POTENTIOMETRIC DETERMINATION OF STABILITY CONSTANTS OF METFORMIN COMPLEXES WITH METALS IN AQUEOUS MEDIA

Ahmed Zain A. Thabet1,2, Mohammad Mohsin2, Fahd Saleh T. Saleh1 and Mohamad Asif1

1Department of Chemistry, Maulana Azad College Aurangabad, India
2Department of Chemistry, Dr. Rafiq Zakaria College for Women, Aurangabad (M.S.). India

Corresponding Author: m7za.su.ahmed@gmail.com

ABSTRACT

The stability constant of coordination complexes of metformin i.e 1,1- Dimethyl guanidine hydrochlorides with metals such as Sm\(^{2+}\), La\(^{3+}\), Cu\(^{2+}\), and Mn\(^{2+}\) has been studied metrically and in the presence of NaClO\(_4\), 27C±0.5. The findings revealed that the sequence of the stabilization constant of the formal complexes increased from La to Cu as La< Sm< Mn< Cu.

Keywords: Samarium, Potentiometric, Stability Constant, Medicinal Drug, Metal Complexes.

INTRODUCTION

The ionic concentration of metal has a remarkable role in electrolytic solutions.\(^1\) Synthesized ligands have a remarkable effect in complex formation with Samarium. Biological activity towards the gram-negative, gram-positive bacteria, and fungi showed vital important results.\(^2\) Nowadays, the pharmaceutical market is at a high peak, so the researchers targeted their work on metal-ligand complexation study keeping transitional metal ions as their priority.\(^3\)-\(^5\) The transition metal, as well as inner transition metals, have a tendency to form coordination complexes with amino acid, Lewis bases, chalcones shiff bases, and even medicinal drugs.\(^6\) According to the current study, we have chosen d-block and f-block metallic ions with medicinal ligand Metformin. The work is also done on the 3d-metal ions with ciprofloxacin. A literature survey reveals that solvents also play an important role in the stability of complexes formed between metal ions with different ligands.\(^7\) Potentiometric studies of stability constants of some amino acids and thiobarbituric acid with metal(II) ions were also done.\(^8\) The metal forms binary and ternary complexes. The order of stability was found to increase in the covalent index. The work pH-meter is the most convenient technique for the metal-ligand complexes. Work carried out to investigate the Gene Metal-Ligand stability constant of Cefadroxil with metal ions\(^9\). Amino acids act as a coordinating agent through the amino group and carboxylic group. Work has been done with L-valin with Cu(II), Co(II), and Ni(II) metals. Valin like other amino acids is associated with insulin resistance.\(^10\) In the view of some medicinal and analytical applications of substituted pyrazoles, it will act as an antibiotic drug and a chelating agent. Therefore, the study of the metal-ligand stability constant has been done on substituted pyrazole with some lanthanide.\(^11\)

EXPERIMENTAL

Materials and Methods

Material and Reagents

3-(diaminomethylidene)-1,1-diamethylguanidine and hydrochloride were gifted samples and all reagents were obtained from Merck and SD fine chemicals and were used without more all reagents were obtained from Merck and SD fine chemicals and used without further refinement. 3-(diaminomethylidene)-1,1-diamethylguanidine and hydrochloride were gift samples, and all reagents were acquired from Merck and SD fine chemicals and used without further purification. Double distilled water was utilized to make the solutions for the potentiometric investigations. The oxalic acid content of the NaOH solution was determined (0.1M).

Rasayan J. Chem., 15(2), 968-971(2022)
http://doi.org/10.31788/RJC.2022.15266724

This work is licensed under a CC BY 4.0 license.
Complexometric titrations were used to standard all of the metal nitrate solutions that had been created. In doubly distilled water, the ligand metformin was easily soluble. Before conducting the experiment, the pH meter (ELICO, LI-120) was calibrated. Double distilled water was utilized to make the solutions for the potentiometric investigations. Oxalic acid (0.1M) was used to standard the NaOH solution. All prepared metal nitrates solutions were standardized by complexometric titrations. In double distilled water, the ligand metformin was easily soluble. Before starting the experiment, the pH meter (ELICO, LI-120) was calibrated.

