Studies of complex formation equilibria of transition metal ions (Fe (II), Co (II), Ni (II) and Cu (II)) with folic acid

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Abstract : **Research of metal complexes with biologically active ligands is one of high scientific and practical interest. The proton-ligand and metal-ligand stability constants of the complexes of Fe(II), Co(II), Ni(II) and Cu(II) with folic acid have been determined by pH-metric method in medium of 20% acetone-water mixture at ionic strength 0.1M $NaNO_3$ solution and 30 ± 0.1 ^{O}C temperature. Proton ligand stability constant ($\log K'_H$) of folic acid is determined by Irving-Rossotti Method. Ligand metal stability constants ($\log K_H$) of metals Fe^{2+}, Co^{2+}, Ni^{2+} and Cu^{2+} were calculated at 303K. The order of stability constant for metal complexes by Irving Rossotti Method, follows the order $Fe^{2+} < Co^{2+} < Ni^{2+} < Cu^{2}$.**

I. INTRODUCTION

Metals are commonly found as natural constituents of proteins, vitamins, enzymes etc. Nature has learned to use the special properties of transition metal ions to perform a wide variety of specific functions associated with the processes. In the formation of metal complexes or metal coordination compounds, transition metal possess a distinctive property. The complexes which acquire dissimilar physicochemical properties are formed by the metal ion coordinated with a mixture of molecular species. In order that they have wide applications in metal extraction, water purification and medicines etc. Folic acid is used in the treatment and prevention of folate deficiencies and pernicious anemia. The absorption of metal-folic acid complexes as drugs are higher than the folic acid itself.

It is essential to measure the stability constant for calculating quantitatively the concentration of free metal ion, ligand and the complex formed in the system, under unusual conditions of pH. Recently, there has been considerable interest in the study of binary and ternary complexes by pH metric method[1-6]. So, attempt has taken to measure the stability constant of transition metal ions with folic acid.

RESEARCH METHODOLOGY

The solutions used in potentiometric titration were prepared in double distilled water. The stock sodium hydroxide solution was standardized by potassium hydrogen phthalate using phenolphthalein as indicator (0.2M) and standard alkali solution was again used for standardization of prepared nitric acid solution. Sodium nitrate solution was used to maintain ionic strength. The pH of the solution was measured by an Electronics India digital pH meter (model 101) set with a reference calomel electrode and magnetic stirrer. The pH meter was calibrated at pH 4.0, 7.0 and 10.0 using the standard buffer solutions before titration. The iron, cobalt, nickel and copper salt solutions were standardized by the reported method. The activity of H^+ was converted to the concentration of hydrogen ion using activity coefficients calculated from Davies equation. All the measurements were done at room temperature 303 K.

At the time of titration, pH measurements made with alkali solution of ligand in the presence and absence of metal ion. According to Calvin and Wilson[7], these pH values could be used to evaluate the formation functions ($\bar{\eta}_A$, $\bar{\eta}$ and ρL) and stability constants. Using Irving Rossotti method, the following solutions are titrated against standard sodium hydroxide solution (N^0) keeping total volume (V^0) constant.

(a) HNO_3 (A)

(b) HNO_3+ Folic acid (A + L)

(c) HNO_3+ Folic acid + Metal ion (A + L + M)

Total initial volume = 50 ml, ionic strength (I) = 0.1, [NaOH] = 0.14 M, $[H^+]$ = 0.1 M **(Fig. 1)**

