Research Journal of Pharmaceutical, Biological and Chemical Sciences

INFLUENCE OF IONIC STRENGTH ON THE ASSOCIATION AND DISSOCIATION CONSTANT OF Ce(III), Tb(III), Dy (III), Nd(III), Gd(III) COMPLEXES WITH SUBSTITUTED HETEROCYCLIC DRUG SUCH AS PHENYTOIN -5,5-DIPHENYLIMIDAZOLIDINE-2,4-DIONE.

GD Tambatkar, RE Khadsan and AS Kalawate

Shri. D.M. Burungale College of Science, Shegaon – 444 203 Dist-Buldana, MS, India.

ABSTRACT

A Proton ligand stability constant (pK) of Substituted Heterocyclic Drug such as phenytoin -5,5-diphenylimidazolidine-2,4-dione with Ce(III), Tb(III), Dy (III), Nd(III), Gd(III) and metal ligand complex of Substituted Heterocyclic Drug such as phenytoin -5,5-diphenylimidazolidine-2,4-dione with some metal ions have been investigated 0.02, 0.04, 0.06, 0.08, 0.1 M ionic strength pH metrically. Phenytion is a commonly antiepileptic. It was approved by the Food and Drug Administration in 1953 for use in seizures. Phenytoin acts to damp the unwanted, runaway brain activity seen in seizure by reducing electrical conductance among brain cells bu stabilizing the inactive state of voltage gated sodium channels. The value of (pK) proton ligand stability constant and (log K) metal ligand stability constant are utilized to estimate the thermodynamic stability at zero ionic strength and to exact nature of complexation equilibria. It is observed from the slope values, that the value of pK and log K are less than expected values. These values donot give a conclusive evidence regarding the magnitude of charge of reacting species. The discrepancy may be due to the limited application of Bronsted equation-
From the plots of pK/log K verses $\frac{\sqrt{\mu}}{1+\sqrt{\mu}}\ and \left(\frac{\sqrt{\mu}}{1+\sqrt{\mu}}-0.3\sqrt{\mu}\right)it$ showed that modifies Debye – Huckel equation also did not show much improvement in the slope values. The discrepancy between observed and expected slope values was thought of to be due to the concentration and did not activity terms use in the equation of stability constant. From thermodynamic stability constants pK^0/log K^0, it is observed that there is good agreement among thermodynamic constants obtained from various plots .

INTRODUCTION

In the view of analytical application, it was an interest to know the physico chemical properties such as stability constants of complexes with Ce (III), Tb (III), Dy (III), Nd (III), Gd (III) metal ion at various ionic strength. In present work the interaction of Ce (III), Tb (III), Dy (III), Nd (III), Gd (III) with substituted heterocyclic drug such as phenytoin 5,5-diphenylimidazolidine-2,4-dione has been investigated potentiometrically in 70 % DMF - water mixture at 0.02 M, 0.04 M, 0.06 M., 0.08 M., 0.1 M. ionic strength.

EXPERIMENTAL

Nitrides of lanthanide (B. D. H. AnalaR) was dissolved in perchloric acid and its concentration was estimated by standard procedure [1]. Since phenytoin in insoluble in water, DMF – water (70 % V/V) was use as solvent. The other solution was prepared in double distilled water. DMF was purified by standard method [2] and its purity was checked by potassium iodide. pH measurements were carried out with ELICO-LI-10 pH meter (accuracy $\pm$ 0.05 unit.) Using glass and calomel electrodes at 27 ± 0.1^0C. The B values (pH meter readings in 70 % DMF – water mixture) were converted to (H^+) values by applying the correction proposed by Van-Uitert and Hass [3].

