Research Journal of Chemical Sciences E-ISSN 2231-606X
Vol. **6(10),** 51-53, October **(2016)** *Res. J. Chem. Sci.*

Short Communication

Thermodynamics of Complexation of Mn (II) Metal Ion with Amoxicillin

Archana Shukla[1] and M.K. Singh[2]
[1]LCIT College of C and S, Bodri, Bilaspur, CG, India
[2]Govt Agrasen College, Bilha, Bilaspur, CG, India
archanasunchu@gmail.com

Available online at: www.isca.in, www.isca.me
Received 11th August 2016, revised 29th September 2016, accepted 8th October 2016

Abstract

In recent time study of metal complexes are used immensely in medicine in the design of slow release and long acting drugs. Now a day the study of chemistry of metal-drug interaction has become more popular in the design of more biologically active drugs. The present work comprises Potentiometric studies of complexation of amoxicillin with Mn (II) ions in 50% aqueous ethanol medium at three different temperatures (30, 35 and 40^oC) and at 0.1 M ($NaNO_3$) ionic strength. Calvin-Bjerrum pH titration process as used by Irving and Rossotti is used for the calculation of stability constants of the metal complexes. It is observed that Mn (II) ions form 1:1 and 1:2 complexes. Various thermodynamic parameters eg. Gibbs free energy change (ΔG), enthalpy changes (ΔH) and entropy changes (ΔS) have also been calculated, which shows formation of metal complexes to be spontaneous, exothermic and stability of complexes at lower temperature.

Keywords: Potentiometric method, Complexation, Stability constant, Free energy, Enthalpy, Entropy, Amoxicillin.

Introduction

Among the outstanding achievement of human being is the discovery of antibiotics. It is called miracle drugs for its effectiveness and efficiency is controlling several diseases[1]. Though considerable amount of work has been done earlier in metal complexes of antibiotics by various experimental methods. The interaction of antibiotics with metal can provide an important information regarding action of antibiotics within the body. Amoxicillin is an important antibiotic. It is a member of the Penicillin family of antibiotics. It is a semi synthetic antibiotic and used for the treatment of infections caused by gram positive and gram negative microorganism[2,3]. It is widely used in the treatment of infections in urinary tract being caused by gram negative rods and also used in treatment of typhoid and enteric fevers.

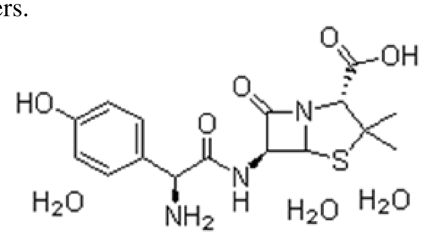

Figure-1
Chemical structure of Amoxicillin

There are number of various methods available for the calculation of values of stability constants of metal-ligand complexes. Potentiometry pH-metric titration method is widely used for the study of complexation of metal with different ligand. In transition metal complexes, metal is co-ordinated by ligands.

The complex formation has wide applicability in different field of drugs containing metal complex in the form of chelate. The study presents the calculation of protonation constants of the ligand and the values of stability constants of the metal -ligand complexes and various thermodynamic quantities of complexation of Mn (II) ions with amoxicillin antibiotic using Potentiometric method[4-7] in 50% aqueous ethanol medium at three different temperatures (30, 35and 40^oC) and at 0.1 M $NaNO_3$ ionic strength.

Materials and Methods

All the chemicals used in present study were of high rank of purity (AR grade). All the solutions were prepared in double distilled deionised water. The solution of antibiotic (ligand) was prepared by dissolving in double distilled ion free water. The solutions of metal salt were also prepared by dissolving the metal salts in double distilled ion free water and standardized by using standard volumetric procedures as explained by Schwarzenbach[8]. The solution of carbonate free sodium hydroxide was prepared by the method of Schwarzenbach and Biedermann and standardized by using standard Oxalic Acid solution before starting an experiment. The titration technique employed here is the modified form of Irving-Rossotti titration technique.