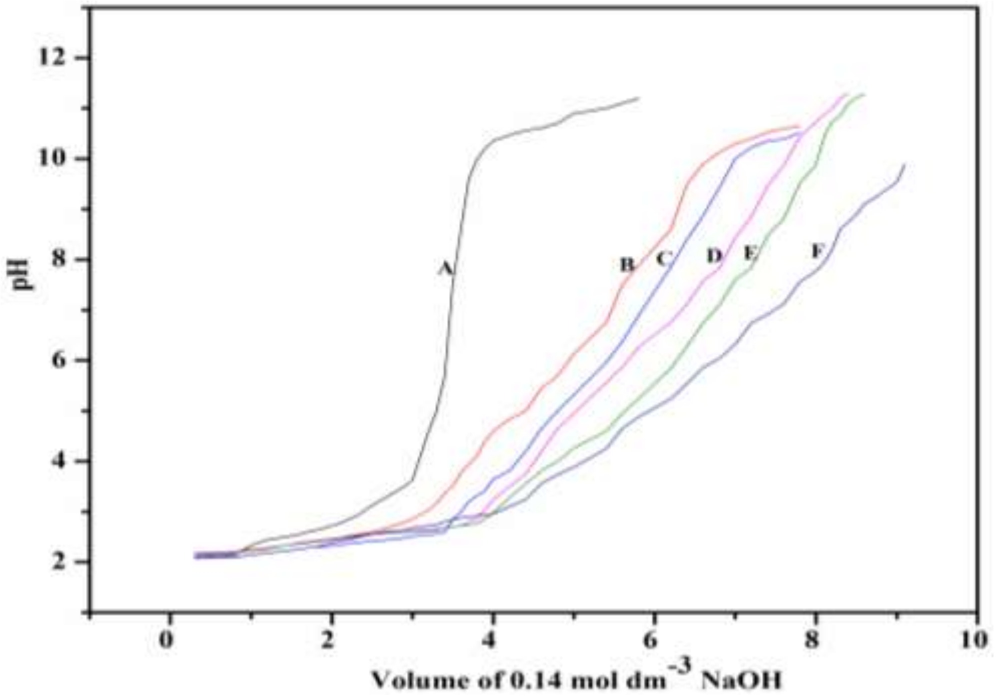


Figure 1 Plot of pH versus volume of NaOH

(A) HNO_3 vs. 0.14 M NaOH titration

(B) HNO_3 + Folic acid vs. 0.14 M NaOH titration

(C) HNO_3 + Cu^{2+} + Folic acid with 0.14 M NaOH titration

(D) HNO_3 + Ni^{2+} + Folic acid with 0.14 M NaOH titration

(E) HNO_3 + Co^{2+} + Folic acid with 0.14 M NaOH titration

(F) HNO_3 + Fe^{2+} + Folic acid with 0.14 M NaOH titration

IV. RESULTS AND DISCUSSION

The following formula is used to calculate the average number of protons attached per ligand ($\bar{n}_A$) **(Table 1)**.

$$\bar{n}_A = Y - \frac{(V'' - V')\,(N^0 + E^0)}{(V^0 + V')T_{C_{L^0}}} \qquad (1)$$

Where

Y = Number of dissociable protons in the ligand

V^0 = Initial volume of the mixture

V' and V'' = Volumes of alkali added to reach the same value of pH in the titration of acid and ligand

N^0 = Strength of alkali in molarity

E^0 = Total initial strength of the free acid used in the system

$T_{C_{L^0}}$ = Total ligand concentration

Table 1 Calculation of $\bar{\eta}_A$ for folic acid

pH	V′	V″	V″ -V′	$\bar{\eta}_A$
3.50	2.9	3.5	0.6	1.66
4.60	3.2	4.0	0.8	1.54
5.0	3.3	4.4	1.1	1.38
5.70	3.4	4.8	1.4	1.23
7.50	3.5	5.6	2.1	0.82
8.60	3.6	6.2	2.6	0.54