Table 1 :- Proton ligand and metal ligand stability constant of Ce (III)+ complexes with phenytoin 5,5-diphenylimidazolidine-2,4-dione in 70 % DMF - water mixture at different ionic strength

Ionic strength	$\sqrt{\mu}$	$\dfrac{\sqrt{\mu}}{1+\sqrt{\mu}}$	pK	Constant Log K_1	Log K_2	Log K_2- Log K_1
0.1 M	0.3162	0.2402	11.30	6.20	8.05	1.85
0.08 M	0.2828	0.2204	11.50	6.45	9.15	2.7
0.06 M	0.2449	0.1967	11.65	6.60	9.50	2.9
0.04 M	0.2000	0.1666	11.75	6.70	9.95	3.25
0.02 M	0.1414	0.1238	11.90	6.95	10.05	3.1

RESULT AND DISCUSSION

Influence of ionic strength on complex equilibria

The stability transition metal complexes with a great variety of ligands have been studied.

Y. K. Meshram et al [4]., have thoroughly investigated the interaction of Cu (II) with 3-(2hydroxy-3 iodo-5 methyl phenyl) 1-phenyl 5-(4 methoxy phenyl) pyrazoline, and 3-(2-hydroxy-3-iodo 5-methyl phenyl) -5-(4-methoxo phenyl) isoxazoline at different ionic strength by potentiometrically.

Rajan and Martell [5] have thoroughly investigated the interaction of uranyl and copper ions with organic legends and correlated the stability constants of their chelates with the dissociation constants of the ligands. Narwade et al., [6] have determined the stability constants of bivalent metel ions with some substituted Pyrazolines and isoxazolines at 0.1M ionic strength.

The interaction of Ce (III), Tb (III), Dy (III), Nd (III), Gd (III) with phenytoin 5,5-diphenylimidazolidine-2,4-dione was undertaken with a view to study the influence of ionic strength on stability constant and to ascertain the exact mechanism of complexation equilibria. The over all ionic strength of the solution was calculated by expression $\mu = \frac{1}{2} \sum C_i Z_i^2$. The contribution of the other ions in addition of Na^+ and ClO_4^- were also taken into consideration.

Proton ligand stability constants

Phenytoin may be consider as a monobasic acids having only one dissociate H^+ ion from –OH group and can therefore be represented as HL.

$$HL \rightleftharpoons H^+ + L^-$$

1M, $NaClO_4^-$ solution was used for maintaining ionic strength constant. The proton ligand formation numbers (n_A) were calculated by Irving and Rossotti's expression [7]. pK values were calculated from formation curves (pH vs n_A) by noting pH at which $n_A = 0.5$ at different ionic strengths. The accurate values of pK were determined by pointwise calculation which are represented in Table 1.

Table 2:

Sr. No.	Reaction equilibria	Constant	Δz^2	
			Expected	Observered
1	$HL \rightleftharpoons H^+ + L^-$	pK	2.0	0.394
2	$L^- + Cu^{2+} \rightleftharpoons CuL^+$	Log K_1	-2.00	- 1.308
3	$L^- + CuL^+ \rightleftharpoons CuL_2$	Log K_2	0.00	-0.838

METAL LIGAND STABILITY CONSTANT

The departure of metal of metal ion curve from ligand curve was observed around pH 5.60 in the media of different ionic strength that commencement of complex formation before the hydrolysis of metal ion set in. the values of n (i.e. metel ligand formation number) were calculated by Irving Rossotti's equation [8]. The values of metal ligand stability constant (LogK, and LogK$_2$) were obtained from the plots of n vs logK$_1$ by half integral method as well as pointwise calculation method at various ionic strength which ate given in table 1 and Table 2

Table 3 :- Thermodynamic stability constants at zero-ionic strength.

System	Plot	pK^0 or $Log\ K^0$
1) Phenytoin (5,5-diphenylimidazolidine-2,4-dione)	pK Vs $\sqrt{\mu}$	13.45
	pK Vs $\dfrac{\sqrt{\mu}}{1+\sqrt{\mu}}$	13.30
	pK Vs $\left(\dfrac{\sqrt{\mu}}{1+\sqrt{\mu}}-0.3\sqrt{\mu}\right)$	13.35
2)Ce(III) Phenytoin 5,5-diphenylimidazolidine-2,4-dione	Log K_1 Vs $\sqrt{\mu}$	13.40
		13.20
	Log K_1 Vs $\dfrac{\sqrt{\mu}}{1+\sqrt{\mu}}$	
		13.25
	Log K_1 Vs $\left(\dfrac{\sqrt{\mu}}{1+\sqrt{\mu}}-0.3\sqrt{\mu}\right)$	11.10
	Log K_2 Vs $\sqrt{\mu}$	12.00
	Log K_2 Vs $\dfrac{\sqrt{\mu}}{1+\sqrt{\mu}}$	11.90
	Log K_2 Vs $\left(\dfrac{\sqrt{\mu}}{1+\sqrt{\mu}}-0.3\sqrt{\mu}\right)$	

