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Research Article

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Quantitative study on the interaction of transition metal ions with allopurinol and 4-aminobutyric acid in aqueous solution

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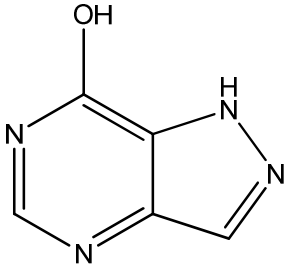
ABSTRACT

The stability constant values of ternary complexation by transition metal ions such as Co(II), Zn(II) with allopurinol and 4-aminobuytyric acid has been evaluated by potentiometry. The ionic strength was maintained by NaNO3 A computer based SCOG program is used to calculate stability constants. The trend in the stability constants varies for ternary complexes Co(II) > Zn (II) > Cu (II) > Ni(II).

INTRODUCTION

Allopurinol is chemically known as 1,2-Dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one . Its structure is.



The allopuriInol is used to reduce the production of uric acid. It is used as medicinal drug. It has two coordinating sites containing N- and /or O-donar atoms. Hence we decided that it should be used as ligand for present investigation of stability constant of ternary complexation. Recently we used different medicinal drugs which form complexes with transition metal ions.[1-6]

EXPERIMENTAL SECTION

Materials: The chemicals such as NaOH, $NaNO_3$, HNO_3 & metal salts were of AR grade and was purchased from Sd fine chemical Ltd. The solutions used in the potentiometric titration were prepared in double distilled water. The NaOH solution was standardized against oxalic acid solution (0.1M) and standard alkali solution was again used for standardization of HNO_3.. Metal salt solution was also standardized using EDTA titration. All the measurements were made at constant ionic strength of 0.1 M $NaNO_3$.The thermostat model SL-131 (Adar Dutt and Co(India) Pvt. Ltd. Mumbai) was used to maintain the temperature constant. The pH measurement were made using a digital pH meter model Elico L1-120 in Conjunction with a glass and reference calomel electrode (reading accuracy ± 0.01 pH units) the instrument was calibrated at pH 4.00 ,7.00 and 9.18 using the standard buffer solutions .

Potentiometric procedure: The proton ligand stability constants (protonation constant) of the primary and secondary chelating agents, and metal ligand stability constants (formation constants) of the complexes were determined by adopting the method suggested by Irving and Rossotti . For the determination of pK and logk values, three sets of the following solutions were titrated potentiometrically against carbonate free sodium hydroxide solution.

i. *Free acid titration*: HNO_3 (0.2M) 5ml.
ii *Free acid + ligand1 titration*: HNO_3 (0.2M) 5ml+Allopurinol (0.01M) 5ml.
iii *Free acid + ligand1 + metal titration* HNO_3 (0.2M) 5ml + Allopurinol (0.01M) 5ml + metal Nitrates (0.01 M) 5ml
iv *Free acid +.ligand2* HNO3 (0.2M) 5ml + 4-amino butyric acid (0.01M)
v *Free acid + ligand2 + metal ion titration*: HNO3 (0.2M) 5ml + Allopurinol (0.01M) 5ml + 4-amino butyric acid (0.01M) + metal Nitrates (0.01 M) 5ml
vi *Free acid + ligand1 +ligand2 + metal ion titration*: HNO3 (0.2M) 5ml + 4-amino butyric acid (0.01M) + metal Nitrates (0.01 M) 5ml

All the systems were studied in 0.1 M $NaNO_3$ 5ml ionic strength at 298K temperature. The total volume of the test solution was raised to 50ml with double distilled water. The titrations were carried out in a 100ml beaker and stirred with magnetic stirrer; the reaction solution was potentiometrically titrated against the standard alkali NaOH (0.2M) at 298K temperature. The titrations were stopped when pH reading became unstable as result of hydrolysis of metal ions, in some cases the titration was stopped in the beginning of precipitation

