International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 045 Published Mar. 2018
Volume No. 04, Issue No.05, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: Potentiometric and thermodynamic studies on …

Potentiometric and thermodynamic studies on transition metal complexes of sulfamethoxazole drug and phenyl alanine in 40% alcohol water medium.

B. K. Magare[1] and M. B. Ubale[2]

*[1]Shivaji Arts, Commerce and Science College Kannad, District Aurangabad-431103(M.S.) (India). Email: magarebk75@gmail.com

[2]Vasantrao Naik Mahavidhyalaya Aurangabad-431001(M.S.) (India). Email: mbubale@yahoo.co.in

---

Abstract

Proton ligand and metal ligand stability constants of Co (II), Ni(II), Cu(II) and Zn(II) transition metal complexes with sulfamethoxazole drug and phenyl alanine amino acid have been studied p^H metrically at different temperatures and 0.1 M ionic strength($NaClO_4$) in 40% v/v alcohol water medium. The pKa of ligands and logK of binary metal complexes were determined and correlated with basicity of ligands and atomic number, atomic radii of metal ions. Thermodynamic parameters ΔG ΔH ΔS were determined by known equations. The complexes of both ligands with metals follow the Irving William natural order of stability.

Keywords: Stability constant, drug, amino acid, ionic strength, pH metrically, Thermodynamic parameters.

Subject Classification: Chemistry 2018

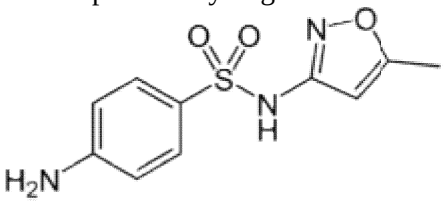
1. Introduction

The complexes of metal ions with ligand plays vital role in biological systems. The knowledge of metal complexes with drugs is essential to understand proper dose of drug, 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 study of complexes of drugs attracts many researchers because of its tremendous application in medicinal study.

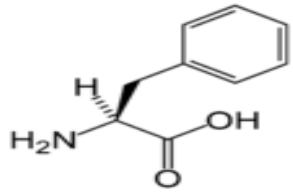
The literature survey reveals that there is still need to study the binary complexes of transition metal ions with drugs to know the coordination behavior[3-6].

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 045 Published Mar. 2018
Volume No. 04, Issue No.05, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: Potentiometric and thermodynamic studies on …

The systematic IUPAC name of sulfamethoxazole is 4-amino-*N*-(5-methylisoxazol-3-yl)-benzenesulfonamide. It is a bacteriostatic antibiotic[9]. 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 converted into tyrosine which forms the harmones like adrenaline, noradrenaline, 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.

2. 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[7].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 25 ^{0}C, 35 ^{0}C and 45^{0}C temperature in 40% v/v alcohol water solution pH metrically by using Irving Rossotti titration technique[8]. 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.

3. Results and Discussion

Proton ligand stability constant (pKa)

The pKa values of sulfamethoxazole drug and phenylalanine amino acid were determined by point wise and half integral methods. Sulfamethoxazole shows only one pKa (6.77) due to sulfonamide 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 amino group. The observed pKa values of amino acids show little deviation with literature values due to different medium and environmental conditions. The phenyl alanine shows two pKa 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 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

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.**

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 045 Published Mar. 2018
Volume No. 04, Issue No.05, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: Potentiometric and thermodynamic studies on …

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.

Table: 1.0
pKa , LogK and logβ values of transition metal ions with sulfamethoxazole drug(Smp) and phenyl alanine (phyA)amino acid

Metal	Stabi	(Smp)L_1			(PhyA)L_2		
		T_1(25^0	T_2(3	T_3(45	T_1(25^0	T_2(35	T_3(45
-	pKa_1	-			3.32	3.31	3.30
-	pKa_2	6.72	6.70	6.67	9.58	9.56	9.55
Co(II)	LogK	2.62	2.60	2.57	5.05	5.00	4.98
	LogK	-			3.92	3.90	3.88
	logβ	**2 .62**	**2.60**	**2.57**			
Ni(II)	LogK	2.90	2.88	2.86	7.44	7.43	7.41
	LogK				5.02	4.98	4.95
	logβ	**2.90**	**2.88**	**2.86**	**12.46**	**12.41**	**12.36**
Cu(II)	LogK	3.27	3.26	3.24	9.39	9.37	9.35
	LogK	-			7.32	7.30	7.27
	logβ	**3.27**	**3.26**	**3.24**	**16.71**	**16.67**	**16.62**
Zn(II)	LogK	2.80	2.78	2.77	6.92	6.91	6.90
	LogK	-			3.96	3.95	3.94
	logβ	**2.80**	**2.78**	**2.77**	**10.88**	**10.86**	**10.84**

Medium: Alcohol/Water (40%) v/v ;**μ**=0.1 M ($NaClO_4$) ;**Temperature**: =25^{0}C (T_1), 35^0(T_2),45^{0}C(T_3)

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 LogK 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[10]. The low values of LogK in L_1 drug indicates ionic interactions whereas high LogK values of L_2 drug may be attributed to covalent interactions[11-12].