The reduction in values may be due to the effect of electron withdrawing iodo group at 3-position. Initially log K_1 and Log K_2 values were obtained by pointwise calculations. The maximum value of n at each ionic strength was around 2.0 which indicated that 1:1 and 1:2 complex formation are possible. One would expect at bigger differences between Log K_1 and Log K_2 values (Table 1,2) due to possible steric hindrance to the linking of the secondary ligand to the metal ion.

The smaller difference may be due to trans structure. The ratio of Log K_1/Log K_2 is positive, it shows that the separator factor between first and second formation constant are well with in the expected range.

The Bronsted equations

$$Log\ K = log\ K^0 + A\ \Delta\ z^2 \text{ and}$$

$$pK = pK^0 - K^0 - A \Delta z^2$$

were used to determine the magnitude of the obtained data of pK and log K values could be utilized to know the exact mechanism of complexation equilibria. The plots of pK and log K values against $\sqrt{\mu}$ gave the straight lines and magnitude of Δz^2 (Debye-Huckel constant) were observed for each plot. It is observed from Table 3, that slope values of pK are less than the expected and for log K less than expected.

There values donot give a conclusive evidence regarding the magnitude of the charge of reacting species. The discrepancy may be due to the limited applicability of Bronsted equations.

$$\text{The plots of pK /log K vs } \quad \frac{\sqrt{\mu}}{1+\sqrt{\mu}} \; and \left(\frac{\sqrt{\mu}}{1+\sqrt{\mu}} - 0.3\sqrt{\mu} \right)$$

Were also plotted and slope values were determined. It showed that modified Debye-Huckel equation also did not show much improvement in the slope values. The discrepancy between observed and expected slope values was thought of to be due to the concentration and not the activity terms used in the equation of stability constant.

Thermodynamic stability constants (pK^0/log K^0)

Thermodynamic stability constants are calculated at zero ionic strength from various plots. Which are given in Table 4. It could be seen from table 4 that agreement between pK^0 and log K^0 values from various plots are found to be fairly good.

ACKNOWLEDGEMENT

REFERENCES

[1] Vogel A.I. A Text Book of quantitative inorganic Analysis, Longmans Green, London, 1975,539.
[2] Vogel A.I. A Text Book of Practical Organic Chemistry, Longmans Green, London,1976,177.
[3]Van Uitert LG and Hass GG. Am Chem Soc 1953;75:451.
[4]YK Mesharam, AU Mandakmare and ML Narwade. Oriental J Chem 1999;15 (3): 531-534.
[5] Martall AE and Sillen LG. The Stability constants of metal ion complexes, Special publication no. 17 and 95, Chem. Soc., London, 1964, 1971.
[6] Narwade ML, Jamode VS. J Indain Chem Soc.(1988)
[7] Invring MM, Rossotti HS. J Chem Soc 1953;3397.

## pH-Metric Titration Data

System-Ce(III) phenytion

Medium -70% DMF+Water

$T^0L = 20 \times 10^4 M$ $T^0M = 4 \times 10^4 M$

$V^0 = 50\ ml$ $N = 0.2 N = 27^0 C$ $\mu = 0.02 M$

	Titration OF		
Volume of Alkali added	Free acid	Free acid + Ligand	Free acid + Ligand + Metals Ce(III)
(ml)	pH	pH	pH
0.0	3.07	3.07	3.07
0.2	3.12	3.12	3.12
0.4	3.27	3.27	3.27
0.6	3.54	3.54	3.52
0.8	4.45	4.45	4.43
1.0	9.05	7.50	5.80
1.2	11.32	10.35	8.70
1.4	11.60	11.20	10.25
1.6	11.73	11.40	11.10
1.8	11.77	11.45	11.40
2.0	11.78	11.70	11.60