3.1 MECHANISM

Folic acid is represented as H_2FA. The step wise dissociation constants are as follows:

$$H_2FA \overset{K_1}{\rightleftharpoons} HFA^- + H^+$$

$$HFA^- \overset{K_2}{\rightleftharpoons} FA^{2-} + H^+$$

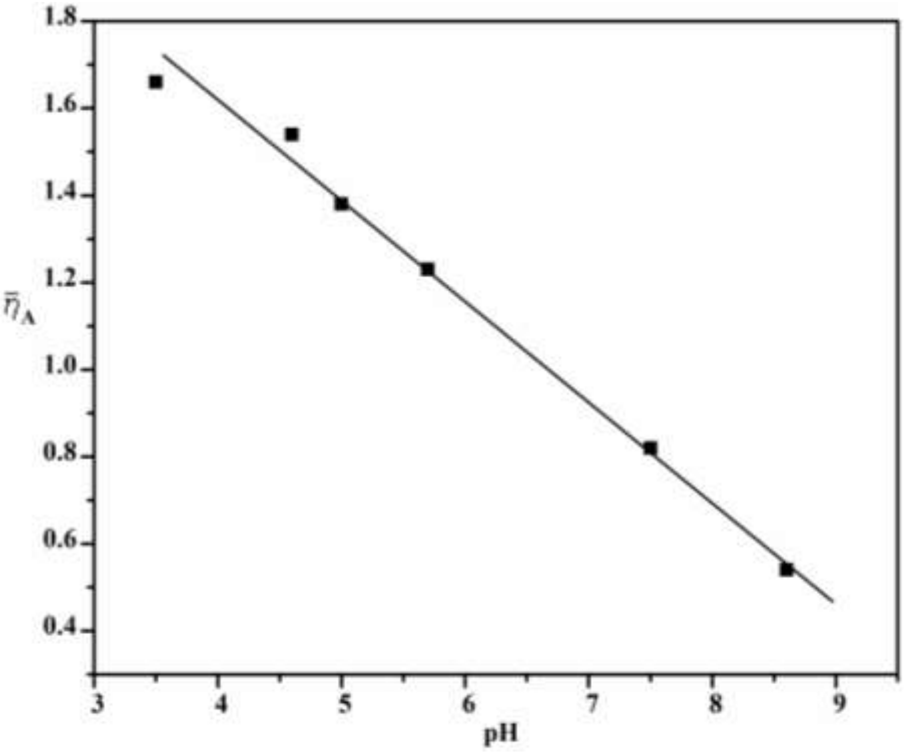
Where K_1 and K_2 are the first and second dissociation constants.

Step wise formation constants are expressed as K_H^1 and K_H^2

$$FA^{2-} + H^+ \rightleftharpoons FAH^- \quad K_H^{\ 1}$$

$$FAH^- + H^+ \rightleftharpoons FAH^{2-} \quad K_H^{\ 2}$$

A graph is plotted between $\bar{\eta}_A$ against pH **(Fig. 2)** to calculate proton ligand association constant. The values of $\log K_1^H$ and $\log K_2^H$ (the first and second association constants of the FA) are the pH values corresponding to $\bar{\eta}_A = 0.5$ and 1.5 respectively



Formation curves of ligands

3.2 Metal-Ligand stability constants

In the present case the formation constants have been obtained by plotting $\bar{\eta}$ against ρL of Cu(II) **(Fig. 3)**, Ni(II) **(Fig. 4)**, Co(II) **(Fig. 5)** and Fe(II) **(Fig. 6)**. The values of $\bar{\eta}$, the average number of ligand molecules attached per metal ion were calculated by using the formula

$$\bar{\eta} = \frac{(V''' - V'')(N^0 + E^0)}{(V^0 + V')\,(\bar{\eta}_A)\,(T_{C_{M^0}})} \qquad (2)$$

Where V'''= volumes of alkali added for the same pH of metal titration curve

V''= Volumes of alkali added for the same pH of ligand titration curve

V^0= Volume of the mixture = 50 ml

$T_{C_{M^0}}$ = Total metal concentration

The free ligand exponent ρL has been calculated by using the following equation (V^0+V''') / V^0 factor is unity. The exponent ρL is represented as by the following formula

$$\rho L = \log_{10}\left[\frac{1 + K_1^H[H] + K_1K_2[H]^2}{T_{C_{L^0}} - \bar{\eta}T_{C_{M^0}}}\right] \times \frac{V^0 + V'''}{V^0} \qquad (3)$$

The method[8] by Dixit and Munshi was used for determination of stability constants of the mixed ligand complexes. The equations (2) and (3) are used to calculate the values of $\bar{\eta}$ and ρL **(Table 2)**.

