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EQUILIBRIUM STUDIES OF BINERY COMPLEXES OF SOME TRANSITION METAL (II) IONS WITH 5-ASA

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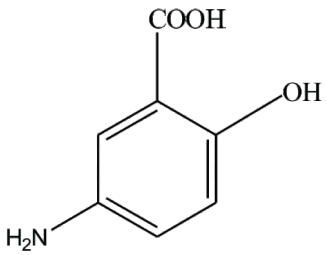
ABSTRACT *Stability constants of Mn(II) and Co(II) transition metal complexes with drug 5-ASA have been evaluated at 40.00°C + 1.00°C temperature and 0.2 M ($NaClO_4$) ionic strength in double distilled water medium by potentiometrically. Proton ligand stability constants (pK) and metal ligand stability constants (logK) were determined by using Calvin Bjerrum titration technique as modified by Irving and Rossotti.*

KEYWORDS : Potentiometry, Stability constant, Metal complexes, 5-amino salicylic acid(5 –ASA)

INTRODUCTION:

The determination of stability constants is an important process for many branches of chemistry. Metal Complexes are widely used in various fields, such as biological processes pharmaceuticals, separation techniques, analytical processes etc. The metal complexes with medicinal drugs and amino acids play a major role in the biological and chemical activity [1,2]. The stability of metal complexes controls the interaction of metal and ligands in complex media [3]. The metal ligand selectivity and strength of metal ligand bonds are depends on stability constants [4]. The determination of the metal – ligand stability constant requires the knowledge of reliable and accurate values of proton-ligand stability constants. Thus, proton-ligand and metal-ligand stability constants are correlated with each other. Potentiometric titration is accepted as a powerful and simple electro analytical technique for determination of stability constants. Many binary complexes of transition and inner transition metals have been studied potentiometrically [5,6,7]. Metal complexes of drugs are found to be more potent than parent drugs [8]. Chemistry of drugs attracts many researchers because of its application in medicinal study. . The 5-amino salicylic acid (5-ASA) has been known for their strong complex forming ability. In the present investigation, we selected medicinal drug 5-ASA, as ligand. Now a day's 5-ASA is the recommended therapy for the induction and maintenance of remission of ulcerative colitis(UC).[9,10] The drug acts topically at the colonic mucosa to reduce mucosal inflammation,[10] yet because the active drug is rapidly absorbed in the stomach and small intestine,[11] a number of oral formulations have been developed to deliver 5-ASA to the colon.[10,12] 5-ASA, also known as Mesalazine or, Mesalamine, is an anti-inflammatory drug used to treat inflammation of the digestive tract ulcerative colitis[13] and mild-to-moderate Crohn's disease.[14] The 5-ASA is β-hydroxy acid; as the name signifies, this compound contains both $-NH_2$ amine and –COOH acidic groups. It also contains hydroxy –OH group. In complexes of transition metals the formation of a coordination bond can be considered as a transfer of a lone electron pair from the coordinated group or ligand to the metal ion.[15] These metal ligand chelates serves as suitable models for the valuable information in the elucidation of biological processes.[16-20]. The Literature survey reveals that no work has been reported on complex formation of 5-ASA with transition metal ions in aqueous medium. The present paper describes study of stability constants of 5-ASA drugs with Mn(II) and Co(II) transition metal ions in double distilled water solution at 0.2M $NaClO_4$ ionic strength and 40.00°C + 1.00°C temperature by potentiometric study.

The structure of, 5-amino salicylic acid is shown as below:



(5 – Amino salicylic acid)

EXPERIMENTAL:

Materials:

All the chemicals used were of high grade of purity (AR Grade). Ligand sample of 5-ASA in pure form was obtained from (HI- MIDIA) pharma industries and used as received. The ligand is soluble in water and its 0.1M concentration standard solution was prepared by dissolving the required quantity of ligand in double distilled water. $NaClO_4$ solution was prepared in carbon dioxide free double distilled water. Metal ions were used in the nitrate form (Indian Rare Earth). A carbonate free NaOH solution was prepared by dissolving the Anlar pellets in double distilled water and standardized against oxalic acid solution (0.2 M) and standard alkali solution was again used for standardization of $HClO_4$(0.2 M). The ionic strength was maintained at 0.2M by using $NaClO_4$ (B.D.H.). The ligand solution and acid solution were transferred into 100 ml beaker and titrated against NaOH solution. The titration was performed first without addition of metal and then in its presence.

METHOD:

The potentiometric titrations are performed by using a Welltronix model PM-300 digital pH meter in conjuction with a combined glass electrode consisting of glass and reference electrode. The combined glass electrode was activated by immersing 24 hours in 0.1 N hydrochloric acid and then 12 hours immersed in distilled water. The precautions suggested by Bates [21], Albert and Sergent [22] were adopted for smooth handling of electrode. The combined glass electrode was connected to pH meter. The metal ion solutions were prepared by dissolving metal nitrates (Indian Rare Earth) and standardized by EDTA [23]. By adopting standard procedure, all titrations were carried out under inert atmosphere by bubbling oxygen free nitrogen gas through an assembly. The buffer solution having the pH ranges 4.00 and 9.18 was used for the standardization of pH meter, before and after each titration. The ligand solution of 5-ASA was prepared in aqueous medium which was used for further titrations i.e. without and with the transition metals Mn(II) and Co(II)

maintaining ionic strength 0.2M $NaClO_4$ at constant temperature 40.00°C + 1.00°C. The titration curves were obtained by plotting experimental data, which were utilized to determine the proton ligand formation constants of ligand and their metals complexes. The relative stabilities of the complexes formed are investigated potentiometrically adopting Irving and Rossotti [24] pH –titration technique. Proton ligand (pK) and metal –ligand Stability constants (log K) are determined using the Microsoft office excel computer program.

