Research Article

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

Ashish Garg, Yogesh Kumar and Rajayashree Pandey*

Department of Chemistry, University of Rajasthan, Jaipur, India.

ABSTRACT

The interaction between Famotidine and Cd^{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 Cd^{2+} complexes with Famotidine. The study was carried out at two different temperatures 20 °C and 30 °C. Cd^{2+}-Famotidine complexes were formed in 1:1 and 1:2 ratios. The electrode processes were reversible and diffusion controlled.

Keywords: stability constant, thermodynamic parameters, Cd^{2+}– Famotidine system.

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.

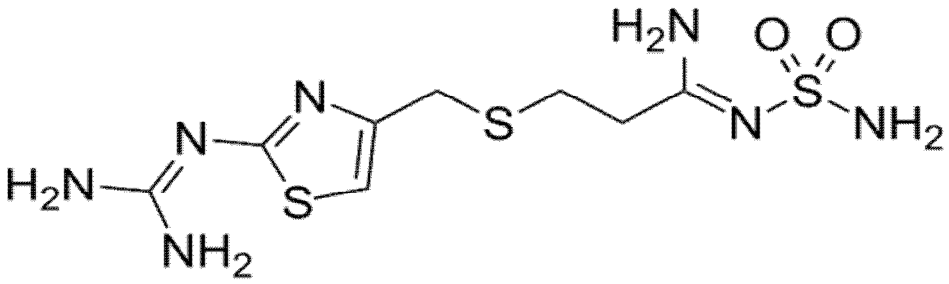

Fig. 1: 3-([2-(diaminomethyleneamino)thiazol- 4-yl]methylthio)-N'-sulfamoylpropanimidamide

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[16-18], Square Wave Voltammetry[19], DPP[20] and others[21-22]. Study of Famotidine complexes have been done with some metals[23-24].

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

2. MATERIALS AND 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.

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 Cadmium Acetate 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 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 DISCUSSIONS

The system Cadmium(II)- Famotidine was investigated polarographically at 20^o C and 30^o C. Half wave potential of Cd(II) (–0.590 V vs. SCE) in Acetate Buffer, has been determined. Half wave potential of Cd(II) shifts towards more negative side with successive addition of Famotidine and diffusion current of metal (id) decreases, which suggests complex formation. Cd(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[25-26] using polarographic measurements.

The plots of *Fj (x)* vs. X (where X is the concentration of Famotidine) are represented in Fig. 2 & 3. By seeing them we can say that at 20^o C and 30^o C the complexes of Cd (II)-Famotidine formed in 1:1 and 1:2 ratio. Value of intercept gives the value of β, where as the value of logβ represents the stability constant. The values of *Fj (x)* with respect to Famotidine concentration are summarised in table 1 to 3. 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: Cd(II)- Famotidine system at 20°C Acetate Buffer (pH = 4.37), Temp = 20°±1°C, $E_{1/2}$ (M) = -0.590 volts vs S.C.E, Im = 11.1.

$C_x \times 10^{-3}$	$\Delta E_{1/2}$ (V)	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^3$	$F_2(x) \times 10^6$
1.32	0.032	0.0367	12.6573	8.7781	6.1153
2.65	0.038	0.0721	20.3739	7.2944	2.4990
3.98	0.046	0.1058	38.3710	9.3802	2.1895
5.31	0.052	0.1368	61.6910	11.4252	2.0271
6.64	0.058	0.1760	99.1932	14.7881	2.1281
7.96	0.062	0.2128	136.1522	16.9618	2.0462
9.29	0.066	0.2529	186.8826	19.9959	2.0803
10.62	0.070	0.2894	256.5111	24.0503	2.2019
11.95	0.073	0.3293	325.2985	27.1334	2.2152

β_1 = 6.57 × 102, **β_2 =** 2.126× 106, **$E1_{/2}$ (M) = Half wave potential of Cd**
Im = Diffusion current of polarographic wave for cadmium
β_1 & β_2 = Overall formation constant or Overall stability constant for 1:1 & 1:2 Cd(II)- Famotidine complexes at **20°C.**

Table 2: Cd(II)- Famotidine system at 30°C Acetate Buffer (pH = 4.37), Temp = 30°±1°C, $E_{1/2}$ (M) = -0.590 volts vs S.C.E, Im = 17.5

$C_x \times 10^{-3}$	$\Delta E_{1/2}$ (V)	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^3$	$F_2(x) \times 10^6$
1.32	0.030	0.0499	10.8211	7.3954	4.4355
2.65	0.034	0.0877	14.8753	5.2241	1.4002
3.98	0.041	0.1224	25.8714	6.2428	1.1892
5.31	0.048	0.1496	44.9851	8.2803	1.2754
6.64	0.053	0.1748	66.8043	9.9102	1.2658
7.96	0.057	0.2096	91.6844	11.3810	1.2394
9.29	0.061	0.2387	125.8234	13.4276	1.2825
10.62	0.064	0.2653	159.5460	14.9233	1.2630
11.95	0.067	0.2839	202.3017	16.8425	1.2832

$\beta_1 = 1.505 \times 10^3$, $\beta_2 = 1.256 \times 10^6$
Here β_1 & β_2 = Overall formation constant or Overall stability constant for 1:1 & 1:2 Cd(II)- Famotidine complexes at **30°C.**

Table 3: Stability constant for Cd (II)- Famotidine

System	Composition of complex	Stability constants	
		20°C	30°C
$[Cd(Famotidine)]^{2+}$	1:1	2.8175	3.1775
$[Cd(Famotidine)_2]^{2+}$	1:2	6.3277	6.0993

Gibb's free energy change, Enthalpy change and Entropy change are listed in Table 4 for 1:1 and 1:2 Cd(II)- Famotidine complexes.

