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Study of Complexation of Co (II) ion with Antibiotics Flumquine by Titrimetric Method

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Abstract

The development and scope of transition metal- coordinated antibiotics have promising pharmacological applications. Metal complexes are very useful to design the slow release and long acting drug. Although most antibiotics do not need metal ions for their biological activities there are a number of antibiotics called metalloantibiotics that require metal ions to function properly, metal ions are therefore known to accelerate drug action. The present study comprises determination of stability constant and thermodynamics of interaction of antibiotics flumequine with transition metal ion Co (II). 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.

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

Introduction

Metal complexes are known to exhibit remarkable antitumor, antifungal, antiviral and special biological activities. In present study flumequine is used as a ligand for complexation with Co (II) ion. **Flumequin** is a synthetic chemotherapeutic[1] antibiotic of the fluoroquinolones drug class used to treat bacterial infections. It is a first-generation fluoroquinolones antibacterial which is used in veterinarian medicine for the treatment of enteric infections (all infections of the intestinal tract),[2] as well as to treat cattle, swine, chickens, and fish.[3] Flumquine is a 9-fluoro-6,7-dihydro-5-methyl-1-oxo-1H,5H-benzo[ij]quinolizine-2-carboxylic acid. The molecular formula is $C_{14}H_{12}FNO_3$. The stability constant of flumequine – Co (II) ion complex is determined by Potentiometric titration method at temperatures 303, 308 and 313 K. it is found that value of stability constant decreases with increasing temperature. This

is in agreement with the conclusion of Pitzer[4]

Material and Methods

A digital Systronics pH meter 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.

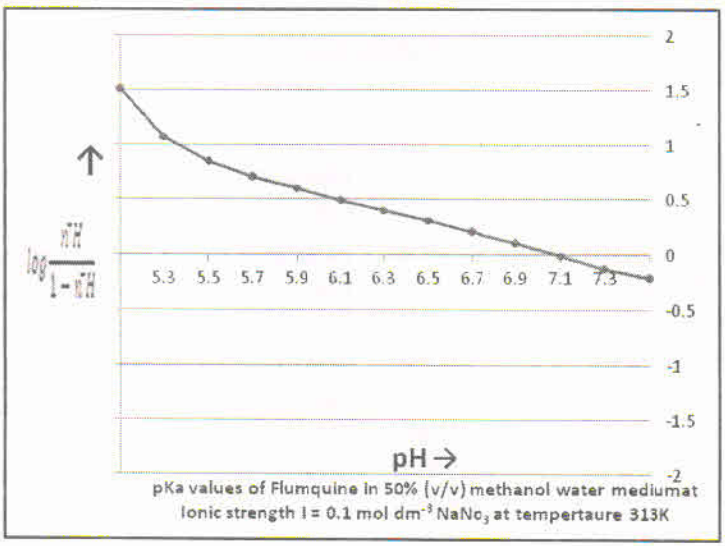
The metal ion solution prepared from the corresponding nitrate of AR grade standardized by titration with disodium salt of EDTA as described by Schwarzenbach[5]. Carbonate free sodium hydroxide prepared by the method of Schwarzenbach and Biedermann and standardized by titration with pure oxalic acid. The modified form of Irving-Rosotti titration technique used[6].

Potentiometric titration carried out at three temperatures 25°C, 30°C, and 35°C, keeping ionic strength of the solution constant (0.1 M KNO_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.

