

Stability Constant Study of Transition Metal Complexes with Pharmacologically Active Nicotinamide and Alanine by pH Metric Technique

D. D.Kayande^{1*}, Shivaji Jadhav², Mazahar Farooqui³ and Megha Rai³

¹ S.B.E.S.Sciene College, Aurangabad, Maharashtra, INDIA

² Tarai Arts and Science College, Paithan, Aurangabad, Maharashtra, INDIA

³ Dr. Rafiq Zakaria College for Women, Aurangabad (M.S), INDIA

* Correspondence: E-mail: drkayande@gmail.com

DOI: <http://dx.doi.org/10.33980/jbcc.2019.v05i01.017>

(Received 26 Feb, 2019; Accepted 27 Apr, 2019; Published 29 Apr, 2019)

ABSTRACT: The main objective of this research work is to carry out the stability constant study of ternary complexes of transition elements with nicotinamide and alanine. Formation of ternary complexes of transition elements like Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) of pharmacologically active Nicotinamide with Alanine was studied by the pH-metric technique at $25 \pm 0.1^\circ\text{C}$ in 70% (v/v) ethanol - water medium at 0.1M (NaClO_4) ionic strength. The stability constants of the Nicotinamide and Alanine were calculated from the half integral method of potentiometric pH titrations data of solutions according to Irving and Rossetti's method. The stability constants of these ternary complexes were evaluated and Order of stability constant found as $\text{Co (II)} > \text{Fe (II)} > \text{Cu (II)} > \text{Ni (II)} > \text{Zn (II)}$.

Keywords: Stability constant; Nicotinamide; Alanine and Ternary complexes.

INTRODUCTION: The metal ligand equilibria plays important role in different fields including the therapeutic values of the drug. It is well known fact that the metal complexes of the drugs shows different therapeutic values compared to the bare drug only, therefore various researchers reports stability constant of bioactive compounds with metal (Chaudhari et al., 2009; Pardeshi et al., 2015). For the determination of stability constant various technique are utilized such as spectrophotometry, polarography, potentiometry etc. pH-metric study is one of the best widely used technique because it has various advantages like, it is simple and low cost technique, easy to operate, economic (Jadhav et al., 2016) etc.

Hetero atom present in bioactive compounds able to bind metal ions present in living organisms due to present of lone pair of electron. Activity of Mixed Metal complexes are found to be improved as compare to parental biomolecule, so now a days many co-workers are interested to carried out complexation study of various heterocyclic compounds which are continuously used in medical field.

Complex formation of metal ions of biological important compounds with amino acids, small peptide and their derivatives are of great significance, as many of these systems offer simple models of otherwise. Com-

plex metal protein equilibria occurring in enzymic processes. At low pH, the peptide group undergoes both protonation and metallation at the carbonyl oxygen atom. Metal ion coordination with amide nitrogen atom takes place only upon substitution of the amide proton, for which primary ligating site at a chelating position is, however, essential researchers are studied the effect of a sulfonamide group at a chelating position on the modes of Cu(II) ion coordination with a series of N- Benzene Sulphonyl derivatives. Nicotinamide is one of the most famous pharmacological active agents which are used to treat pellagra discovered in 1935 -1937. Structural configuration of nicotinamide shows the presence of pyridine ring and attachment of amide group at metaposition. Hetero atom present in the structure of Nicotinamide is helpful for the formation of metal complexation which may improve the stability and pharmacological role of parental biomolecule.

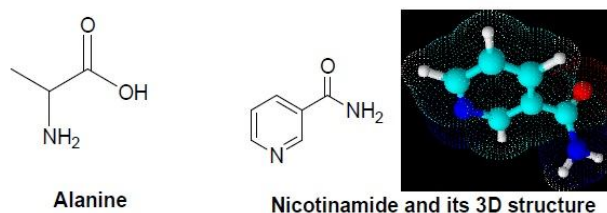


Figure 1: Structures of ligands.

