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The Effect Of Different Concentrations Of DMF-H_2O On The Proton Ligand Dissociation Constant (Pk) And The Stability Constant Of Mn-Glycine Complex

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ABSTRACT: *The stepwise stability constant values of glycine with Mn(II) have been studied using pH measurements in 50%DMF- 50%Water and 70%DMF- 30%Water medium. The values of proton-ligand stability constants and metal – ligand stability constants were calculated. The metal- ligand stability constant of binary complex was evaluated using Irving- Rossotti titration technique.*

KEYWORDS: *Binary solvent mixture, dissociation constant, glycine, potentiometric, stability constant*

I. INTRODUCTION

The first aminoacid isolated from hydrolysis of protein was glycine, obtained in 1820 from gelatinby Braconnot as reported by Lehninger [1]. The physiological function of glycine is as a precursor to proteins, such as its periodically repeated role in the formation of collagen helix in conjunction with Hydroxyproline. It is also a building block to numerous natural products. Glycine has tremendous pharmaceutical applications in management of seizures [2]. It is also used in the treatment of enduring negative symptoms of schizophrenia [3]. It has also shown to have beneficial effects on memory and attention in young and middle-aged adults [4]. It also has neuroprotective effects for therapy of acute ischaemic stroke [5]. It is also used in the treatment of hypostatic leg ulceration [6]. It prevents the development of liver tumors caused by the peroxisome proliferator WY-14,643 [7] and it accelerates recovery from alcohol-induced liver injury[8]. The metal complexes with aminoacids play a major role in the biological and chemical activity [9], [10].The stability of metal complexes controls the interaction of metal and glycine in complex media [11]. Literature survey reveals that a very few researchers have done such type of work in organo aqueous media [12], [13], [14].Stability constants of metal complexes have been determined by different methods such as spectroscopy and potentiometry [15]. The essential metals such as iron, manganese, cobalt and nickel play vital roles in biological processes in form of complexes and their stability contributes to their efficiency. The roles played by these metals include catalysing enzymatic process, storage, checking of toxicity of metal at certain concentration [16].The stability constant is a measure of the strength of the interaction between the reagents that come together to form the complex. This helps in the pharmaceutical applications of the complex. This work is an endeavor to achieve that and this work emphasizes the effect of different concentrations of the binary solvent on the stability constant.

II. MATERIALS AND METHODS

All the chemicals used in this work were of Analar grade. The metal ion solution, acid solution, KNO_3 solution and NaOH solution were prepared in double distilled water. NaOH was standardized with standard oxalic acid solution and it was used for further potentiometric titration. Systronics pH meter with a combined glass electrode were used for the pH measurements .

The experimental procedure for binary metal complexes involves the following titrations.

[1] Free HNO_3
[2] Free HNO_3 + Glycine
[3] Free HNO_3 + Glycine + Metal ion
[4] The above mentioned solutions are titrated against standardized 0.1M NaOH in 0.2 ml aliquots, under an inert atmosphere of nitrogen. The ionic strength of the solutions was maintained at 0.1M by addition of calculated amounts of 1M KNO_3. The concentration of glycine and metal ions were 20 x 10^{-4}M and 4 x 10^{-4}M.

III. RESULTS AND DISCUSSION

Proton-Ligand stability constant:

The plot of volume of NaOH against pH was used to evaluate the proton-ligand stability constant of glycine. The deviation between free acid titration curve & secondary ligand titration curve was used to evaluate the formation function nA.. The proton-ligand formation curves were then obtained by plotting the values of $n_A$verses pH. From the graphs the value of pKwas evaluated by half-integral method and pointwise calculation method reported in the Table-3.

Metal-Ligand stability constants of Binary complexes:

[1] The metal titration curves showed displacement with respect to the ligand titration curves along the volume axis. This indicated the affinity of ligand with metal ions which released protons and produced the difference in volume ($V_3 - V_2$).

[2] The colour change of the ligand was in presence of metal ions appeared showing the formation of new species.

[3] The hydrolysis of metal ions was suppressed due to complex formation and the precipitation did not appear during the titrations.

