Spectrophotometric and pH-Metric Studies of Ce(III), Dy(III), Gd(III), Yb(III) and Pr(III) Metal Complexes with Rifampicin

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Abstract: The metal-ligand and proton-ligand stability constant of Ce(III), Dy(III), Gd(III), Yb(III) and Pr(III) metals with substituted heterocyclic drug (Rifampicin) were determined at various ionic strength by pH metric titration. NaClO₄ was used to maintain ionic strength of solution. The results obtained were extrapolated to the zero ionic strength using an equation with one individual parameter. The thermodynamic stability constant of the complexes were also calculated. The formation of complexes has been studied by Job's method. The results obtained were of stability constants by pH metric method is confirmed by Job's method. .

Keywords: Stability constant, Ionic strength, Rifampicin, pH metric

Introduction

The substituted heterocyclic drug (Rifampicin-5,6,9,17,19,21-hexahydroxy-23-methoxy-2,4,12,16,18,20,22-heptamethyl-8-[N-(4-methyl-1-piperazinyl)formimidoyl]-2,7-(epoxypentadeca [1,11,13]trienimino)-naphtho[2,1-*b*]furan-1,11(2*H*)-dione 21-acetate) has anti-tuberculosis, protein transporter, anti-hyperglycemics, anti-epileptic, neuropsychiatry therapeutics, anti-bacterial properties¹. The complex of rifampicin with cyclodextrin is used as anti-tubercular drug². Das³ *et al.* have studied the effect of ionic strength on the stability constant of complexes of Fe(III) with salicylic acid and its derivatives. Sanchez⁴ *et al.* have studied the influence of ionic strength on ionization constant and stability constant of 4-amino-1,6-dihydro-2-methylthio-5-nitroso-6-oxo-pyrimidine and its complex with Fe(II), Co(II), Ni(II) and Cu(II). Majlesi⁵ *et al.* have studied the stability constant of tugesten(VI) and molybdenum(VI) with nitrilo triacetic acid and glutamic acid at different ionic strength. Meshram⁶ *et al.* have studied the association and dissociation constant of Pr(III) complexes with 3-(2-hydroxy-3-iodo-5-methyl phenyl)1,5 diphenyl pyrazoline at different ionic strength. The stability constant of vanadium with glycine at various ionic strength was investigated by potentiometric titration technique⁷. Majlesi⁸ *et al.* have studied the stability constant of Mo(IV) with iminodiacetic acid at different ionic strength maintained by using

sodium per chlorate. Sharma *et al.* have studied the effect of ionic strength and solvent effect on thermodynamic parameters⁹. They have also studied the mechanism of protonation and complex formation of binary complexes of La(III), Ce(III), Pr(III) and Nd(III) with aminopyridines.

Tekade¹⁰ *et al.* have studied the apparent metal-ligand stability constant and confirmation of complexes. The compositions of complexes were confirmed by Job's method as modified by Vasburgh and Gold¹¹. In the present work, the values of pK, metal-ligand stability constant at different ionic strength have been determined in the 70% dioxane-water mixture. We attempted to study the effect of ionic strength on thermodynamic parameters of complexes of rifampicin with Ce(III), Dy(III), Gd(III), Yb(III) and Pr(III) metals in 70% dioxane-water mixture by pH metrically and spectrophotometrically.

Experimental

The pH measurements were carried out with equip-tronic EQ-610 pH meter (accuracy ± 0.01 units) using combine glass electrode at 208 K. All the rare earth nitrates were used of 99.9% pure. All metal nitrates used were purchased from Sigma Aldrich Chem. Co., U.S.A. Metal nitrate solutions were prepared in triply distilled water and concentration was estimated by standard method. The drug solutions were prepared in 70% 1,4 dioxane solution. The 1, 4 dioxane was purified by the method described by Vogel¹². The pH metric readings were taken in 70% 1, 4 dioxane-water mixture and were converted to $[H^+]$ value by applying the correction. The overall ionic strength of solution was maintained constant by adding $NaClO_4$. All the solutions were titrated with standard carbonate free NaOH (0.2 N) solution at different ionic strengths using $NaClO_4$ (0.02, 0.04, 0.06, 0.08 M). The solutions involved in the experimental procedure for pH metric titrations are:

