Received: 27-12-2013
Accepted: 25-01-2014

ISSN: 2321-4902
Volume 1 Issue 5

Online Available at www.chemijournal.com

International Journal of Chemical Studies

Studies on metal ligand stability constant of allopurinol and succinic acid with some metal ions in aqueos media

Jamilkhan Pathan [1], D M Janrao [2], B R Agarwal [2], Mazahar Farooqui [3*]

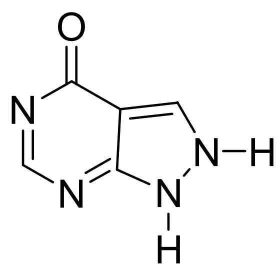
1. Sant Ramdas College, Ghansawangi. Dist Jalna.
2. J. E. S. College, Jalna, (M.S.), India
3. Dr. Rafiq Zakaria College for women, Aurangabad, India. 431001
   *[Email: Mazahar_64@rediffmail.com, Tel: 91 9422214785, (Off) +91 240 2402462]

The PH-Metric stability constant of binary & ternary complexes of allopurinol with bivalent metal & Succinic acid in aqueous solution has been determined. The ionic strength was kept constant by sodium nitrate. The stability constant of ternary complexes have been quantitatively compared with those of corresponding binary complexes in terms of the parameter ΔlogK.

Keyword: pH-metric; stability constant; binary & ternary complexes; allopurinol; Succinic acid.

1. Introduction

For the last few years the interest has been increased to study the interaction between metal ions and biologically active compounds. This may due to the fact that some of the complexes show different activities than the drug allopurinol itself [1-3]. Allopurinol is also known as lopurin, zyloprim, antisuril etc. molecular formula $C_5H_4N_4O$ molecular wt.136.1 a xanthine oxidase inhibitor that decreases uric acid production. It also acts as an antimetabolite on some simple organisms.



It has 4- nitrogen heteroatoms in the ring system. Nitrogen contains lone pair electrons which can be used for the bonding purpose. Succinic acid possesses oxygen donor atom & can form complex with metal with in presence of allopurinol there will be competition for binary both of these ligands with metal ion. At low pH, metal coordinates with o-atom is replaced by deprotonated N-atom involving a structural equilibrium, this results in the formation of strong binary complexes [4] in constitution of previous work [5-9] we hereby report coordination behavior of Allopurinol elements belonging to transition metals.

2. Material and Methods

All chemicals used were of analytical grade. Allopurinol was obtained from Dr. Zahed Zaheer (Assi. prof. Y. B. Chavan College of pharmacy, Aurangabad.) The ligands & metal nitrates were obtained from research laboratory. The potentiometric pH titrations of ligands were performed at 30 ^{0}C fresh solids were weighed out directly in to the reaction cell. The stock solution of analytically pure cobalt nitrate was prepared and standardized volumetrically by titration with the disodium salt of EDTA in the presence of suitable indicator carbonate free NaOH was prepared & was standardized by titration with potassium hydrogen phthalate. The ionic strength was kept constant using 0.1M $NaNO_3$ as supporting electrolyte and relatively low concentration of ligands and metal ions (10^{-3}) M. An Elico digital pH meter fitted with a combined glass micro-electrode was used to determined hydrogen ion concentration. For determination of pH values below 3.5 & above 10.5. the system was calculated with standard HCl & NaOH solution respectively, each experiment was repeated at least three times.

3. Results and Discussion

The dissociation constant of ligands Allopurinol were determined by using the data from the experimental titration curve with help of computer program. The equilibria involved for the dissociation reaction are.

$$H_2L \overset{K_1}{\rightleftharpoons} HL + H^+$$

$$HL \overset{K_2}{\rightleftharpoons} H^+ + L$$

$$H_2L \overset{K}{\rightleftharpoons} 2H^+ + L$$

3.1 Stability Constant

To determine stability constant for 1:1 binary metal ligand complexes the following equation were used

$$M + L \rightleftharpoons ML$$

$$K^{L}_{(ML)} = \frac{[ML]}{[M][L]}$$

Table 1: Metal ligand stability constant of APN.

