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Polarographic study of Cd(ii)-Ranitidine complex

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Abstract
The Polarographic behaviour of Cd (II) Ranitidine hydrochloride complex have been studied. Cd (II) forms complexes with Ranitidine hydrochloride 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 (ΔG°, ΔH°, ΔS°) have also been reported.

Keywords: Ranitidine hydrochloride, direct current polarography, stability constant, thermodynamic parameter

Introduction

Ranitidine is a histamine-2 blocker, which decreases the amount of acid created by the stomach. Prescription ranitidine is approved for multiple indications, including treatment and prevention of ulcers of the stomach and intestines and treatment of gastroesophageal reflux disease.
Chemically it is - N[2-[[[5-[(dimethylamino)methyl]-2-furanyl] methyl] thio] ethyl]-N-methyl-2-nitro-1,1-ethenediamine, It has the following structure

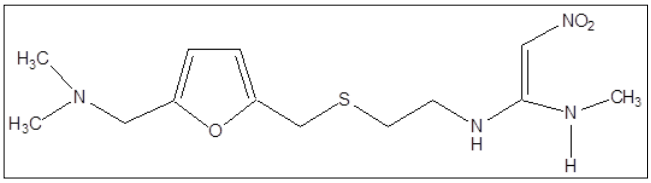

Fig 1: Ranitidine hydrochloride (HCl)

Molecular formula - $C_{13}H_{23}ClN_4O_3S$
Molar mass - 350.86472
Melting point - 69-70 °C
CAS number - 66357-59-3
Half life - 2.8-3.1 hours

Ranitidine HCl is a white to pale yellow crystalline powder with slightly bitter taste and sulfur like odor. Freely soluble in water, methanol and ethanol, sparingly soluble in ethanol, very slightly soluble in chloroform and dichloro methane. Used in the treatment of peptic ulcer disease (PUD), dyspepsia, stress ulcer prophylaxis, and gastroesophageal reflux disease (GERD). Complexation of therapeutic compounds with metals may influence their nature, properties and pharmacokinetics. So metal drug complexes are being widely studied by different techniques [1-5].
Cadmium is a very unique metal. Cadmium is first transported to the liver through the blood. There, it is bond to proteins to form complexes that are transported to the kidneys. Cadmium accumulates in kidneys, where it damages filtering mechanisms. This causes the excretion of essential proteins and sugars from the body and further kidney damage. It takes a very long time before cadmium that has accumulated in kidneys is excreted from a human body.
It is essential to study complexation of Cadmium with drugs.

Earlier, the studies of Cadmium complexes with different drugs like sulfamethoxazole [6], Anti-inflammatory Drugs Piroxicam, Tenoxicam [7] and diclofenac sodium [8] etc have been done
Present study includes the complexation behavior of Ranitidine hydrochloride with metal present in human body in least amount such as Cd by direct current polarography.

Experimental

Apparatus

A digital DC recording Polarography (CL-357) was used to record the current – voltage curves. Measurements were performed with three electrode assemblies, dropping mercury (DME) as working electrode, platinum electrode as counter electrode and a saturated calomel electrode as reference electrode. Capillary of 120 mm length and 0.05mm diameter was used. The dropping mercury electrode had the following characteristics m = 2.422 mg/sec., t = 3.5 sec./drop, h = 60 cm. Elico digital pH meter was employed to measure pH of solution. The current responses and applied potentials were recorded at scan rate100 mv/min.

Materials and Reagents

Analytical grade salts of Cadmium Chloride [$CdCl_2$] of strength 1.25×10^{-2} M were used for present study. Aqueous buffers of different pH values were prepared. pH was adjusted by 0.1 M HCl and 0.1 M NaOH. 1.0 M KCl was used as supporting electrolyte for $CdCl_2$. 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.

Procedure

Electrochemical measurement were performed in the solution (10ml) containing Ranitidine hydrochloride, Cd(II), Triton X-100(maximum suppress maxima), 1.0 M KCl. The solution (10ml) were purged with nitrogen for at least 15 minutes. Prior to each experiment. The polarograms were recorded in following order-pure supporting electrolyte, after Cd (II) addition and addtion of each aliquot of Ranitidine hydrochloride.

