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The pH-metric Study of Acetyl Salicylic Acid Metal Complexes in Mixed Solvent Media

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ABSTRACT

The stepwise stability constant values of Acetyl Salicylic Acid with Cu(II) and Zn(II) have been studied using pH measurements in 70% DMF-30% water medium and 50% DMF-50% water. The values of proton- ligand stability constants and metal-ligand stability constants were calculated. The metal-ligand stability constant of binary complex was evaluated using Irving-Rossotti titration technique.

Keywords: Acetyl-salicylic acid, Stability constant, Irving-Rossotti titration

INTRODUCTION

Currently, there has been extensive interest in the study of binary complexes of drugs by pH-metric methods [1,2]. The ligand acetyl salicylic acid (Aspirin) is well known for its analgesic, antipyretic and anti-inflammatory actions [3]. Many researchers have studied the metal-ligand binary and ternary complexes of transition metals with simple or substituted acids [4]. Mc Byrde and his co-workers studied the stability constants of three iron salicylates [5]. Ashiq studied the complexation of aspirin at different pH range by both potentiometric and spectrophotometric methods [6]. Ternary complexes of Cu(II) with tryptophan as primary ligand and aspirin as secondary ligand have been studied by Beril Anilanmert [7]. From the literature it has been clearly noted that Aspirin forms a weak binary complex with metals in aqueous medium. In order to increase its stability, in this work we studied the binary complex of aspirin in binary solvent medium.

In this paper, the stability constants of binary complexes of Cu(II) and Zn(II) metal ions with aspirin at 302 ± 0.5 K and at fixed ionic strength μ=0.1 M using Irving-Rossotti pH-metric technique in binary solvent medium have been studied.

EXPERIMENTAL SECTION

The ligand acetyl salicylic acid and solvent Dimethylformamide (DMF) were obtained from Sigma-Aldrich and used as such. Carbonate free sodium hydroxide solution was prepared by standard method [8]. All other chemicals like hydrochloric acid, sodium hydroxide and potassium nitrate were of annular grade and their solutions are prepared in double distilled water. Systronics pH meter with a combined glass electrode were used for the pH measurements. For determination of proton-ligand stability constant and metal ligand stability constant of binary complexes, the following set of solutions were prepared and titrated against standardized NaOH solution.

Binary system: (i) Free acid, (ii) Free acid + Acetyl salicylic acid**,** (iii) Free acid + Acetyl salicylic acid + Metal ion. The above mentioned solutions are titrated against standardized 0.1 M NaOH in 0.2 ml aliquots, under an inert atmosphere of nitrogen. The ionic strength of the solutions is maintained at 0.1 M by addition of calculated amounts of 1 M KnO_3. The concentration of acetyl salicylic acid and metal ions are 20×10^{-4} M and 4×10^{-4} M respectively. The ratio of metal to ligand is maintained at 1:5 in each of the binary systems Tables 1 and 2.

RESULTS AND DISCUSSION

Proton-ligand dissociation constant

The dissociation constant of acetyl salicylic acid at different solvent compositions have been reported [9]. The value of pKa in binary solvent medium is slightly greater than the literature value (pKa=3.49) in water [7,10]. The increase in pKa in binary solvent medium than pure water shows that DMF plays a major role to enhance the basicity. It is well known that the addition of DMF to pure water breaks the three dimensional network of water and it forms the H-bonded complexes between DMF-nH_2O [11]. These H bonded complexes are presumably more basic than pure water by considering the +I effect of the methyl group which tends to increase the mesomeric shift of the lone pair of electrons on nitrogen to the more electronegative oxygen of DMF. It is further enhanced when a molecule capable of delocalizing this excess charge on oxygen of

DMF is present. Since water molecules are capable of forming H-bonds with such sites the excess negative charge on oxygen of DMF (arising due to mesomeric shift) is now partially transferred on to the oxygen of water. Hence, the co-operative nature of H-bonding in all DMF-nH_2O molecule complexes is expected to be more basic than the water molecule in pure solvent and thereby reduces its protonation constant.

