STUDIES OF STABILITY CONSTANT OF DRUG WITH TRANSION METAL IONS AT 303.15K.

A. N. Sonar*

Shri. V.S. Naik Arts, Com, and Science College, Raver Dist. Jalgaon (M.S.) India.

*Corresponding Author: Dr. A.N. Sonar

Shri.V.S. Naik Arts, Com, and Science College, Raver Dist. Jalgaon (M.S.) India.

ABSTRACT

The stability constant of substituted heterocyclic drug with rare earth metal ion have been investigated by Calvin-Bjerrum's pH-metric titration technique, as modified by Irving and Rossoti, was used to determine at 0.1 M ionic strength at room temperature in 70 % Ethanol-Water mixture. The data obtained use to estimate the values of proton-ligand stability constant (P^k) and Metal -ligand stability constant (logK). It is observed that transition metal ion form 1:1, 1: 2 complexes with all the systems.

INTRODUCTION

Favipiravir is an antiviral medication used to treat influenza in Japan. It is also being studied to treat a number of other viral infections, including SARS-CoV-2[1,2] It is used in the treatment of covid-19.Raman Jee Jha was investigated the stability constant of 1-phenyl – 3 - (2' – mercaptophenyl) – N – (3"– hydroxy – 5" – ethyl – 1", 2", 4" – triazolyl) propene – 1 – imine with transition metal ion at constant ionic strength.[3] The researchers have been studied the stability constant of Iron(III) plant based oxalate complexes at constant ionic strength and they concluded that the consumption of half-boiled vegetables like Spinach may enhanced the formation of oxalate-related kidney stones which are serious health challenges nowadays since a stable complex can easily be formed[4] Researcher investigated the Stability Constants of Mixed Ligand Complexes of Transition Metal(II) ions with 1-[(1E)-N-(2,4-dibromophenyl)ethanimidoyl]naphthalen-2-oland 2-{(E)-[(4-chlorophenyl) imino] methyl}phenol at constant ionic strength by using KCl in 1,4-dioxne-water medium.[5] Zamzam Taher Omaret. al have been studied the stability constant of N-[-(4-chlorophenyl) methylene] nicotinohydrazide with transition metal ion at constant ionic strength in 70% ethyl alcohol.[6] The studies of metal-ligand complexes in solution of a number of metal ions with carboxylic acids, oximes, phenols etc. would be interesting which throw light on the mode of storage and transport f metal ion in the biological kingdom.

In the earlier papers extensive data base on metal complexes with substituted heterocyclic drugs was presented. Narwade et.al. studies the Formation and Stability constant of thorium (IV) complex with some substituted pyrazolines.[7] Mathieu W.A. Steenland et.alstudies stability constant of Cu(II) and Ni(II)

complexes of trans –dioxopentaaza macrocycles in aqueous solution by different technique.[8] Hong-Wen Gaoet.alhas studied the stability constant of Cu (II) and Co (II) complexes with CNBAC in water sample spectrophotometrically.[9] Tuba Sismanoglu have studied the stability constant of binary complexes of Nicotinamide with Mn (II) by pH metrically.[10] He also determines change in free energy, change in enthalpy and change in entropy from stability constant at different temperature. Tekade et.al. have been studied complex formation of Cu (II) and Co (II) metal ion complex with substituted isoxazolines.[11] O.Yamauchi et.al. studied stability constant of metal complexes amino acids with charged side chain by pH–metrically.[12] Hayati Sari et.alstudied the stability constant of glyoxime derivative and their Nickel, Copper, Cobalt and Zinc complexes potentiometric and theoretically.[13]

After review of literature survey the detail study of complex under identical set of experimental condition is still lacking. It was thought of interest to study the chelating properties of Olmesartan under suitable condition with metal ions by pH metrically.

MATERIAL AND METHOD

pH measurement were carried out with equip-tronic EQ-610 pH meter (accuracy ± 0.01 units) using combine glass electrode at room temperature. Metal ions solutions were prepared in triply distill water and concentration estimated by standard method.[14] The solution of drug prepared in solvent. The pH metric reading in 70% ethanol – water mixture were converted to [H+] value by applying the correction proposed by Van Uitert Haas.

The overall ionic strength of solution was constant and calculated by the equation and mentain by adding standard solution of NaCl.