Graph of pH Vs ml of Alkali added

System 70% DMF+Water (phenytion)-Ce(Ⅲ)
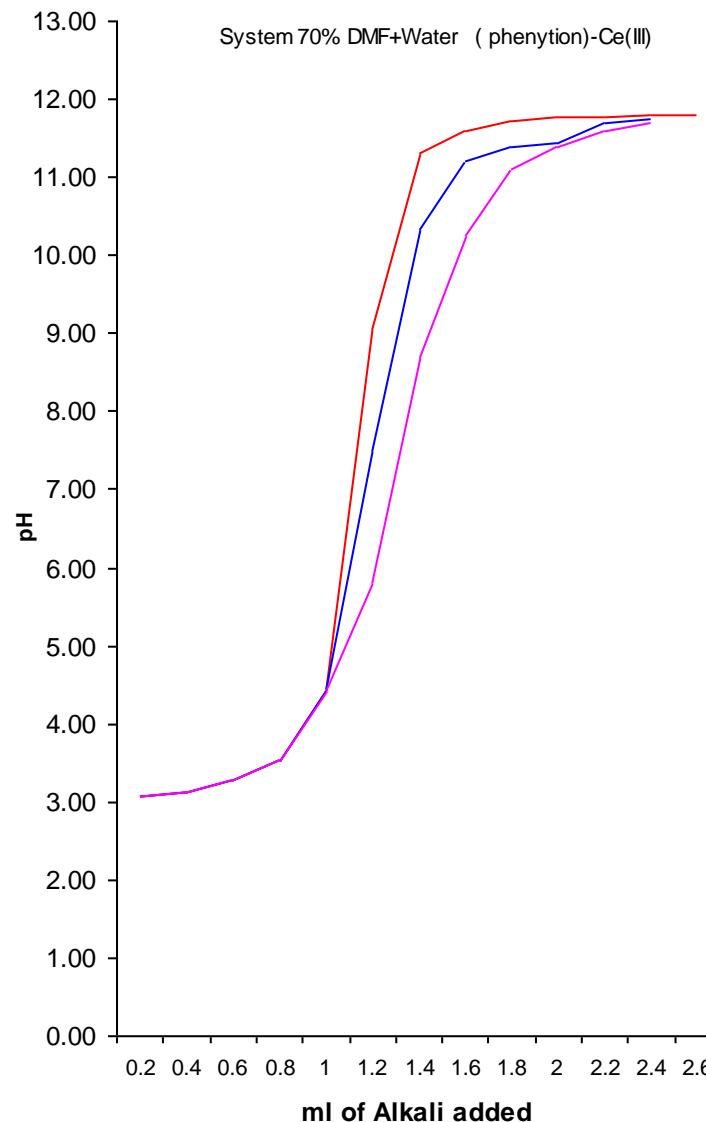
2.2	11.81	11.75	11.70
2.4	11.81		

Determination of $\bar{n}_A$

System-Ce(III)-Phenytion

Medium -70%

DMF+Water

$T^0L = 20 \times 10^4 M$ $T^0M = 4 \times 10^4 M$

$V^0 = 50\, ml$ $N = 0.2N$

$tempt = 27^0 C$ $\mu = 0.02M$

$$\frac{A}{A+L}$$

Ce(III)

pH	V_1	V_2	$(V_2 - V_1)$	$\bar{n}_A$
5.00	0.82	0.85	0.03	0.911
5.50	0.83	0.89	0.06	0.822
6.00	0.85	0.92	0.07	0.793
6.50	0.88	0.97	0.09	0.734
7.00	0.90	1.00	0.10	0.705
7.50	0.92	1.02	0.10	0.675
8.00	0.94	1.05	0.11	0.646
8.50	0.96	1.07	0.11	0.646