RESULTS AND DISCUSSION

The titrations curves are analysed and protonation constant is determined using pointwize calculation and half integral method. The protonation constant for Allopurinol is found to be 9.36. The basic pKa may be because of nitrogen imbedded in the ring. There are four nitrogen present in the structure, out of these four, two are tertiary and remaining two are secondary nitrogen. One ketonyl group is also present. The pK value is in basic range indicating the involvement of nitrogen atom for binding purpose. Out of these two types of nitrogen, the secondary nitrogen is found to be dominating group.It is reported that the pKa values for Diadenosine 5', 5'', P^1P^4 tetra-phosphate (AP_4A) which is a micro molecular containing free NH_2 attached to ring along with tertiary nitrogen, enclosed in the ring structure. The values are reported to be 8.74 & 11.32 using potantiometry [7] In the same way the protonation constant related to the imidazole rings are in the range of hexadiene containing peptides. [8] The presence of imidazolyl side chains results in some decrease in the basicity of the amino groups. [9]

In the bianary titration using metal and allopurinol , the metal ligand stability constants are evaluated, The observed order in the stability constants is

Fe (III) < Cu(II) < Ni(II) < Zn(II) < Co(II).

Assuming the interaction of the metal ion and the ligand was electrostatic; the stability constant for complexes of metal ions of the same charge should be inversely proportional to metal ion radii for ions of similar electronic configuration this relationship may be approximately valid, but incompletely fails with metal ions of different groups of the periodic system. The metal chelates of the ligand show more or less linear behavior when their logk values are plotted against the reciprocal ionic radii R.

Allopurinol in complexation is used as one of the ligand, along with secondary carboxylic acids. The potentiometric method Kelvin BJerrum method is used as discussed in the chapter II. The metal ligand stability constants for binary as well as ternary are determined for which Δlog k values has been evaluated. The pKa values and $LogK_1$, $LogK_2$ values for different acids has been shown in the table .2.

Different methods are known to estimate the formation of ternary complexes Δlog k has been widely accepted and used for many years and the advantages in using ΔlogK in comparing stabilities of ternary and binary complexes have been reviewed. The parameter ΔlogK expresses the effect of bounded primary ligand (AMBI in this case) towards an incoming secondary ligand $[L]_1$. ΔlogK values are positive when indicates that ternary complex more stable as compared to binary complexes.

The theoretical Δlogk value, for a square planner copper (II) complex is – 0.6 the tendency to form ternary complexes was compared with this value, so that if Δlogk is greater than – 0.6, this should be taken to indicate that the ternary complex is favored. The ΔlogK value for ternary complexes are more positive than –0.6. This may be

explained on the premise that the non coordinating aromatic side groups of these acids can approach the aromatic moiety of primary ligand stacking interaction.

Since the presence of an aromatic ring above the Cu(II) coordination plane is probably essential for preferential formation of ternary complexes [10].

In the present investigation we get following order of stability constant

Cu(II) > Ni(II) > Co(II) > Zn(II).

For ternary complexation of transition metal ions with N-(2-hydroxybenzyl)-L-histidine & 1.10 phenanthroline (phen)-2, 2 bipyridine (bipy), ethylenediamine (en) shows the order Co(II) < Ni(II) < Cu(II) < Zn(II) [11]The difference in order may be due to the nature of ligands present for ΔlogK values. In the case of Ni(II) & Cu(II) is much higher greater than one which can only justified by the presence of interaction between the ligands. This much higher stability of the ternary complexes can be expected since formation of stacking interactions and possibly formation of Π-back bonding a synergy that will favored considerable the formation of these complexes [12].

Table:1 Binary and ternary complex formation parametrs

Ligands [L_2]	Metal	$Log\beta_L$ $_{LogK1}$ (Logk2)	$Log\beta_R$ $_{LogK1}$ (Logk2)	$Log\beta_{MLR}$	ΔLogK	KL_1	KL_R	Kr
4-amino butyric acid	Fe(III)	03.25	3.42					
	Co(II)	03.28	2.55 (0.67)	8.3304	2.5004	5.0504	5.7804	63.5656
	Ni(II)	03.13	4.33	9.7109	2.1009	6.4309	5.3809	86.6916
	Cu(II)	03.10	3.09	7.8009	1.4109	4.5209	4.7109	54.4841
	Zn(II)	03.23	3.42	7.1504	0.4504	3.8704	3.7304	44.4283

For 4-aminobutyric acid the stability constant difference i.e. Δlogk is positive(table 1) and greater than one except in the case of Zn this indicates that ternary complexation is more favored compound to binary. The stability constant for ternary complexation shows the trend Ni(II) > Co (II)> Cu(II) > Zn(II).The ternary complexation of Fe(III) was not possible, because of precipitate formation.