RESULT AND DISCUSSION

Substituted heterocyclic drugs may be ionized as acid having replaceable H^+ ion from -OH group. Therefore it is represented as HL i.e. HL $\longrightarrow$ $H^+ + L^-$

The titration data used to construct the curves between volume of NaOH and P^H. They are called acid-ligand titration curves.

It is observed from titration curves for all systems ligand start deviating from the free acid curves at P^H 2.5 and deviating continuously up to P^H =11. The deviation shows that dissociation of proton in substituted drugs.

The average number of proton associated with the ligand (n_A) was determined from free acid and acid – ligand titration curves employing the equation of Irving and Rossotti.[15] The P^k values were determined from formation curves $(n_A$ v^s P^H) by noting the P^H at which n_A =0.5. The accurate values of pk were calculated by point wise calculations which are presented in table -1. The pK values are found.

Table-1: Proton ligand stability constant of ligandat 0.1M ionic strength.

System	Constant pK	
	Half integral	Point wise calculation
Ligand-1	6.75	6.690. ± 0.06

METAL -LIGAND STABILITY CONSTANT (Log k)

Metal-ligand stability constant of transition metal ion chelate with drug were determined by employing Bjerrum calvin P^H metric titration method as adopted by

Irving and Rossotti. The formation of chelate between transition metal ion with drug was indicated by the significant separation starting from pH =2.5 for transition metal ion with ligand -1.

Table-2: Determination of metal –ligand stability constant (logK) of transition metal ion with drug at 0.1M ionic strength.

System	Logk$_1$	Logk$_2$	Logk$_2$ - Logk$_1$	Logk$_2$ / Logk$_1$
Ce(III)-Ligand	3.75	5.50	1.75	1.4666
Gd(III)-Ligand	3.90	5.65	1.75	1.4487
Pr(III)-Ligand	3.85	5.70	1.85	1.4805
Dy(III)-Ligand	3.45	4.70	1.25	1.3623
Yb(III)-Ligand	4.25	5.95	1.70	1.4000

The result shows the ratio of Logk$_2$/ Logk$_1$ is positive in all cases. This implies that there is little or no steric hindrance to the addition of secondary ligand molecule .The smaller difference may be due to trans structure.

REFERENCES

1. Du YX, Chen XP "Favipiravir: pharmacokinetics and concerns about clinical trials for 2019-nCoVinfection". *Clinical Pharmacology and Therapeutics*, 2020; 242–247.
2. Shiraki K, Daikoku T "Favipiravir, an anti-influenza drug against life-threatening RNA virus infections". *Pharmacology & Therapeutics*, 2020; 20: 107512.
3. Raman Jee Jha, *Res J. Chem. Environ. Sci*, 2020; 01-12.
4. Gongden, J. J., 1Gurumyen, K. K, Danja, B. A., Uduah, O. V. and Lohdip Y. N., *Nigerian Journal of Chemical Research*, 2020; 69-80.
5. Atmaram K. Mapari, *International Journal of Applied Chem*., 2017; 211-218.
6. ZamzamTaher Omar (Al-Ahdal)*, Shivaji Jadhav,Mazahar Farooqui, Megha Rai, *International Journal of ChemTech Res*., 2018; 211-216.
7. M. L. Narwade, V.S. Jamode, and S.K. Gudadhe, *Acta.Ciencia Indica* , 1985.
8. Mathieu W.A. steenland, Use dirack Gerrit G. turnan, Bart Devreese, Werner Lippens, Jozef Van Beeuman and Andre M. Goeminne, *J.Chem.Soc. Dalton trans,* 1997; 3637-3647.
9. Hong Wen Gao and Jian-Fu-Zhao, *Croatica Chem. Acta ,CCACAA*, 2003; 1-6.
10. Tuba sismanoglu, , *Chinese Chemical Letters*, 2003.
11. P.V. Tekade, K. N. Patil, M.L. Narwade, P.S. Bodake, Y.K. Meshram, *Asian J. Chem,* 2006; 2657.
12. O. Yamauchi and A. Odani, *Pure and Applied chemistry*, 1996.
13. Hayati Sari, Muzaffer Can and Mustafa macit,*Acta Chim Slov*, 2005.
14. A.I. Vogel, Longmans Green A *Text Book of Quantitative Inorganic Analysis*, London, 1975; 589.
15. H.S. Irving and H.S. Rossotti, *J. Chem. Society,* 1954.