9.00	0.97	1.10	0.13	0.617
9.50	1.00	1.14	0.14	0.588
10.00	1.03	1.18	0.15	0.559
10.50	1.05	1.21	0.16	0.529
11.00	1.13	1.33	0.20	0.413
11.50	1.30	1.70	0.40	0.169

Determination of $\bar{n}$

System-Ce(III)-Phypention

Medium - 70% DMF Water

$V^0 = 50\,ml$

$tempt = 27^0C$

$T^0L = 20X10^4M$ $I = 4X10^4M$

$N = 0.2N$

$\mu = 0.1M$

pH	V_2	V_3	$(V_3 - V_2)$	$\bar{n}$
5.00	0.85	0.88	0.03	0.476
5.50	0.89	0.96	0.07	1.230
6.00	0.94	1.09	0.15	1.485
6.50	0.95	1.05	0.10	1.604
7.00	1.00	1.09	0.09	1.877

Graph of $\bar{n}$ Vs $\overline{pH}$ A

Medium -70% DMF+Water   System-Phenytion
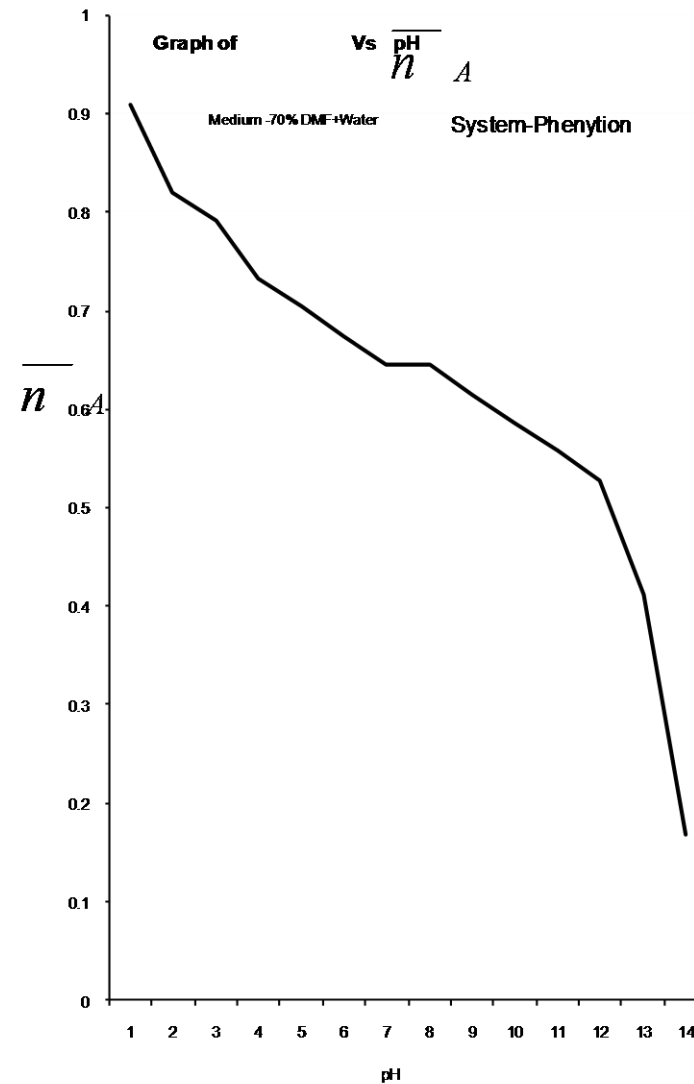
7.50	1.02	1.12	0.10	2.177
8.00	1.05	1.14	0.09	2.501
8.50	1.07	1.18	0.11	2.727
9.00	1.10	1.23	0.13	3.092
9.50	1.14	1.28	0.14	3.491
10.00	1.18	1.34	0.16	4.194
10.50	1.21	1.44	0.23	6.367
11.00	1.33	1.56	0.23	8.137
11.50	1.70	1.96	0.26	

Graph of $\bar{n}$ s pH

Medium -70% DMF+Water

System-Ce(III)-Phenytion

$\bar{n}$ A

pH