Systronic pH meter (model 132E) has been used for measurement of pH by using a combination electrode in 50% aqueous ethanol medium at three temperatures (30, 35, and 40^oC) and at 0.1 M ($NaNO_3$) ionic strength. Suitable buffer solution was used for the calibration of pH meter at regular intervals during the course of study.

For each set of metal –antibiotic interaction three different solutions (Keeping total volume 20 mL) were prepared as mentioned below: i. 1.5 ml HNO_3 (0.01 M) +2.0 ml $NaNO_3$ (1.0 M) +3 ml KNO_3 (0.01 M) +3.5 ml H_2O +10.0 ml ethanol. ii. 1.5 ml HNO_3 (0.01 M) +2.0 ml $NaNO_3$ (1.0 M) +3 ml KNO_3 (0.01 M) +5 ml amoxicillin (0.01 M) +1.0 ml H_2O +7.5 ml ethanol. iii. 1.5 ml HNO_3 (0.01 M) +2.0 ml $NaNO_3$ (1.0 M) +0.5 ml metal nitrate (0.01 M) +5 ml amoxicillin (0.01 M) +3.5 ml H_2O +7.5 ml ethanol.

Solutions (i), (ii) and (iii) were titrated against standard sodium hydroxide solution (0.01 M) prepared in 50% aqueous ethanol. The plots of pH versus volume of alkali required for the titration give three curves referred as (i) acid (ii) ligand and (iii) metal complex and are shown in Figure-2.

The procedure adopted by Bjerrums[9], Calvin and Wilson[10], Fronaeous, Schwarzenbach and Irving[11] and Rossoti[12] were used for the measurement of pKa values of antibiotic used as ligand and stability constants values of metal-ligand complexes.

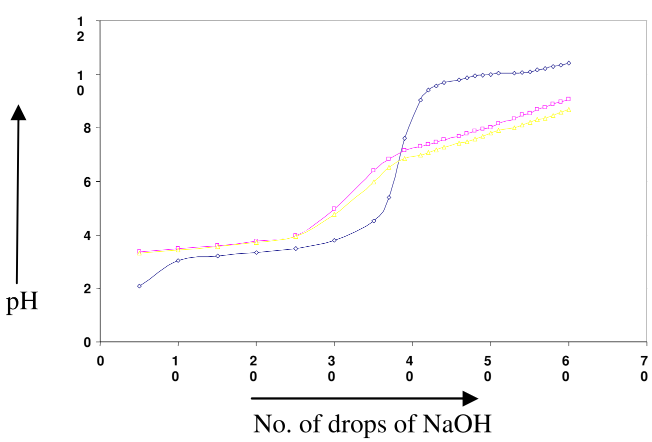

Figure-2
Titration curves of (i) HNO_3 (ii) Amoxicillin and (iii) Complex at temperature 303K in 50% aqueous ethanol medium

Calculation of the Thermodynamic Parameters: The various thermodynamic quantities eg. Gibbs free energy change (ΔG), enthalpy change (ΔH) and entropy change (ΔS) for formation of metal-antibiotic complexes were determined. The Gibbs free energy change (ΔG) is calculated by using

$$\Delta G = -2.303\, RT \log K$$

R= Universal gas constant, log K = Stability constant, T= temperature in K

The enthalpy change is evaluated by finding the slope of logK vs 1/T plot

$$\text{Slope} = -\Delta H / 2.303\, R$$

The entropy change for complex formation were calculated by $\Delta S = (\Delta H - \Delta G) / T$

Results and Discussion

The values of stability constants of complexation of Mn (II) ion with Amoxicillin and various thermodynamic quantities ΔG, ΔH and ΔS have been calculated and present below in the table (01) and table (02) respectively.

Conclusion

Stability constant values are very important for biological system. This value decreases with an increase in temperature. This confirms the conclusion of Pitzer that high temperature is not favorable for metal complexation process[4]. The metal ion Mn (II) forms 1:1 and 1:2 complexes with amoxicillin antibiotic. The negative values of free energy change (ΔG) indicate that the complex formation process is spontaneous[13]. The negative value of entropy change (ΔS) indicates higher order in the complex formation process. The negative values of enthalpy change (ΔH) indicate the complex formation reaction is an exothermic.

