

Polarographic study of Cu(II)-ranitidine hydrochloride complex at D.M.E.

Dr. Chandrakanta Verma

Department of Chemistry, Govt. Raj Rishi College, Alwar, Rajasthan, India

Abstract

The electrochemical behavior of complex between Ranitidine hydrochloride and Cu (II) was investigated using direct current polarography. Study of Cu (II)- Ranitidine complex carried out with different concentration of drug at two temperatures (20°C and 30°C). Complexes were formed in 1:1 ratio. Complex at 30°C is more stable than 20°C. Since Cu (II) Ranitidine complex shows reversible wave. So thermodynamic parameters (ΔG° , ΔH° , ΔS°) and stability constants of complexes have been determined by Deford and Hume's method.

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

Introduction

Ranitidine hydrochloride (HCl) is - a histamine H₂-receptor antagonist. Ranitidine, like other H₂ blockers, suppresses histamine stimulation of gastric parietal cells to decrease gastric acid secretion.

Chemically it is -

N [2-[[[5-[(dimethyl amino)methyl]-2-furanyl] methyl] thio] ethyl]-N-methyl-2-nitro-1,1-ethenediamine, It has the following structure-

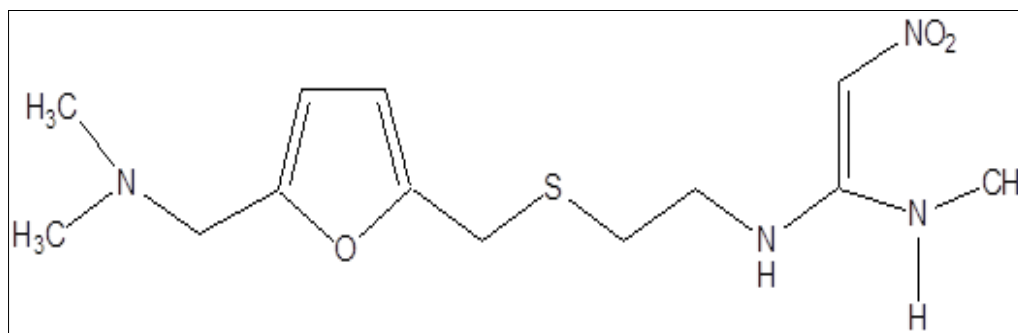


Fig 1: Ranitidine hydrochloride (HCl)

Molecular formula - C₁₃H₂₃ClN₄O₃S

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, 3]. The investigation of the Ranitidine as mixed ligand complex has been done [4, 5].

Copper exhibits considerable biochemical action either as an essential trace metal or as a constituent of various exogenously administered compounds in humans. In its former role it is bound to ceruloplasmin, albumin, and other proteins, while in its latter it is bound to ligands of various types forming complexes that interact with biomolecules,

mainly proteins and nucleic acids [6]. It is essential to study complexation of copper with drugs.

Earlier, the studies of copper complexes with different drugs like Antituberculosis agent- Isoniazid [7], 4 Chlorobenzyl Dene 4-aminoacetanilide [8], 3-hydroxy-3-m-tolyl-1-p (sulphonamido) phenyltriazene [9] etc have been done.

Present study includes the complexation behavior of Ranitidine hydrochloride with metal present in human body in least amount such as Cu 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 rate 100 mv/min.

Materials and reagents

Analytical grade salts of Copper Chloride [CuCl₂] 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 CuCl₂. 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, Cu (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 Cu (II) addition and addition 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 Cu²⁺ was -0.141 V vs. SCE. Single and well defined polarograms were obtained for complexes of Cu (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 Cu (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 $\log\beta$ of the complexes have been determined by Deford and Hume's method using polarographic measurements.

The plots of $F_j(x)$ vs. X (where X is the concentration of Ranitidine) are represented in Fig. (2,3). By seeing them we can say that at 20° C and 30° C the complexes of Cu (II)-Ranitidine hydrochloride are in 1:1 ratio. Value of intercept gives the value of β , where as the value of ($\log \beta$) represents the stability constant. The values of $F_j(x)$ with respect to Ranitidine hydrochloride concentration are summarized in table (1,2). From the plots of $F_j(x)$ vs. X values of stability constants $\log\beta_1$ have been evaluated. More will be the value of stability constant more will be stability of complex. From the values of stability constants ^[10], thermodynamic parameters have also been evaluated.

Values of stability constants for 1:1 complexes are 2.1072 and 2.3201 at 20° C and 30° C respectively. This shows that stability of complexes increase with increase in temperature table (3)

Table 1: Cu (II)- Ranitidine hydrochloride system at 20°C CuCl₂= 1.25×10^{-2} M, Temp = $20 \pm 1^\circ\text{C}$, $E_{1/2}$ (M) = -0.140 , volts vs S.C.E.