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The SCOG programme is used to identify various species present in the solutions along percentage concentration of free metal and free ligand etc. These are plotted pH (Fig 1 to 4). The system involving Allopurinol (L_P) and 4-aminobutyric acid (L_S) shows different equilibria such as

For six species

$HL_P \rightleftharpoons H_+ L_P$ C_1

$HL_S \rightleftharpoons H_+ L_S$ C_2

$M_+ L_P \rightleftharpoons ML_P$ C_3

$M_+ L_S \rightleftharpoons ML_S$ C_4

$M L_{S+} L_S \rightleftharpoons ML_{2s}$ C_5

$M_+ L_{P+} L_S \rightleftharpoons M L_P L_S$ C_6

For seven species

$HL_P \rightleftharpoons H_+ L_P$ C_1

$H_2L_S \rightleftharpoons H_+ HL_S$ C_2

$HL_S \rightleftharpoons H_+ L_S$ C_3

$M_+ L_P \rightleftharpoons ML_P$ C_4

$M_+ L_S \rightleftharpoons ML_S$ C_5

$M L_{S+} L_S \rightleftharpoons ML_{2s}$ C_6

$M_+ L_{P+} L_S \rightleftharpoons M L_P L_S$ C_7

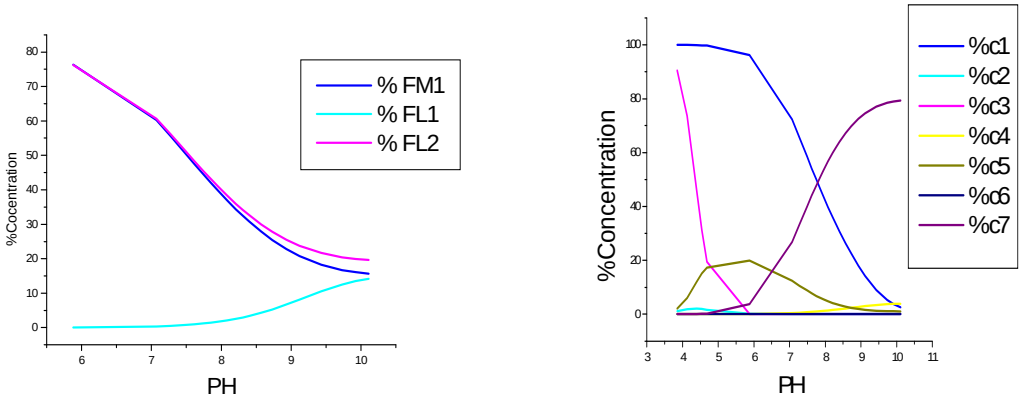

Fig 1 (a)% concentration of free Cobalt(FM), Free Allopurinol (FL_1) and free 4- aminobutyric acid
(b) Species disturbed curve for Cobalt(II)+ Allopurinol + 4- aminobutyric acid