- 1) Free $HClO_4$ (A);
- 2) Free $HClO_4$ + Ligand (A+L), Free $HClO_4$ + Ligand +Metal ion (A+L+M)

The volume of NaOH added in each titration was plotted against pH and the corresponding volume at successive pH for each set was determined and calculated. The metal-ligand stability constant of lanthanide metal complexes with rifampicin were investigated spectrophotometrically. The absorbance measurements were carried out with Shimadzu UV-1800 ENG 240V, Japan spectrophotometer. The solutions of metal nitrates and rifampicin were prepared in 70% dioxane-water mixture. $NaClO_4$ was used for maintaining the constant ionic strength. The different composition of metal ion (1×10^{-4} M) and ligand ion (1×10^{-4} M) were prepared in ten series. For determination of λ_{max} , 50% metal ion solution was used, at which maximum absorbance observed. The absorbance of all composition was measured at constant wave length (λ_{max}) and at constant pH.

Results and Discussion

In the present investigation the dependence of proton-ligand stability constant (pK) and metal-ligand stability constant (log K) on ionic strength of medium was examined by keeping fixed concentration of metal nitrates and ligand solution during pH metric titration. The system has been studied at 0.02, 0.04, 0.06 and 0.08 M ionic strength by varying the concentration of sodium per chlorate. The total ionic strength of medium was calculated

The values of proton-ligand and metal-ligand constant of lanthanide metal complexes at different ionic strength 0.02, 0.04, 0.06 and 0.08 M were determined. These values were determined by using Irving-Rossotties method¹³. From Table 1, it shows that the values of proton-ligand stability constant (pK) decreases with increasing ionic strength of medium. The metal-ligand stability constant (log K) also decrease with increasing ionic strength. For determination of stability constant at zero ionic strength the Bronsted equation was used.

$$\log K = \log K^0 + A \sum \Delta Z^2 \sqrt{\mu}$$

$$pK = pK^0 - A \Delta Z^2 \sqrt{\mu}$$

Table 1. Proton-ligand (pK) and metal-ligand stability constant (log K) values for Ce(III), Dy(III), Gd(III), Yb(III) and Pr(III) metal ions with rifampicin at various ionic strength (μ)

μ	$\sqrt{\mu}$	$\sqrt{\mu}/1+\sqrt{\mu}$	$[\sqrt{\mu}/1+\sqrt{\mu}] - 0.3\sqrt{\mu}$	Pk	logK ₁	logK ₂
Rifampicin + Ce(III)						
0.02	0.1414	0.1239	0.0815	8.035234	7.00	4.95
0.04	0.2000	0.1667	0.1067	7.982331	6.45	4.55
0.06	0.2450	0.1968	0.1233	7.853715	6.25	4.25
0.08	0.2828	0.2205	0.1356	7.615693	5.80	4.00
Rifampicin + Dy(III)						
0.02	0.1414	0.1239	0.0815	8.035234	7.15	5.20
0.04	0.2000	0.1667	0.1067	7.982331	6.90	4.95
0.06	0.2450	0.1968	0.1233	7.853715	6.75	4.80
0.08	0.2828	0.2205	0.1356	7.615693	6.25	4.50
Rifampicin + Gd(III)						
0.02	0.1414	0.1239	0.0815	8.035234	7.55	5.15
0.04	0.2000	0.1667	0.1067	7.982331	6.95	4.75
0.06	0.2450	0.1968	0.1233	7.853715	6.75	4.55
0.08	0.2828	0.2205	0.1356	7.615693	5.90	4.20
Rifampicin + Yb(III)						
0.02	0.1414	0.1239	0.0815	8.035234	7.75	5.45
0.04	0.2000	0.1667	0.1067	7.982331	7.55	4.95
0.06	0.2450	0.1968	0.1233	7.853715	7.25	4.80
0.08	0.2828	0.2205	0.1356	7.615693	6.50	4.15
Rifampicin + Pr(III)						
0.02	0.1414	0.1239	0.0815	8.035234	7.70	5.10
0.04	0.2000	0.1667	0.1067	7.982331	7.45	4.90
0.06	0.2450	0.1968	0.1233	7.853715	7.25	4.70
0.08	0.2828	0.2205	0.1356	7.615693	6.40	4.10