Metal-ligand stability constant

The metal-ligand stability constants of binary complexes are evaluated in different solvent composition. An examination of titration curves indicates that complex formation has taken place in the solution. The metal titration curves showed a marked shift with respect to the ligand titration curves along the volume axis. This indicated the affinity of the ligand with metal ions which released protons and the difference in volume is obtained from (V_3-V_2). In addition, the color change of the ligand in the presence of metal ions appeared after the required volume of NaOH showing the formation of new species. From the ligand and metal titration curves the value of n is calculated. From n value the pH values are obtained. The variation of n is found be 0-0.8 for 1:1 complexes and 1.2-1.8 for 1:2 complexes.

The data in Table 3 clearly indicates the effect of solvent properties on the stability of complexes. The stability of a complex formed in a solution strongly depends on the nature of the solvent medium. During complexation, the metal ion should be able to replace the solvent molecule with the ligand or the ligand should be able to replace the solvent molecules in the first solvation shell of the cation. Since, the different solvent ratio yields a compelling change in their binding properties and their selectivity of ligand for certain cation over the others. The stability constants of all complexes increase with increase in DMF concentration in the binary mixture. The solvating of the metal ions and the ligand in DMF mixture should be less than water. The donor number of DMF (26.2) is less than the water (33) which makes the weak solvating nature of DMF [12]. The difference between log K_1 and log K_2 values are smaller which shows the simultaneous complex formation. The value of log K_1 for the formation of Cu $(C_9H_7O_4)^+$ appear to be fairly good while log K_2 is small due to low metal concentration. The deviations may be due to the difficulty caused by the hydroxide formation at higher pH values. The Irving-Williams order of stability constant is followed for the Cu(II) and Zn(II) complexes (Figures 1-3).

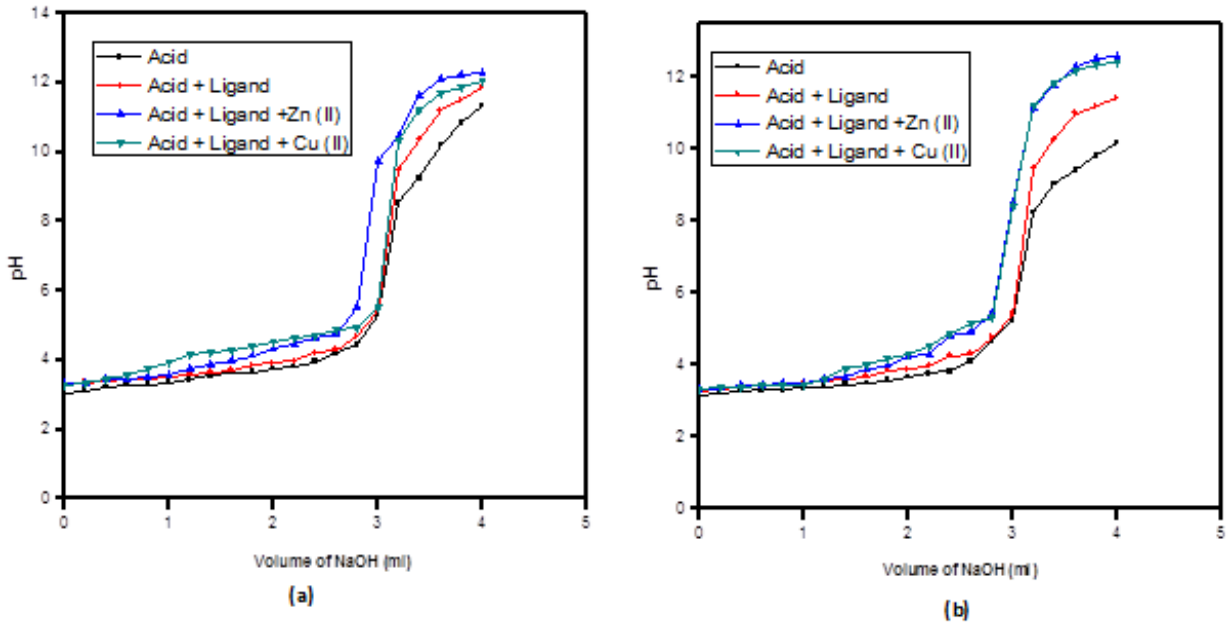

Figure 1: pH metric titration of free acid + Ligand + Zn(II) ion + Cu(II) ion, (a) 70% DMF-30% water system, (b) 50% DMF- 50% water system

