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INTERACTION OF Co (II), Ni (II), Cu (II) AND Zn (II) TRANSITION METAL IONS WITH SULFAMETHOXAZOLE DRUG AND PHENYL ALANINE IN 40% ALCOHOL WATER MEDIUM

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ABSTRACT

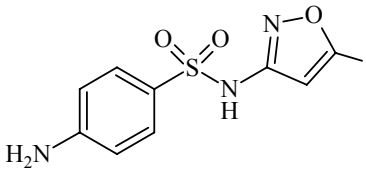
The interaction of Co (II), Ni (II), Cu (II) and Zn (II) transition metal ions with sulfamethoxazole drug and phenyl alanine amino acid have been studied pH metrically at 27°C temperature and 0.1 M ionic strength ($NaClO_4$) in 40% v/v alcohol water medium. The pKa of ligands and log K of binary metal complexes were determined and correlated with basicity of ligands and atomic number, atomic radii of metal ions.

Key words: Interaction, drug, amino acid, ionic strength, pH metrically.

INTRODUCTION

The interaction of metal ions with ligand plays vital role in biological systems. The knowledge of metal complexes with drugs is essential to understand the complex physiological process and mode of action drugs and their effect on various body systems. The formation of metal complexes depends on metal ligand selectivity in complex media. The stability constant of metal complexes with drugs are important to measure the metal ligand selectivity in terms of relative strength of metal ligand bonds[1]. The metal complexes of drugs are found to more potent than drugs[2]. It plays a vital role in transportation, detoxification and catalytic process. The literature survey reveals that no systematic study of binary complexes of transition metal ions with drugs has been reported[3-10].

The systematic IUPAC name of sulfamethoxazole is 4-amino-*N*-(5-methylisoxazol-3-yl)-benzenesulfonamide. It is a bacteriostatic antibiotic[11]. It is most often used as part of a synergistic combination.



The phenyl alanine is aromatic, essential, glycogenic and ketogenic amino acid. In metabolism, it is

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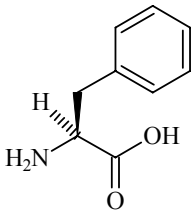
converted into tyrosine, which forms the hormones like adrenaline, nor adrenaline, melanin pigments. The abnormalities observed in the phenyl alanine metabolism are phenylketonaria and alkaptonaria.



It is found in the breast milk of mammals. It is used in manufacture of food and drink products. It is a direct precursor to neuromodulator phenyl ethylamine commonly used dietary supplement. Hence, the study of complexes of sulfamethoxazole drug and phenyl alanine with Co(II), Ni(II) Cu(II) and Zn(II) transition metal ions were carried out in 40% v/v alcohol water media.

EXPERIMENTAL

The chemicals used for present study were of analytical grade. Pure drugs were obtained as a gift sample. The solution of drug was prepared in pure alcohol. The other solutions were prepared in double distilled water having pH 6.70-6.90. The alcohol was purified by standard procedure. The concentrations of solutions were determined by standard procedures[12]. The determination of stability constants of binary complexes were involved three steps.

(i). Free acid (A)

(ii). Free acid + Ligand (A+L)

(iii). Free acid + Ligand + Metal (A + L + M)

These three sets were titrated separately with standard sodium hydroxide solution at 27^{o}C temperature in 40% v/v alcohol water solution pH metrically by using Irving Rossotti titration technique[13]. The ionic strength of each solution was maintained constant at 0.1 M 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 (pK_a)

The pK_a values of sulfamethoxazole drug and phenylalanine amino acid were determined by point wise and half integral methods. Sulfamethoxazole shows only one pK_a (6.77) due to sulphonamide sec amino (= NH) group. It is a weak acidic group due to powerful electron withdrawing effect of SO_2 group. The ligand curve shows higher pH than acid curve and lies above the acid curve indicates the deprotonation of that secondary amino group. The observed pK_a values of ligands show little deviation with literature values due to the different solution media.The phenyl alanine shows two pK_a values. The highest valu**es** of $n^{-}A$ are two indicates the presence of pK_1 and pK_2. The values observed in the present study are in good agreement with earlier reported work[14-15]. 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

The displacement of metal titration curves with respect to ligand titration curve along volume axis indicates the formation of complex species. The log K values were determined by pointwise calculation method as well as half integral method. The pK_a, log K and log β values were enlisted in Table 1.

Table 1: pK_a, log K and log β values of transition metal ions with sulfamethoxazole drug (Smp) and phenyl alanine (phyA) amino acid

Medium: Alcohol/Water (40%) v/v; μ = 0.1 M ($NaClO_4$); Temperature: 27°C

Metal ions	Stability constants	(Smp)L1	(PhyA)L2
-	pK_a 1	-	3.32
-	pK_a 2	6.77	9.58
Co(II)	log K1	2.62	5.05
	log K2	-	3.92
	log β	2 .62	8.97
Ni(II)	log K1	2.90	7.44
	log K2	-	5.02
	log β	2.90	12.46
Cu(II)	log K1	3.28	9.39
	log K2	-	7.32
	log β	3.28	16.71
Zn(II)	log K1	2.81	6.92
	log K2	-	3.96
	log β	2.81	10.88

The highest value of n^- in sulfamethoxazole is around 1.0 and 2.0 for phenyl alanine. It indicates that the formation of 1 : 1 complex in sulfamethoxazole and phenyl alanine shows 1 : 1 and 1 : 2 complexes. The transition metal complexes of L_1 drug show low stability than L_2 ligand. It may be attributed to monodentate and bidentate nature and different basicity of ligands.

The order of stability of transition metal complexes with drugs in the present study are as follows:

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

Phenyl alanine L_2: Co (II) < Ni(II) < Cu(II) > Zn(II)

The plots of log K versus atomic number, atomic radii were plotted and it is observed that the complexes of L_1 and L_2 ligands follow the Irving William natural order of stability[16]. The low values of log K in L_1 drug indicates ionic interactions whereas high log K values of L_2 drug may be attributed to covalent interactions[17,18].

CONCLUSION

Nature of acid and ligand titration curves indicates deprotonation of secondary amino group. Sulfamethoxazole shows one pK_a value and phenyl alanine shows two pK_a values. Complex formation has confirmed by displacement of metal titration curve from ligand titration curve. Sulfamethoxazole forms 1 : 1 complex whereas phenyl alanine 1 : 2 complex. The complexes of transition metal ions follow natural order of stability.

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