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To study stability constants and thermodynamic properties of complexation of Paracetamol with Co^{2+}, Zn^{2+} and Cd^{2+} by PH metrically

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ABSTRACT

The equilibrium constants for metal complex formation have been employed from long as an effective measure and parameter of the affinity of a ligand for a metal ion in solution. PHmetry is one of the most convenient and successful technique employed for metal complex equilibrium measurements. pHmetric measurement of hydrogen ion concentration may be employed when the degree of complex formation is sensitive to the hydrogen ion concentration thus the degree of complex formation undergoes increase/ decrease with change in pH. In the present work, we investigate the stability constants of Paracetamol complexes with Co^{2+}, Zn^{2+} and Cd^{2+}pHmetrically using pH metric technique at three temperatures (25 ±0.1, 30 ±0.1 and 35± 0.1^0 C) and at an ionic strength of 0.1 mol L^{-1} (KNO_3). The method of Calvin and Bjerrum as adopted by Irving and Rossotti has been employed to determine log K1 values. The thermodynamic parameters ΔG, ΔH and ΔS are calculated. System tend to progress in the direction of increasing entropy as entropy is a measure of a system's tendency towards spontaneous change.

Introduction

Paracetamol (para-acetylaminophenol) is useful in the management of more severe pain, where it allows lower dosages of additional non - steroidal anti-inflammatory drugs (NSAIDs) to be used, there by minimizing overall side effects. It is considered safe for human use at recommended doses; however, acute overdose can cause potentially fatal liver damage Paracetamol is a sparingly soluble bitter tasting drug. It is widely used as an analgesic and antipyretic. It is only slightly

soluble in cold water, moderately soluble in water at room temperature (1 g dissolves in approx. 70 ml) but considerably more soluble in hot water and soluble in organic solvents such as methanol, ethanol, dimethyl formamide, ethylene dichloride, acetone, and ethyl acetate [1,2]. Published literature on the analgesic and antipyretic effects of paracetamol revealed a therapeutically effective plasma concentration range of 10–30g/ml [3]. The relatively high dissociation constant Complexation of drug with different cyclodextrins was attempted to improve solubility of Paracetamol.The Chemistry of paracetamol has gain importance due to its analgesic and antipyretic activities,complex forming abilities of these with various metal ion have been worked earlier The pKa values of ligands and stability constants of the complexes with some hydroxamic acids a comparative study of three different potentiometric methods was reported by Senthilnithy [4]. The data obtained by pH-metric method were analyzed by three standard methods namely, Bjerrum's method, Irving and Rossotti method, and Sarkar and Kruck method. Aectohydroxamic acid, $CH_3CONHOH$, forms highly stable complexes with vanadium (V) and vanadium (IV) in 1: 1, 1: 2 and 1 : 3 mole ratios [5]. The stability of these complexes can be determined in terms of thermodynamic parameters; ΔG, ΔH and ΔS . The preliminary data, obtained through pH titration at various temperatures, was processed. Another study on the stability constant of the transition metal complexes with some medicinally important compounds was reported by Chaudhari [6]. The formation of bioligand complexes of some medicinal drugs with Co (II), Ni (II) and Cu (II) ions were investigated. The formation const. of Ranitidine Hydrochloride and 6-methoxy naphthaldehyde has been carried out pH metrically in aq. soln. at 30°C, at 0.1 M fixed ionic strength [6]. The method of Calvin and Bjerrum [7,8] as adopted by Irving and Rossotti [9] has been employed to determine log *K* value

Material and Methods

The titration were carried out in a100 ml Pyrex glass beaker kept in a water bath maintain at constant temperature Chemicals and ligand used were of analytical grade. Ligand solutions were prepared in twice distilled deionized, carbon dioxide free water. Metal salt solutions were prepared by dissolving the corresponding metal salt in twice distilled deionized water and standardized by standard volumetric methods.

The free hydrogen ion concentrations were measured with a combined glass electrode attached to digital pH meter model-361; the accuracy of pH meter was ± 0.01 at three temperatures (25 ± 0.1, 30 ± 0.1 and 35 ± 0.1° C) and at an

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ionic strength of 0.1 mol L^{-1} (KNO_3). The pH meter was calibrated with suitable buffers before use.

a) Calvin – Bjerrum Titration

The experimental procedure involved pHmetric titration of,

i) Free acid (0.01M) titration,

ii)Free acid (0.01 M) and ligand (0.05M) titration.

iii) Free acid (0.01M), ligand (0.05M) and metal ion (0.01M) against std. NaOH solution.

