Mixed Ligand Complexes with Nucleic acid Constituents-A pH-metric Study

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Formation constants of ternary complexes of Co(II), Ni(II), Cu(II) and Zn(II) with Kojic acid or Maltol in presence of nucleic acid constituents (viz. Adenine, Hypoxanthine, Guanine, Adenosine, Inosine and Guanosine) have been determined pH-metrically. The ligands Kojic acid or Maltol coordinate as secondary ligands in presence of nucleic acid constituents under study.

It is well known that hydroxy γ -pyrones and their derivatives play an important role in a number of natural systems. These compounds are extensively used as fugicides and insecticides [1]. In present communication, we report the interaction of nucleic acid constituents with bivalent metal ions in presence of hydroxy γ - pyrone in aqueous medium at 30°C and I=0.1 M KNO_3.

The ligands used in this study include Adenine, Hypoxanthine, Guanine, Adenosine, Inosine, Guanosine, 3-Hydroxy-2-methyl-pyran-4-one(Maltol) 3-Hydroxy-6-(hydroxymethyl)-pyran-4-one (Kojic acid).

EXPERIMENTAL

3-Hydroxy-2-methyl-pyran-4-one (Maltol), 3-Hydroxy-6-(hydroxymethyl)-pyran-4-one (Kojic acid) were obtained from Fluka (Switzerland). The other ligands - Adenine, Hypoxanthine, Guanine, Adenosine, Inosine and Guanosine were obtained from Aldrich Chemical Company. All bivalent metal ions, EDTA, potassium hydrogen phthalate, KNO_3, NaOH were of BDH AnalaR grade. A stock solution of bivalent metal ions were prepared and standardized by the various methods available in literature [2,3]. Carbonate-free sodium hydroxide was prepared and standardized by titrating with potassium hydrogen phthalate. Acid dissociation constants of the free ligands and formation constants of metal complexes were determined by potentiometric titrations of the various ligands and metal - ligand mixtures (in the ratio 1:1 and 1:1:1) with standard carbonate-free NaOH. The pH measurements were carried out with a Control dynamics pH meter fitted with gel filled combined electrode assembly.

RESULTS AND DISCUSSION

Acid Dissociation Constants

The free ligand titration curves for the mono-protonated form of all the ligands under study, show a steep inflection at

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a=1 (where a = moles of base added per mole of ligand). The pK_a and pK_{2a}^{M}, were calculated in the buffer region a = 0 to a = 1 and a = 1 to a = 2 respectively. The pK_a's calculated are in good agreement with literature values.

Binary Systems

The potentiometric titration curves for the binary 1:1 M(II)-ligand systems show a single steep inflection at m = 1 (where m = moles of base added per mole of metal ion). The formation constants for the binary complexes were calculated in the buffer region m = 0 to m = 1. Once again the stability constants obtained are in good agreement with literature values. The trends with respect to ligands and with respect to metal ions are discussed elsewhere [4].

Ternary Systems

The potentiometric titration curves (Fig. 1) of the 1:1.:1 ternary system [M(II)-L-Kojic acid] show inflection at m = 1 and another feeble inflection at m = 2. The ternary curve coincides with the binary titration curve of [M(II)- Guanosine], in the beginning upto m = 1 and later it deviates from the curve indicating stepwise formation. The stability constants of the 1:1:1 ternary complexes [M(II)-L-Kojic

Table 1

Log K of Ternary Complex with Bivalent Metals
Kojic Acid pK_a = 7.62; Maltol pKa = 8.55 as Secondary Ligands in presence of Nucleic acid Constituents; T = 30°; I = 0.1M KNO_3; Medium = Aqueous

