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Determination of The Stability Constants of Furosemide Complexes with Metals in Aqueous Media by Potentiometric Measurement

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Abstract: *Study showed the higher values of Metal stability constant with Furosemide diuretic drug. The stability constant of co-ordination complexes of Furosemide diuretic drugand metals such as Co^{+2}, La^{+3}, Ni^{+2} and Cu^{+2} has been studied potentio-metrically and in the presence of $NaClO_4$ by pH-metric technique at 27^0C, the order of the stability constant of the formed complexes increase for La to Cu as La<Co< Ni< Cu..*

Keywords: Lanthanum, Potentiometric, Stability Constant, Medicinal drug, Metal complexes

I. INTRODUCTION

Electrolyte solutions are greatly affected by the ionic concentrations of metals [1].Gram-negative and Gram-positive bacteria are significantly affected by the complex formation of complexes using samarium-assembled ligands. Biological activity against gram positive, gram negative bacteria, and fungi showed moderate to significant results [2]. Now a day's pharmaceutical market is at high peak, so the researchers targeted their work on metal ligand complexation study keeping transitional metal ions as their priority [3-5].The Transition elements as well as internal transition elements tend to form coordination complexes with Lewis bases, amino acids, Chalcone-Schiff bases, and even medicinal drugs[6]. In this study, we relied on the selection of a medicinal furosemide ligand with d-block and f-block metal ions. Three-dimensional metal ions were also synthesized using ciprofloxacin. A literature survey reveals that solvents also play an important role, in the stability of the complex formed between different bonds with metal ions. [7 Potentiometer studies of the stability constants of some metal (II) ions were also carried out using amino acids and thiobarbituric acid. [8].The mineral forms binary and triple complexes. Order stability is found an increase in the covalent index. A work was carried out to examine the stability of the metal-ligand gene to cefadroxil with metal ions.[9]. Amino acids act as a coordinating agent through the carboxylic group and the amino group. L-valin has been worked on with Ni(II), Co(II) and Cu(II) metals. Valine like other amino acids is associated with insulin resistance. [10]. In the view of some medicinal and analytical application of substituted pyrazoles will act as antibiotic drug and a chelating agent. Therefore, study of metal-ligand stability constant have been done on substituted pyrazole with some lanthanide [11].

II. MATERIAL & METHOD

Materials and Reagents:3-(diaminomethylidene)-1,1-diamethylguanidine;hydrochloride was a gifted sample and all reagents were purchased from Merck and SD fine chemicals and used without further purification. The solution used for potentiometric studies were prepared in double distilled water. The NaOH solution was standardized against oxalic acid (0.1M). All prepared metal nitrates solutions were standardized by complexometric titrations. The Furosemide diuretic is freely soluble in double distilled water. The pH meter (ELICO, LI-120) used was calibrated before proceeding for experiment.

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Potentiometric experiment

The pH meter was calibrated with three different buffer solution of pH 4.01, 7.0 & 9.2 before starting of titrations. For the determination of protonation constant of the ligand and the formation constant of the complexes in distilled water by varying metal ions, following trials of solution were prepared.

(A) $HClO_4 + NaClO_4$

(A + L) $HClO_4 + NaClO_4 + C_{12}H_{11}ClN2O5S$

(A + L + M) $HClO_4 + NaClO_4 + C_{12}H_{11}ClNO5S$ + metal ions

Above sets of solutions were prepared as M:L ratio, the solution of complex

was titrated against standard NaOH solution at room temperature by using pH-meter and recorded the readings until a constant pH is obtained of three systems : (i) [A] 0.2N $HClO_4$ (5 mL) + 1M $NaClO_4$ (5 mL); (ii) [A + L] 0.2N $HClO_4$ (5 mL) + 1M $NaClO_4$ (5 mL) + 0.01N ligand (10 mL); (iii) [A + L + M] 0.2N $HClO_4$ (5 mL) +1M $NaClO_4$ (5 mL) + 0.01N ligand (10 mL) + 0.01N Lanthanum metal solution (10 mL).

