Ph-Metric Study of Stability Constant of Ternary Complexes Involving Transition Metals, Nicotinamide and Penicillamine

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Abstract

Role of Pharmacologically important compounds (Nicotinamide and Penicillamine) as ligand has been focused on the coordination complexes with transition metal ions such as Fe (III), Co (II), Ni (II), Cu (II) and Zn (II). Complexation of metal ions with Nicotinamide as primary ligand whereas Penicillamine as secondary ligand has been evaluated by the potentiometric technique at 25±0.1°C and 0.1M ($NaClO_4$) ionic strength. The protonation constants of the ligand were calculated from the half-integral method of potentiometric pH titrations data of solutions according to Irving and Rossetti's method.

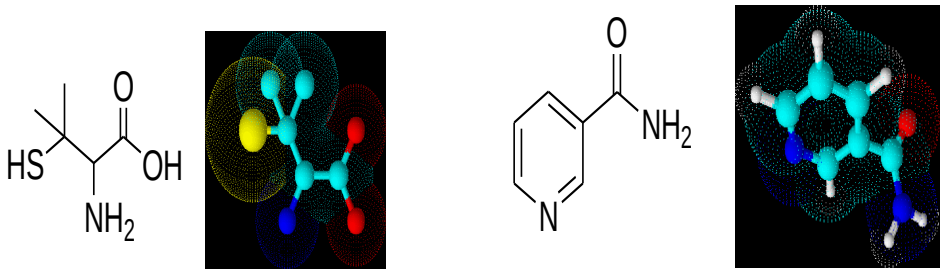
Keywords: Stability Constant, Nicotinamide, Penicillamine, Mixed Ligand Complexes.

Introduction:

Various functional groups, active sites present in bioactive compounds able to bind metal ions are present in living organisms. As compare to original biomolecule, Mixed Metal complexes of biomolecule are found to be more effective. Due to this importance of complexation of metal ions with biomolecule most of the researchers are attracted towards mixed metal complexation study of pharmacologically active compounds and it plays life-sustaining role in the bio - chemical activity [1-3]. It is widely used in various fields such as biological processes, pharmaceuticals, separation techniques, analytical processes etc. Complex formation of metal ions of biological importance with amino acids, small peptide and their derivatives are of great significance, as many of these systems offer simple models of otherwise.

Complex metal protein equilibria are occurring in enzymatic 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 G.N. Mukherjee and P. K. Chakraborty studied the effect of a sulfinamide group at a chelating position on the modes of Cu(II) ion coordination with a series of N- Benzene Sulphonyl derivatives [4].

Nicotinamide is a form of vitamin B3 found in food and used as a dietary supplement and medication. As a supplement, it is used by mouth to prevent and treat pellagra. Nicotinamide was discovered between 1935 and 1937. It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. The structure of nicotinamide consists of a pyridine ring to which a primary amide group is attached in the *meta* position. It is an amide of nicotinic acid Penicillamine is a medication primarily used for the treatment of the patients which is suffering through kidney stones that have high urine cysteine levels, rheumatoid arthritis, and various heavy metal poisonings. It is taken by mouth. It is also used as a chelating agent: In Wilson's disease, a rare genetic disorder of copper metabolism, Penicillamine treatment relies on its binding to accumulated copper and elimination through urine.



Penicillamine and its 3D structure Nicotinamide and its 3D structure

Fig.1: Structure of ligands

In the present investigation the formation and stability of ternary mixed metal complexes containing Nicotinamide (N.O) donor secondary ligands with Penicillamine (N,O,S) Donor primary ligands **(fig.1)** are reported at 25±0.10C in 0.1 M (NaClO4). The effect of the substituent on the dissociation constants and on the stability & formation of the binary and ternary complexes **(fig.2)** have been evaluated by comparing the relevant data for systems containing determined under identical experimental conditions.

Experimental Section:

Materials and Solution: Nicotinamide were 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 [5]. 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 Procedure:

In this study of binary and ternary chelates by the potentiometric titration technique.

The following sets were prepared in the standard:

(1) Free HClO4

(2) Free HClO4 +Ligand (LP)

(3) Free HClO4 +Ligand (LP) +Metal ion

(4) Free HClO4 +Ligand (LS)

(5) Free HClO4 +Ligand (LS) +Metal ion (M)

(6) Free HClO4 +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 precipitation 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 [6]. For this purpose, the average proton-ligand formation number (na) at various pH for the ligand was determined according to the literature [7]. The value of pKa was read directly from na = f (pH) graph at na =0.5. For the calculation of stability constants of binary complexes (using the potentiometric titration data of the solutions and according to Irving and Rossotti's method [8], the metal-ligand (M-NA and M-2NA) formation number (n-) at various pH for the ligand was determined according to the literature [9]. Then pL values were calculated with using the equation from the literature [10]. 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 MLp or MLs titration curve. The method of Thomson and Loraas [11] for calculation of stepwise stability constants is widely used.