Table–1
Stability Constant of Amoxicillin Mn (II) Complex at temperature 303,308 and 313K

Temperature	Bjerrum half integral method			Weighted least square method		
	$\log k_1$	$\log k_2$	$\log \beta_2$	$\log k_1$	$\log k_2$	$\log \beta_2$
303K	6.270	4.179	10.449	5.942	4.284	10.226
308K	6.010	4.128	10.138	5.846	4.244	10.09
313K	5.730	4.110	9.840	5.621	4.218	9.839

Table–2
Thermodynamic parameters for Amoxicillin Mn (II) complex in 50% aqueous ethanol medium at 0.1 mol dm^{-3} $NaNO_3$

Temperature K	**Gibbs Energy Change ($KJmol^{-1}$)**			**Enthalpy Change (303-313K $KJ\ mol^{-1}$)**			**Entropy Change at 308 $KJmol^{-1}k^{-1}$**		
	$-\Delta G_1$	**$-\Delta G_2$**	**$-\Delta G_{\beta 2}$**	**$-\Delta H_1$**	**$-\Delta H_2$**	**$-\Delta H_{\beta 2}$**	**$-\Delta S_1$**	**$-\Delta S_2$**	**$\Delta S_{\beta 2}$**
303	34.5730	25.8539	60.3269						
308	34.4757	25.0282	59.5039	55.0418	11.5303	66.5721	66.7732	-43.8243	22.9488
313	33.6869	24.2787	57.9656						

References

1. Waksman S.A. (1947). What Is an Antibiotic or an Antibiotic substance?. *Mycologia,* 39(5), 565-569**.**
2. Janjic Dalhoff A. and Echols R.N. (2006). Redefining penems. *Biochem Pharmacol E pub.*, 71(7), 1085-1095.
3. McEvoy G.K. (2016). AHFS Drug Information, American Society of Health-system Pharmacists. Inc., Bethesda, MD.
4. Pitzer K.S. (1937). The Heats of Ionization of Water, Ammonium Hydroxide, Cabonic, Phosphoric, and Sulfuric Acids. The Variation of Ionization constants with Temperature and the entropy Change with Ionization. *J.Am.Chem Soc*., 59(11), 2365-2371.
5. Martell A.E. (1971). Co-ordination chemistry. 1, Von Nostrand Reinhold Company, London, 577.
6. Mendoza-Diaz G., Perez-Alanso R. and Moreno-Esparza R. (1996). Stability constants of copper (II) mixed complexes with some 4-quinolone antibiotics and (NN) donors. *J. Inorg, Biochem.*, 64(3)*,* 207-214.
7. Obaleye J.A., Nde-aga J.B. and Balogun J.BE.A. (1997). Some Antimalaria Drug Metal Complexes: Synthesis characterization and their in-vivo Evaluation against malaria parasite. *Afr.J.Sci*, 1,10-12.
8. Jaffery G.H., Basset J., Mendham J. and Denny R.C. (1978). Vogel's Textbook of Quantitative Chemical Analysis. 5th edition, Longman group UK Limited, ISBN-0-470-21517-8.
9. Bjerrum J. et. al. (1941). Metal Ammine formation in Aqueous Solution. P. Haase and Son, Copenhagen Denmark, 296.
10. Calvin M. and Wilson K.W. (1945). Stability of Chelate Compounds. *J. Am. Chem. soc*., 67(11), 2003-2007.
11. Franaeous S. (1948). Komplexsystem Hos Kopper. Gleerupska Univ. Bokhandeln, Lund, 139.
12. Schwarzenbach G. and Ackermann H. (1947). Metal Chelates of EDTA and related substances. *Helv. Chim. Acta*, 30, 1798-1804.
13. El-Sherbiny M.F. (2005). Potentiometric and thermodynamic studies of 2-Thioxothiazolidin-4-one and its metal complexes. *Chem. Pap*., 59(5), 332-335.
14. Irving H.M. and Rossotti H.S. (1954). The calculation of formation curves of metal complexes from pH titration curves in mixed solvents. *J.Chem.Soc*, 2904-2910.