Journal of Advanced Scientific Research

Available online through http://www.sciensage.info/jasr

ISSN
0976-9595
Research Article

Thermodynamic Studies of Rare Earth Metal Complexes with Metformin Hydrochloride Drug in Mixed Solvent System

S.V.Thakur[a], Mazahar Farooqui[b], S.D. Naikwade[c]
[a]Milliya Art's Science & Management Science College Beed, (M.S.)-India
[b]Dr Rafiq Zakaria College for women, Aurangabad, (M.S.)-India
[c]Mrs.K.S.K.College, Beed (M.S.)-India.
*Corresponding author: mazahar_64@rediffmail.com

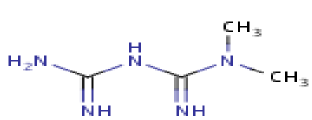
ABSTRACT

In the present work we investigate the stability constant of Metformin Hydrochloride drug with rare earth (Lanthanides) metal ions La(III),Ce(III),Nd(III),Sm(III),Gd(III),Tb(III) and Dy(III) using pH metric technique in 20%(v/v) ethanol-water mixture at 298K, 308K, 318K and at an ionic strength of 0.1M $NaClO_4$. The method of Calvin and Bjerrum as adopted by Irving and Rossotti has been employed to determine metal-ligand stability constant (logK) values. It is observed that rare earth (Lanthanide) metal ions forms 1:1 and 1:2 complexes.The thermodynamic parameter ΔG, ΔH and ΔS were calculated from values of stability constant at different temperatures. The formations of metal complexes were found to be spontaneous and exothermic in nature.

Keywords: pH-metry, Stability Constant, rare earth metal, Metformin Hydrochloride drug, thermodynamic parameter.

1. INTRODUCTION

Metal complexes of drugs are found to be more potent than parent drugs. Chemistry of drugs attracts many researchers because of its application in medicinal study. The stability of metal complexes with medicinal drugs play a major role in the biological & chemical activity Metal Complexes are widely used in various fields, such as biological processes pharmaceuticals, separation techniques, analytical processes etc. Most of the f-block elements form complexes. There are different kinds of ligand used for complexation. For the present investigation, we selected antidiabetic drug Metformin Hydrochloride. Metformin Hydrochloride [1, 1 dimethylbiguanide hydrochloride] is a hypoglycemic agent having molecular formula $C_4H_{12}ClN_5$ and IUPAC name 3-(diaminomethylene)-1,1- dimethylguanidine hydrochloride.



. HCl

Metformin Hydrochloride ($C_4H_{12}ClN_5$)

Metformin hydrochlorid is a biguanide antihyperglycemic agent used for treating non-insulin-dependent diabetes mellitus (NIDDM). It improves glycemic control by decreasing hepatic glucose production, decreasing glucose absorption and increasing insulin-mediated glucose uptake. Metformin hydrochloride is the only oral antihyperglycemic agent that is not associated with weight gain. Metformin hydrochloride may induce weight loss and is the drug of choice for obese NIDDM patients. When used alone, metformin hydrochloride does not cause hypoglycemia; however, it may potentiate the hypoglycemic effects of sulfonylureas and insulin. Its main side effects are dyspepsia, nausea and diarrhea. Dose titration and/or use of smaller divided doses may decrease side effects. Lower doses should be used in the elderly and those with decreased renal function. Metformin hydrochloride decreases fasting plasma glucose, postprandial blood glucose and glycosolated hemoglobin (HbA1c) levels, which are reflective of the last 8-10 weeks of glucose control. Metformin hydrochloride may also have a positive effect on lipid levels.

Literature survey reveals that very few researchers were investigated thermodynamic stability constant and thermodynamic parameters ΔG, ΔH and ΔS of complexes at different temperature range. The detail study of complex under identical set of experimental condition is still lacking. Therefore we decide to study the effect of temperature on thermodynamic parameters ΔG, ΔH and ΔS of complexes of Metformin Hydrochloride drug with rare earth metal ions(Lanthanides) La(III),Ce(III),Nd(III),Sm(III),Gd(III),Tb(III) and Dy(III) using pH metrically in 20% ethanol-water mixture at constant ionic strength of 0.1M $NaClO_4$.