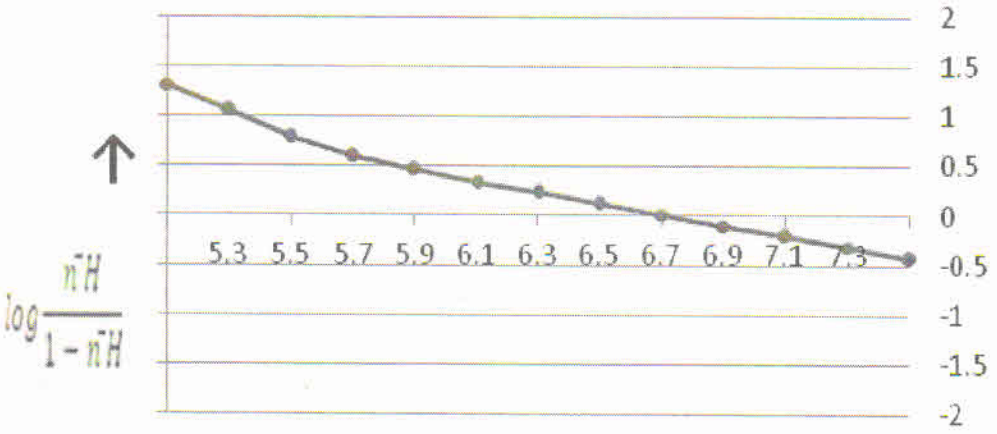
The pKa values of ligand and stability constants have determined as the method described by Bjerrum[7], Calvin and Wilson[8] Fronaeous[9], Schwarzenbach and Irving and Rossoti.

Result and Discussion

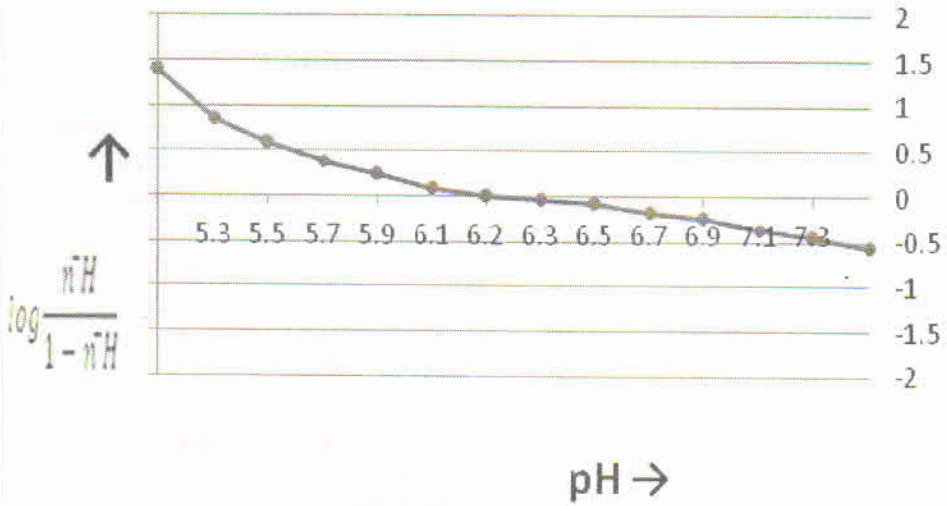
The stability constant values for complexation of flumequine with Co (II) by Potentiometric titration method have been presented in table 1 and the thermodynamic parameters have been given in table 2. The formation of 1:1 and 1:2 metal ligand complexes[10] are found to be formed in 50 %(v/v) methanol–water system. The comparative study of



pKa values of Flumquine in 50% (v/v) methanol water mediumat Ionic strength I = 0.1 mol dm^{-3} $NaNo_3$ at tempertaure 313K



pKa values of Flumquine in 50% (v/v) methanol water mediumat Ionic strength I = 0.1 mol dm^{-3} $NaNo_3$ at tempertaure 308K



pKa values of Flumquine in 50% (v/v) methanol water mediumat Ionic strength I = 0.1 mol dm^{-3} $NaNo_3$ at tempertaure 303K

Table 1. Stability constant values for complexation of flumequine and Co (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		
	$\log K_1$	$\log K_2$	$\log \beta_2$	$\log K_1$	$\log K_2$	$\log \beta_2$
303	4.5521	3.5571	8.109	5.7739	5.472	11.245
308	4.2087	3.2245	7.432	4.258	3.967	8.215
313	3.5211	3.0021	6.523	4.123	3.822	7.945

Table 2. Thermodynamic parameters for Flumequine– Co (II) Complex at temperatures 303, 308, and 313K

Tempe-rature 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	33.497	31.751	65.249						
308	25.114	23.338	48.452	3.193	3.404	6.597	3.112	3.328	6.440
313	24.711	22.907	47.619						

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.

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