Effect of Temperature
The proton ligand stability constant and metal ligand stability constant have been determine at 25 ^{0} C , 35 ^{0}C and 45 ^{0}C. Effect of temperature shows that there is decrease of logKa and Pka values with increase in temperature[13] .

Thermodynamic parameters
Thermodynamic parameters(ΔG, ΔH and Δ S)parameters have been determined by using following equations
ΔG = -2.303 RT log K
The values of ΔH and ΔS were calculated by plotting graph between logK vs 1/T (ln K = -ΔH/RT+ΔS/R). The slope of straight is equal to -ΔH/R and Intercept is ΔS/R. and
The ΔS = (ΔH- ΔG)/T.[14]
The ΔG, ΔH and Δ S values of metal complexes of sulfamethoxazole were determined at 25 ^{0}C and shown in Table 2. The negative values Gibbs free energy ΔG indicates the formation of complexes is spontaneous process and ΔH indicates the formation of complexes is exothermic in nature and it is favorable at low temperature. The - ΔG_1> - ΔG_2 in case of logK_1 and log K_2 values of phenyl alanine due to steric hindrance of molecules[15].

Table : 2 Thermodynamic parameters ΔG, ΔH and ΔS at 25 ^{0}C

Compl	Temp	pKa/l	-ΔG	-ΔH	-ΔS
CO(II)	298	2.62	14.9	19.1	14.0
Ni(II)-	298	2.90	16.5		72.9
Cu(II)	298	3.27	18.6	19.1	16.4
Zn(II)-	298	2.80	15.9	38.3	74.9

4. Conclusion

The complexes of L_1 and L_2 ligands follow the Irving William natural order of stability[10]. The low values of LogK in L_1 drug indicates ionic interactions whereas high LogK values of L_2 drug may be attributed to covalent interactions[11-12]. The logK of metal complexes decreases with increase in temperature. The

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 045 Published Mar. 2018
Volume No. 04, Issue No.05, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: Potentiometric and thermodynamic studies on …

negative values of thermodynamic parameters show formation of complexes.

5. Acknowledgement

One of the authors Dr. B. K. Magare, Department of Chemistry, Shivaji Arts, Commerce and Science College Kannad is very much thankful to the UGC (WRO) Pune for providing financial assistance.

6. References

[1] G. Thomas,"*Medicinal Chemistry*", John Wiley and Son Co. Ltd. London. 2002.

[2] B. Sarkar "*Medicinal Inorganic Chemistry* Rev. Med. 41, 2535-2544,1999.
[3] L. Gandhi and B. S Sekhon., *J Indian Chem. Soc*. Vol. **83,**868-870,2006,.

[4a] B.K.Magare and M. B. Ubale, *Int J. Chem. Sci:***9(2)**, ,589-592. , 2011
[4b] P.M. Deore, B.M. Khade, A. Khalkar and B. R. Arbad, *J. Chem. Bio. Phy.* ,Sec.A, Vol-**2(1),**14-18, 2011.

[5] A. Tiwari, H. N Sharma and P. B. Chakrawarti, *J Indian Chem. Soc*.Vol.LVII,134-136, 1980.
[6]B. K. Magare, M. N. Farooqui, R.S. Shelke and M. B. Ubale, *Orient. J. Chem*. Vol. **25(2)**,387- 390 ,2009.
[7] A. I. Vogel "*A Text Book of Quantitative Inorganic Analysis*", Pergamon Green and Co. Ltd 1975.
[8] H. Irving and H.S., Rossotti *J. Chem. Soc*. 2904, 1954.
[9] Merck Index , *Merck and Co. INC*. Whitehouse station 14 Edn. NJ USA p-908 and 180, (2006).
[10] H. Irving and R.J.P Williams., *Nature*,**162**, 746, 1947.
[11] P.B. Chakrawarti , M. Chakrawarti and P. Maini, *J. Indian Chem. Soc*. Vol. **77,**217-219,2000.
[12] G. N. Mukherji. and T. K. Ghosh, *J. Indian Chem. Soc*. Vol. **68,**194-196,1991.
[13] M M Mohrouka ,A.T. Abdelkarim, A A ElSherif, M. M. Shoukry, *Int J of Elect Sci*, 10,456-471,2015.
[14] G.D Rawate,*Int J of Sci and Research*,Vol5, 4 350-351,2016
[15] A Samir , A Lathif, S E Mansour, A A Fatouh, *Natural Science*, Vol 2, 8,793-802,2010.