System	Co(II)	Ni(II)	Cu(II)	Zn(II)
Binary Complex with Kojic Acid				
log K^{M}_{ML} of KA	4.75	4.93	6.57	5.14
Ternary Complexes with Kojic acid as Secondary Ligand				
Adenine + KA	4.59±0.03	4.81±0.08	6.48±0.02	5.04±0.05
Hypoxanthine + KA	4.63±0.04	4.89±0.06	6.50±0.08	5.01±0.04
Adenosine + KA	4.64±0.05	4.99±0.08	6.69±0.05	5.18±0.06
Ionosine + KA	4.59±0.06	4.76±0.09	6.51±0.08	4.94±0.06
Guanosin + KA	4.85±0.05	5.09±0.05	6.78±0.07	5.22±0.08
Binary Complex with Maltol				
log K^{M}_{ML} of KA	5.35	5.57	7.61	5.77
Ternary Complexes with Maltol as Secondary Ligand				
Adenine + MA	5.30±0.09	5.61±0.04	7.59±0.05	5.74±0.01
Hypoxanthine + MA	5.28±0.08	5.59±0.05	7.57±0.05	5.71±0.07
Adenosine + MA	5.33±0.05	5.67±0.07	7.76±0.01	5.83±0.07
Ionosine + MA	5.23±0.03	5.51±0.08	7.58±0.09	5.69±0.08
Guanosin + MA	5.51±0.01	5.83±0.09	7.81±0.08	5.98±0.01

Guanine titration could not be carried out because of the insolubility of the ligand in aqueous medium

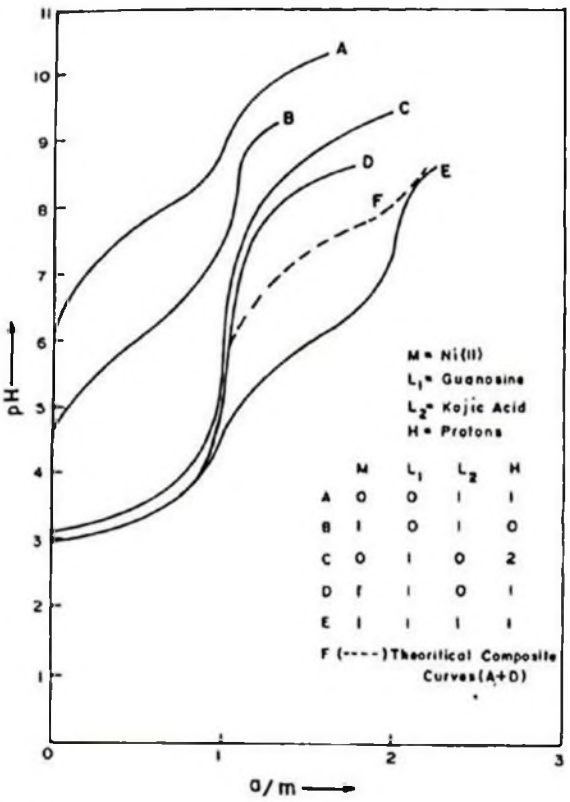


Fig1 : Titratation Courves with Kojic Acid

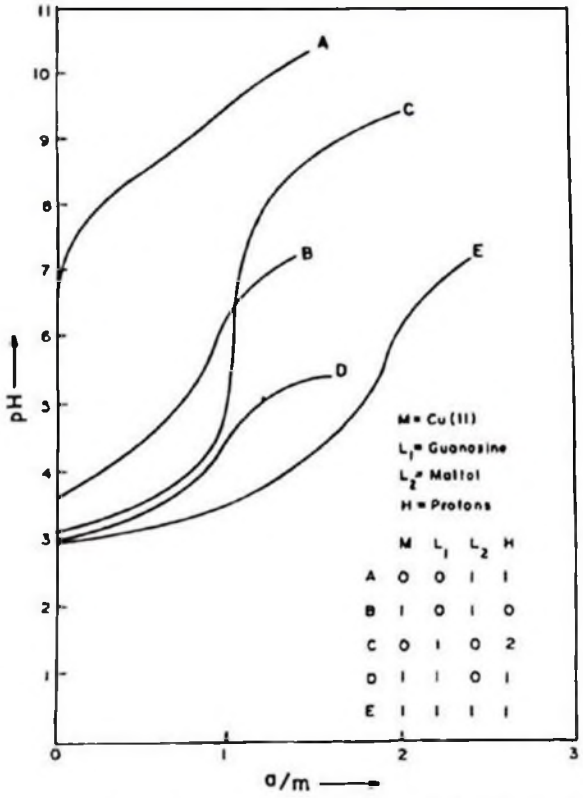


Fig2 : Titratation Courves with Maltol

Table 2

Comparison of Stability of Binary and Ternary Complexes with Nucleic acid constituents (Δlog K Values)