Allopurinol-	Pk_1	pK_2	$logK_1$	$logK_2$
Fe(II)	-	9.36	2.57	-
Co(II)	-	9.36	3.28	-
Ni(II)	-	9.36	3.13	-
Cu(II	-	9.36	3.10	-
Zn(II)	-	9.36	3.23	-

Table 2: Metal ligand stability constant of Succinic Acid

Succinic acid	Pk_1	pK_2	$logK_1$	$logK_2$
Fe(II)			3.32	
Co(II)	2.62	3.89	3.33	3.29
Ni(II)			2.93	
Cu(II			2.94	
Zn(II)			3.41	

The protonation constant of allopurinol was determined by using following equation.

$$n^{-} = \frac{(v_3 - v_2)}{(v_0 + v_2)} \frac{(N + \varepsilon^0)}{n^{-}{}_A T^0{}_M}$$

Table 3: Stability constant of ternary complexes

Allopurinol-succinic acid	$log\beta_L$		$log\beta_R$		$log\beta_{MLR}$	$\Delta logK$	KL_L	KL_R	Kr
	$logK_1$	$logK_2$	$logK_1$	$logK_2$					
Fe(III)	03.25		03.32						
Co(II)	03.28		03.33	03.29	7.1548	0.5448	3.8748	3.8248	44.5812
Ni(II)	03.13		02.93		7.3109	1.2509	4.1809	4.3809	47.3893
Cu(II	03.10		02.94		9.0838	3.0438	5.9838	6.1438	76.4755
Zn(II)	03.23		03.41		6.6539	0.0139	3.4239	3.2439	37.6344

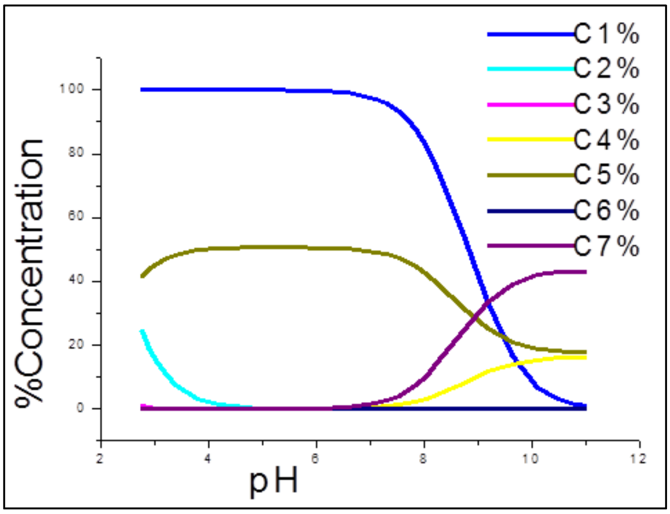


Fig 1: Species distribution curves for APN +SA +Fe(III)

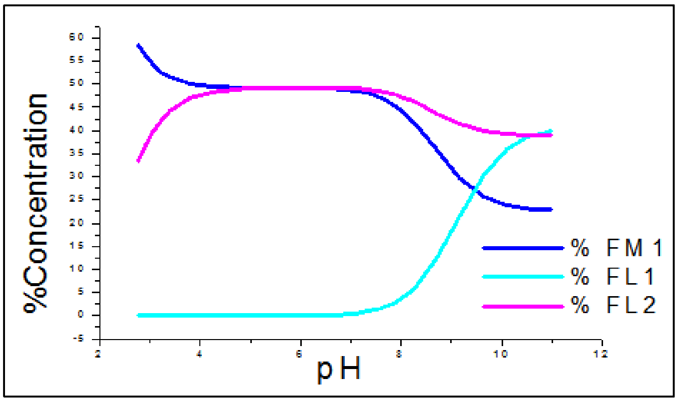


Fig 2: Percentage conc. of free metal and free ligands for APN +SA +Fe(III)

