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Potentiometric determination of Stability Constant of Levofloxacin and Mn (II) Ion Complex

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ABSTRACT: Transition metal complexes are cationic, anionic or neutral species in which transition metal is coordinated by ligands. Metals can play an important role in modifying the pharmacological properties of known drugs after coordinating with it. Stability constants of complexes also have an important role in the design of drugs for alleviation of metal poisoning. In the present study levofloxacin is used as a ligand for complexation. It is a member of fluoroquinolones group of antibiotics which is very active against aerobic Gram negative microorganism. The object of the present work is a physicochemical investigation of the interaction of bivalent metal ion [Mn(II)] with levofloxacin antibiotics and is aimed at understanding the mechanism of inhibitory or lethal effect of antibiotics against fixed types of microorganisms. The stability constants data can also be used for determination of various thermodynamic parameters such free energy (ΔG^0), enthalpy (ΔH^0), and entropy ΔS^0. From these parameters important information about mechanism of interaction can be deduced.

Key Words: Ligand, Stability constant, Complexation, Complex, Thermodynamic parameters.

INTRODUCTION

Levofloxacin is a member of fluoroquinolones group of antibiotics which is very active against aerobic Gram negative microorganism chemically it is 9-fluoro-2, 3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido [1, 2, 3-de]-1, 4-benzoxazine-6-carboxylic acid[1]. Levofloxacin is a zwitter ion at physiological pH, possessing a carboxylic group with pK_a=5.5, a piperazinyl group with pK_a=8.0 and another proton accepting function with $pK_a = (6.8 \pm 0.3)$[2]. In present study it is used as a ligand for the complexation with Mn(II) ion. The object of the present work is the study of interaction between metal and ligand by Potentiometric method[3-6]. The stability constant values of complexes formed between levofloxacin and Mn(II) ion have determined at three temperatures, 303K, 308K, and 313K. Bjerrum half integral method and least square method have been used for calculating it[7]. The formation of 1:1 and 1:2 metal ligand complexes are found to be formed in 50 %(v/v) methanol – water system. The stability constant values for metal-ligand system compared at three temperatures, it is found that value of stability constant decreases with increasing temperature. This is in agreement with the conclusion of Pitzer[3].

MATERIAL AND METHODS

A digital Systronics pH meter (MODEL 371) and a combination electrode (pH range 0-14) with an accuracy of 0.01 pH unit were used for the measurement of pH. In the present work chromatographically pure sample of antibiotics used (obtained from Fluka). For each titration fresh samples of antibiotics weighed and solution prepared to avoid the possibility of hydrolysis and photochemical decomposition. The metal ion solution prepared from the corresponding nitrate of AR grade standardized by titration with disodium salt of EDTA as described by Schwarzenbach[8]. Carbonate free sodium hydroxide prepared by

the method of Schwarzenbach and Biedermann and standardized by titration with pure oxalic acid. The modified form of Irving-Rosotti titration technique used[9].

Potentiometric titration carried out at three temperatures 25^0C, 30^0 C, and 35^0 C, keeping ionic strength of the solution constant (0.1M $NaNO_3$). Presaturated N_2 gas passed through the experimental solution before titration. During the titration the change in pH of the solution measured by a digital pH –meter provided with an electrode previously calibrated standard method.

The pK_a values of ligand and stability constants have determined as the method described by Bjerrum[10], Calvin and Wilson[11] Fronaeous, Schwarzenbach and Irving[12] and Rossoti[13].

RESULTS AND DISCUSSION

The pK_a values of levofloxacin at 303,308 and 313K have been presented in figure (1A, 1B and1C) respectively. The values of pK_a shows that it is weakly acidic in nature. The $\bar{n}$ and pLvalues of Mn(II) with levofloxacin at temperature 303, 308, and 313K presented in Table 1.

The stability constant values for complexation of levofloxacin with Mn(II) by Potentiometric titration method have been presented in (table 02) and the thermodynamic parameters have been given in (table 03). The formation of 1:1 and 1:2 metal ligand complexes are found to be formed in 50 %(v/v) methanol - water system. The comparative study of stability constant values for metal-ligand system at three temperatures shows that value of stability constant decreases with increasing temperature. This is in agreement with the conclusion of Pitzer that higher temperatures are not favorable for complex formation.

