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Study of equilibrium constants of 5-ASA with transition metal ions

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ABSTRACT

Potentiometry is one of the most convenient and successful technique employed for metal complex equilibrium measurements. In the present work, the interactions of transition metal ions Mn(II) and Co(II) with 5-ASA has been investigated in double distilled water mixture at 0.2 M ionic strength at temp 30 °C $\pm$ 1.0^{0}C 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, Stability constant, Transition metals, 5-amino salicylic acid(5 –ASA) .

INTRODUCTION

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. The stability of metal complexes with medicinal drugs plays a major role in the biological & chemical activity [1-2]. 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 [3,4]. 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 [5]. Metal complexes of drugs are found to be more potent than parent drugs [6]. 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).[7,8] The drug acts topically at the colonic mucosa to reduce mucosal inflammation,[8] yet because the active drug is rapidly absorbed in the stomach and small intestine,[9] a number of oral formulations have been developed to deliver 5-ASA to the colon.[8,10] 5-ASA, also known as Mesalazine or, Mesalamine, is an anti-inflammatory drug used to treat inflammation of the digestive tract ulcerative colitis[11] and mild-to-moderate Crohn's disease.[12] 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. During complex formation reaction, ligand acts as a base and hence greater the basicity of the ligand more stable is the complex formed. In other words, the stability is proportional to the proton ligand stability constants provided other factors affecting the stability are constant. The formation constants of the binary complexes formed due to interaction of bivalent transition metal (II) ion with 5-ASA were calculated by measuring the magnitude of the

proton liberated during the titration of the ligand in absence and presence of metal against standard sodium hydroxide solution.

Based on the growing importance of both, the metal ions as well as the ligand, this combination is selected for the present study.

MATERIALS AND METHODS

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. All the chemicals used were of high grade of purity (AR Grade). The solutions used in the potentiometric titration were prepared in double distilled water. The pH of this water was found ~ 6.8 to ~7.0. 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 metal ion solutions were prepared by dissolving metal nitrates (Indian Rare Earth) and standardized by EDTA [13]. The pH measurement was made using a digital pH meter model Welltronix PM-300 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. All the measurements were made at 30 °C ± 1.0°C in double distilled water mixture at constant ionic strength of 0.2M $NaClO_4$ .The relative stabilities of the complexes formed are investigated potentiometrically adopting Irving and Rossotti [14] 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 $30^0C \pm 1.0^0C$ 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. It is found that in the ligand $\bar{n}$**H** values ranges between 1 and 3 indicating the liberation of three proton 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 [15] 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 ligands form more stable complexes. Similar linear relationship was shown by several workers [16-19] between the logK of a series of metal complexes derived from one metal ion with a set of similar ligands and their pK values.