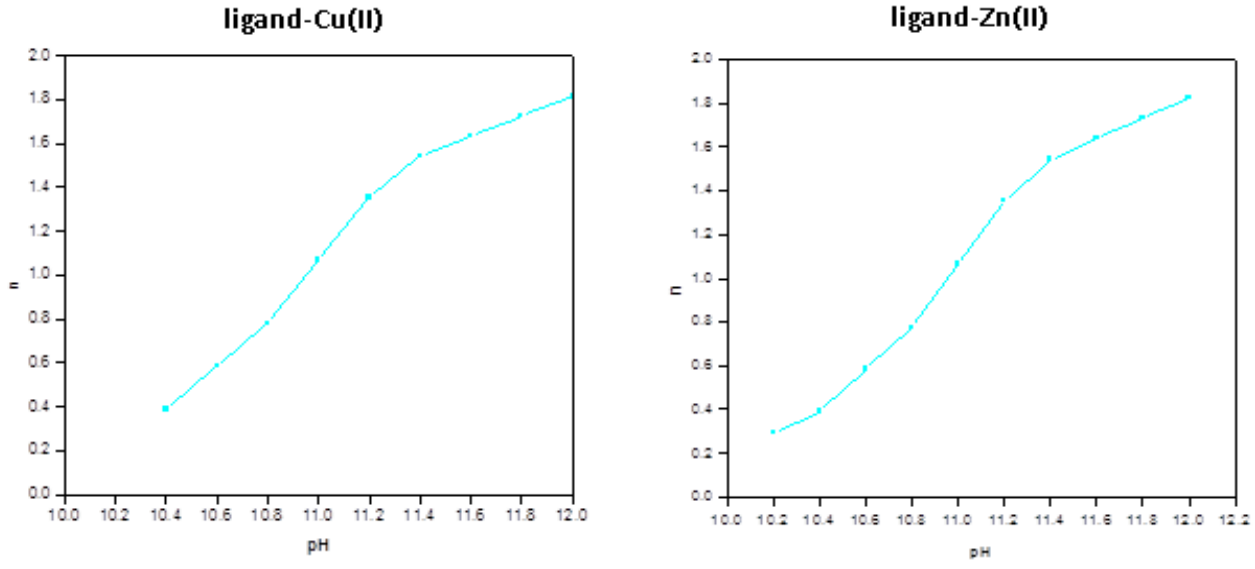

Figure 2: Plot of n Vs pH of ligand-Cu(II), ligand-Zn(II) system in 70% DMF medium

