AQUEOUS CHEMISTRY OF ME BIO-METAL (II) COMPLEXES WITH NICOTINIC ACID AND ADENINE

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ABSTRACT

Objective: (i) To determine the stability constant of some bio of some bio-metal and (ii) complexes with nicotinic acid and adenine. The knowledge of stability constant may help in rationalizing our understanding of the behaviors of metal chelate in the solution and thus in biological systems.

Methods: Stock solutions of all reagents were prepared in double distilled water. Metal nitrate solutions were prepared and standardized by EDTA titration. The ionic strength of all mixture solutions was kept 0.1 M $NaNO_3$. The free acid concentration was kept 0.02 M in each case. From the titration curves between pH of solution and volume of NaOH, the species distribution curves were obtained through software with % concentration and pH of the solution. The stability constant of complex in the solution is usually determined by the knowledge of measurement of equilibrium constants (K) for complex forming reaction.

Results: The results have shown that in the case of binary complexes ML_1 and ML_2 with nicotinic acid and adenine, respectively, the order of the stability constants found as Cu > Ni > Co > Cd. While in the case of ternary complexes, the order is almost reversed, as, Ni > Co > Cd > Cu.

Conclusion: It was found that the stability constant of the ternary system is higher than binary system, but the order of the stabilities with metal ions are almost reversed.

Keywords: ???

INTRODUCTION

The study of mixed ligand complexes is one of the major applications of coordination chemistry. It has extreme importance because it helps to predict the probable chemistry of elements in solution. It makes possible to understand the mechanism and kinetics of analytical reactions giving new prospects for the development of selective and sensitive methods for the determination and separation techniques. Further, mixed ligand complexes have received much attention because of their biochemical reactions which often leads to the formation of ternary complexes involving biologically significant ligands through a dynamic equilibrium [1-6].

One of the most common naturally occurring purine bases in a biological system is adenine. It is also found to be associated with all living cells as mono-, di- and triphosphate of a-nucleosides, namely, adenosine monophosphate, adenosine diphosphate, and adenosine triphosphate. These nucleosides play key roles in metabolic processes. Due to the presence of four nitrogen labeled: N(1), N(3), N(7), and N(9) (Scheme 1), it possess chelating properties which make suitable for the activity study and administering metal complexes in the biological system [7-9]. Protonation at N(1) of adenine [10] takes place at pH<4. On the other hand, adenine loses [11] its N(9) proton at pH>10.

Nicotinic acid (Scheme 2), commonly known as vitamin B_3 or niacin(3-pyridine carboxylic acid), a white translucent crystalline solid with a carboxyl side chain at the 3-position, is essential for number of biological and metabolic activities as for healthy skin, cell respiration, circulation and metabolism of carbohydrates, fats, proteins, etc. [12]. It decreases the risk of cardiovascular diseases in a number of controlled human trials by increasing levels of HDL cholesterol in the blood. Nicotinic acid has also been used in the treatment of schizophrenia, Alzheimer [13], and other mental ailments [14].

The increasing importance of ternary complexes, especially those involving ligands containing functional groups identical to those present
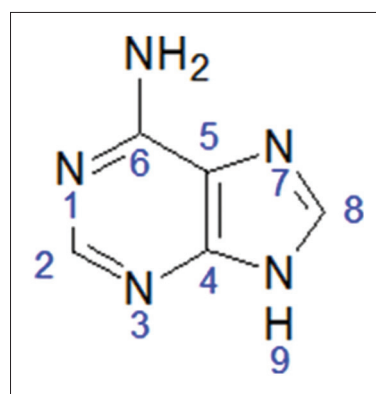
Scheme 1: 9*H*-purin-6-amine
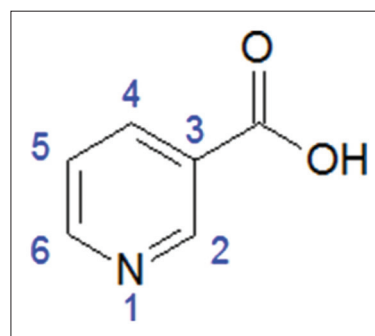
Scheme 2: Pyridine-3-carboxylic acid

