# Potentiometric Studies of the Samarium(III) and Gadolinium(III) Complexes with Mesalamine in Aqueous Solution

**Dr. Sanjay B. Dalicha[1], Dr. Arvindbhai S. Prajapati[*2]**

[1]Department of Chemistry, B.C.J Science College Khambhat ,Gujarat, India
[2]Department of Chemistry, Government Science College, Limkheda, Dist: Dahod, Gujarat, India

## ABSTRACT

Potentiometric titration is accepted as a powerful and simple electroanalytical technique for determination of stability constants. The binary complexes of some transition metal (III) ions with Mesalamine were studied using potentiometric titrations. In the present work, the interactions of transition metal ions Sm(III) and Gd(III) with Mesalamine has been investigated in double distilled water mixture at 0.2 M ionic strength at temp 25 °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 formation of a coordination bond in complexes of transition metals can be considered as a transfer of a lone electron pair from the coordinated group or ligand to the metal ion. It is well known that proton transfer plays an important role in the reactions such as complexation, acid–base catalyzing and enzymatic reaction [1] in aqueous solution. The stability constants can be of significance in order to predict different chemical processes such as isolation, extraction, or preconcentration methods [2,3]. Thus, the accurate determination of acidity and stability constants values are fundamental to understanding the behavior of ligands and their interaction with metal ions in aqueous solution.

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 [4-5]. Stability order of metal ions transition metal ions is found by Irving and Williams[6] by comparing the ionic radius and second ionization potential of the metal ions because it is valid for most nitrogen and oxygen doner ligands.

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-ASA. Mesalamine have been known for their strong complex forming ability. Now a day's Mesalamine is the recommended therapy for the induction and maintenance of remission of ulcerative colitis(UC).[7,8], Mesalamine is an anti-inflammatory drug used to treat inflammation of the digestive tract ulcerative colitis[9] and mild-to-moderate Crohn's disease.[10] 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,[12] a number of oral

formulations have been developed to deliver 5-ASA to the colon.[8,11]

The Mesalamine is β-hydroxy acid; as the name signifies, this compound contains both -NH2 amine and –COOH acidic groups. 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. 25 °C + 1.00C is studied.

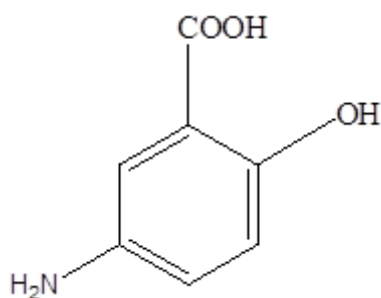The structure of Mesalamine is shown as below:



**Figure 1**

## II. MATERIALS AND METHODS

### 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. NaClO4 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 HClO4(0.2 M). The ionic strength was maintained at 0.2M by using NaClO4 (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 glass distilled water. The precautions suggested by Bates [9], 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 Sm(III) and Gd(III) maintaining ionic strength 0.2M NaClO4 at constant temperature 25°C + 1.00C. 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 HClO4 (A)
2. Free HClO4 + Ligand (A+L)
3. Free HClO4 + Ligand +Metal ion (A+L+M)

The solutions were titrated against standard carbonate free sodium hydroxide at 250C + 1.00C 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 ligands 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- 25°C ± 1.0°C.

| 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$_2$ |
|---|---|---|---|---|
| Sm(III) | $log\beta_2$ | 6.175 | 1.254 | 0.697 |
| | $logK_1$ | 3.436 | | |
| | $logK_2$ | 2.739 | | |
| Gd(III) | $log\beta_2$ | 6.176 | 1.255 | 0.700 |
| | $logK_1$ | 3.438 | | |
| | $logK_2$ | 2.738 | | |
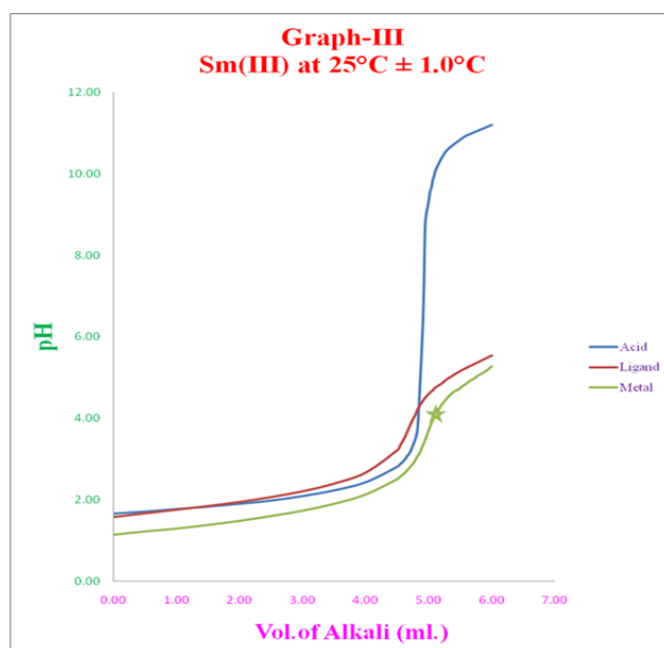


