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Study of Pb^{2+}- Famotidine Complexes by Polarography

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ABSTRACT

The interaction between Famotidine and Pb^{2+} was investigated using direct current polarography. The polarographic technique was used to determine the stability constants and thermodynamic parameters such as enthalpy change ($\Delta H^{\#}$), free energy change ($\Delta G^{\#}$) and entropy change ($\Delta S^{\#}$) of Pb^{2+} complexes with Famotidine. The study was carried out at two different temperatures 20 °C and 30 °C. Pb^{2+}-Famotidine complexes were formed in 1:1 and 1:2 ratios. The electrode processes were reversible and diffusion controlled.

1. Introduction

Famotidine (Fig. 1) is pale yellowish-white, crystalline powder. It is sensitive to light, freely soluble in dimethylformamide and in glacial acetic acid, slightly soluble in methanol, very slightly soluble in water, practically insoluble in acetone, in alcohol, in chloroform, in ether and in ethyl acetate.

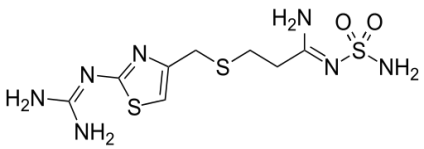

Fig. 1 3-([2-(diaminomethyleneamino)thiazol- 4-yl]methylthio)- N'-sulfamoylpropanimidamide

Famotidine, a competitive histamine H_2-receptor antagonist, is used to treat gastrointestinal disorders such as gastric or duodenal ulcer, gastroesophageal reflux disease, and pathological hypersecretory conditions. Famotidine inhibits many of the isoenzymes of the hepatic CYP450 enzyme system. Other actions of famotidine include an increase in gastric bacterial flora such as nitrate-reducing organisms. Famotidine is given to surgery patients before operations to prevent postoperative nausea and to reduce the risk of aspiration pneumonitis. Famotidine is also given to some patients who take NSAIDs, to prevent peptic ulcers. It serves as an alternative to proton-pump inhibitors. Famotidine has also been used in combination with an H1 antagonist to treat and prevent urticaria caused by an acute allergic reaction. It has been found to decrease the debilitating effects of chronic heart failure by blocking histamine [1-4].

Famotidine has been studied and determined by several procedures /techniques including spectrophotometric/spectrophotometry [5-8], Spectrofluorimetry [9], colorimetry [10], potentiometry [11-12], HPLC [13-15]. Many electrochemical procedures have been reported for the determination of famotidine. Famotidine has been determined in different samples by different techniques as Square wave adsorptive stripping voltammetric [15-17], Square wave voltammetry [18], DPP [19] and others [20,21]. Study of famotidine complexes have been done with some metals [22,23].

Here attempts have been made to study the electroreduction of various complexes of famotidine in various experimental conditions using direct current polarography.

Lead is a poisonous metal that can damage nervous connections (especially in young children) and cause blood and brain disorders. Lead exposure also causes small increases in blood pressure.

In the human body, lead inhibits porphobilinogen synthase and ferrochelatase, preventing both porphobilinogen formation and the incorporation of iron into protoporphyrin IX, the final step in heme synthesis. This causes ineffective heme synthesis and subsequent microcytic anemia [24]. At lower levels, it acts as a calcium analog, interfering with ion channels during nerve conduction.

Due to effect of lead on health, it becomes necessary to study the lead – famotidine complex. Present work incorporate this study by polarography.

Present research represents the study of complex formation of Lead (II) with famotidine. Pb (II) forms complexes with Famotidine in 1:1 and 1:2 ratios. Stability constants of complexes have been determined at 20 °C and 30 °C by Deford and Hume's method. Thermodynamic parameters ($\Delta G°$, $\Delta H°$, $\Delta S°$) have also been reported.

2. Experimental Methods

2.1 Apparatus

The digital D.C. polarograph (CL-357) of Elico Limited was used to record current-voltage data. This equipment has the three electrode assembly, dropping mercury electrode as working electrode, calomel as reference electrode and platinum electrode as counter electrode. The current responses and applied potential were recorded at scan rate 150 mV/min. Dropping mercury electrode had the characteristics m = 2.422 mg/sec, t = 2.5 sec and h = 60 cm.

The Elico digital pH meter model 111E was used to measure the pH of the analytes.