in enzymes, *viz.* –COOH, –NH$_2$, etc., is obvious from the application of such complexes in many analytical, biological, and physiological reactions [15,16]. Therefore, to understand the physiological activities of nicotinic acid together with adenine, the study of their interaction with metal ions in an aqueous medium, we have investigated mixed ligand ternary complex equilibria potentiometrically with nicotinic acid as a primary ligand and adenine as a secondary ligand with some biologically activated metals, *viz.* Cu(II), Ni(II), Co(II), and Cd(II). We have also studied the comparative stabilities of binary and ternary complexes.

EXPERIMENTAL

Stock solutions of nicotinic acid and adenine were used as such. Carbonate-free sodium hydroxide solution is prepared by a standard method [17] and standardized against standard oxalic acid. All the reagents and salts were purchased from BDH (India) and were treated as such. Metal nitrate solutions were prepared and standardized by EDTA titration. The other experimental details have been described elsewhere [18].

The ionic strength of all mixture solutions was kept 0.1 M NaNO$_3$. The free acid concentration was kept 0.02 M in each case. The following sets of solutions were prepared keeping the total volume 50 ml in each case. The molar ratios of binary and ternary systems were taken in the same ratios.

(i)   5 ml NaNO$_3$ (1.0 M)+5 ml HNO$_3$ (0.02 M)+H$_2$O
(ii) 5 ml NaNO$_3$ (1.0 M)+5 ml HNO$_3$ (0.02 M)+5 ml L$_1$ (0.01 M)+H$_2$O
(iii) 5 ml NaNO$_3$ (1.0 M)+5 ml HNO$_3$ (0.02 M)+5 ml L$_2$ (0.01 M)+H$_2$O
(iv) 5 ml NaNO$_3$ (1.0 M)+5 ml HNO$_3$ (0.02 M)+5 ml M (0.01 M)+H$_2$O
(v)   5 ml NaNO$_3$ (1.0 M)+5 ml HNO$_3$ (0.02 M)+5 ml M (0.01 M)+
      5 ml L$_1$ (0.01 M)+H$_2$O
(vi) 5 ml NaNO$_3$ (1.0 M)+5 ml HNO$_3$ (0.02 M)+5 ml M (0.01 M)+
      5ml L$_2$ (0.01 M)+H$_2$O
(vii) 5 ml NaNO$_3$ (1.0 M)+5 ml HNO$_3$ (0.02 M)+5 ml M (0.01 M)+
      5 ml L$_1$ (0.01 M)+5 ml L$_2$ (0.01 M)+H$_2$O

Where, M is Cu(II)/Co(II)/Ni(II)/Cd(II) metal ions and L$_1$, L$_2$ are nicotinic acid and adenine, respectively. From the titration curves between pH of solution and volume of NaOH, the species distribution curves (Figs. 1-4) were obtained through software with % concentration and pH of the solution.

RESULTS AND DISCUSSION

The stability constant of complex in the solution is usually determined by the knowledge of measurement of equilibrium constants (K) for complex forming reaction. The knowledge of stability constant is, therefore, of immense help to rationalize our understanding of the behaviors of metal chelate in the solution and thus in biological systems.

Sayce [19] developed a computer-based program Stability Constant of Generalized Species (SCOGS) which employs the conventional non-linear least square approach. It is capable of calculating simultaneously the association/formation constants for any of the species formed in the system containing up to two metals and two ligands and provided that the degree of complex formation should be pH dependent. Thus, SCOGS may be utilized to analyze appropriate pH titration data to yield metal-ion hydrolytic constants and stability constants of simple complexes such as ML$_1$, ML$_2$ and ML$_1$L$_2$. The protonation constants of the ligands were calculated from the potentiometric pH titration data of solutions according to Irving and Rossetti's method [20]. The pH value of solution regulated the equilibrium of metal-ligand complex formation due to the protonation of respective ligands which participated in the complexes formation. At higher pH, titration curves of 1:1:1 ternary complex strongly overlapped with the titration curves of the 1:1binary complexes due to dissociation of binary complexes. The calculated protonation constants of ligand and stability constant of selected bio-metal ions were shown in Table 1.