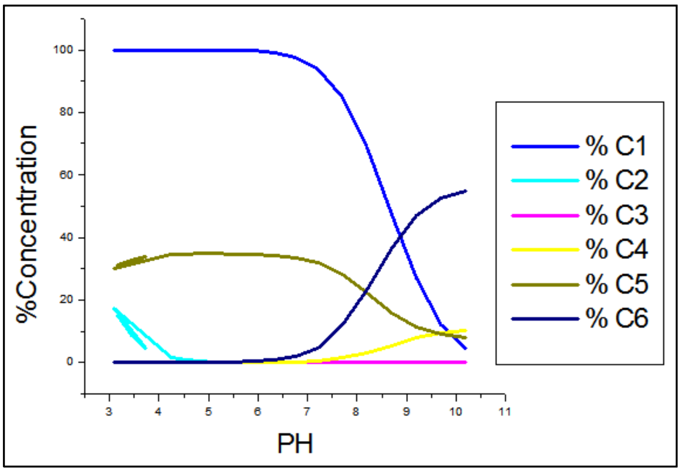


Fig 3: Species distribution curves for APN +SA +Co(II)

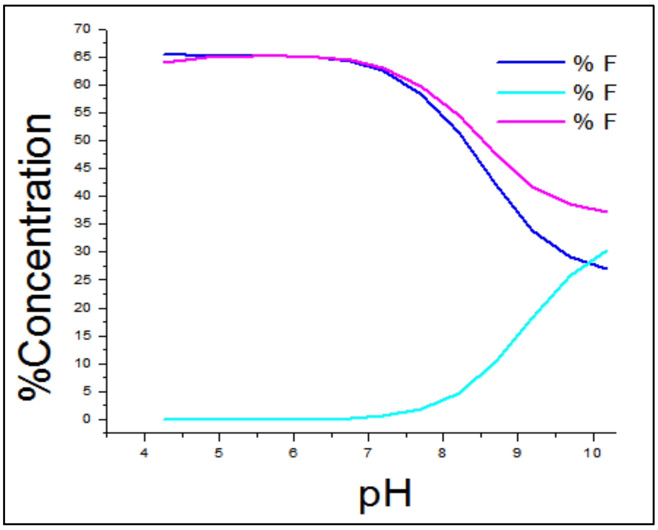


Fig 4: Percentage conc. of free metal and free ligands for APN +SA +Co(II)

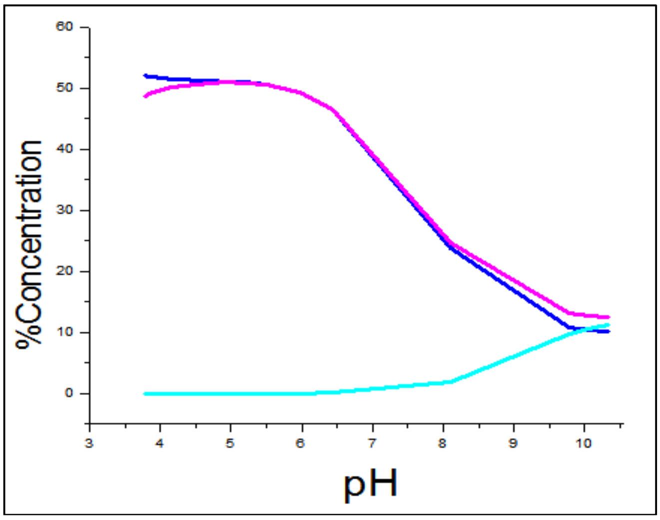


Fig 5: Percentage conc. of free metal and free ligands for APN +SA +Cu(II)