Results and Discussions

A well–defined two-electron reversible reduction and diffusion controlled wave observed in 1.0 M KCl. The value of $E^{1/2}$ reversible for Cd^{2+} was – 0.645 V vs. SCE. Single and well defined polarograms were obtained for complexes of Cd(II) with Ranitidine hydrochloride in the concentration range 1.6×10^{-3} to 5.4×10^{-3} at 20° C and 30° C. With successive addition of Ranitidine hydrochloride Half wave potential of Cd(II) shifts towards more negative side and diffusion current of metal (i_d) decreases, which suggests complex formation (table-1,2). 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 logβ 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 Ranitidine hydrochloride) are represented in Fig. (2,3). By seeing them we can say that at 20° C and 30°C the complexes of Cd (II)- Ranitidine hydrochloride 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 Ranitidine concentration are summarized in table (1,2). From the plots of Fj (x) vs. X values of stability constants $\log\beta_1$ 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) - Ranitidine hydrochloride system at 20°C $CdCl_2 = 1.25 \times 10^{-2}$ M, Temp = 30°±1°C, $E_{1/2}$ (M) = -0.651 Volts vs S.C.E

$C_x \times 10^{-3}$	Id (µA)	$\Delta E_{1/2}$ (Volt)	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^2$	$F_2(x) \times 10^4$
1.6	4.8	0.653	0.0184	1.1206	0.7542	4.2138
2.2	4.6	0.654	0.0193	1.2528	1.1494	4.8613
2.8	4.4	0.656	0.0292	1.4507	1.6096	5.4631
3.5	4.3	0.658	0.0499	1.7362	2.1035	5.7814
4.1	4.1	0.661	0.0829	2.0880	2.6536	6.2772
4.8	3.8	0.663	0.0945	2.4333	3.1262	6.0546
5.4	3.7	0.665	0.1064	2.8267	3.3828	6.1163

$\beta_1 = 2.3201\text{x}10^6$ $\beta_2 = 4.7433\text{x}10^6$

$E_{1/2}$ (M) = Half wave potential of Cadmium

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)- Ranitidine hydrochloride complexes at 20°C.

Table 2: Cd(II)- Ranitidine hydrochloride system at 30°C $CdCl_2 = 2.5 \times 10^{-2}$ M, Temp = 20°±1°C, $E_{1/2}$ (M) = -0.646 volts vs S.C.E

$C_x \times 10^{-3}$	Id (µA)	$\Delta E_{1/2}$ (Volt)	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^2$	$F_2(x) \times 10^4$
1.6	4.9	0.648	0.0173	1.1740	1.0879	3.0495
2.2	4.7	0.649	0.0354	1.2938	1.3357	3.3445
2.8	4.6	0.650	0.0448	1.4456	1.5917	3.5420
3.5	4.5	0.652	0.0543	1.6623	1.8925	3.6929
4.1	4.3	0.653	0.0741	1.8641	2.1077	3.6775
4.8	4.2	0.655	0.0843	2.1549	2.4060	3.7626
5.4	4.1	0.657	0.0947	2.4715	2.7251	3.9353

$\beta_1 = 2.2718\text{x}10^6$ $\beta_2 = 4.5529\text{x}10^6$

$E_{1/2}$ (M) = Half wave potential of Cadmium

Im = Diffusion current of polarographic wave for Cadium

β_1 & β_2 = Overall formation constant or Overall stability constant for 1:1 & 1:2 Cd(II) - Ranitidine hydrochloride complexes at 30°C.

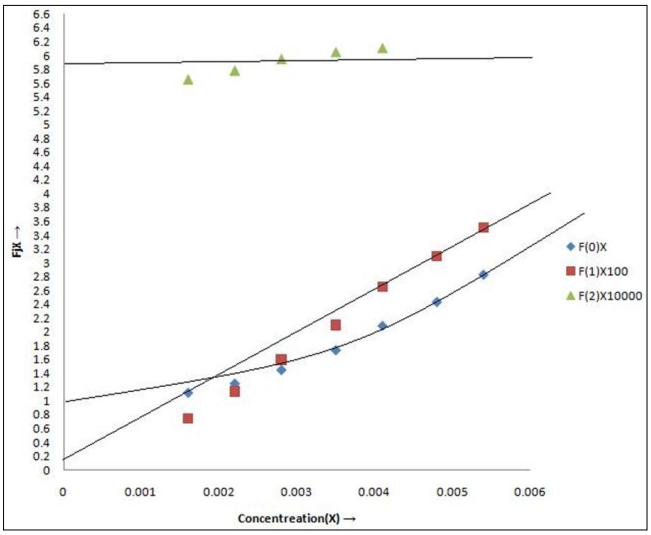

Fig. -2 - $F_j(X)$ vs. (X) for Cd^{+2}- Ranitidine hydrochloride system at T=20°C