**Figure 1.** Representative titration curves for formation of Sm (III)- Mesalamine complexes at 25° ±1.0°C and 0.2M ionic strength in aqueous solution.
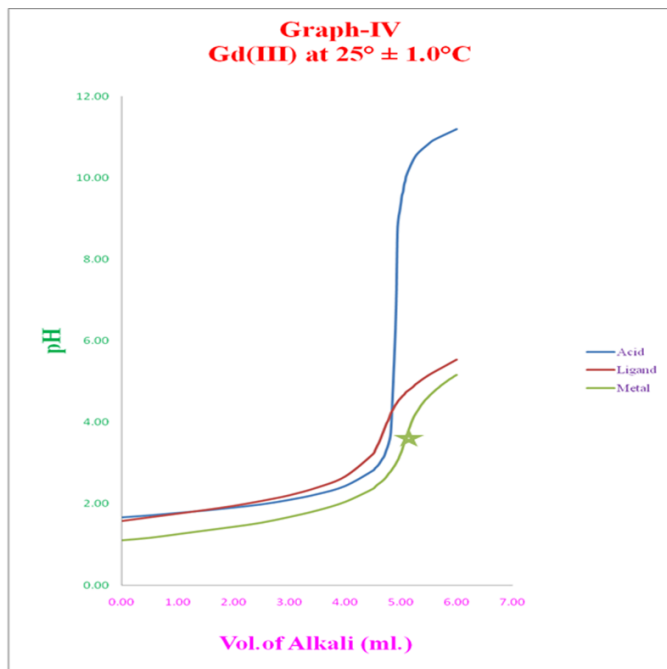
**Figure 2.** Representative titration curves for formation of Gd(III)- Mesalamine complexes at 25º ±1.0ºC and 0.2M ionic strength in aqueous solution.

## IV. CONCLUSION

The metal ligand formation curve data for Mesalamine with transition metal ions indicate that the $\bar{n}$ value range between 0.758 to 1.654 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 $\log K_1 / \log K_2$ 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 $\log K_1$ and $\log K_2$ was 0.697 and 0.700 in both cases indicating the formation of 1:1 complexes.

## V. REFERENCES

[1]. I. Ando, K. Ujimto, H. Kurihara, Bull. Chem. Soc. Jpn., 1982, 55, 713.

[2]. E.A. Gracia, D.B. Gomis, Mikrochem. Acta, 1996, 124, 179.

[3]. S. Cao, M.J. Zhang, Trace Microprobe Tech., 1999, 17, 157.

[4]. a) Mukharjee G.N & Ghosh T.K. Indian J. of chem.30,(1991)1033-1037. b) Mukharjee G.N & Ghosh T.K. J. of Indian Chem. SOC 68, (1991) 194-196.

[5]. Thomas G. medicinal chemistry –John wiley & son ltd.London256 (2003).

[6]. Irving. H and Williams RJP : Jchem. Soc .75,3192. 1953.

[7]. Travis SPL, Strange EF, Lemann M, et al.European evidence-based Consensus on the management of ulcerative colitis: Current management. Journal of Crohn's and Colitis 2008; 2: 24–62

[8]. Qureshi A. I, Cohen R. D.,Mesalamine delivery systems: do they really make much difference? Adv Drug Deliv Rev 2005; 57: 281–302.

[9]. Kruis, W; Schreiber, I; Theuer; Brandes; Schütz; Howaldt; Krakamp; Hamling et al."Low dose balsalazide (1.5 g twice daily) and mesalazine (0.5 g three times daily) maintained remission of ulcerative colitis but high dose balsalazide (3.0 g twice daily) was superior in preventing relapses". Gut 49 (6): 783–9. (2001)..

[10]. Sandborn W. J, Feagan B .G, and Lichtenstein G. R., "Medical management of mild to moderate Crohn's disease: evidence-based treatment algorithms for induction and maintenance of remission". Alimentary Pharmacology & Therapeutics 26 (7): 987–1003. (October 2007).

[11]. Cohen R D.Review article: evolutionary advances in the delivery of aminosalicylates for the treatment of ulcerative colitis.Aliment Pharmacol Ther 2006; 24: 465–74.

[12]. Myers B, Evans DN, Rhodes J, et al.Metabolism and urinary excretion of 5-amino salicylic acid in healthy volunteers when given intravenously or released for absorption at different sites in the gastrointestinal tract. Gut 1987; 28: 196–200

[13]. A. Albert, E.P. Serjeant, Determination of Ionisation Constants, Chapman and Hall Ltd., 2nd Edn, London, 1971, 10.

[14]. G.H.Jaffery,J.Basset,J.mendham,R.C.Denney,Vo gels textbook of quantitative chemical analysis .5th edition, Long man, group UK limited 1978,1989.

[15]. H. Irving and H. S. Rossoti, J. Chem. Soc, (1954), 2904.

[16]. J. Bjerrum, Chem. Soc.,1950, 46, 381.

[17]. R. Gupta, N. Agrawal, K.C. Gupta, Der Chemica Sinica, 2012, 3(1):91-98.

[18]. B. K. Magarea, M.B. Ubale, Der Chemica Sinica, 2011, 2 (2):158-164.

[19]. A. A. Zaida, M. Farooqui, D.M. Janrao Der Chemica Sinica, 2012, 3(1):64-70.