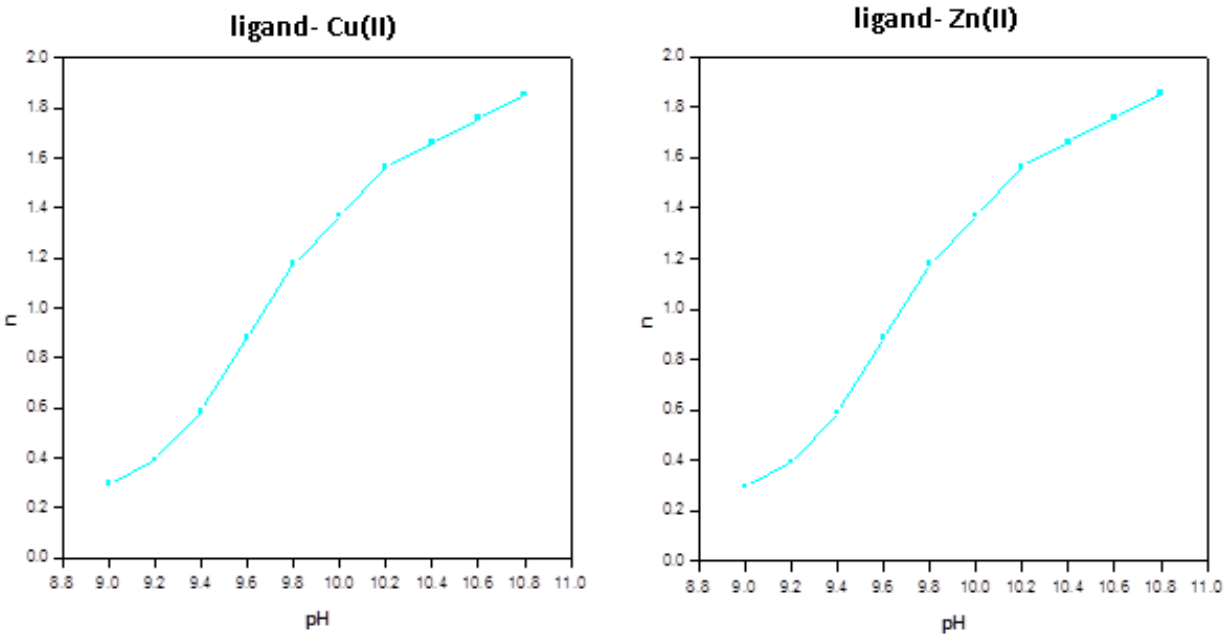

Figure 3: Plot of n Vs pH of ligand-Cu(II), ligand-Zn(II) system in 50%DMF medium

Table 1: Determination of n

70% DMF-30% Water system									
Acetyl salicylic acid+Cu(II)					Acetyl salicylic acid+Zn(II)				
pH	**V_2**	**V_3**	**V_3–V_2**	**n**	**pH**	**V_2**	**V_3**	**V_3–V_2**	**n**
10.4	3.2	3.24	0.04	0.390	10.4	3.25	3.29	0.04	0.389
10.6	3.25	3.31	0.06	0.584	10.6	3.3	3.36	0.06	0.583
10.8	3.3	3.38	0.08	0.777	10.8	3.35	3.43	0.08	0.776
11.0	3.35	3.46	0.11	1.067	11	3.4	3.51	0.11	1.065
11.2	3.4	3.54	0.14	1.356	11.2	3.45	3.59	0.14	1.353
11.4	3.5	3.66	0.16	1.544	11.4	3.5	3.66	0.16	1.544
11.6	3.6	3.77	0.17	1.635	11.6	3.53	3.7	0.17	1.6386
11.8	3.7	3.88	0.18	1.725	11.8	3.56	3.74	0.18	1.733
12.0	3.8	3.99	0.19	1.814	12	3.6	3.79	0.19	1.827

Table 2: Determination of n

50% DMF-50% Water system									
Acetyl salicylic acid+Cu(II)					Acetyl salicylic acid+Zn(II)				
pH	**V_2**	**V_3**	**V_3–V_2**	**n**	**pH**	**V_2**	**V_3**	**V_3–V_2**	**n**
9	3.00	3.03	0.03	0.295	9.8	3.1	3.13	0.03	0.294
9.2	3.02	3.06	0.04	0.392	10	3.11	3.15	0.04	0.391
9.4	3.04	3.1	0.06	0.588	10.2	3.12	3.18	0.06	0.585
9.6	3.06	3.15	0.09	0.882	10.4	3.14	3.24	0.1	0.977
9.8	3.08	3.2	0.12	1.175	10.6	3.16	3.28	0.12	1.172
10.0	3.10	3.24	0.14	1.370	10.8	3.18	3.32	0.14	1.366
10.2	3.12	3.28	0.16	1.565	11.0	3.20	3.36	0.16	1.560
10.4	3.14	3.31	0.17	1.6613	11.2	3.23	3.4	0.17	1.656
10.6	3.16	3.34	0.18	1.758	11.4	3.26	3.44	0.18	1.752
10.8	3.18	3.37	0.19	1.854	11.6	3.3	3.49	0.19	1.846

Table 3: Stability constant of acetyl salicylic acid with metal ions

Ratio of DMF-water	Log K_1	Log K_2	Log K_1-Log K_2	Log K_1/Log K_2
70% DMF Cu(II)	3.19	2.71	0.48	1.177
70% DMF Zn(II)	3.01	2.71	0.30	1.111
50% DMF Cu(II)	2.99	2.81	0.18	1.064
50% DMF Zn(II)	2.89	2.51	0.38	1.151

CONCLUSION

The stability constant is more in the 70%-30% binary solvent media than in the 50%-50% binary solvent media. These studies help to compute the usage of Acetyl Salicylic Acid in medicinal applications.

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