Calculation

Irving and Rossotti method was adopted to calculate the average number of protons associated with the ligand, $\overline{\eta_a}$ at different pH values using acid and ligand titration curves.

$$\overline{\eta_a} = \gamma - \frac{(V_L - V_a)(N^0 + E^0)}{(V_0 + V_a)T_L}$$

Where V_a and V_L are the volumes of sodium hydroxide needed to reach the same pH in acid and ligand titration curves. T_L the total ligand concentration γ is the total number of protons free attached to the ligand molecule, N^0 is the normality of alkali, E^0 is the initial concentration of the free acid and V_0 is the total volume of the titrated solution. The protonation constant is related to the $\overline{\eta_a}$ by the equation:

$$K_1 = \frac{\overline{\eta_a}}{(1-\overline{\eta_a})[H^+]}$$

For monobasic acid

$$K_1 = pH + \log\frac{\overline{\eta_a}}{1-\overline{\eta_a}}$$

For dibasic acid

$$K_1 = pH + \log\frac{\overline{\eta_a} - 1}{2-\overline{\eta_a}}$$

$$K_1 = pH + \log\frac{\overline{\eta_a} - 1}{2-\overline{\eta_a}[H^+]}$$

The proton ligand formation constant K_1 and K_2 were calculated rom the formation curve obtained by plotting $\overline{\eta_a}$ Vs pH where the pH values at $\overline{\eta_a}$ = 0.5 and 1.5 gives log K_1 and log K_2 respectively. The average number of metal ions associated with the ligand $\overline{\eta}$ at different pH values is calculated from the metal ions and ligand titration curves using Irriving and Rossotti equation as follows.

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$$\bar{\eta} = \frac{(V_m - V_1)(N^0 + E^0)}{(V_0 + V_1)\overline{\eta_a} T_m}$$

and

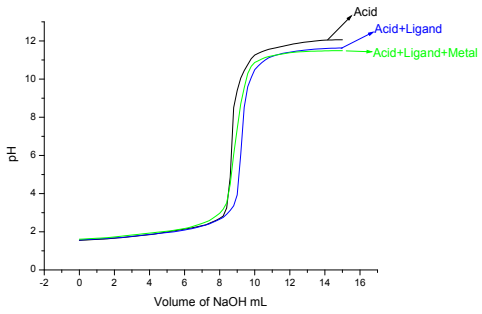
$$pL = \log_{10}\left[\frac{\sum_{n=0}^{n=1} \beta_n^H \left(\frac{1}{anti\log pH}\right)}{T_1 - RT_m} \cdot \frac{V_0 + V_m}{V_0}\right]$$

Where T_m denotes the total concentration of metal present in solution, β_n^H is the overall proton ligand stability constant, the other terms have their usual meaning as mentioned before. The successive stability constants are computed using the interpolation at half $\bar{\eta}$ values from $\bar{\eta}$ Vs pL formation curves. The values of $\log K_1$ and $\log K_2$ were obtained by interpolation at 0.5, 1.5 respectively, the least square method was used for calculation of $\log K_1$ and $\log K_2$ by plotting $\log \frac{\overline{\eta_a}}{1-\overline{\eta_a}}$ Vs pL or $\log \frac{\overline{\eta_a} - 1}{2 - \overline{\eta_a}}$ Vs pL, respectively.

III. RESULT AND DISCUSSION

Coordination compounds play an important role in many branches like chemistry, biochemistry, Biology, medicine etc. Stability constant used in the determination of metal-ligand complex [12-14].

As far as solution study of transition series is concerned it is very interesting Cu shows greater lattice energy and has higher formation constant for complexes of Cu(II) ions observed. Cu(II) shows complexes with ligand is more stable than Ni(II) complexes [15].



The order of stability of metal chelates are investigated Irving William natural order of stabilities [16] as La (II) < Co(II) < Ni(II) < Cu(II). A Kalvin-Bjerrum method used for the determination of stability constant for metal ion with ligands.

For the present study La, Cu, Co,Ni are taken as metal ion withFurosemide as a ligand. Furosemideis used for the treatment of edema secondary to exacerbation of congestive heart failure, hepatic failure, or renal failure, including nephrotic syndrome.Furosemide is water soluble. Furosemide has one free amino group and two terminals –NH group. Furosemide has more capacity of forming complex.

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Table 1. Metal-Ligand stability Constant

Metals	LogK	pL
La	0,7852	3,264
Co	1,063	3,525
Ni	3,2498	3,742
Cu	1,354	4,783

The highest value of metal ligand complexes between Fe and boric acid are also observed by earlier researchers[17-18]. Also workers showed the higher values of Metal-ligand stability constant of Ni with cysteine and Schiff's base [19]. For the present study the metal ion selected from transition and inner transition elements. It has been observed that the values obtained having variation with ligand. Similarly, we have studied pL for metal ions with ligand Furosemide and is observed in the range 3.20-6.83 shown in table 1.

IV. CONCLUSION

The stability constant of co-ordination complexes of Furosemide diuretic drug and metals such as Co^{+2}, La^{+3}, Ni^{+2} and Cu^{+2} has been studied potentio-metrically and in the presence of $NaClO_4$ by pH-metric technique at 27^0C, the order of the stability constant of the formed complexes increase for La to Cu as La< Co< Ni< Cu.

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