2. MATERIAL AND METHODS

2.1. Material and Solution

The ligand Metformin Hydrochloride is soluble in double distilled water. NaOH, $NaClO_4$, $HClO_4$ & metal salts were of Analar grade. The solutions used in the potentiometric titration were prepared in double distilled water. The NaOH solution was standardized against oxalic acid solution (0.1M) and standard alkali solution was again used for standardization of $HClO_4$. The metal salt solutions were also standardized using EDTA titration. All the measurements were made at 298 K, 308K &318K in 20% ethanol-water mixture at constant ionic strength of 0.1M $NaClO_4$. The Thermostat model SL-131 (Adar Dutt and co (India) pvt. ltd. Mumbai) was used to maintain the temp constant. The pH measurement were made using a digital pH meter model Elico L1-120 in conjunction with a glass and reference calomel electrode (reading accuracy ±0.01 pH units) the instrument was calibrated at pH 4.00, 7.00 and 9.18 using the standard buffer solutions.

2.2. Potentiometric procedure

For evaluating the protonation constant of the ligand & the formation constant of the complexes in 20 % (v/v) ethanol-water mixture with different metal ions we prepare the following sets of solutions.

(A) $HClO_4$ (A)
(B) $HClO_4$+ Metformin Hydrochloride (A+ L)
(C) $HClO_4$+ Metformin Hydrochloride + Metal (A+ L+ M)

The above mentioned sets prepared by keeping M:L ratio, the concentration of perchloric acid & sodium perchlorate (0.1M) were kept constant for all sets. The volume of every mixture was made upto 50ml with double distilled water and the reaction solution were potentiometerically titrated against the standard alkali at temp 298K, 308K &318K.

2.3. Determination of the Thermodynamic parameters

The thermodynamic parameters such as Gibb's free energy, entropy change and enthalpy change for formation of complexes were determined. The change in free energy of the ligands is calculated by using following equation.

$$\Delta G = -2.303\ RT \log K \qquad (1)$$

R- Universal gas constant, T- temperature in K, logK – Stability constant.
The changes in enthalpy (ΔH) are calculated by plotting 1/ T vs logK. The equation utilized for the calculation of changes in enthalpy is as under

$$\text{Slope} = -\Delta H / 2.303\ R \qquad (2)$$

The evaluation of changes in entropy (ΔS) is done by the following equation.

$$\Delta S = (\Delta H - \Delta G) / T \qquad (3)$$

Table-1 Proton-ligand& metal-ligand stability constant of Metformin Hydrochloride drug at 0.1M ionic strength in 20% ethanol-water medium

Temp	pK	logK	La(III)	Ce(III)	Nd(III)	Sm(III)	Gd(III)	Tb(III)	Dy(III)
298K	pK_1=2.9052	$\log K_1$	6.861	7.629	7.718	7.813	7.687	7.903	8.044
	pK_2=11.100	$\log K_2$	5.304	6.176	6.207	6.400	6.092	6.725	6.876
308K	pK_1=2.6184	$\log K_1$	6.720	7.487	7.556	7.634	7.545	7.761	7.822
	pK_2=10.958	$\log K_2$	5.146	6.035	6.068	6.247	5.959	6.582	6.735
318K	pK_1=2.3459	$\log K_1$	6.597	7.375	7.454	7.495	7.412	7.633	7.700
	pK_2=10.856	$\log K_2$	5.020	5.920	5.970	6.121	5.814	6.480	6.618