Table 4: Thermodynamic parameters for Cd (II)- Famotidine at 20°C

System	Composition of complex	Thermodynamic parameters		
		ΔG° Kcal/mole	ΔH° Kcal/mole	ΔS° Cal/degree/mole
$[Cd(Famotidine)]^{2+}$	1:1	-3.7635	14.5691	0.0625
$[Cd(Famotidine)_2]^{2+}$	1:2	-8.4522	-9.2452	-0.0027

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

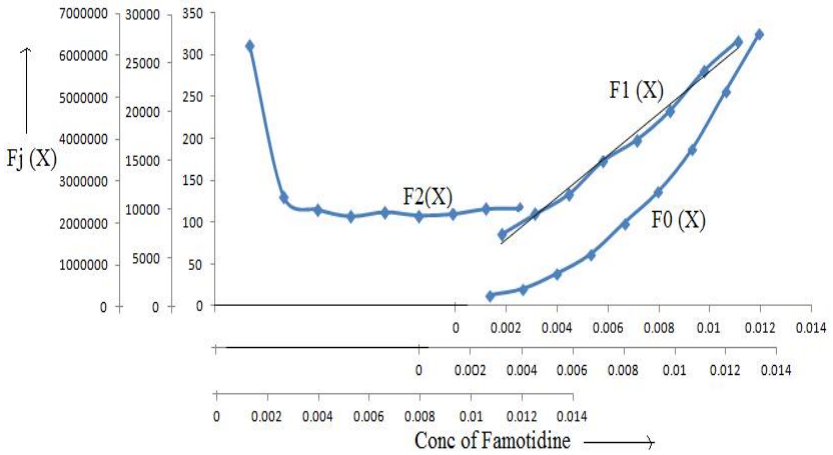

Fig. 2: [Cd(II)- Famotidine system at 20°C]

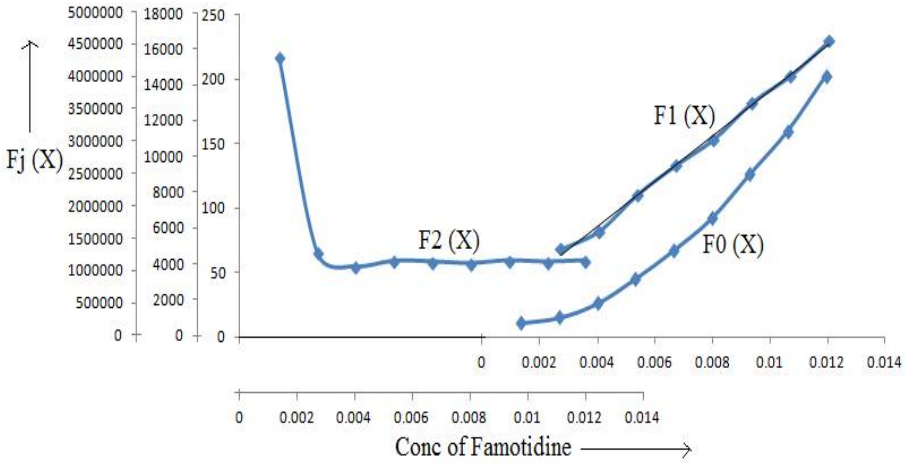

Fig. 3: [Cd(II)- Famotidine system at 30°C]

4. CONCLUSION

Cd (II) forms complexes with Famotidine in 1:1 and 1:2 ratio. The stability constants of $[Cd(Famotidine)_2]^{2+}$ are greater than $[Cd(Famotidine)]^{2+}$ at both temperatures, it suggest that Cd(II)- Famotidine complexes are more stable in 1:2 ratio than in 1:1. Moreover complex $[Cd(Famotidine)_2]^{2+}$ is slightly more stable at 20^o C than 30^o C as stability at 20^o C is slightly greater than 30^o C. while [Cd (Famotidine)]$^{2+}$ is more stable at 30^o C than 20^o C.

As we know from chemical thermodynamics that the complex which have less value of Gibb's free energy change is more stable, here for $[Cd(Famotidine)_2]^{2+}$ Gibb's free energy change is more negative, which suggest that $[Cd(Famotidine)_2]^{2+}$ complex is more stable than $[Cd(Famotidine)]^{2+}$. The Enthalpy change in 1:1 complex is more (positive value) than for 1:2 complex (negative value), which suggest that the formation of $[Cd(Famotidine)]^{2+}$ complex is accompanied with absorption of energy in comparison to $[Cd(Famotidine)_2]^{2+}$. Positive value of entropy for 1:1complex reveals the formation of comparatively disordered complex.

5. ACKNOWLEDGMENT

The authors are thankful to Head, Dept. of Chemistry, University of Rajasthan, Jaipur, Rajasthan (India) for providing lab facilities.

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