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

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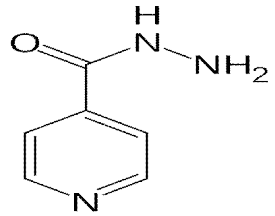
Abstract: The polarographic study of Copper complex of Antituberculosis drug Isoniazid carried out at dropping mercury electrode (DME). Study of Cu(II)-Isoniazid complex carried out with different concentration of drug at two temperatures (20 & 30°C). Complexes were formed in 1:1 and 1:2 ratios. $[Cu(Isoniazid)_2]^{2+}$ complex is more stable than $[Cu(Isoniazid)]^{2+}$. Since Cu(II)-Isoniazid complex shows reversible wave so thermodynamic parameters (ΔG^o, ΔH^o and ΔS^o) evaluated using Deford and Hume's method.
Keywords: Cu(II)-Isoniazid complex, Direct current polarography and Thermodynamic parameters.

Introduction:

Isoniazid (pyridine-4-carboxylic acid hydrazide) also known as isonicotinylhydrazine (INH) used as Antituberculosis - agent. Isoniazid also has an antidepressant effect, and it was one of the first antidepressants discovered. Isoniazid is odorless, and occurs as a colorless or white crystalline powder or as white crystals. It is freely soluble in water, sparingly soluble in alcohol, and slightly soluble in chloroform and in ether. Isoniazid is slowly affected by exposure to air and light.



Structure:- ISONIAZID

Iupac Name : pyridine-4-carboxylic acid hydrazide
Formula : $C_6H_7N_3O$
Mol. Mass : 137.139 g/mol
CAS No. : 54-85-3.

INH forms metal chelates with many bivalent ions. These complexes have been used in the determination of the structure of isoniazid[1-2]. The study of antiviral activity of copper complexes of isoniazid against RNA tumor viruses has been done[3]. It is known that copper ions enhance the in vitro activity of INH against mycobacterium tuberculosis, prompting speculation that a Copper-INH complex may be an important entity in the mycobacterial action[4]. The studies have been done of various metal complexes with isoniazid[5-7]. Structural study of copper-isoniazid complex has been done by crystallographic method[8]. Rieber and Bemski studied and postulated a 1:1 or 1:2 Cu(II)-INH complex[9].

The present study is related to the polarographic behaviour of Cu(II)-INH complex formed in 1:1 and 1:2 ratio.

Experimental:

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. Dropping mercury electrode had the characteristics m = 2.422 mg/sec, t = 2.5 sec and h = 60 cm.

2) Reagents

All the solutions were prepared from doubly distilled water and analytical reagent grade chemicals (MERCK).

Isoniazid {from Alpha Chemica India.} solution was prepared freshly every 5 days.

1.0 M KCl has been used as supporting electrolyte. Triton X-100 (0.001%) was used to suppress polarographic maxima.

3) Proposed Procedure

An aliquot (10 ml) of experimental solution was placed in a dry, clean polarographic cell and deoxygenated with nitrogen for 15 min. the negative potential was applied to the working electrode with 150 mV/min span rate and 100 nA/div sensitivity of current measurement, then current-voltage curves were measured.

Results and Discussion:

A well-defined two-electron reversible reduction and diffusion-controlled wave of Cu^{2+} was observed in 1.0 M KCl. The value of $E_{1/2}$ reversible for Cu^{2+} was –0.141 mV vs. SCE. Single and well defined polarograms were obtained for complexes of Cu(II) with INH in the concentration range 2.9×10^{-4} to 2.61×10^{-3} at 20^{o} C and 30^{o} C. The nature of the C–V curves of Cu^{2+} complexes with INH were also reversible and diffusion-controlled. With increasing the concentration of INH, half wave potential shifts towards more negative direction i.e. towards more cathodic value and diffusion current 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.

As the complexation of Cu(II) with Isoniazid is reversible, hence thermodynamic parameters like Gibb's free energy change, Enthalpy change and Entropy change have been evaluated using Deford and Hume method [10].

The plots of *Fj (x)* vs. X (where X is the concentration of INH) are given in Fig. 1 & 2. By seeing them we can say that at 20^{o} C and 30^{o} C the complexes of Cu (II)-INH formed in 1:1 and 1:2 ratio. From the plots of *Fj (x)* vs. X values of β_1 and β_2 have been evaluated. Value of intercept gives the value of β, where as value of logβ represents the stability constant. More will be the value of stability constant more will be stability. The stability constants of $[Cu(Isoniazid)_2]^{2+}$ are greater than $[Cu(Isoniazid)]^{2+}$ at both temperature, it suggest that Cu(II)-INH complexes are more stable in 1:2 ratio than in 1:1. Moreover complex $[Cu(Isoniazid)_2]^{2+}$ 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. Stability constants are reported in Table-3.

Table (1): Cu(II)-Isoniazid system at 20°C

$CuCl_2 = 2.5 \times 10^{-2}$, Temp = 20°±1°C, $E_{1/2}$ (M) = -0.141 volts vs S.C.E, Im = 2.6.