In the present investigation the formation and stability of ternary mixed metal complexes containing Nicotinamide (N, O) donor secondary ligands with Alanine (N,O) Donor primary ligands (figure 1) are reported at $25 \pm 0.10^\circ\text{C}$ in 0.1 M (NaClO_4). The effect of the substituent on the dissociation constants and on the stability & formation of the binary and ternary complexes have been evaluated by comparing the relevant data for systems containing determined under identical experimental conditions. Due to these valuable findings observed in literature review, present work was planned and well executed for the formation of ternary complexes of Nicotinamide (as primary ligand) with Alanine (as secondary ligand). Complexation of biologically active ligand was carried out with transition metals to determine the order of stability constants by using pH-metric technique.

MATERIALS AND METHODS: Nicotinamide was of analytical grade and NaOH, NaClO_4 , HClO_4 and copper salt were of local grade. The solutions used in the potentiometric titrations were prepared in double distilled water. The NaOH (0.041M) solution was standardized against oxalic acid solution (0.1M) and the standard alkali solution was again used for standardization of HClO_4 . The copper salt solution was standardized using EDTA titrations. The ligand (NA) is soluble in double distilled water. The pH meter was calibrated before each titration with standard buffer solutions of 4.00, 7.00, and 9.2. The pH-meter (ELICO, L1-120) was used with a combined glass electrode assembly.

Potentiometric method: In this study of binary and ternary chelates by the potentiometric titration technique. The following sets were prepared in the standard:

- (1) Free HClO_4
- (2) Free HClO_4 + Ligand (LP)
- (3) Free HClO_4 + Ligand (LP) + Metal ion
- (4) Free HClO_4 + Ligand (LS)
- (5) Free HClO_4 + Ligand (LS) + Metal ion (M)
- (6) Free HClO_4 + Ligand (LP) + Ligand (LS) + Metal ion (M)

Against standard sodium hydroxide, the ionic strength of solutions was maintained constant by adding appropriate amount of (0.1M) Sodium perchlorate solution. The titrations were carried out at room temperature in inert atmosphere by bubbling oxygen free nitrogen gas through an assembly containing the electrode to keep out CO_2 by noting the pH of precipita-

tion for ML_p , ML_s and ML_pL_s titration, the formation of mixed ligand complexes can be concluded.

Calculations: The protonation constants of the ligand were calculated from the potentiometric pH titrations data of solutions according to Irving and Rossetti's method. For this purpose, the average proton-ligand formation number (n_a) at various pH for the ligand was determined according to the literature. The value of pK_a was read directly from $n_a = f(\text{pH})$ graph at $n_a = 0.5$. For the calculation of stability constants of binary complexes (using the potentiometric titration data of the solutions and according to Irving and Rossetti's method the metal-ligand (M-NA and M-2NA) formation number (n) at various pH for the ligand was determined according to the literature. Then pL values were calculated with using the equation from the literature. Having thus obtained corresponding values of n - and pL , the formation curve of the metal-ligand system is drawn and the stability constant is read directly at $n = 0.5, 1.5$. The calculation of the stability constant of ternary complex by the stepwise equilibria in solution would be confirmed when the mixed ligand curve could be superimposed over the binary ML_p or ML_s titration curve. The method of Thomson and Loraas for calculation of stepwise stability constants is widely used.

RESULTS AND DISCUSSION: Schwarzenbech and Ackermann (Pathan et al., 2014) found that the stability of chelate decreases as the size of ring increases. Mellor & Maley (Farooqui et al., 2014) 50% Dioxane-Water medium. The order of stability was: $\text{Pa} > \text{Cu} > \text{Ni} > \text{Co} > \text{Zn} > \text{Cd} > \text{Fe} > \text{Mn} > \text{Mg}$. Irving – William (Kayande et al., 2018) have correlated their data by plotting the stability constant against the atomic number of the metal ion. The order is, $\text{Mn} < \text{Fe} < \text{Co} < \text{Ni} < \text{Cu} < \text{Zn}$.

In complexation, Nicotinamide is used as one of the ligand, along with secondary Alanine. The potentiometric Calvin Bjerrum method is used as discussed in the experimental section. The metal ligand stability constants for binary as well as ternary are determined. The protonation constant of Nicotinamide and Alanine was determined by half integral method and Metal-ligand stability constant are shown in **Table 1**.