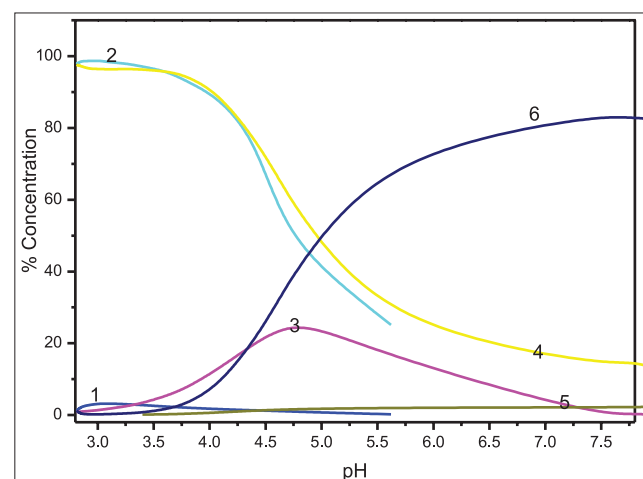The ionization of nicotinic acid and adenine may occur according to the following equilibria.

$$HL_1 \rightleftharpoons H^+ + L_1^- \tag{1}$$

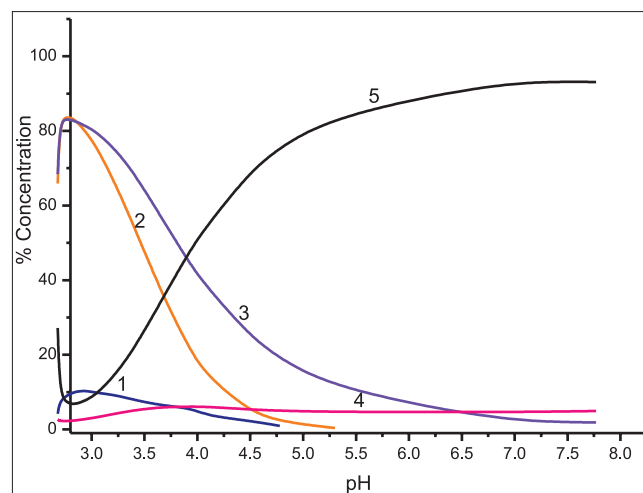**Fig. 1: Species distribution curve for 1:1:1 Co(II)L$_1$L$_2$ ternary complex**

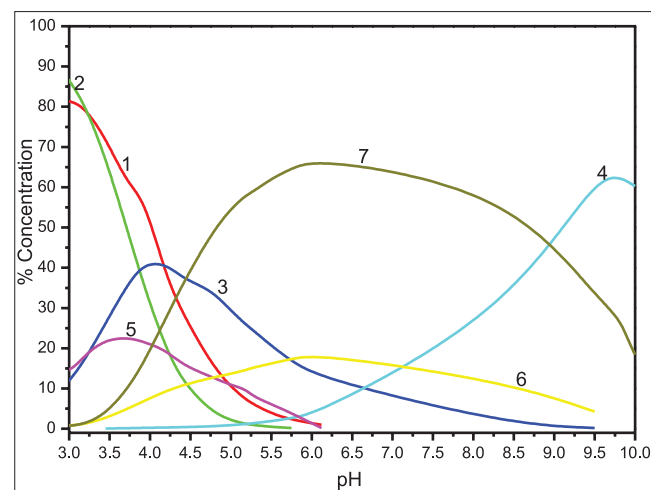**Fig. 2: Speciation curve of Ni(II)L$_1$L$_2$ complexes**