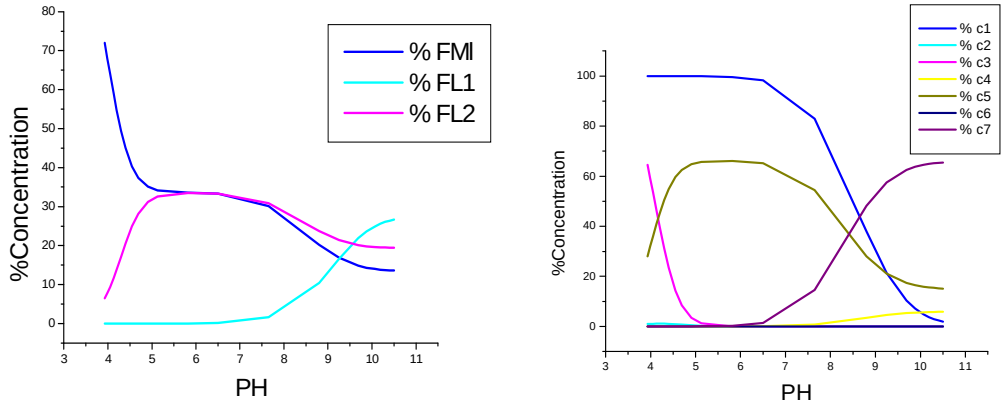

Fig 2 (a)% concentration of free Copper(FM), Free Allopurinol (FL_1) and free 4- aminobutyric acid
(b) Species disturbed curve for Copper(II)+ Allopurinol + 4- aminobutyric acid

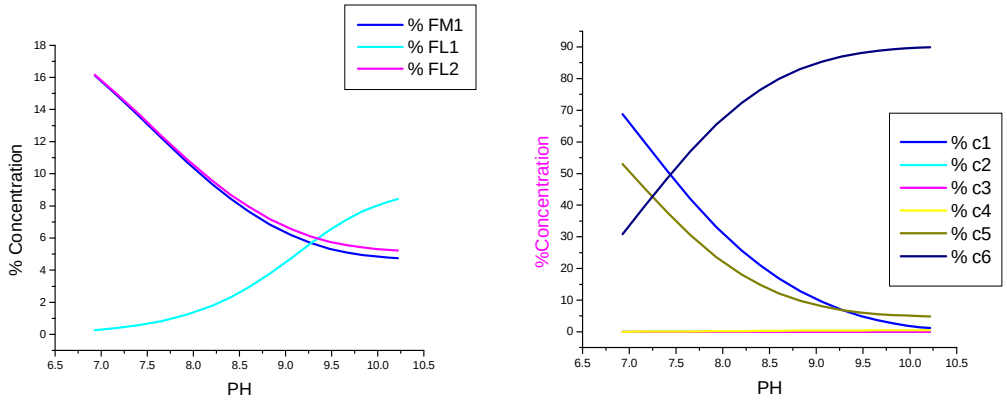

Fig 3(a)% concentration of free Nickel(FM), Free Allopurinol (FL_1) and free 4- aminobutyric acid
(b) Species disturbed curve for Nickel(II)+ Allopurinol + 4- aminobutyric acid

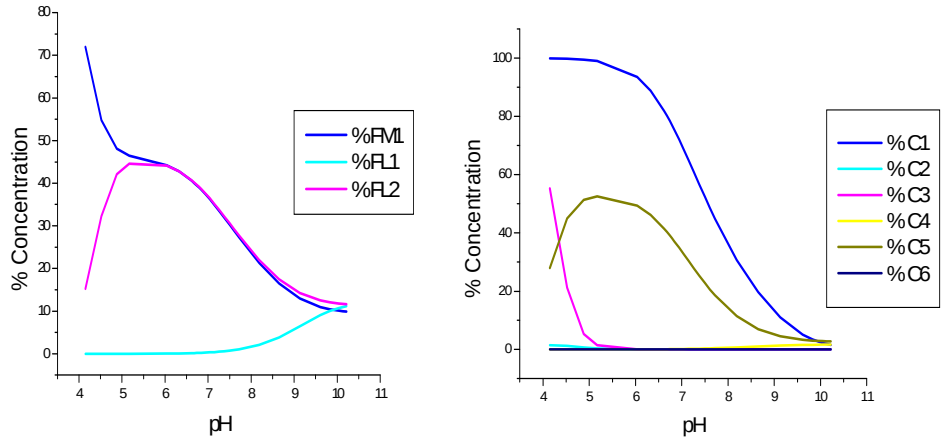

Fig 4 (a)% concentration of free Zinc(FM), Free Allopurinol (FL_1) and free 4- aminobutyric acid
(b) Species disturbed curve for Zinc(II)+ Allopurinol + 4- aminobutyric acid

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