Table 2 Calculation of $\bar{\eta}$ and ρL for folic acid

Metal	**pH**	**$\bar{\eta}$**	**ρL**
Copper	3.10	0.34	8.70
	4.60	0.81	6.24
	6.74	1.03	3.98
	8.90	1.62	2.27
Nickel	4.60	0.35	6.16
	5.0	0.82	5.78
	5.70	1.34	4.99
	7.50	2.04	3.23
Cobalt	4.71	0.39	6.15
	5.35	0.86	5.36
	6.19	1.00	4.47
	6.98	1.73	3.71
Iron	2.70	0.30	7.48
	3.80	0.39	5.90
	4.60	0.65	5.04
	7.60	3.16	2.51

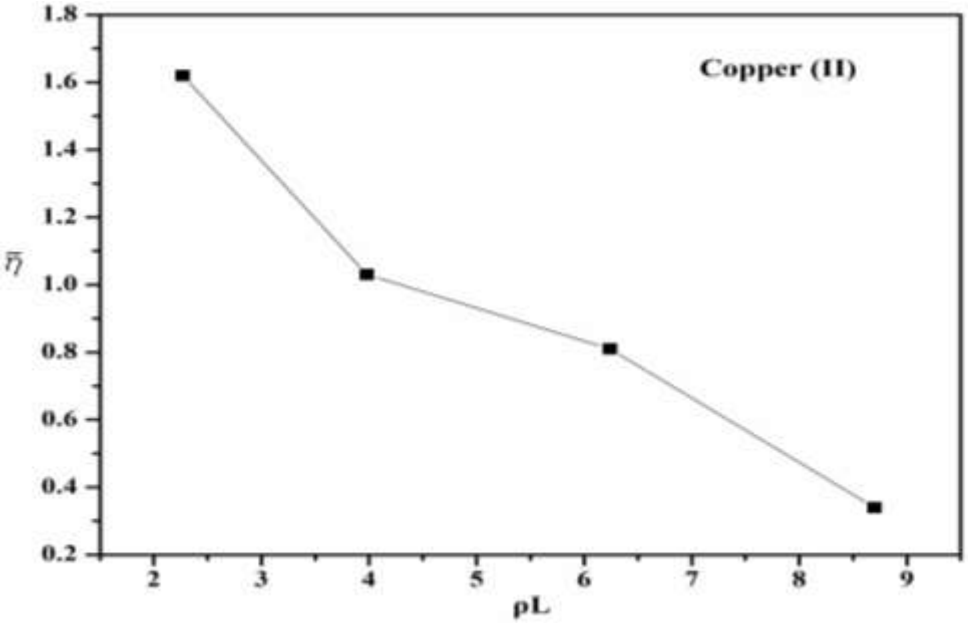


Figure 3 Formation curve of copper (II) metal complex

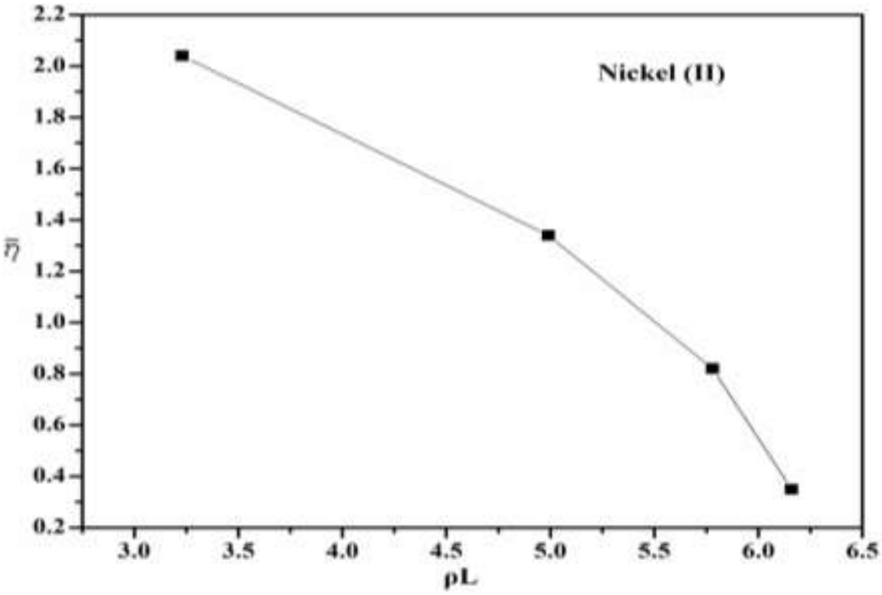


Figure 4 Formation curve of nickel (II) metal complex

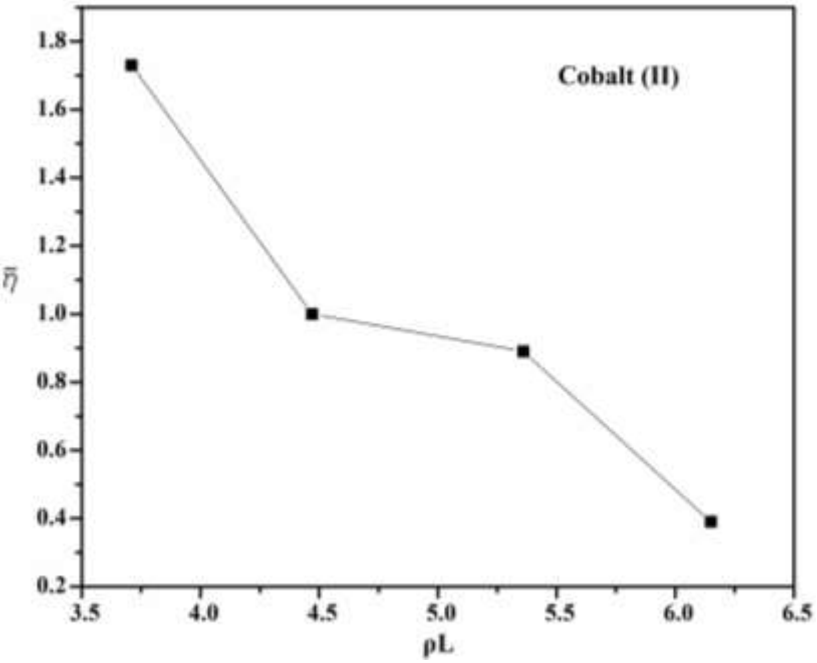


Figure 5 Formation curve of cobalt (II) metal complex

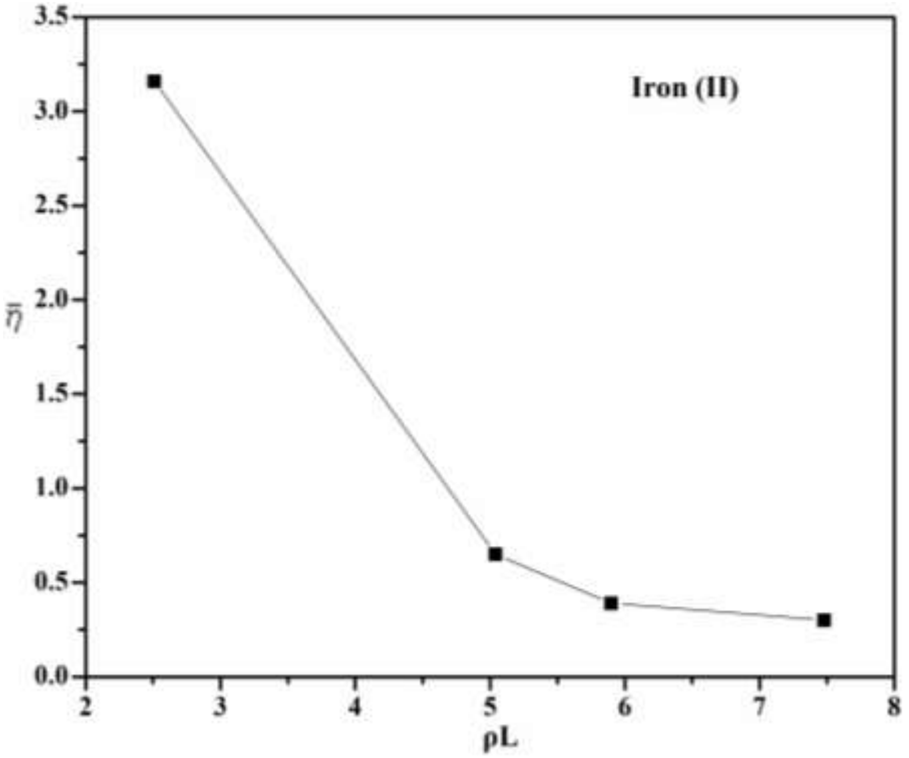


Figure 6 Formation curve of iron (II) metal complex

It is significant that the ligand do not hydrolyses under experimental conditions due to maintaining equilibrium at the time of titration. The titration curves of the metal-ligand solutions (C) are well separated from the ligand solution (B) **(Fig. 1)**. Thus, replacement of H^+ ion is due to complexation. From these data, the proton-ligand and metal-ligand stability constants were obtained **(Table 3)**.