The values of all the thermodynamic parameters calculated are found to be negative. The negative value of ΔG indicates that the complex formation is spontaneous. The negative value of ΔH indicates that reaction is exothermic. The negative value of ΔS indicates that the complex formation is highly ordered.

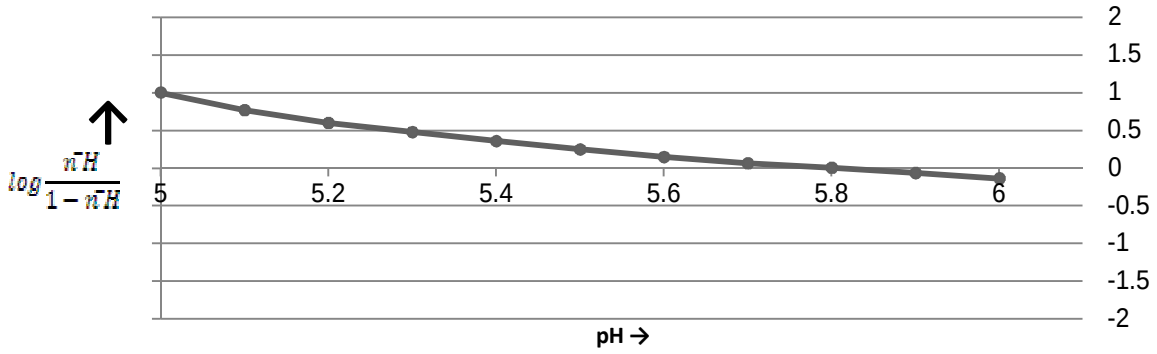

Figure 1(A): pKa values of Levofloxacin in 50% (v/v) methanol water medium at Ionic Strength (I)=0.1 mol dm^{-3} $NaNO_3$ at temperature 303K.

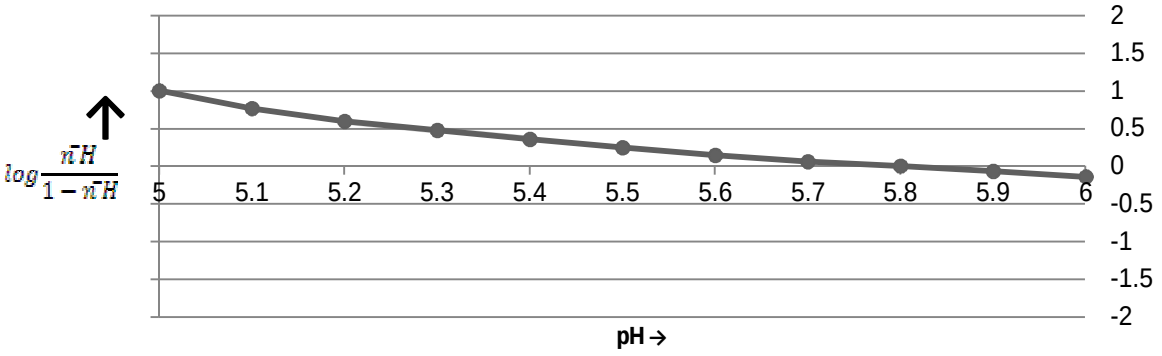

Figure 1(B): pKa values of Levofloxacin in 50% (v/v) methanol water medium at Ionic Strength (I)=0.1 mol dm^{-3} $NaNO_3$ at temperature 308K.