Results and Discussion:

Schwarzenbech and Ackermann [12] found that the stability of chelate decreases as the size of ring increases. Mellor & Maley [13] 50% Dioxane-Water medium. The order of stability was: Pa > Cu > Ni > Co > Zn > Cd > Fe > Mn > Mg. Irving – William [14] have correlated their data by plotting the stability constant against the atomic number of the metal ion. The order is, Mn < Fe < Co < Ni < Cu < Zn. In complexation Nicotinamide is used as one of the ligand, along with secondary Penicillamine **(fig.2).**

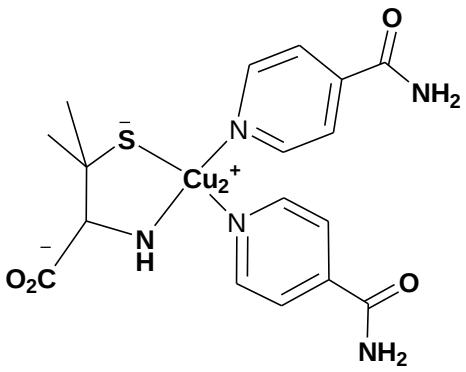


Fig.2:probable structre of Cu-complex with Nicotinamide and penicillamine

The potentiometric Celvin 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 of Nicotinamide and Penicillamine was determined by half integral method. The protonation constant of Nicotinamide and Metal-ligand stability constant are shown in **Table 1.**

Table1. Protonation constant of Nicotinamide and Metal-Ligand Stability

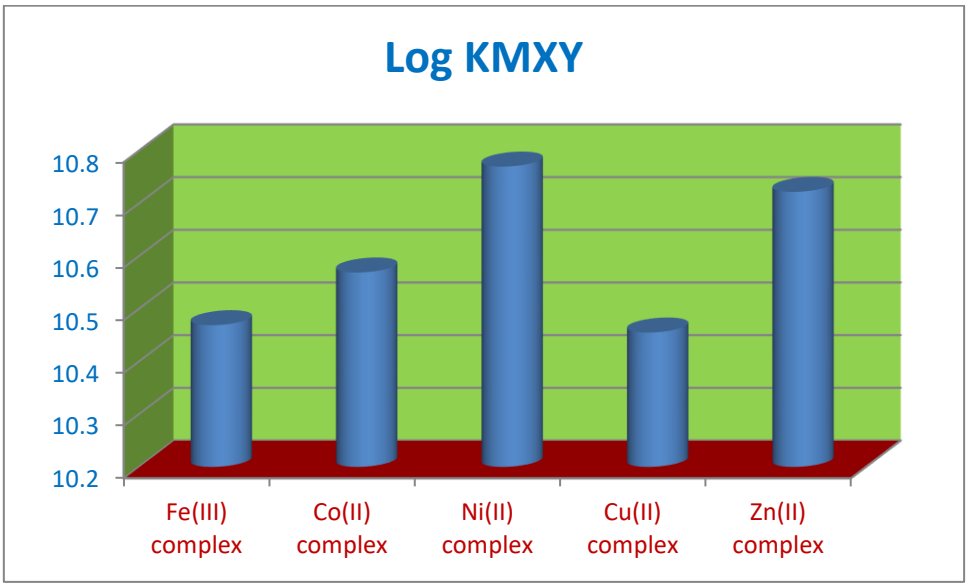
Metal	Nicotinamide Stability Constant(logK1)
Fe(III)	4.141
Co(II)	3.980
Ni(II)	2.704
Cu(II)	2.671
Zn(II)	3.710

The stability parameters of ternary complexes of Nicotinamide with Penicillamine and transition metal ions like Fe, Co, Ni, Cu, Zn. The logK values for these are given in **table 2.**

Table 2: A Complex metric parameters of ternary complexes of Nicotinamide With Penicillamine as Secondary ligand

Metal ion	Mixed Ligand	Log K_{MXY}
Fe(III)	Nicotinamide+ Penicillamine	10.469
Co(II)	Nicotinamide + Penicillamine	10.569
Ni(II)	Nicotinamide + Penicillamine	10.770
Cu(II)	Nicotinamide + Penicillamine	10.455
Zn(II)	Nicotinamide + Penicillamine	10.722

Graphical representation of stability constant data as shown below:



The order of stability constant of ternary complexes of Nicotinamide with Penicillamine were found to be Cu < Fe < Co< Zn < Ni.

Conclusion

The present work describes the complex formation equilibria of transition metal ions with Nicotinamide with Penicillamine. 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 Penicillamine were found to be Cu < Fe < Co< Zn < Ni. The ternary metal complexes of Nicotinamide and Penicillamine may be improving its application in drug industry. This would require specially designed research conducted by specialized drug chemist.

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