

Equilibrium Studies of the Calcium (II) and Barium(II) Complexes with Mesalamine in Aqueous Solution

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ABSTRACT

The binary complexes of some transition metal(II) ions with Mesalamine were studied using potentiometric pH titrations. Potentiometric titration is accepted as a powerful and simple electroanalytical technique for determination of stability constants. In the present work, the interactions of transition metal ions Ca(II) and Ba(II) with Mesalamine has been investigated in double distilled water mixture at 0.2 M ionic strength at temp 30 °C + 1.00C by potentiometrically. Proton ligand (pK) and metal-ligand (logK) stability constant were determined by using Calvin Bjerrum titration technique as modified by Irving & Rossoti.

Keywords : Potentiometry, Transition Metals, Stability Constant, Mesalamine

I. INTRODUCTION

The ligand Mesalamine is slightly soluble in cold water, ethanol, more soluble in hot water, soluble in hydrochloric acid. Mesalamine also known as Mesalazine or 5-aminosalicylic acid (5-ASA).

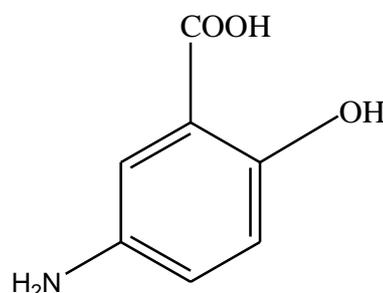
In the present investigation, we selected medicinal drug Mesalamine, as ligand. Now a day's Mesalamine is the recommended therapy for the induction and maintenance of remission of ulcerative colitis(UC).[1,2] The drug acts topically at the colonic mucosa to reduce mucosal inflammation,[2] yet because the active drug is rapidly absorbed in the stomach and small intestine,[3] a number of oral formulations have been developed to deliver Mesalamine to the colon.[2,4] Mesalamine, is an anti-inflammatory drug used to treat inflammation of the digestive tract ulcerative colitis[5] and mild-to-moderate Crohn's disease.[6]

Mesalamine ligand contains both -NH₂ amine and -COOH acidic groups. . It also contains hydroxyl -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.[7] These metal ligand chelates serves as suitable models for the valuable information in the elucidation of biological processes.[8-11].

The Literature survey reveals that no work has been reported on complex formation of Mesalamine with transition metal ions in aqueous medium. Therefore in order to understand the complex formation behavior of Mesalamine at ionic strength 0.2M NaClO₄ at constant temperature i.e. 30 °C ± 1.0°C is studied.

The structure of Mesalamine is shown as below:



II. METHODS AND MATERIAL

Materials:

All the chemicals used were of high grade of purity (AR Grade). Ligand sample of Mesalamine 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 conjunction 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 glass distilled water. The precautions suggested by Bates [12], Albert and Sergent [13] 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 [14]. 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

Mesalamine was prepared in aqueous medium which was used for further titrations i.e. without and with the transition metals Ca(II) and Ba(II) maintaining ionic strength 0.2M NaClO_4 at constant temperature $30^\circ\text{C} \pm 1.0^\circ\text{C}$. 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 [15] 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 $30^\circ\text{C} \pm 1.0^\circ\text{C}$ 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.

III. EXPERIMENTAL RESULTS AND DISCUSSION

The potentiometric titration curves of Mesalamine 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 Mesalamine. 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-2. It is found that in the ligand nH 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 [16] pointed out that the bases which have the strongest affinity for hydrogen ions form most stable complexes. This trend was observed in Mesalamine. The more basic ligandss form more stable complexes. Similar linear relationship was shown by several workers [17-19] between the logK of a series of metal complexes derived from one metal ion with a set of similar ligands and their pK values.

Table 1. Proton ligand stability constants of Mesalamine at 0.2M ionic Strength Medium – Water, Temperature- 30°C ± 1.00C.

Proton Ligand stability constants	Ionic Strengths
	0.2M
pK ₁ ^H	2.822
pK ₂ ^H	6.194
pK ₃ ^H	8.894

Table 2. Metal ligand stability constants of of Mesalamine at 0.2M ionic Strength.