$C_x \times 10^{-3}$	I_d (μA)	$\Delta E_{1/2}$ (Volt)	$\log (I_m/I_c)$	$F_0(x)$	$F_1(x) \times 10^2$
1.6	4.7	0.141	0.0180	1.2165	0.7911
2.2	4.6	0.142	0.0274	1.2178	0.9902
2.8	4.5	0.143	0.0369	1.3358	1.1992
3.5	4.3	0.144	0.0567	1.4850	1.3859
4.1	4.1	0.145	0.0774	1.6235	1.5208
4.8	4.0	0.146	0.0881	1.7354	1.5321
5.4	3.9	0.147	0.0991	1.8403	1.5562

$$\beta_1 = 2.1072 \times 10^5$$

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

I_m = Diffusion current of polarographic wave for copper

β_1 = Overall formation constant or Overall stability constant for 1:1 Cu (II)-Ranitidine hydrochloride complexes at 20°C

Table 2: Cu (II) - Ranitidine hydrochloride system at 30°C CuCl₂= 1.25×10^{-2} M, Temp = $30 \pm 1^\circ\text{C}$, $E_{1/2}$ (M) = -0.142 , volts vs S.C.E.

$C_x \times 10^{-3}$	I_d (μA)	$\Delta E_{1/2}$ (Volt)	$\text{Log} (I_m/I_c)$	$F_0(x)$	$F_1(x) \times 10^2$
1.6	5.1	0.144	0.0084	1.2288	1.4303
2.2	5.0	0.146	0.0170	1.3860	1.7549
2.8	4.8	0.147	0.0347	1.5823	2.0798
3.5	4.7	0.149	0.0439	1.7933	2.2666
4.1	4.5	0.150	0.0627	1.9370	2.2855
4.8	4.3	0.151	0.0825	2.1216	2.3367
5.4	4.2	0.152	0.0927	2.2774	2.3656

$$\beta_1 = 2.3201 \times 10^6$$

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

I_m = Diffusion current of polarographic wave for copper

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

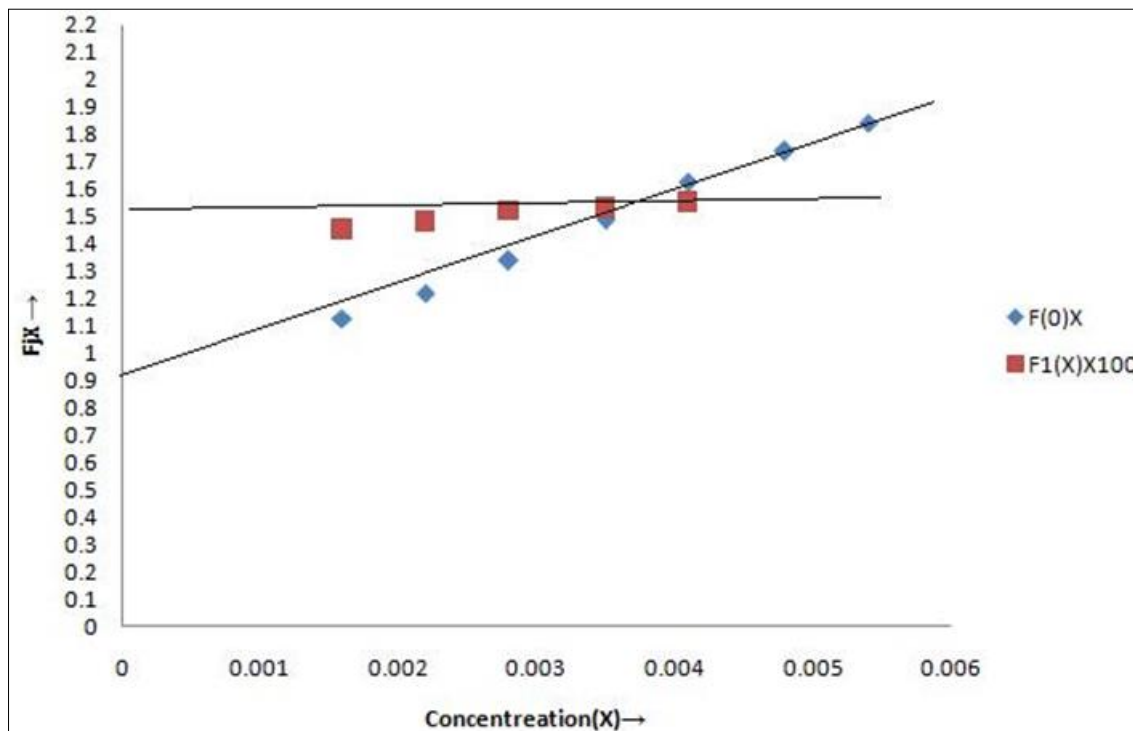


Fig 2: $F_j(X)$ vs. (X) for Cu^{+2} - Ranitidine hydrochloride system at $T=20^{\circ}C$