Fig. 3: Species distribution curve of 1:1:1 Cu(II)L$_1$L$_2$ ternary complex
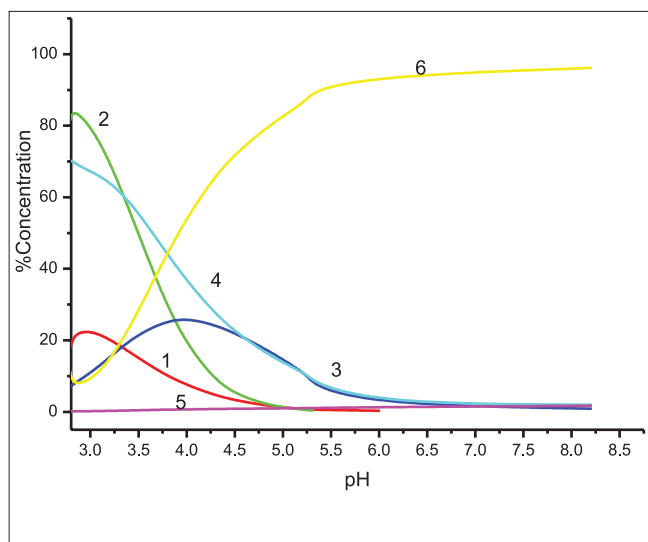
Fig. 4: Species distribution curve for 1:1:1 Cd(II)L$_1$L$_2$ ternary complex

Table 1: Protonation constant, and other related constants of the binary and ternary species of some bio-metal complexes with nicotinic acid (L$_1$) and adenine (L$_2$)

Species	Protonation Constant log (β_{pqrst})						
	Ligand		**Metal hydroxide**		**Metal complex**		
	L$_1$	L$_2$	M (OH)$^+$	M (OH)$_2$	ML$_1$	ML$_2$	ML$_1$L$_2$
H$_2$L	-	13.34	-	-	-	-	-
HL	4.67	9.38	-	-	-	-	-
Cu(II)	-	-	−6.29	−13.10	3.72	8.65	9.64
Co(II)	-	-	−8.23	−17.83	3.60	8.26	12.12
Ni(II)	-	-	−8.10	−16.87	3.63	8.41	12.74
Cd(II)	-	-	−9.84	−15.54	3.51	6.05	11.74

$$K=[H^+] [L_1^-]/[HL_1] \tag{1a}$$

$$H_2L_2 \rightleftharpoons H^+ + HL_2^- \tag{2}$$

$$K_1=[HL_2^-][H^+]/[H_2L_2] \tag{2a}$$

$$HL_2^- \rightleftharpoons H^+ + L_2^{2-} \tag{3}$$

$$K_2=[H^+][L_2^{2-}]/[HL_2^-] \tag{3a}$$

Where: L$_1^-$ represents the dissociated nicotinic acid anion, the ionization constants of the nicotinic acid is K, L$_2^{2-}$ represents the fully dissociated adenine anion, the ionization constant of the H$_2$L$_2$ is K$_1$ and of HL$_2^-$ is K$_2$.

The formation of ternary complexes in an aqueous solution may be conveniently expressed with the help of the following equilibrium:

$$pM_1+qM_2+rL_1+sL_2+tOH \rightleftharpoons (M_1)_p(M_2)_q(L_1)_r(L_2)_s(OH)_t \tag{4}$$
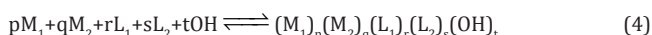
The overall stability constant can be given by the following equation:

$$\beta_{pqrst}= [(M_1)p(M_2)q(L_1)_r(L_2)_s(OH)_t]/[M_1]^p[M_2]^q[L_1]^r[L_2]^s[OH]^t \tag{5}$$

The stoichiometric numbers p, q, r, s are either zero or positive integer and t is a negative integer for a protonated species. Hydroxo or deprotonated species carries positive values and zero for a neutral species.

