Formation Constant of Transition Metal Complexes with Adenosine Biomolecule and Glutamic Acid and Isoleucine Amino Acids

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Abstract

Formation constants of transition metal complexes with Adenosine biomolecule, Glutamic acid, and isoleucine amino acids have been studied pH metrically in 20% v/v ethyl alcohol and water medium at 30°C temperature and 0.1 M ionic strength. The proton ligand stability constant (pKa) of ligands and metal ligand stability constant (logK) of binary metal complexes were determined. It is correlated with atomic numbers, basicity of ligands, and atomic radii of metal ions. The transition metal complexes of ligands follow the Irving William natural order of stability.

Keywords: Formation Constants, Metal Complexes, Adenosine, Amino Acids.

Introduction

The formation of metal complexes depends on metal ligand selectivity in complex media. The formation constant of metal complexes with biomolecule and amino acids are important to measure the metal ligand selectivity and strength of metal ligand bonds (Thomas,2002). The metal complexes of drug are found more potent than drugs (Sarkar,1999). It plays a vital role in metabolism, transportation, detoxification and catalytic process. The knowledge of metal complexes with drugs is essential to understand proper dose of drug. In addition, it helps to know the complex physiological process and mode of action of drugs and their effect on various body systems. The literature survey reveals that there is still need to study the binary complexes of transition metal ions with drugs and amino acids to know the coordination behavior (Deore et. al, 2011; Gandhi and Sekhon., 2006;Magare and Ubale,2011;Magare and Ubale,2018;Magare,2019;Phase et al ,2013;Sakhare et al,2019)

Adenosine (Fig.**1.0**) being a purine nucleoside performs many important functions in human body and biological processes (Cummings,1994). It modulates physiological function in heart and brain, regulates oxygen supply during cell stress and play an important role in the regulation of renal function (Kloor,2000;Zhang,1997). It is a potent anti-inflammatory and anti-arrhythmic agent which is important for the control of coronary and cerebral blood flow (Phillis,2004; Tesch,2004). It is an inhibitory neurotransmitter (Gruber,1991; Nishiyama et al,2004) and play a role in promoting sleep and suppressing arousal (Bashir et al,2000). Adenosine is an endogenous vasodilation agent (Martin et al,2000) and also administered for the treatment of gastrointestinal diseases in many cases (Ye and Rajendran,2009). The amounts of Adenosine in the urine and plasma samples are considered be marker of some diseases such as carcinoma or liver diseases (Yang et al,2002).

Glutamic acid (Meister,1965) (Fig. **2.0**) is acidic non-essential glycogenic amino acid with one amino group and two carboxylic groups. It takes part in transamination, transamidation and inter conversion of amino acids and also participate in ammonia transport and urea formation. Glutamic acid involve in

glycogenic function, on deamination it form oxaloacetate and α-ketoglutarate and form glycogen. Its wide range contribution in urea formation, purine, and pyrimidine rings synthesis. Glutamic acid on decarboxylation gives rise to gamma aminobutyric acid. It controls the neuronal activity. Glutamic acid is one of the constituent of glutathione which is important in the activity of sulphadryl enzyme system. Studies over the last several years have explored the physiological role and therapeutic utility of these molecules in various diseases conditions (Colquhonn and Newsholme,1997;Pitha et al 1980). Recently Satyajit Datta et al. have reported glutamic acid analogues used as potent anticancer (Kato et al,1984).

Isoleucine (Fig. **3.0**) is an essential amino acid, which means that human cannot synthesize it, so it must be part of our diet. It promotes muscles recovery, needed for the formation of haemoglobin regulation of blood sugar level and blood clot formation. Deficiency of isoleucine is only found in people deficient in dietary protein but symptoms may include headache, dizziness, fatigue, depression & confusion. Isoleucine has also several significant applications in biological systems (Li et al,2009; Mitrophanov,2008;Papp et al 2010) .

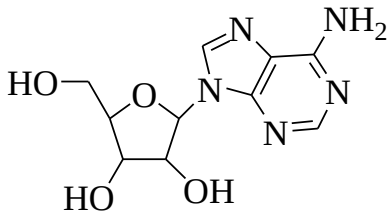

Figure 1.0

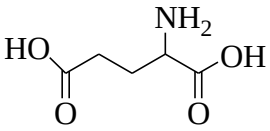

Figure 2.0

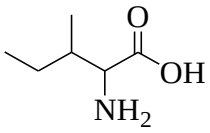

Figure 3.0

Hence formation constants of Co (II), Ni (II) Cu (II) and Zn (II) transition metal ion complexes with biomolecule nucleoside, glutamic acid and isoleucine amino acids were carried out in 20% v/v alcohol water media.