The stability parameters of ternary complexes of Nicotinamide with Alanine and transition metal ions like Fe, Co, Ni, Cu, Zn. The $\log K$ values for these are given in **Table 2**.

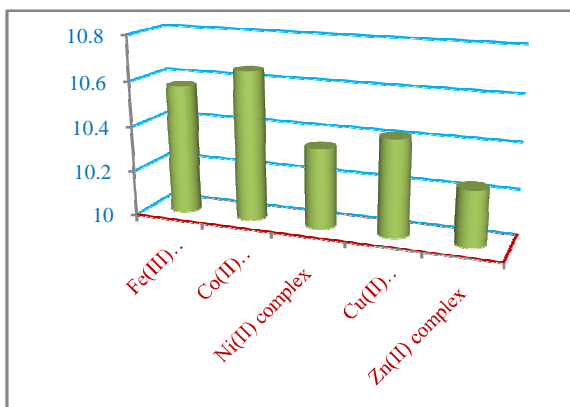
The order of stability constant of ternary complexes of Nicotinamide with Alanine were found to be $\text{Zn} < \text{Ni} < \text{Cu} < \text{Fe} < \text{Co}$.

Table 1: Protonation constant of Nicotinamide and Metal-Ligand Stability.

Stability constant data	
Metal	Nicotinamide Stability Constant (log K ₁)
Fe(III)	4.141
Co(II)	3.980
Ni(II)	2.704
Cu(II)	2.671
Zn(II)	3.710

Table 2: A Complex metric parameters of ternary complexes of Nicotinamide with Alanine as secondary ligand.

Log K _{MX} Data of mixed ligands with metal ion		
Metal ion	Mixed Ligand	LogK _{MX}
Fe(III)	Nicotinamide + Alanine	10.569
Co(II)	Nicotinamide + Alanine	10.657
Ni(II)	Nicotinamide + Alanine	10.351
Cu(II)	Nicotinamide + Alanine	10.422
Zn(II)	Nicotinamide + Alanine	10.242

**Figure 2: Graphical representation of stability constant data of ternary complexes.**

CONCLUSION: Formation of ternary metal complexes of Nicotinamide with Alanine has been suc-

cessfully and conveniently carried out with transition metal ions like Fe, Co, Ni, Cu and Zn. Role of pharmacological properties of biologically active compounds on the stability of the complexes was investigated and the order of stability constant of ternary complexes of Nicotinamide with Alanine were found to be Zn < Ni < Cu < Fe < Co. The ternary metal complexes of Nicotinamide and Alanine may be improving its application in drug industry. This would require specially designed research conducted by specialized drug chemist.

REFERENCES:

1. V. T . Chaudhari and Mazahar Farooqui (2009) Synthesis, characterization and potentiometric study of stability constant of N-[2-hydroxy-1-naphthylidene]-2-methylaniline complexes with transition elements, *J. Ind. Chem. Soc.*, 86, 166.
2. R. K. Pardeshi et al. (2015) TDR approach towards Dielectric relaxation studies of binary mixtures of organic compounds in polar solvents at room temperature, *Arab J. phy. Chem.*, 2(4), 97-101.
3. Shivaji Jadhav et al. (2015) Determination of stability constant of metal ligand equilibria with special reference to Schiff base and transition elements, *Der pharmacia Letter.*, 7(12), 316-320.
4. Shivaji Jadhav et al. (2016) Synthesis, characterization and potentiometric study on stability of N-[2-hydroxy-1-naphthylidene]-2-methylaniline complexes with transition elements, *J. chem. Pharm. Res.*, 8(1), 245-249.
5. Jamil khan Pathan et al. (2014) Studies on metal ligand stability constant of allopurinol and succinic acid with some metal ions in aq. Media, *Int. Journal of chemical studies*, 1(5), 35- 41.
6. Mazhar Farooqui et al. (2014) Characterization by potentiometric procedure of metal binding properties of allopurinol in presence of ascorbic acid, *J. Chem and Pharm Research*, 6(6), 1001-1003.
7. D. D. Kayande et al. (2018) Mixed metal Complexation study of transition series with Thiourea and alanine, *International Jou. Universal Print.*, 4(8), 495-499.