The proton-ligand stability constant and the metal ligand stability constants are found for Mn(II) with Glycine in 70%-30% DMF-water and 50%-50% DMF-water. Irving Rossotti expression was used to calculate the proton ligand formation number n_A.Bjerrum proposed the half integral method in 1957 by which we calculated the pK values at n_A=0.5 (Figure-1). The pointwise calculations were also done and the results were similar to the half integral method (Table 1). The n_A values were calculated by using the following equation

$$n_A = \gamma - \frac{(E° + N) \text{ X } (V_2 - V_1)}{(V° + V_1) \text{ x } T°_L}$$

where γ is the replaceable H^+ ions, E° is the concentration of acid, N is the normality of the base, $T°_L$ is the concentration of ligand, V° is the total volume and V_2-V_1 is the horizontal difference in the volume at the given pH.

Figure-1 Half integral method for determining pK (70%DMF-30% water)

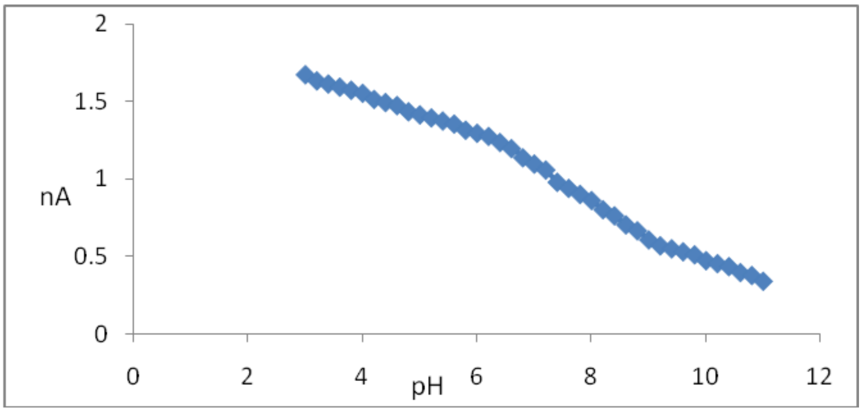

Table-1Pointwise method for calculation of pK(70%DMF-30% water)

pH	V_1	V_2	ΔV	n_A
8.0	2.88	2.95	0.07	0.8619
8.2	2.89	2.99	0.10	0.8027
8.4	2.90	3.02	0.12	0.7634
8.6	2.95	3.10	0.15	0.7048
8.8	2.98	3.15	0.17	0.6658
9.0	3.00	3.20	0.20	0.6071
9.2	3.04	3.26	0.22	0.5684
9.4	3.07	3.30	0.23	0.5493
9.6	3.08	3.32	0.24	0.5299
9.8	3.10	3.35	0.25	0.5106
10.0	3.15	3.42	0.27	0.4724

The metal-ligand stability constants were calculated by the half integral method by plotting n vspL. The n values were obtained by using the equation.

$$n = \frac{(E^\circ + N) \times (V_3 - V_2)}{(V^\circ + V_2) \times T^\circ_m}$$

Where E° is the concentration of acid, N is the normality of the base, T°_m is the concentration of metal, V° is the total volume and V_3-V_2 is the horizontal difference in the volume at the given pH.

The proton-ligand stability constant and the metal ligand stability constants for Mn(II) with Glycine in 50%-50% DMF-water can be found by the half integral method (Figure-2) and pointwise calculation method (Table -2).

Figure- 2 Half integral method for determining pK (50% DMF-50% water)