2.2 Proposed Procedure

The general procedure used to produce DC polarograms was as follows: An aliquot (10 mL) of experimental solution which contains drug (famotidine), metal solution, supporting electrolyte/ buffer, Triton-X-100 (maxima suppresser) and water was placed in a dry, clean polarographic cell and deoxygenated with nitrogen for 15 min. the current-voltage values were measured manually.

The negative potential was applied to the working electrode with 150 mV/min span rate and 100 nA/div sensitivity of current measurement. After the background polarogram had been obtained, aliquots of the required amounts of Famotidine solution were added.

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2.3 Reagents

Famotidine was obtained from Panchseel Organics Ltd., Mumbai, Maharashtra, India. Famotidine was dissolved in water. All solutions were prepared freshly with triple distilled water and analytical reagent grade chemicals (MERCK).

Analytical grade salts of lead nitrate ($PbNO_3$) of strength 2.5×10^{-2} M were used for present study. Aqueous buffers of different pH were prepared. pH was adjusted by 0.1 M HCl and 0.1 M NaOH. 1.0 M KNO_3 was used as supporting electrolyte for $NiNO_3$, $ZnSO_4$, $PbNO_3$ and 1.0 M acetate buffer (pH = 4.37) for $Cd(CH_3COO^-)_2$. All solutions were prepared in triple distilled water. Triton X-100 (0.001%) was used to suppress polarographic maxima. The depolariser (metal) and ligand (drug) were taken in different ratio.

3. Results and Discussion

The system lead (II)- famotidine was investigated polarographically at 20 °C and 30 °C. Half wave potential of Pb(II) (–0.390 V vs. SCE) in 1.0 M KNO3 supporting electrolyte, has been determined. Half wave potential of Pb (II) shifts towards negative direction with successive addition of famotidine and the diffusion current (id) of the metal ion Pb(II) decreases with increasing concentration of complexing agent suggesting complex formation. Pb (II) undergoes $2e^-$ reduction process at d.m.e. The reduction is found to be reversible and diffusion controlled. The plots of log $[i/(i_d-i)]$ vs $E_{d.e}$. were linear with lower slope values suggesting electrode reactions to be reversible.

Overall formation constant (log β) of the complexes have been determined by Deford and Hume's method using polarographic measurements.

The plots of Fj (x) vs. X (where X is the concentration of famotidine) are represented in Fig. 2 and Fig. 3. By seeing them we can say that at 20 °C and 30 °C. The Pb (II) - famotidine complexes formed are in 1:1 and 1:2 ratio. Value of intercept gives the value of β, whereas the value of logβ represents the stability constant. The values of Fj (x) with respect to famotidine concentration are summarised in Table 1 and Table 2. From the plots of Fj (x) vs. X values of stability constants logβ1 and $\log\beta_2$ have been evaluated. More will be the value of stability constant more will be stability of complex. From the values of stability constants, thermodynamic parameters have also been evaluated.

Table 1 Pb(II)- famotidine system at 20 °C. ($PbNO_3 = 2.5 \times 10^{-2}$ M Temp = 20°±1°C, $E_{1/2}$ (M) = -0.390 volts vs S.C.E, Im = 20.6.)

$C_x \times 10^{-3}$	$\Delta E_{1/2}$ (V)	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^3$	$F_2(x) \times 10^5$
1.32	0.020	0.0885	4.9658	2.9863	20.3713
2.65	0.024	0.1179	6.8139	2.1889	7.1836
3.98	0.032	0.1406	12.7613	2.9521	6.7046
5.31	0.038	0.1646	20.4664	3.6646	6.3697
6.64	0.043	0.1835	30.3537	4.4207	6.2345
7.96	0.048	0.2066	45.0421	5.5273	6.5843
9.29	0.052	0.2239	61.7781	6.5380	6.7309
10.62	0.055	0.2383	78.3082	7.2767	6.5848
11.95	0.058	0.2531	99.2702	8.2220	6.6441

$\beta_1 = 2.81 \times 10^2$; $\beta_2 = 6.5505 \times 10^5$
$E_{1/2}$ (M) = Half wave potential of lead
Im = Diffusion current of polarographic wave for Lead
β_1 & β_2 = Overall formation constant or Overall stability constant for 1:1 and 1:2 Pb(II)- famotidine complexes at 20 °C.