**Potentiometric Experiment**

Before beginning the titrations, the pH meter was calibrated with three different buffers: 4.01, 7.0, and 9.2. Following trials of solution were prepared to determine the protonation constant of the ligand and the formation constant of the complexes in distilled water by altering metal ions.

\[
\begin{align*}
(A) & \text{HClO}_4 + \text{NaClO}_4 \\
(A + L) & \text{HClO}_4 + \text{NaClO}_4 + \text{C}_4\text{H}_{12}\text{ClN}_5 \\
(A + L + M) & \text{HClO}_4 + \text{NaClO}_4 + \text{C}_4\text{H}_{12}\text{ClN}_5 + \text{metal ions}
\end{align*}
\]

The previous mentioned sets of solutions were prepared as m: L and the complex solution was titrated against a standard NaOH solution at room temperature using a pH meter, with measurements recorded until a constant pH was achieved in 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 Samarium metal solution (10 mL).

**Calculation**

Using acid and ligand titration curves, the Irving and Rossotti approach was used to compute the average number of protons associated with the ligand at various pH levels. In acid and ligand titration curves, \(V_a\) and \(V_L\) are the volumes of sodium hydroxide required to achieve the same pH. The total ligand concentration \(T_L\) while \(N^0\) is equal to the total number of free protons connected to the ligand molecule, \(N^0\) is the normality of alkali, \(E^0\) is the initial concentration of the free acid, and \(V_0\) total volume of titrated solution. The protonation constant may be calculated using the equation.

\[
K_1 = \frac{\bar{\eta}_a}{(1-\bar{\eta}_a)[H^+]} \\
K_1 = pH + \log \frac{\bar{\eta}_a}{1-\bar{\eta}_a} \\
K_1 = pH + \log \frac{\bar{\eta}_a-1}{2-\bar{\eta}_a}
\]

The proton ligand formation constant \(K_1\) and \(K_2\) were determined from the formation curve obtained by plotting \(\bar{\eta}_a\) Vs pH, where pH values at \(\bar{\eta}_a = 0.5\) and 1.5 yield \(K_1\log\) and \(K_2\log\), respectively. Using the Irving and Rossotti equation, the average number of metal ions associated with the ligand at different pH levels was estimated from the metal ions and ligand titration curves as follows.

\[
\bar{\eta} = \frac{(V_m - V_l)(N^0 + E^0)}{(V_0 + V_l)\bar{\eta}_a T_m}
\]

Ahmed Zain A. Thabet et al.
and

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

Where \( T_m \) represents the total concentration of metal in solution and is the overall proton ligand stability constant, the other variables have their normal meanings as previously stated. The successive stability constants were then calculated using half-\( \eta \) value interpolation from \( \eta \) Vs pL formation curves. The values of \( K_1 \log \) and \( K_2 \log \) were acquired using interpolation at 0.5 and 1.5, respectively, and the least square approach was used to calculate \( K_1 \log \) and \( K_2 \log \) by plotting vs pL or s pL, respectively.

**RESULTS AND DISCUSSION**

Coordination compounds play an important role in many branches like chemistry, biochemistry, biology, medicine, etc. Stability constant used the determination of metal-ligand complex.\(^{12-14}\)

As far as the solution study of transition series is concerned, it is very interesting that Cu shows greater lattice energy and higher formation constants for complexes of Cu(II) ions. Cu(II) shows complexes with a ligand that are more stable than Ni(II) complexes.\(^{15}\)

![Fig.-1: The pH titration reading of acid, acid + Ligand, acid + Ligand + Metal at T = 27±10°C, solvent Ethanol-water (70:30)](image)

The order of stability of metal chelates was investigated by using Irving William’s natural order of stabilities\(^{16}\) as Mn (II)< Co(II)< Ni(II)< Cu(II). A Kalvin-Bjerrum method was used for the determination of the stability constant for a metal ion with ligands.