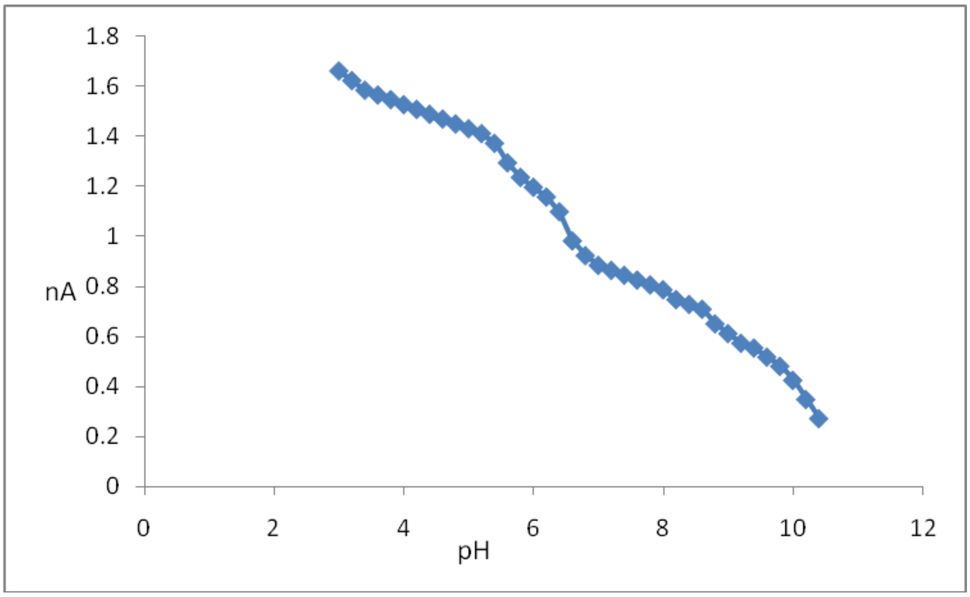

Table-2 Pointwise method for calculation of pK(50%DMF-50% water)

pH	V_1	V_2	ΔV	n_A
7	3.09	3.15	0.06	0.8825
7.2	3.10	3.17	0.07	0.8629
7.4	3.11	3.19	0.08	0.8434
7.6	3.12	3.21	0.09	0.8239
7.8	3.13	3.23	0.10	0.8044
8.0	3.15	3.26	0.11	0.7850
8.2	3.16	3.29	0.13	0.7460
8.4	3.17	3.31	0.14	0.7266
8.6	3.18	3.33	0.15	0.7072
8.8	3.19	3.37	0.18	0.6488
9.0	3.20	3.40	0.20	0.6099
9.2	3.22	3.44	0.22	0.5712
9.4	3.25	3.48	0.23	0.5522
9.6	3.40	3.65	0.25	0.5158
9.8	3.50	3.77	0.27	0.4789
10.0	3.60	3.90	0.30	0.4230
10.2	3.61	3.95	0.34	0.3463
10.4	3.62	4.00	0.38	0.2697

The pK values and the metal ligand stability constants are summarized in Table-3 and Table-4.

Table -3pK values at different solvent concentrations

Ratio of DMF-water	pK_1(Half integral method)	pK_2 (Half integral method)	pK_1 (pointwise calculation)	pK_2 (pointwise calculation)
70%-30%	3.80	9.80	4.37	9.74
50%-50%	3.70	9.70	4.22	9.41

Table -4 Stability constant values at different solvent concentrations

Ratio of DMF-water	Log K_1	Log K_2
70%-30%	3.29	3.41
50%-50%	2.89	3.17

This shows that the stability of the Mn(II)-Glycine complex is slightly more in DMF-water concentration of 70%-30%.The present study has great importance in the development of co-ordination chemistry and metal-ligand stability constant of Mn(II) is given in the table. The deviation of metal titration curves from ligand curve indicates the formation of binary complex. The connection between metal-chelation and at least a type of cancer was suggested by Furst [17].

IV. CONCLUSION

- This is a rapid method of determination of stability of a complex.
- The difference in pKvalues at two different concentrations is probably due to the action of DMF as a base competing with that of water.
- In the present study, the stability constants of glycine with Mn(II) complex in 50%DMF- 50%Water and 70%DMF- 30%Waterconcluded that the difference between log K_1 and log K_2 values are less. The difference between log K_1 and log K_2 complexes indicated the simultaneous formation of 1:1 and 1:2 complexes. They showed the linear relationships between log K and pK values of ligands suggesting identical binding sites in all ligands.
- The increase in the stability constant value from 50% DMF- 50%Water and 70%DMF- 30%Water is because the dielectric constant value of DMF is lower than water which is responsible for the less solvation of the metal ion in DMF, which in turn, makes the approach of the ligand (Glycine) to occupy a coordination site in the coordination sphere of metal ion easier and hence greater the stability of the complex.
- The higher values account for the stability of the complexes and this further explain the ability of the metals to function effectively in biological systems.
- The method can be extended to real life samples where the stability of metal-glycine complex can be studied.
- This method helps in studying the stability of pharmaceutically important samples so that its behavior can be studied.

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