Potentiometric procedure:

The experimental procedure involved potentiometric titrations of the solutions of:

1. Free $HClO_4$ (A)
2. Free $HClO_4$ + Ligand (A+L)
3. Free $HClO_4$ + Ligand +Metal ion (A+L+M)

The solutions were titrated against standard carbonate free sodium hydroxide at 40.00°C + 1.00°C using Irving – Rossotti pH titration techniques. The concentration of Perchloric acid(0.2M) and sodium perchlorate (1M) were kept constant for all sets. The water thermostat was used to maintain the temperature constant. The solutions were equilibrated in the thermostat for about 15 minute before titrations. The volume of every mixture was made up to 50 ml with double distilled water. The curves of pH versus ml-base solution were plotted (Figure-1 and 2) and Proton ligand (pK) and metal–ligand Stability constants (log K) are determined.

RESULTS AND DISCUSSION:

The potentiometric titration curves of 5 -ASA with transition metal ion is shown in fig.1 and fig.2. The pH of complex formation is much below than the pH of metal ion hydrolysis. These features of the pH metric studies confirm the formation of complexes by all the metal ions with 5 -ASA. The basicities of the ligand have been measured in term of their proton-ligand stability constant. Proton ligand stability constants (pK) of drugs were determined by point wise calculation method as suggested by Irving & Rossotti and are given in table 1. The formation constants for these complexes are given in table-1. It is found that in the ligand $\bar{n}$**H** values ranges between 1 and 3 indicating the liberation of three protons during complexation. Therefore the drug gives three (pK). The basicity of the ligand have been measured in terms of their proton-ligand stability constant. The interaction of metal ion with a base is similar to the neutralization reaction involving hydrogen ion. J. Bjerrum [25] pointed out that the bases which have the strongest affinity for hydrogen ions form most stable complexes. This trend was observed in 5-ASA.The more basic ligandss form more stable complexes. Similar linear relationship was shown by several workers [26-28] between the logK of a series of metal complexes derived from one metal ion with a set of similar ligands and their pK values.

CONCLUSION:

The metal ligand formation curve data for 5 -ASA with transition metal ions indicate that the n value range between 0.209 to 0.989 and this suggests that metal ions form 1:1 complexes with ligand in solution. The logK values are evaluated by the computational techniques are in good agreement. The ratio of $LogK_1$ / $LogK_2$ is positive and greater than one in both cases. This implies that there is little or no steric hindrance to the addition of ligand molecule. The difference between $logK_1$ and $logK_2$ was 0.694 indicating the formation of 1:1 complexes.

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Table-1: Proton ligand and binary metal ligand formation constants of 5 -ASA at 40.00°C ±1.00°C and at 0.2M ionic Strength.

Ligand pK^H Values	Transition Metals	Metal Ligand stability constants		$LogK_1/LogK_2$	$LogK_1$-$LogK_2$
pK_1^H=2.728	Mn(II)	$log\beta_2$	6.177	1.253	0.695
		$logK_1$	3.436		
pK_2^H=5.876		$logK_2$	2.741		
	Co(II)	$log\beta_2$	6.176	1.253	0.694
pK_3^H=9.179		$logK_1$	3.435		
		$logK_2$	2.741		

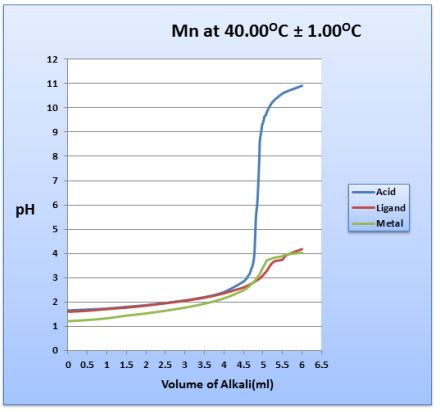

Figure- 1 Representative titration curves for formation of Mn (II)- 5-ASA complexes at 40.00° C ±1.00°C and 0.2M ionic strength in aqueous solution

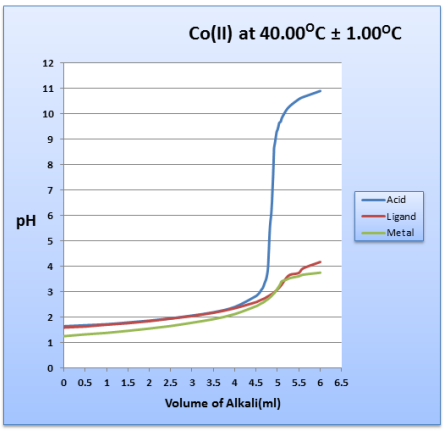

Figure- 2 Representative titration curves for formation of Co (II)- 5-ASA complexes at 40.00°C ±1.00°C and 0.2M ionic strength in aqueous solution.

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