The ionic strength of all solutions were maintain constant (0.1M) by adding appropriate quantity of 1M KNO_3solution.

The titration were carried out in a100 ml Pyrex glass beaker kept in a water bath maintain at constant temperature (25,30and 35 ^{0}C) nitrogen gas was purged for chemically inert atmosphere. The readings were recorded for each addition of 0.1ml. The graphs of volume of alkali added against pH were plotted. The curve has been designated as below:-

(i) Acid curve (A)

(ii) Ligand titration curve (A+L)

(iii) Metal – ligand titration curve (A+L+M)

Method for determination of stability constants

The dissociation constants of paracetamol was determined at 0.1 M ionic strength pH – acid having only one dissociable H^+ ion from –OH group and can therefore represented

$$HL \rightleftharpoons H^+ + L^{-1}$$

The titration curve of the acid and the ligand deviates at about pH 3.0 and then increase up to pH 12.0. The deviation between acid curve from ligand curve for the systems showed the dissociation of H^+ from OH groups of the ligands. (Table)

Proton – ligand formation Number (n^-A)

Proton – ligand formation number (n A) were calculated by Irving and Rossotti expression.

$$nA = \gamma - (E^0 + N)(V_2 + V_1) / (V^0 + V_1) T^0{}_L$$

Where,

V^0 = Initial volume of solution (50 ml)

N = Normality of sodium hydroxide

$T^0{}_L$ = Concentration of ligand in 50 ml solution

E^0 = Initial concentration of free acid (HNO_3)

γ = Number of dissociable proton from ligand

V_1 and V_2 – Volume of alkali consumed by acid and ligand on same pH

Metal- ligand formation number (n)

The deviation of (A + L +M) curve from (A +L) started at about pH 3.5, It indicate the commencement of complex formation .

Metal – Ligand formation number (n) was calculated by following expression.

$$\mathbf{n = (E^0 + N)(V_3 - V_2) / (V^0 + V_2)(T^0{}_M) \times nA}$$

V^0 = Initial volume of solution (50 ml)

N = Normality of sodium hydroxide

$T^0{}_M$ = Concentration of the metal ions

nA = Proton – ligand formation number

E^0 = Initial concentration of free acid (HNO_3)

Where, V_2 and V_3 – volume of NaOH consumed by ligand and metal ions at same pH.

Metal – Ligand Formation curves

Formation Curves were plot ted between n and p^H .The metal-ligand stability constants were determination by half integral method

Half Integral Method:-The metal- ligand stability constants (log, k_1 values) are calculated from formation curves. The values of n = 0.5 which corresponds to value of The values of Pk are presented in Table No.

The values of metal – ligand stability constants i.e. log k_1 for all the systems were presented in tables.

Table. Stability constants and thermodynamic parameters of Co^{2+},Zn^{2+} and $Cd^{2+}$with paracetamol

System	Temperature (oC)	pKa	logK	-Δ H ($KJmol^{-1}$) At 30^{0}C	-Δ G ($KJmol^{-1}$)	-Δ S ($KJmol^{-1}$ deg^{-1}) At 30^{0}C
Zn(II)Paracetamol	25	9.54	3.98	7.147	22.709	0.049
	30	9.50	3.96		22.162	
	35	9.45	3.94		22.52	
Co(II)Paracetamol	25	9.54	4.01	10.721	22.880	0.040
	30	9.50	3.97		23.032	
	35	9.45	3.94		23.235	
Cd(II)Paracetamol	25	9.54	4.429	17.86	25.271	0.025
	30	9.50	4.428		25.689	
	35	9.45	4.427		26.107	

Conclusion

The results obtained from the pH metric measurements, the values of pKa were found to decrease with increasing temperature. The values of the thermodynamic functions ΔG, ΔH and ΔS were calculated. The values of stability constants reveal that the stability constants decrease with increasing temperature, along with the pKa value.

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