3. RESULTS AND DISCUSSION

Proton ligand stability constants (pK) of Metformin Hydrochloride drug is determined by point wise calculation method as suggested by Irving & Rossoti. Metal ligand stability constant (log k) of rare earth (Lanthanide) metal ions with Metformin Hydrochloride drug (ligand) were calculated by point wise and half integral method of Calvin and Bjerrum as adopted by Irving and Rossotti has been employed. For the present investigation we have studied the stability constants of trivalent rare earth metal ions. Since we got $\bar{n}_A$ between 0.2 to 0.8 and 1.2 to 1.8 indicating 1:1 and 1:2 Complex formations. The proton-ligand stability constants values decreases with increase in temperature for all systems. This suggested that liberation of protons becomes easier at higher temperature. The values of metal-ligand stability constant decreases with increase in temperature. This suggests that the complex formation is exothermic and favorable at lower temperature. The negative values of ΔH and ΔG of complex formation indicates the complex formation process is spontaneous. All

the metal complexes are accompanied by negative enthalpy (ΔH) changes suggesting that the metal-ligand bonds are fairly strong. Positive entropy changes accompanying a given reaction are due to the release of bound water molecules from the metal chelates .During formation of metal chelates, water molecules from the primary hydrationc sphere of the metal ion are displaced by the chelating ligand. Thus there is an increase in the number of particles in the system i.e. randomness of the system increases. The order of stability constants for these metal complexes was as follows:
$\mathbf{La^{3+}<Ce^{3+}<Nd^{3+}<Sm^{3+}>Gd^{3+}<Tb^{3+}<Dy^{3+}}$ and shows a break at gadolinium

Table-2 Thermodynamic parameters of Metformin Hydrochloride complexes formation with rare earth metal ions at 0.1M ionic strength in 20% ethanol-water medium.

Metals	$-\Delta G$(KJ/mol)			$-\Delta H$(KJ/mol)	$+\Delta S$(J/mol)		
	298K	308K	318K		298K	308K	318K
La(III)	ΔG_1 =39.147	39.624	40.161	ΔH_1= 24.055	ΔS_1 = 50.64	50.54	50.64
	ΔG_2 =30.263	30.341	30.565	ΔH_2= 25.794	ΔS_2 = 14.99	14.76	15.00
Ce(III)	ΔG_1= 43.524	44.153	44.904	ΔH_1= 23.016	ΔS_1 = 68.81	68.62	68.83
	ΔG_2= 35.239	35.584	36.039	ΔH_2= 23.248	ΔS_2 = 40.23	40.05	40.22
Nd(III)	ΔG_1 =44.031	44.554	45.385	ΔH_1= 24.004	ΔS_1 = 67.20	66.72	67.23
	ΔG_2=35.416	35.784	36.343	ΔH_2= 21.575	ΔS_2 = 46.44	46.13	46.44
Sm(III)	ΔG_1 =44.579	45.020	45.629	ΔH_1= 28.913	ΔS_1 = 52.57	52.29	52.56
	ΔG_2 =36.517	36.834	37.269	ΔH_2= 25.335	ΔS_2 = 37.52	37.33	37.52
Gd(III)	ΔG_1 =43.860	44.495	45.124	ΔH_1= 24.953	ΔS_1 = 63.44	63.44	63.43
	ΔG_2 =34.759	35.142	35.394	ΔH_2= 25.205	ΔS_2 = 32.06	32.26	32.04
Tb(III)	ΔG_1 =45.093	45.769	46.469	ΔH_1= 24.506	ΔS_1 = 69.08	69.03	69.06
	ΔG_2 =38.366	38.817	39.455	ΔH_2= 22.265	ΔS_2 = 54.03	53.74	54.05
Dy(III)	ΔG_1 =45.897	46.128	46.883	ΔH_1= 31.305	ΔS_1 = 48.96	48.12	48.98
	ΔG_2 =39.233	39.712	40.234	ΔH_2= 23.427	ΔS_2 = 53.04	52.87	52.85

4. REFERENCES

1. Sayyed Hussain, Rashid Munjewar, Mazahar Farooqui. *Current Pharma Research*, 2010; **4(1):**44-48.
2. Farooque Basheer Ansari, Mazahar Farooqui, S H Quadri. Orient J Chem, 2010; **26(2):**667-670.