect[6], in case of Cu(FA)(L) complexes, the ligand is strained in occupying the axial position and its tendency to coordinate with the MA is much less than in the binary complexes where the bidentate ligand occupies two equatorial positions. Hence the stability of Cu^{II} complexes becomes low. In the absence of Jahn-Teller effect in Ni^{II} complexes, the bidentate ligand does not face any strain in occupying one equatorial and one axial position and hence $\Delta \log K$ is increased. Besides of the fact, the intramolecular interligand interaction is also possible.

Electron-transfer properties of the M(FA)(L) complexes have been studied in 50% aqueous-dioxane (v/v) by cyclic voltammetry. Voltammetric data are presented in Table 3. Each complex shows two volammetric responses, one oxidative response on the positive side of SCE and the other reductive response on the negative side. From the cyclic voltammetry measurement it is possible to explain the order of stability of ternary complexes. The anodic and cathodic potential gives us information about the relative stability of complexes. The potential is required to show anodic and cathodic peak is called anodic (E_{pa}) and cathodic potential (E_{pc}). Greater the value of cathodic and anodic potential, greater will be the stability of complex. The potential difference between E_{pa} and E_{pc} also helps us to ascertain the relative stability of complexes. An increase in

Table 3. Results of cyclic voltammograms of metal perchlorates and their different complex compounds

Compd.	E_{pa}	E_{pc}	$\Delta E_p = E_{pa}-E_{pc}$	pH
Cu(ClO$_4$)$_2$	50	−90	140	3.00
Ni(ClO$_4$)$_2$	60	−100	160	3.00
Cu(FA)	65	−100	165	3.25
Ni(FA)	75	−150	225	2.80
Cu(FA)(tryp)	110	−175	285	4.30
Ni(FA)(tyr)	250	−175	425	4.80
Cu(FA)(tyr)	175	−125	300	5.50
Ni(FA)(tyr)	225	−120	445	3.30
Cu(FA)(DPA)	150	−110	260	5.80
Ni(FA)(DPA)	240	−160	400	5.60
Cu(FA)(ATP)	200	−120	320	5.10
Ni(FA)(ATP)	300	−155	455	4.40

potential difference between E_{pa} and E_{pc} is observed in Table 3 indicates the higher stability of complex compound. In the light of the above discussion it is said that the order of stability of the ternary complex is as follows : Ni(FA)(L) > Cu(FA)(L), where L = tryp, tyr, DPA, ATP.

Experimental

The microburette was calibrated to 0.01 cm^3 by the method described by Vogel[7].

All reagents were of A.R. grade and their standard solutions were prepared in carbonate free deionised water. Copper perchlorate was prepared by treating copper carbonate (A.R.) with 70% perchloric acid (A.R.). It was washed with ethanol till free from excess acid and recrystallized from ethanol. Copper perchlorate solution was standardized by iodometric method[7]. Carbonate free sodium hydroxide and sodium perchlorate solutions were prepared by the method described elsewhere[8] and standardized by standard oxalic acid solution. Nickel perchlorate, was also prepared by the same method.

Determination of formation constants :

Irving-Rossotti titration technique[8,9] was used to determine protonation constants and formation constants of binary and ternary complexes using SCOGS (Stability Constant of Generalized Species) computer programme[10,11].

Formation constants were determined by titrating all solutions potentiometrically against standard (0.02 M) sodium hydroxide solution keeping acid concentration and total ionic strength (I) at 2.00 × 10^{-2} M and 0.2 M respectively.

Formation constants of the ternary complexes MAL, were determined by titrating 50 cm^3 aqueous solution containing M, A and L in the ratio 1 : 1 against standard alkali in dioxane-water (1 : 1, v/v) at 25 ± 1°. Titration was carried out by using TOA pH-meter HM-20S, having an accuracy of ±0.01 pH unit. The glass electrode was calibrated using buffer solution of pH 4.00 and 6.86.

The values of protonation constants of the ligands and the formation constants of the binary complexes have been presented in Table 1. The values of formation constant for the ternary complexes, Δ log K have been presented in Table 2.

Cyclic voltammetry measurement :

Cyclic voltammograms of metal perchlorates and their complexes were recorded at a scan rate of 100 mV/sec. The cathodic potentials (E_{pc}), anodic potentials (E_{pa}) and difference between them (ΔE_p) have been calculated from cyclic voltammograms. Optimum pH for the maximum formation of complexes was obtained from computer output (shown in Table 3). The voltammetric characteristics are presented in Table 3.

Acknowledgement

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