Table 2 Pb(II)- famotidine system at 30 °C. ($PbNO_3 = 2.5 \times 10^{-2}$, Temp = 30°±1°C, $E_{1/2}$ (M) = -0.390 volts vs S.C.E, Im = 26.0)

$C_x \times 10^{-3}$	$\Delta E_{1/2}$ (V)	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^3$	$F_2(x) \times 10^5$
1.32	0.017	0.0476	3.7258	2.0526	12.5800
2.65	0.022	0.0765	5.4717	1.6836	4.9007
3.98	0.029	0.0990	9.3230	2.0891	4.2849
5.31	0.035	0.1205	14.7275	2.5842	4.1458
6.64	0.040	0.1362	21.5615	3.0966	4.0882
7.96	0.045	0.1549	31.5812	3.8380	4.3373
9.29	0.049	0.1819	42.8779	4.5049	4.4351
10.62	0.052	0.2027	53.9314	4.9822	4.3300
11.95	0.055	0.2218	67.8341	5.5918	4.3590

$\beta_1 = 3.82 \times 10^2$; $\beta_2 = 4.2829 \times 10^5$
β_1 & β_2 = Overall formation constant or Overall stability constant for 1:1 and 1:2 Pb(II)- famotidine complexes at 30 °C.

Table 3 Stability constant for Pb (II)- famotidine

System	Composition of complex	Stability constants	
		20 °C	30 °C
$[Pb(Famotidine)]^{2+}$	1:1	2.4487	2.5820
$[Pb(Famotidine)_2]^{2+}$	1:2	5.8162	5.6317

Table 4 Thermodynamic parameters for Pb (II)- famotidine at 20 °C

System	Composition of complex	Thermodynamic parameters		
		ΔG° Kcal/mole	ΔH° Kcal/mole	ΔS° Cal/degree/ mole
$[Pb(Famotidine)]^{2+}$	1:1	-3.2708	5.3973	0.0295
$[Pb(Famotidine)_2]^{2+}$	1:2	-7.7690	-7.4684	0.0010

ΔG° = Standard Gibb's free energy change.
ΔH° = Standard enthalpy change.
ΔS° = Standard entropy change.

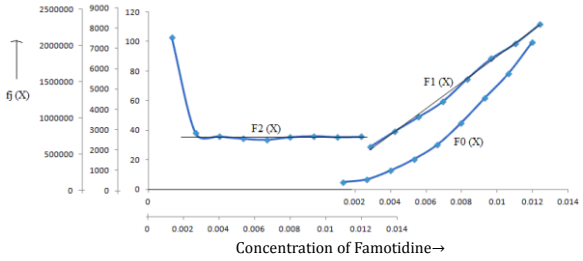

Fig. 2 Pb(II)- famotidine system at 20 °C

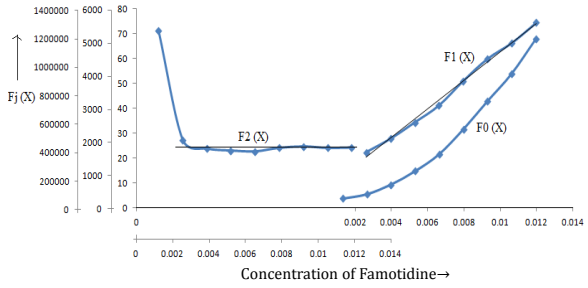

Fig. 2 Pb(II)- famotidine system at 30 °C

4. Conclusion

Pb (II) forms complexes with famotidine in 1:1 and 1:2 ratio. The stability constants of $[Pb(famotidine)_2]^{2+}$ are greater than $[Pb(famotidine)]^{2+}$ at both the temperatures, it suggests that Pb (II)-famotidine complexes are more stable in 1:2 ratio than in 1:1. Moreover complex $[Pb(Famotidine)_2]^{2+}$ is slightly more stable at 20 °C than 30 °C as stability at 20 °C is slightly greater than 30 °C. while $[Pb(famotidine)]^{2+}$ is more stable at 30 °C than 20 °C. From chemical thermodynamics that the complex which have less value of Gibb's free energy change is more stable, for $[Pb(famotidine)_2]^{2+}$ Gibb's free energy change is more negative, which suggest that $[Pb(famotidine)_2]^{2+}$ complex is more stable than $[Pb(famotidine)]^{2+}$. The enthalpy change in 1:1 complex is more (positive value) than for 1:2 complex (negative value), which suggests that the formation of $[Pb(famotidine)]^{2+}$ complex is accompanied with absorption of energy in comparison to $[Pb(famotidine)_2]^{2+}$. Positive value of entropy in ratio 1:1 & 1:2 reveals the formation of comparatively disordered complex.

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