Medium Aqueous: I = 0.1 M KNO_3; T = 30°C

System	Co(II)	Ni(II)	Cu(II)	Zn(II)
Adenine +KA	-0.16	-0.12	-0.09	-0.10
Hypoxanthine + KA	-0.12	-0.04	-0.07	-0.13
Adenosine + KA	-0.11	+0.06	+0.12	+0.04
Ionosine + KA	-0.16	-0.17	-0.06	-0.20
Guanosin + KA	+0.10	+0.16	+0.21	+0.08
Adenine + MA	-0.05	+0.04	-0.02	-0.03
Hypoxanthin + MA	-0.07	+0.02	-0.04	-0.06
Adenosin + MA	-0.02	+0.10	+0.15	+0.06
Ionosine + MA	-0.12	-0.06	-0.03	-0.08
Guanosin + MA	+0.16	+0.26	+0.20	+0.21

acid] were calculated in the region m = 1 to m = 2 by considering that the 1:1 [M(II)-L] complex is completely formed before the coordination of secondary ligand (Kojic acid or Maltol) take place. The theoretical composite curve is constructed by adding horizontal distances of binary complex curve and free ligand curve of the secondary ligand (Kojic acid / Maltol). Again non-superimpossable nature of theoretical composite curve over the mixed ligand curve also indicates the formation of stepwise complexes.

But in the case of Cu(II) complexes, the mixed ligand titration curve E (Fig. 2) shows a single inflection at m = 2, indicative of release of two protons simultaneously upon coordination. The related equilibrium can be represented as follows :

$$Cu(II) + AH + HL^{\bullet} \longrightarrow [Cu\text{-}A\text{-}L]^{\bullet} + 2H^{\bullet} \qquad (1)$$

The stability constants for the ternary complexes and their corresponding ΔlogK values are given in Table 1 & 2 respectively.

Δlog K values are usually negative. In the absence of electronic effect [5] or of any specific interaction between the two ligands [6,7] and assuming all the metal ions are in octahedral geometry the expected statistical factor for these systems would be -0.2. Often the observed values are about the same as expected statistically. Larger negative than -0.2 for Δlog K suggests that some other factors apart from statistical reasons are causing destabilisation. The data in Table 2 show that the observed Δlog K values are less negative than -0.2. The positive effects causing stabilisation in ternary complexes may be due to π bond formation between metal ion and ligands.

A comparison of the Δlog K values reveals

(a) the order of stability in terms of secondary ligands is as Maltol > Kojic acid. This order is in line with basicity order of these ligands.

(b) The order of stability of ternary complexes in terms of metal ions is in conformity with Irving Williams natural order of stabilities [8].

(c) The stability sequence of ternary complexes with respect to i) Nucleic bases is as Hypoxanthine > Adenine and ii) Nucleosides is as Guanosine > Adenosine > Inosine. Srivastava [9] reported the binary stability constants of Cu(II) with nucleosides. Stability order reported decrease in the order : Guanosine > Cytidine > Adenosine.

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REFERENCES

1. J.R. Schenk and M.A. Spielman, *J. Am. Chem. Soc.*, **67** (1945) 2279.
2. H.A. Flaska, *EDTA Titrations*, **Pergamon Press, Oxford** (1964).
3. G. Schwarzenbach, *Complexometric Titrations*, **Interscience, New York** (1957) pp. 77-82.
4. N. Yogi Babu, **Ph.D. Thesis** submitted to Osmania University (1996).
5. H. Sigel, *Angew. Chem.*, **87** (1975) 391.
6. H. Sigel, B.E. Fischer and B. Prijis, *J. Am. Chem. Soc.*, **99** (1977) 4489.
7. H. Sigel and C.F. Nauman, *J. Am. Chem. Soc.*, **98** (1976) 285.
8. H. Irving and R.J.P. Williams, *J. Chem. Soc.*, **(1953)** 3192.
9. V.K. Srivastava, *J. Ind. Chem. Soc.*, **6** (1969) 149.