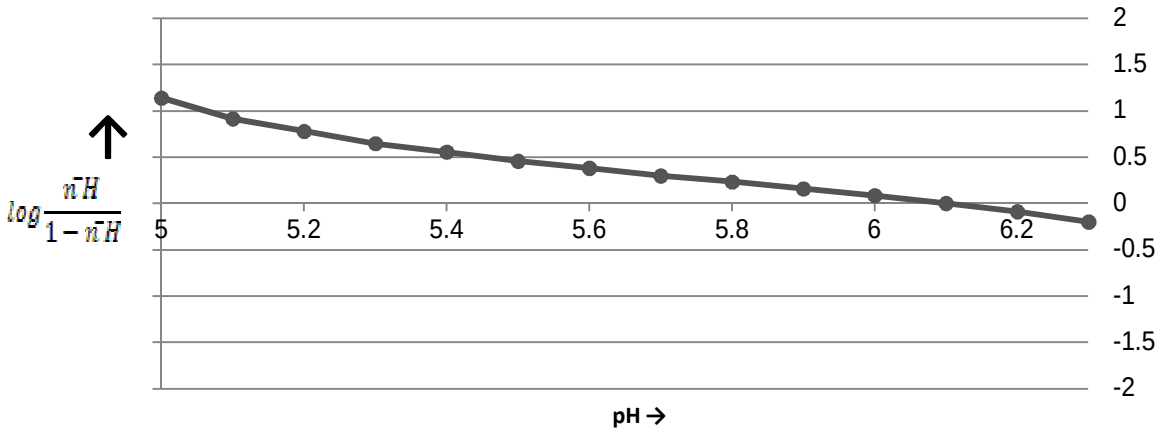

Figure 1(C): pKa values of Levofloxacin in 50% (v/v) methanol water medium at Ionic Strength (I)=0.1 mol dm^{-3} $NaNO_3$ at temperature 313K.

Table 1: $\bar{n}$ and pL values of Mn(II) with Levofloxacin at temperature 303, 308, and 313K.

303K (pK_a= 5.5)		308K (pK_a= 5.8)		313K (pK_a= 6.2)	
$\bar{n}$	pL	$\bar{n}$	pL	$\bar{n}$	pL
0.1	-	0.1	-	0.1	-
0.2	-	0.2	5.402	0.2	5.102
0.3	6.701	0.3	5.204	0.3	5.052
0.4	6.652	0.4	5.152	0.4	5.002
0.5	6.604	0.5	5.053	0.5	4.952
0.6	6.542	0.6	4.952	0.6	4.852
0.7	6.469	0.7	4.903	0.7	4.752
0.8	6.394	0.8	4.852	0.8	4.603
0.9	6.301	0.9	4.800	0.9	4.554
1.0	6.260	1.0	4.753	1.0	4.504
1.1	6.194	1.1	4.705	1.1	4.455
1.2	6.152	1.2	4.641	1.2	4.404
1.3	6.045	1.3	4.590	1.3	4.353
1.4	6.002	1.4	4.530	1.4	4.309
1.5	5.954	1.5	4.453	1.5	4.253
1.6	5.884	1.6	4.390	1.6	4.200
1.7	5.752	1.7	4.352	1.7	4.152

Table 2: Stability constant values for complexation of levofloxacin and Mn(II) ion in 50 % (v/v) water- methanol at 0.1mol dm^{-3} $NaNO_3$

Temperature K	Bjerrum half integral method			Weighted least square method		
	$logK_1$	$log\ K_2$	$log\ \beta_2$	$logK_1$	$log\ K_2$	$log\ \beta_2$
303	6.602	5.954	12.556	6.565	6.264	12.830
308	5.053	4.453	9.506	5.088	4.787	9.876
313	4.952	4.253	9.205	4.739	4.438	9.178

Table 3: Thermodynamic parameters for Levofloxacin – Mn (II) Complex at temperatures 303 , 308 , and 313K

Temperature K	Gibbs Energy change ($kJmol^{-1}$)			Enthalpy change (303-313K $kJmol^{-1}$)			Entropy change at 308K ($kJmol^{-1}k^{-1}$)		
	$-\Delta G_1$	$-\Delta G_2$	$-\Delta G\beta_2$	$-\Delta H_1$	$-\Delta H_2$	$-\Delta H\beta_2$	$-\Delta S_1$	$-\Delta S_2$	$\Delta S\beta_2$
303	38.091	36.345	74.436	-	-	-	-	-	-
308	30.009	28.234	58.243	25.698	27.172	52.87	25.601	27.080	52.681
313	28.405	26.601	55.007	-	-	-	-	-	-

$\Delta G_1, \Delta H_1,$ and ΔS_1 values have been derived from log K_1
$\Delta G_2, \Delta H_2,$ and ΔS_2 values have been derived from log K_2
$\Delta G\beta_2, \Delta H\beta_2,$ and $\Delta S\beta_2$ values have been derived from log β_2

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