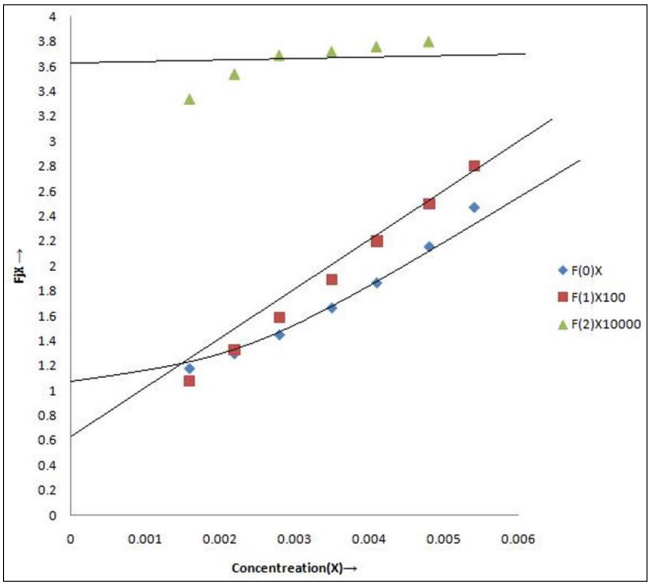

Fig 3: $F_j(X)$ vs. (X) for Cd^{+2}- Ranitidine hydrochloride system at T=30°C

Table 3: Stability constant for Cd(II)- Ranitidine hydrochloride

System	Composition of complex	Stability constants	
		20°C	30°C
$[Cd(Ranitidine)]^{2+}$	1:1	2.320146	2.271842
$[Cd(Ranitidine)_2]^{2+}$	1:2	4.743376	4.552924

Table 4: Thermodynamic parameters for Cd(II)- Ranitidine hydrochloride at 20°C&30°C

System	Composition of complex	Thermodynamic parameters		
		ΔG° Kcal/mole	ΔH° Kcal/mole	ΔS° Cal/degree/mole
$[Cd(Ranitidine)]^{2+}$	1:1	-13.1801	-8.2111	1.6394
$[Cd(Ranitidine)_2]^{2+}$	1:2	-26.4145	-32.3743	1.9672

$\Delta G°$ = Standard Gibb's free energy change.
$\Delta H°$ = Standard enthalpy change.
$\Delta S°$ = Standard entropy change

Stability Constants

Cd(II) forms complexes with Ranitidine hydrochloride in 1:1 and 1:2 ratio. The stability constants [9] of $[Cd(Ranitidine)_2]^{2+}$ are greater than $[Cd(Ranitidine)]^{2+}$ at both temperature, it suggest that Cd(II)- Ranitidine hydrochloride complexes are more stable in 1:2 ratio than in 1:1.

Moreover complex $[Cd(Ranitidine)_2]^{2+}$ is slightly more stable at 30ºC than 20ºC as stability at 30ºC is slightly greater than 20ºC. Stability constants are reported in table (3).

Thermodynamic Parameters

The Thermodynamic parameters [10] such as free energy change (ΔG), enthalpy change (ΔH) and entropy change (ΔS) have been calculated using the following equations and listed in table (4).

1. $\Delta G = -2.303RT \log \beta$
2. $\Delta H = -\dfrac{2.303RT_1T_2\left[\log \frac{\beta_{T_1}}{\beta_{T_2}}\right]}{T_2 - T_1}$
3. $\Delta G = \Delta H - T\Delta S$

As we know from chemical thermodynamics that the complex which have less value of Gibb's free energy change is more stable, here for $[Cd(Ranitidine)_2]^{2+}$ Gibb's free energy change is more negative, which suggest that $[Cd(Ranitidine)_2]^{2+}$ complex is more stable than $[Cd(Ranitidine)]^{2+}$ .The enthalpy change in 1:2 complex is more (negative value) than for 1:1 complex, which suggest that the formation of $[Cd(Ranitidine)_2]^{2+}$ complex is relished more energy in comparison to $[Cd(Ranitidine)]^{2+}$. Positive value of entropy in ratio 1:1 & 1:2 reveals the formation of comparatively disordered complex[33].

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