Where, K^0 is the formation constant at zero ionic strength. pK^0 is proton-ligand stability constant at zero ionic strength. 'A' is the Debye-Huckel constant. ΔZ^2 is the difference in square of the changes of product and reactant ion. The pK^0 and $\log K^0$ values were calculated by plotting the graph of pK, log K₁, log K₂ versus $\sqrt{\mu}$ (Figures 1-3).

Figure 1. Plot of pK vs. $\sqrt{\mu}$

Figure 2. Plot of log K₁ vs. $\sqrt{\mu}$

Figure 3. Plot of $\log K_2$ vs. $\sqrt{\mu}$

From Table 2, it is seen that the good agreement among thermodynamic constant obtained from different plots. The plots of pK , $\log K_1$, $\log K_2$ versus $\sqrt{\mu}$ gives straight line over the entire range of ionic strength for both systems. It shows that the Bronsted relationship is valid for dissociation equilibrium. Fazlur Rahman *et al.*¹³ have determined similar results of stability constant of different metal complexes with substituted acetophenone oxime at 0.1, 0.05 and 0.01 M ionic strength in 70% dioxane-water mixture.

Table 2. Thermodynamic stability constant (pK^0 and $\log K^0$) values for Ce(III), Dy(III), Gd(III), Yb(III) and Pr(III) metal ions with rifampicin

	pK vs. $\sqrt{\mu}$	$\log K_1$ vs. $\sqrt{\mu}$	$\log K_1$ vs. $\sqrt{\mu}/1+\sqrt{\mu}$	$\log K_2$ vs. $[\sqrt{\mu}/1+\sqrt{\mu}]$ $-0.3\sqrt{\mu}$	$\log K_2$ vs. $\sqrt{\mu}$	$\log K_2$ vs. $\sqrt{\mu}/1+\sqrt{\mu}$	$\log K_2$ vs. $[\sqrt{\mu}/1+\sqrt{\mu}]$ $-0.3\sqrt{\mu}$
Rifampicin + Ce(III)							
pK^0	8.4893	--	--	--	--	--	--
$\log K_1^0$	--	8.1314	8.4623	8.7185	--	--	--
$\log K_2^0$	--	--	--	--	5.8975	6.1738	6.3883
Rifampicin + Dy(III)							
$\log K_1^0$	--	8.0467	8.2752	8.4488	--	--	--
$\log K_2^0$	--	--	--	--	5.8907	6.0795	6.2460
Rifampicin + Gd(III)							
$\log K_1^0$	--	9.1301	9.5563	9.8824	--	--	--
$\log K_2^0$	--	--	--	--	6.0683	6.3315	6.5349
Rifampicin + Yb(III)							
$\log K_1^0$	--	8.9488	9.5184	9.7952	--	--	--
$\log K_2^0$	--	--	--	--	6.7128	7.1528	7.4532
Rifampicin+Pr(III)							
$\log K_1^0$	--	9.0234	9.3378	9.5739	--	--	--
$\log K_2^0$	--	--	--	--	6.1292	6.3780	6.5657

The values of ΔZ^2 were calculated from the slope of plots pK vs. $\sqrt{\mu}$, $\log K_1$ vs. $\sqrt{\mu}$, $\log K_2$ vs. $\sqrt{\mu}$. The value of 'A' was taken¹⁴ equal to 0.5161. The value of ΔZ^2 shown in Table 3. The observed value of ΔZ^2 is different from the expected value. These values do not give conclusive evidence regarding the magnitude of the charge of reacting species. This discrepancy may be due to the limited applicability of Bronsted equation. The conditional stability constant of rifampicin-lanthanide metals complexes were determined for all systems by using the following equation.