Transition Metals	Metal Ligand stability constants		LogK ₁ /LogK ₂	LogK ₁ -LogK ₂
	logβ ₂	logK ₁		
Ca(II)	6.175		1.253	0.695
	3.435			
	2.740			

Ba(II)	logβ ₂	6.176	1.254	0.696
	logK ₁	3.436		
	logK ₂	2.740		

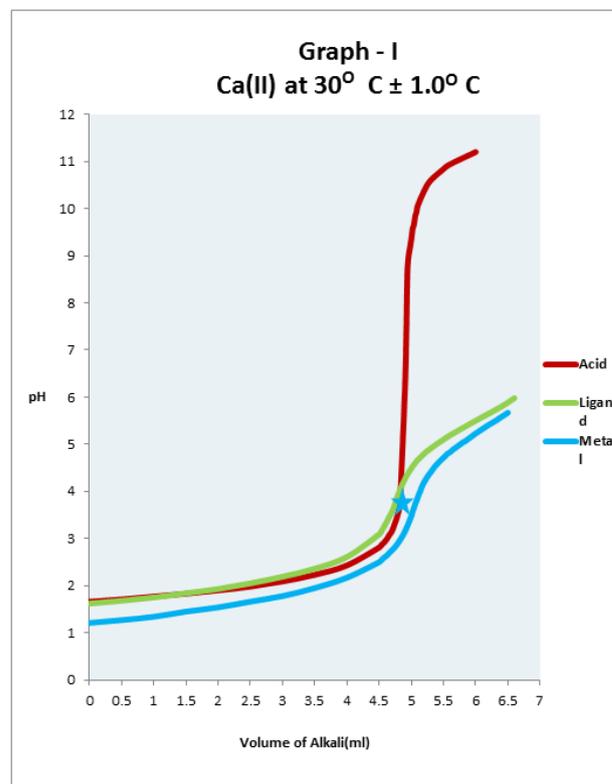


Figure 1. Representative titration curves for formation of Ca(II)- Mesalamine complexes at 30°C ± 1.0°C and 0.2M ionic strength in aqueous solution.

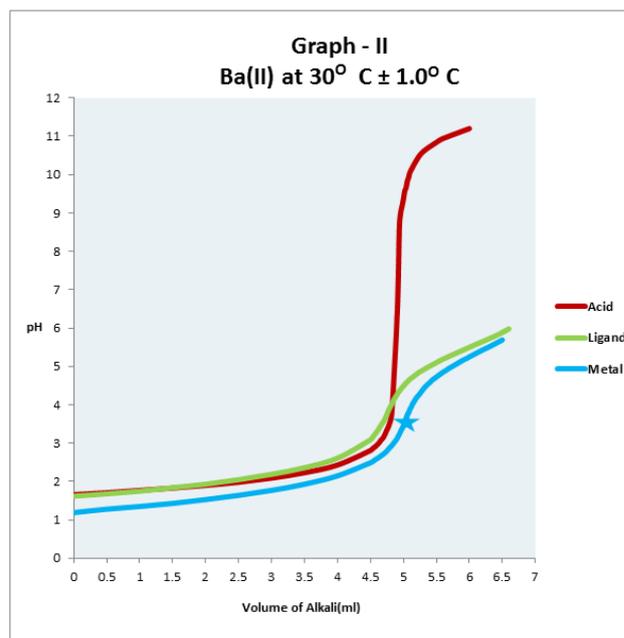


Figure 2. Representative titration curves for formation of Ba (II)- Mesalamine complexes at 30°C ± 1.0°C and 0.2M ionic strength in aqueous solution.

IV. CONCLUSION

The metal ligand formation curve data for Mesalamine with transition metal ions indicate that the n value range between 0.758 to 1.425 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 $\text{LogK}_1 / \text{LogK}_2$ 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 0.695 and 0.696 in both cases indicating the formation of 1:1 complexes.

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