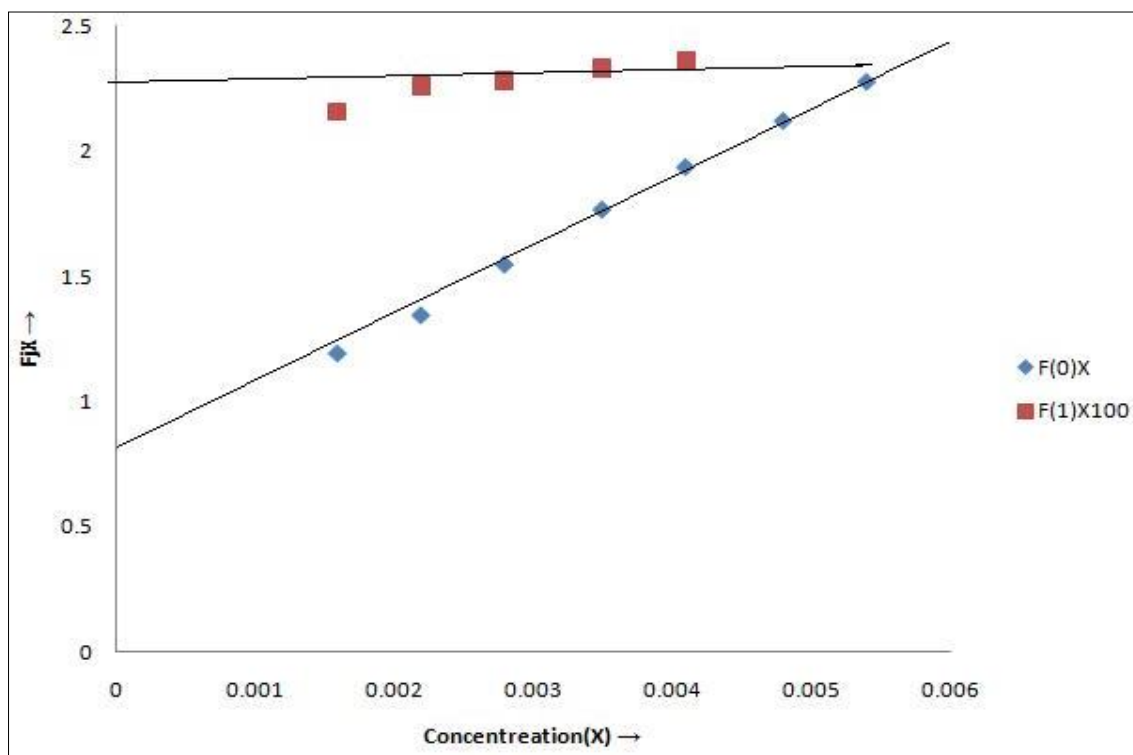


Fig 3: $F_j(X)$ vs. (X) for Cu^{+2} - Ranitidine hydrochloride system at $T=30^{\circ}C$

Table 3: Stability constant for Cu (II)- ranitidine hydrochloride

System	Composition of complex	Stability constants	
		20°C	30°C
$[Cu (Ranitidine)]^{2+}$	1:1	2.10721	2.32014

Table 4: Thermodynamic parameters for Cu (II)- ranitidine hydrochloride at 20°C

System	Composition of complex	Thermodynamic parameters		
		ΔG° Kcal/mole	ΔH° Kcal/mole	ΔS° Cal/degree/mole
$[Cu (Ranitidine)]^{2+}$	1:1	-13.4605	-35.4864	7.7614

ΔG° = Standard Gibb's free energy change.

ΔH° = Standard enthalpy change.

ΔS° = Standard entropy change.

Thermodynamic parameters

The Thermodynamic parameters ^[11, 12] 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).

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

$$(2) \Delta H = - \frac{2.303RT_1T_2 \left[\log \frac{\beta_{T_1}}{\beta_{T_2}} \right]}{T_2 - T_1}$$

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

Positive value of (ΔG), suggests non-spontaneous nature of electrode process and negative value of (ΔG), suggests spontaneous nature of electrode process. Similarly positive value of (ΔS) suggests that formation of activated state is accompanied by increase of entropy. The (ΔH) values are negative, meaning that these processes are exothermic.

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