The overall stability constant (β_{pqrst}) defined may be used to calculate the species distribution curves that provides the clues for the formation

equilibria of the complexes. The following equilibria have been proposed on the basis of distribution curve through SCOGS,

$$L_1^- + M^{2+} \rightleftharpoons ML_1^+ \tag{6}$$

$$L_2H^- + M^{2+} \rightleftharpoons ML_2 + H^+ \tag{7}$$

The formation of ternary complex may be explained as per the following equilibrium:

$$ML_1 + L_2H^- \rightleftharpoons MHL_1L_2^- \tag{8}$$

$$ML_1^+ + L_2H^- \rightleftharpoons ML_1L_2^- + H^+ \tag{9}$$

Other general hydrolytic equilibrium can be shown as:

$$M^{2+} + H_2O \rightleftharpoons M (OH)^+ + H^+ \tag{10}$$

$$M^{2+} + 2H_2O \rightleftharpoons M (OH)_2 + 2H^+ \tag{11}$$

The ternary (1:1:1) complexes have been used in this study to ensure the exclusive formation of the ML$_1$L$_2$ type complex, considering protonation constants of the ligand and hydrolytic constants of the metal (M^{2+}) aqueous ions.

The species distribution curve for 1:1:1 Co(II) L$_1$L$_2$ ternary complex shown in Fig 1. The curve shown in the beginning of the reaction protonated species start to form. The protonated species HL$_1$ form in lower concentration and become constant with increasing pH whereas another protonated species H$_2$L$_2$ form in higher concentration at lower pH and then to be decreased with increasing pH protonated species HL$_2$ formed slowly and attain a maximum concentration at 4.8 pH after that to be decreased as binary species start to form ML$_1$ binary species formed in higher concentration than the ML$_2$ binary species. Formations of ternary Co(II)L$_1$L$_2$ species increased with increasing pH and attain a maximum concentration of 82.9% at (pH ~7.3).

The speciation curve of Ni(II)L$_1$L$_2$ complexes shown in Fig. 2 clearly reveals that at the starting of reaction the protonated species HL$_1$ formed in very small extent and protonated species H$_2$L$_2$>HL$_1$ increases with increasing pH like other binary ML$_2$ species formed in lower concentration and become constant with increasing pH. Binary species ML$_1$ get dissociate with increasing pH as the ternary species start to formed and attain a maximum concentration of 93.2% at (pH ~7.4) and become constant.

Species distribution curve of 1:1:1 Cu(II)L$_1$L$_2$ ternary complex shown in Fig. 3; all the protonated species start to formed as the reaction begin and decrease with increasing pH binary species formed with the dissociation of protonated species metal mono-hydroxide species is also formed and increased with increasing pH. The ternary mixed ligand metal complex formed gradually as the pH increase and attains a maximum concentration 67.4% (pH ~6.1) after that ternary species is decreased as that metal monohydroxide is dominated among all the species formed.

The species distribution curve for 1:1:1 Cd(II)L$_1$L$_2$ ternary complex shown by Fig. 4. All the protonated species formed in higher concentration at lower pH and decreased with increasing pH and the dissociation of protonated species both the binary species formed in lower concentration and become constant with increasing pH; while, the ternary species formed with increasing pH and attained a maximum concentration at 96.2% (pH ~8.2) after that it decreased sharply.

The results have shown that in the case of binary complexes ML$_1$ and ML$_2$ with nicotinic acid and adenine, respectively, the order of the stability constants found as Cu > Ni > Co > Cd. While in the case of ternary complexes, the order is almost reversed, as, Ni > Co > Cd > Cu. The reason for the maximum stability of Ni^{2+} ternary complex may be

attributed to the presence of vacant inner "3d" orbital for the formation of dsp^2 hybridized square planar complex without any steric hindrance. In other cases, which may preferred to form octahedral complexes may suffer with steric hindrance, which in turn reduced their stability. Moreover, the results are in good agreement with the literature.

CONCLUSION

Overall formation constant, the percentage of species formed, and relative stability of binary and ternary complexes was investigated. The ternary complexes occur in larger concentration at higher pH in each of the systems studied. At high pH, it was observed that 1:1:1 ternary complex titration curves strongly overlap with the titration curves of the 1:1 binary complexes due to dissociation of binary complexes which also depend on the nature of both metal and ligand. The protonation constants of ligand and stability constant of selected various bio-metal complexes were calculated. It was found that the stability constant of the ternary system is higher than binary system, but the order of the stabilities with metal ions are almost reversed.

ACKNOWLEDGMENT

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