Chemicals and Methods

The solution of ligands were prepared in pure alcohol. The other solutions were prepared in double glass distilled water having pH 6.70-6.90. The chemicals used for present study were of A.R. grade. The alcohol was purified by standard procedure. The concentrations of solutions were determined by standard procedures (Bates,1973;Vogel,1975). The determination of stability constants of binary complexes were involved three steps.

1) Free acid (A)

2) Free acid + Ligand (A+L)

3) Free acid + Ligand + Metal (A+L+ M)

These three sets were titrated separately with standard sodium hydroxide solution at 30^0C temperature in 20% v/v alcohol water solution pH metrically by using Irving Rossotti titration technique (Irving and Rossoti,1953). The 0.1M ionic strength of each solution was maintained constant by addition of $NaClO_4$. Initial volume of solution was kept 50 ml constant by adding requisite amount of distilled water and pure alcohol.

Results and Discussion

Proton ligand stability constant (pKa)

The pKa values of Adenosine and amino acids were determined by point wise and half integral methods. Adenosine shows only one pKa (3.44) due to (-OH) group. It is a weak acidic group due to powerful electron

withdrawing effect. The observed pKa values of amino acids show little deviation with literature values due to different medium and environmental conditions.

TABLE: 1.0 STABILITY CONSTANT OF METAL IONS WITH BIOMOLECULE AND AMINO ACIDS.

Medium: - 20% (v/v) Ethanol-Water mixture Temp = 30°C μ = 0.1 M $NaClO_4$

Ligand	pK_1	pK_2	Cu (II)			Zn (II)			Ni (II)			Co (II)		
			Log K_1	Log K_2	Log β	Log K_1	Log K_2	Log β	Log K_1	Log K_2	Log B	Log K_1	Log K_2	Log β
Adenosine (L_1)	3.44	----	5.07	4.33	9.40	4.32	3.88	8.20	3.56	3.25	6.81	3.43	3.27	6.70
Glutamic acid (L_2)	2.59	4.99	10.29	8.33	18.62	5.10	4.29	9.39	7.77	5.99	13.76	5.57	4.52	10.09
Iso leucine (L_3)	2.53	9.72	9.54	6.69	16.23	4.28	3.44	7.72	5.01	3.75	8.76	3.95	3.03	6.98

The glutamic acid and isoleucine show two pKa values. The values of $\bar{n}_A$ are indicates the presence of pK_1 and pK_2. The values observed in the present study were in good agreement with literature values (**Table 1.0**). The slight deviation observed may be due to the difference in experimental conditions like temperature, ionic strength, techniques, and medium used.

Metal ligand stability constants (LogK)

The displacement of metal titration curves with respect to ligand titration curve along volume axis indicates the formation of complex species. The LogK values were determined by pointwise calculation method as well as half integral method. The pKa, LogK and logβ values were enlisted in **Table 1.0.**

The values of $\bar{n}$ of Adenosine, glutamic acid and isoleucine are shows the formation of 1:1 and 1:2 complexes. The transition metal complexes of ligand L_1 show low stability than L_2 and L_3 ligands. It may be attributed to monodentate and bidentate nature and different basicity of ligands.

The order of stability of transition metal ions complexes with L_1 ligand and amino acids L_2 and L_3 in the present study are as follows:

Adenosine L_1: Co (II) < Ni (II) < Cu (II) >Zn (II)

Glutamic acid L_2: Co (II) < Ni (II) < Cu (II) >Zn (II)

Isoleucine L_3: Co (II) < Ni (II) < Cu (II) >Zn (II)

The plots of LogK versus atomic number, atomic radii were plotted and it is observed that the complexes of L_1, L_2 and L_3 ligands follow the Irving William natural order of stability (Irving and William,1946). The low values of LogK in L_1 drug indicates ionic interactions whereas high LogK values of L_2 and L_3 ligands may be attributed to covalent interactions (Rajbhoj et al,2007;Rao et al,2006).

Conclusion

The complexes of L_1, L_2 and L_3 ligands follow the Irving William natural order of stability. The low values of LogK in L_1 drug indicates ionic interactions whereas high LogK values of L_2 and L_3 ligands may be attributed to covalent interactions.

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Conflicts of Interest

Authors have declares that he has no conflicts of interest.