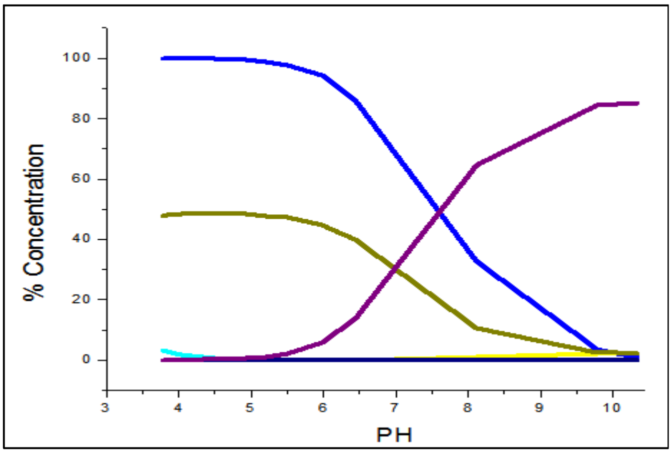


Fig 6: Species distribution curves for APN +SA +Cu(II)

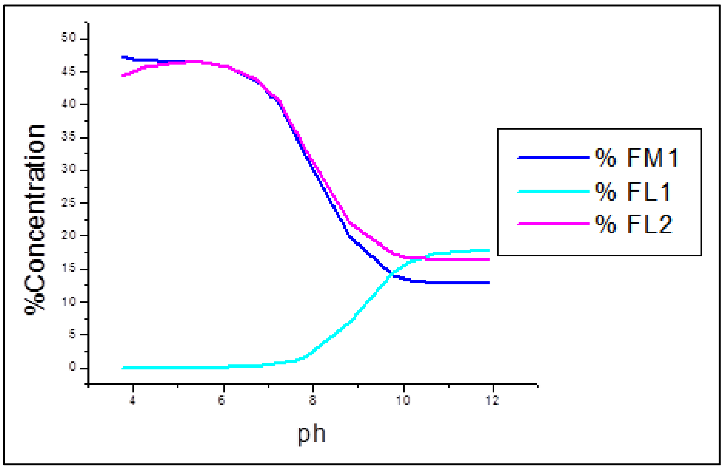


Fig 7: Percentage conc. of free metal and free ligands for APN +SA +Zn(II)

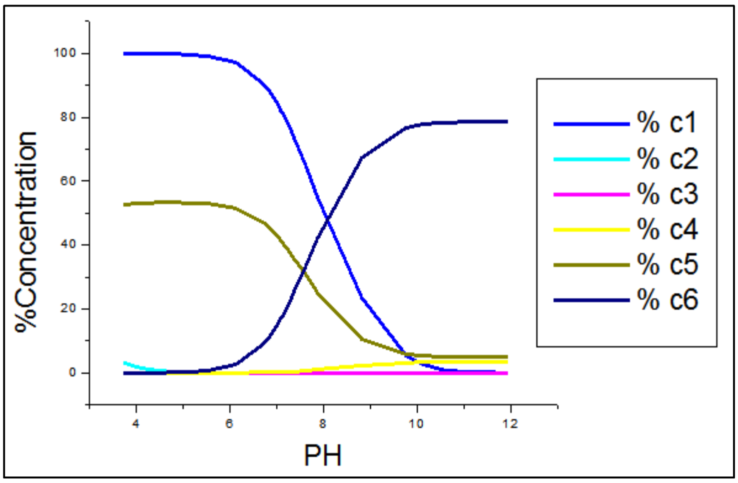


Fig 8: Species distribution curves for APN +SA +Zn(II)

The pka values of allopurinol were found to be 9. 36.&that of Succinic acid was found to be 2.62 & 3.89, this is due to presence of –NH-group the values are different than secondary imines because in the present situation nitrogen is part of hexagonal and pentagonal rings. The metal ligand stability constant was determined (Table 1-2) by using following equation.

$$n^{-}{}_{A} = \gamma - \frac{(v_2 - v_1)(N + \varepsilon^0)}{(v_0 + v_1)T^0 L}$$

To insure the nature of species present in the solution when stiochiometry is in doubt several titrations were performed. It was observed that in 1:1 ratio the predominant species is ML. Though other species are also observed (Figure 1-8). Analysis of complexing ligands curve (not shown) indicates that addition metal ion-ns to the free ligands solution shifts the buffer region towards lower PH value hence complexation proceeds by release of protons from horizontal displacement of complex curve. It can be inferred that complex is strong [10].