Table 3. Values of ΔZ^2 determined from the plots of pK vs. $\sqrt{\mu}$

Reaction equilibria	System	ΔZ^2 Expected	Slope	ΔZ^2 Observed
$\text{HL} \rightarrow \text{H}^+ + \text{L}^-$	Ce(III)+ Rifampicin	2.00	-2.8401	-5.5030
$\text{L}^- + \text{M}^{+3} \rightarrow \text{ML}^{+2}$		-6.00	-8.0820	-15.659
$\text{ML}^{+2} + \text{L}^- \rightarrow \text{ML}_2^{+1}$		-4.00	-6.7186	-13.0180
$\text{L}^- + \text{M}^{+3} \rightarrow \text{ML}^{+2}$	Dy(III)+ Rifampicin	-6.00	-5.9100	-11.4513
$\text{ML}^{+2} + \text{L}^- \rightarrow \text{ML}_2^{+1}$		-4.00	-4.317	-9.1682
$\text{L}^- + \text{M}^{+3} \rightarrow \text{ML}^{+2}$		-6.00	-10.7810	-20.8894
$\text{ML}^{+2} + \text{L}^- \rightarrow \text{ML}_2^{+1}$	Gd(III)+ Rifampicin	-4.00	-6.4694	12.5352
$\text{L}^- + \text{M}^{+3} \rightarrow \text{ML}^{+2}$		-6.00	-7.9892	-15.4799
$\text{ML}^{+2} + \text{L}^- \rightarrow \text{ML}_2^{+1}$		-4.00	-8.5748	-16.6146
$\text{L}^- + \text{M}^{+3} \rightarrow \text{ML}^{+2}$	Pr (III)+ Rifampicin	-6.00	-8.3912	-16.2589
$\text{ML}^{+2} + \text{L}^- \rightarrow \text{ML}_2^{+1}$		-4.00	-6.5769	-12.7435

$$K = x / (a_1 - x) (b_1 - x) = x / (a_2 - x) (b_2 - x)$$

Where, K = conditional stability constant, x = concentration of complex, a_1 and b_1 were concentration of metal ion and ligand before dilution. a_2 and b_2 were concentration of metal ion and ligand after dilution. The values of 'x' were calculated from the graph plotted between optical density and % composition of metal ions in solution (Figure 4-7). From Table 4, it is seen that there is good agreement among thermodynamic constant obtained from pH metry and spectrophotometrically.

Figure 4. Plots of O.D. vs. % composition of metal ions -Yb(III) **Figure 5.** Plots of O.D. vs. % composition of metal ions -Pr(III) **Figure 6.** Plots of O.D. vs. % composition of metal ions -Gd(III) **Figure 7.** Plots of O.D. vs. % composition of metal ions -Dy(III)

Table 4. Metal-ligand stability constants (log K) values obtained by pH-metry and spectrophotometry techniques (Ionic strength = 0.08 M)

System	pH-metry	Spectrophotometry
Dy(III)+ Rifampicin	4.50	4.75
Gd(III)+ Rifampicin	4.20	4.34
Yb(III)+ Rifampicin	4.15	4.40
Pr(III)+ Rifampicin	4.10	4.58

Conclusion

The calculated values of stability constant at various ionic strength are high. From the results obtained in this experiment, the complexes of rifampicin with Ce(III), Dy(III), Gd(III), Yb(III) and Pr(III) metal ions were quite stable at over all range of ionic strength. The values of thermodynamic parameters are nearly same from all plots, were good agreement of results. The values of conditional metal-ligand stability constant shows good agreement with the values determined by pH-metrically.

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