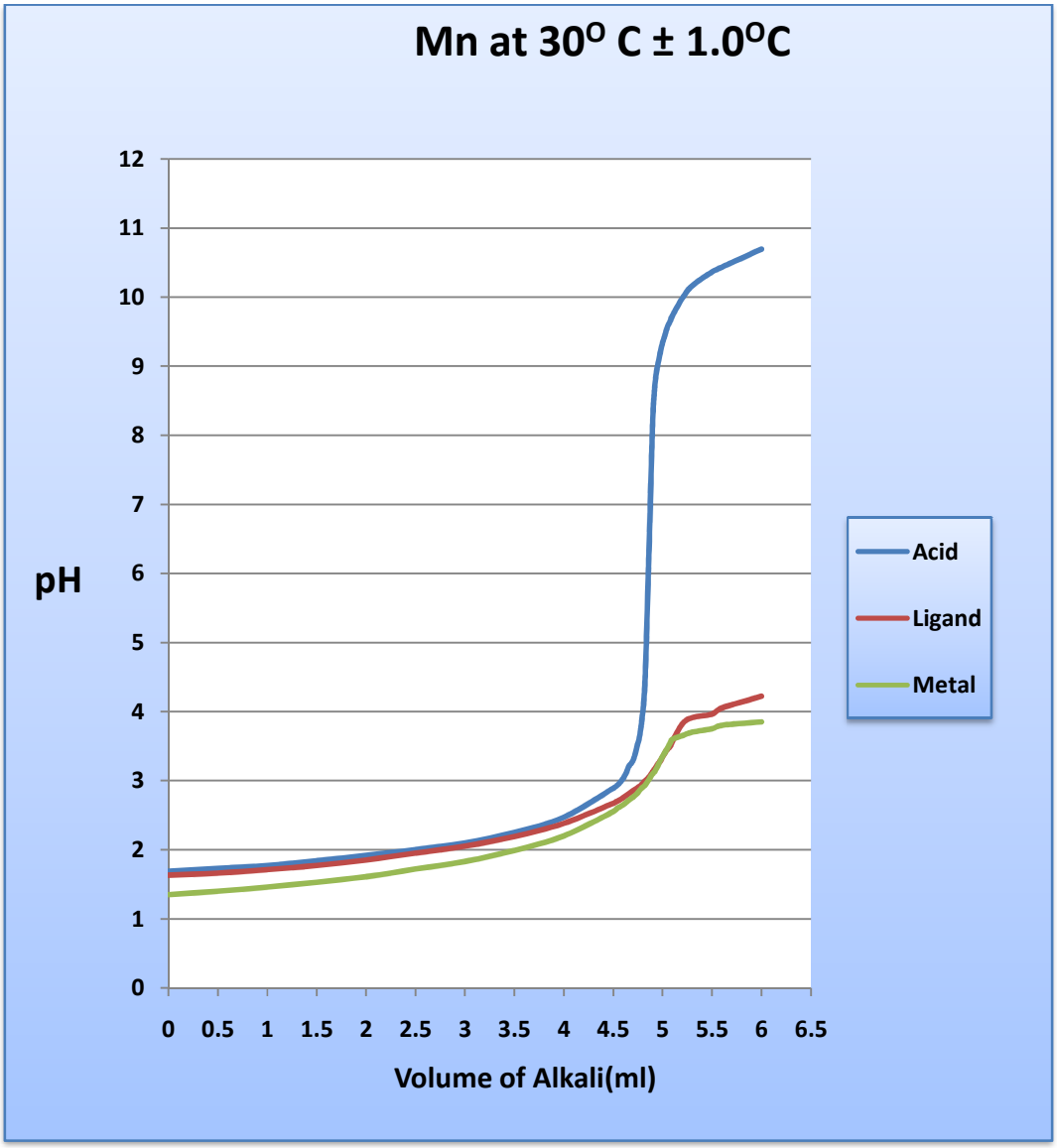

Figure- 1 Representative titration curves for formation of Mn(II)- 5-amino salicylic acid complexes at 30 ± 1.0°C and 0.2M ionic strength in aqueous solution

Table-1: Proton ligand and binary metal ligand formation constants of 5 -ASA at 30^0C ±1.0^0C 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=2.822	Mn(II)	$log\beta_2$	6.175	1.253	0.695
		$logK_1$	3.435		
pK_2^H=6.194		$logK_2$	2.740		
	Co(II)	$log\beta_2$	6.172	1.253	0.695
pK_3^H=8.894		$logK_1$	3.433		
		$logK_2$	2.738		

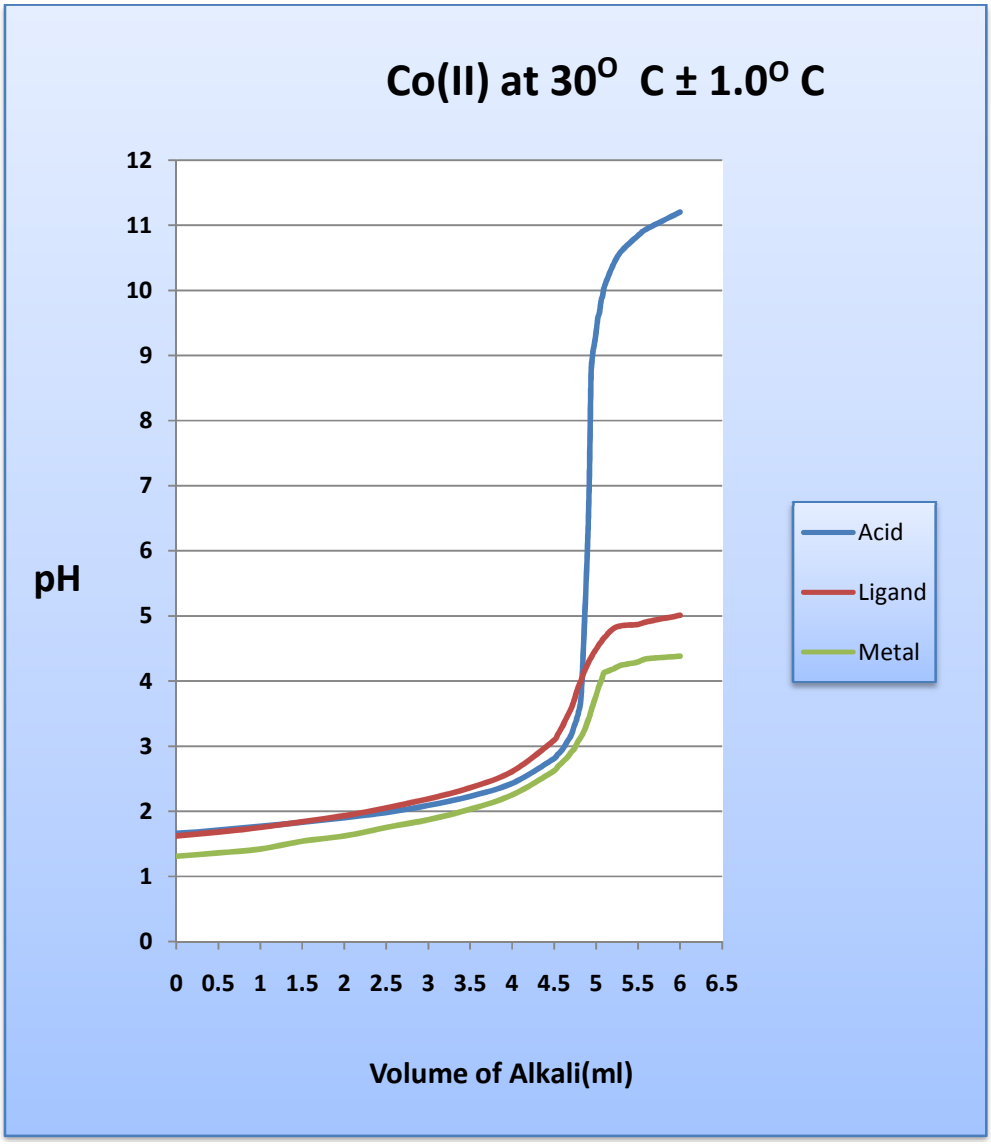

Figure- 2 Representative titration curves for formation of Co(II)- 5-amino salicylic acid complexes at 30 ± 1.0°C and 0.2M ionic strength in aqueous solution

CONCLUSION

The metal ligand formation curve data for 5 -ASA with transition metal ions indicate that the $\bar{n}$ value range between 0.757 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 $LogK_1$ / $LogK_2$ 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 0.695 indicating the formation of 1:1 complexes.

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