The present study shows that 1:1 metal to ligand types of species are important .the titration curve (not shown) shows two inflections. After the addition of NaOH this suggests the dissociation of two protons from Succinic acid in stepwise manner while in case of allopurinol single step is observed. These equilibria can be represented as.

$M+HL \leftrightarrow ML+H$
$Log\ K^{M}_{ML}=logk(ML) - (log[M]+log[L])$
$ML+HL \leftrightarrow ML_2+H$
$Logk^{M}_{ML2}=log[ML_2]-(log[ML]+log[[L])$
Similarly for allopurinol(L^1)
$Logk^{M}_{ML1}=log[ML^1]-(log[M]+log[L^1])$
$Logk^{M}_{ML^1_2}=log[ML^1_2]-(log[ML^1]+log[L^1])$
$\{log\beta = logk^{M}_{ML}+logkML_2ML\}$.

The binary stability constant for allopurinol is observed to be Fe(II)< Cu(II)< Ni(II)< Zn(II)< Co(II) for Succinic acid the trend observed is Ni(II)< Cu(II)< Fe(II)< Co(II)<Zn(II).The difference in trend was observed due to different nature of donor atoms. The steric hindrance is more in heterocyclic allopurinol. In the ternary the trend observed was Zn (II) < Co (II) < Ni (II) < Cu (II).
ΔlogK values are found to be positive which indicate that the ternary complexation is more favorable than binary.

4. Acknowledgements
We are thankful to Dr. Zahed Zaheer Associate Professor, Y B Chavan College of Pharmacy, for providing Medicinal drugs.

5. References

1. Hosny WM, El-Medani SM, Shoakry MM. Equilibriums studies of the binary and ternary complexes involving tetracycline and amino acid on DNA constituents. Talanta 1999; 48:913–921.
2. Sthanumeorthy R, Madhavan SN. Studies on Cu(II) ternary complex involving an amino penicillin drug and imidazole containing ligands. Spectrochemica Acta part A 2010; 75:656–663.
3. Sekhon BS, Srivastava J, Kaur S, Randhawa SK. Complexation equilibria of ciprofloxacin with proton and metal ions in aqueous organic mixtures. J Indian Chem Soc 2008; 85:200–202.
4. Regupathy S, ivasankaran MN. Studies on Cu(II) ternary complexes involving an aminopenicillin drug and imidazole containing ligands. Spectrochemica Acta part A 2010; 75:656–663.
5. Thakur S, Farooqui M, Naikwade SD. Comparative Study of Stability Constant of Antibacterial Drugs with Transition Metals in Ethanol-Water Media. Inter J Recent Trends Sci Tech 2013; 29-31.
6. Thakur S, Farooqui M, Naikwade SD. Mixed Ligand Complexes of Cobalt (II) Metal Ion With Medicinal Drugs Metformin, Imipramine And Adenosine In Mixed Solvent System. Inter J Pharm Tech Res 2013; 5(4):1508-1515.
7. Abdulbaset AZ, Farooqui M, Janrao DM. Study of Stability constant of binary & ternary complexes of Gabapentin with transition metal ions using potentiometric titration. Asian J Biochem Pharm Res 2011; 4(1)22-27.
8. Abdulbaset AZ, Farooqui M, Janrao DM. The Determination of the Stability Constants of Mixed Ligand Complexes of Ascorbic Acid, Pyridoxine HCl and Some Amino Acids with Some Metal Ions by Potentiometric Titration Method. Asian J Research Chem 2011; 4(10):1630-1631.
9. Abdulbaset AZ, Farooqui M, Janrao DM. Study of Stability constant of biological active molecules (drug) using potentiometric titration technique. J Chem Bio Phy Sci 2011; Sec.A 2(1):67-81.
10. Amrallah AH, Abdalla NA, El-Haty EY. Mixed ligand complexes of benzimidazole and pyrimidine hydroxyl azo dyes with some transition metals and glycine, DL-alanine or DL-Leucine. Talanta 1998; 46:491–500.