For the present study Sm, La, Cu, Mn were taken as metal ions with Metformin as a ligand. Metformin is an oral antihyperglycemic drug that is used in diabetes. Metformin is water-soluble. Metformin has one free amino group and two terminals–NH group. Metformin has more capacity for forming complexes.

| Metals | \( \log K \) | pL |
|--------|-------------|----|
| Sm     | 4.4279      | 3.5727 |
| La     | 0.8726      | 3.2959 |
| Cu     | 1.023       | 6.8310 |
| Mn     | 0.0873      | 3.7580 |

The highest value of metal-ligand complexes between Fe and boric acid has also been observed by earlier researchers.\(^{17-18}\) Works also showed the higher values of the Metal-ligand stability constant of Ni with cysteine and Schiff’s base.\(^{19}\) For the present study, the metal ion was selected from transition and inner transition elements. It has been observed that the values obtained have variations with the ligand. Similarly, we have studied pL for metal ions with ligand metformin and it was observed in the range 3.20-6.83 as shown in Table-1.
ACKNOWLEDGEMENT

We are so grateful to Dr. Rafiq Zakaria College for Women's principle for providing infrastructure for this research study.

REFERENCES

1. A. A. Zaid, M. Mohsin, M. Farooqui and D.M. Janrao. Journal of Saudi Chemical Society, 17, 43 (2013), https://doi.org/10.1016/j.jscs.2011.02.020
2. Z. T. Omar, S. Jadhav, M. Mohsin, A. S. Faizaa, and M. Rai, Russian Journal of Inorganic Chemistry, 65(14), 2046 (2020), https://doi.org/10.1134/S0036023620140053
3. S. Jadhav, R. Megha, R. K. Pardeshi, and F. Mazahar. Pharma Letter, 7, 12(2015), http://dx.doi.org/10.33980/jbcc.2019.v05i01.015
4. E. V. Zhuravlev, V. G. Alekseev, M. A. Feofanova, and S. S. Ryasenskii. Russian Journal of Inorganic Chemistry, 61, 877(2016), https://doi.org/10.1134/S0036023616070214
5. A. A. Metlin, G. G. Gorbolotova, S. A. Bychkova, and N. M. Berezina, Russian Journal of Inorganic Chemistry; 62, 1116(2017), https://doi.org/10.1134/S0036023617080149
6. M.V. Hathi, K.B. Vyas, K.S. Nimavat and G.R. Jani, International Journal of Chemical Sciences, 7(3), 2103(2009).
7. V.T. Chaudhari, A. Durrani, B.R. Agrawal, M. Farooqui, Oriental Journal of Chemistry, 25(3), 767 (2009).
8. K. T. Ishola, M. A. Oladipo, O. A. Odedokus, O. T. Olanipekun, American Journal of Applied Chemistry, 8(1), 23 (2020).
9. D. B. Kamkhede. International Journal of Research in Pharmacy and Chemistry, 6(1), 147(2016).
10. N. A. Belkher, A. A. Alabbas and M. Zidan. Journal of Pure & Applied Sciences, 18(3), 59(2019), https://doi.org/10.51984/jopas.v18i3.240
11. V.B. Khobragade and M.L. Narwade, Journal of Chemical and Pharmaceutical Research, 5(10), 189(2013).
12. M.P. Wadekar, A.S. Shirrao and R.R. Tayade. Advances in Applied Research, 5(6), 132(2014).
13. S.V. Thakur, M. Farooqui and S.D. Naikwade. Journal of Advanced Scientific Research, 4(1), (2013).
14. A. Durrani and M. Farooqui. International Journal of Chemical Studies, 1(10), 10 (2014).
15. M.V. Hathi, K.B. Vyas, K.S. Nimavat and G.R. Jani. International Journal of Chemical Sciences, 7(3), 2103 (2009).
16. H. Irving and R.J.P. William. American Chemical Society, 8, 3193 (1953).
17. Z. Omar, S. Jadhav, M. Farooqui and M. Rai. International Journal of ChemTech Research, 11, 211 (2008).
18. G.N. Mukherjee and D. Ansuman Das. Journal of Chemical Sciences, 114(3), 163(2002), https://doi.org/10.1007/BF02704261
19. S. Fatima, M. Hassan. The Arabian Journal for Science and Engineering, 30 (1A), (2005).