Table 3 Protonation constants of FA and stability constants of metal ion complexes at 0.1 M $NaNO_3$ and 30 ± 0.1°C

Metal ion	log K_1	log K_2
H^+	8.60	4.60
Cu(II)	7.89	2.83
Ni(II)	6.28	4.75
Co(II)	5.97	4.11
Fe(II)	5.74	4.53

Variations are obtained in the values in case of proton-ligand stability constant calculation. As the solvents are polar in nature, this may be caused by intermolecular interactions like solute-solvent and solvent-solvent interactions.

It is the nature of ligands that they have different splitting ability. The ligands are arranged in order of their increasing splitting ability and this series is called spectrochemical series. Metal-ligand stability constants of complexes follow the order

$$Mn^{2+} < Fe^{2+} < Co^{2+} < Ni^{2+} < Cu^{2+} > Zn^{2+}$$

according to Irving-Williams series[9,10]. At the time of titration the color was changed from colorless to yellow or green which establish the formation of complex in the current study.

CONCLUSIONS

The folic acid ligand acts as a multidentate ligand. It results in the simultaneous arrangement of 1:1 and 1:2 (M:L) complexes through transition metal ions i.e Cu(II), Ni(II), Co(II) and Fe(II). The stability constant of transition metals are arranged in the order $Cu^{2+}>Ni^{2+}>Co^{2+}>Fe^{2+}$ which was supported by the literature[11]. Due to Jahn-Teller distortion, Cu^{2+} complexes have higher stability constant with its configuration as $3d^9$, which is the unique nature of copper than other transition metal. Proton ligand stability constant ($\log K'_H$) of folic acid is determined by Irving-Rossotti Method[12,13]. Ligand metal stability constants ($\log K_H$) of metals Fe^{2+}, Co^{2+}, Ni^{2+} and Cu^{2+} were calculated at 303K.

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Acknowledgment

Thepreferredspellingoftheword “acknowledgment” inAmericaiswithoutan “e” afterthe “g”.Avoidthestiltedexpression, “Oneofus(R.B.G.)thanks...”
Instead,try“R.B.G.thanks”.Putapplicablesponsoracknowledgmentshere;DONOTplacethemonthefirstpageofyourpaperorasafootnote.

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