$C_x \times 10^{-3}$	$E_{1/2(c)}$v vs SCE	$\Delta E_{1/2}$ v vs SCE	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^3$	$F_2(x) \times 10^5$
0.29	-0.145	0.004	0.034762	1.40764	1.405	18.677
0.58	-0.151	0.01	0.092754	2.301166	2.243	23.782
0.87	-0.156	0.015	0.159701	3.44156	2.806	22.326
1.16	-0.161	0.02	0.210853	5.087935	3.524	22.931
1.45	-0.165	0.024	0.30103	6.996669	4.135	22.562
1.74	-0.169	0.028	0.373581	9.565877	4.922	23.327
2.03	-0.173	0.032	0.460731	13.08063	5.951	25.059
2.32	-0.177	0.036	0.569875	17.89546	7.282	27.666
2.61	-0.18	0.039	0.636822	22.61097	8.280	28.414

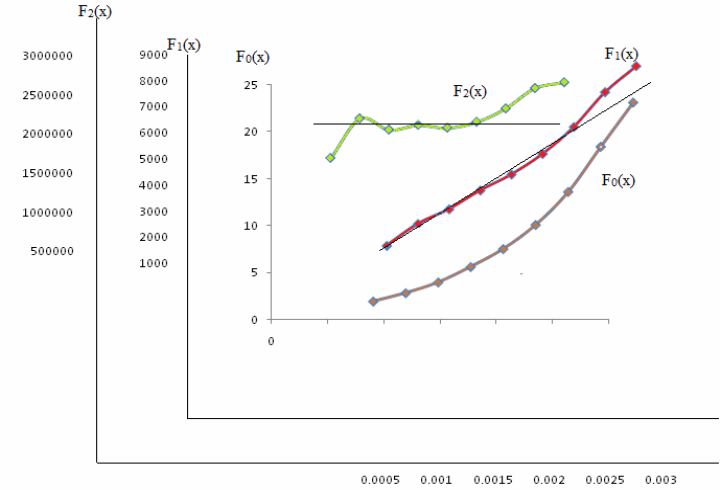
$\boldsymbol{\beta_1} = 8.64 \times 10^2$ $\boldsymbol{\beta_2} = 23.5 \times 10^5$

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

Im = Diffusion current of polarographic wave for copper

β_1 & β_2 = Overall formation constant or Overall stability constant for 1:1 & 1:2 Cu(II)- Isoniazid complexes at 20°C.

Figure-1



Concentration of Isoniazid→ [Cu(II)-Isoniazid system at 20°C]

Table (2): Cu(II)-Isoniazid system at 30°C

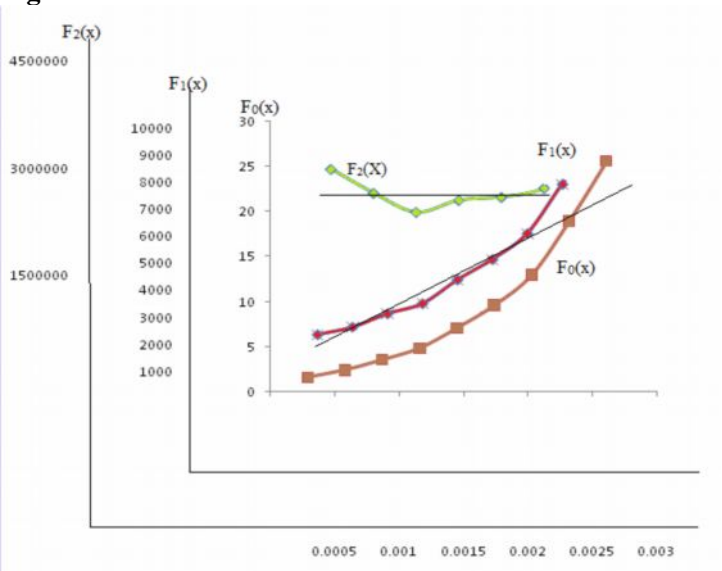
$CuCl_2 = 2.5 \times 10^{-2}$, Temp = 30°±1°C, $E_{1/2}$ (M) = -0.141 volts vs S.C.E, Im = 3.1

$C_x \times 10^{-3}$	$E_{1/2(c)}$v vs SCE	$\Delta E_{1/2}$ v vs SCE	log(Im/Ic)	$F_0(x)$	$F_1(x) \times 10^3$	$F_2(x) \times 10^5$
0.29	-0.147	0.006	0.044204	1.627864	2.165	46.139
0.58	-0.152	0.011	0.093422	2.41641	2.442	27.846
0.87	-0.157	0.016	0.148939	3.556409	2.938	24.268
1.16	-0.161	0.02	0.212608	4.842171	3.312	21.424
1.45	-0.166	0.025	0.287242	7.078105	4.191	23.205
1.74	-0.17	0.029	0.377418	9.603834	4.944	23.665
2.03	-0.174	0.033	0.449969	12.98545	5.904	25.010
2.32	-0.179	0.038	0.537119	18.92476	7.726	29.737
2.61	-0.183	0.042	0.588272	25.57066	9.414	32.900

$\beta_1 = 5.86 \times 10^2$ $\beta_2 = 23.2 \times 10^5$

Here β_1 & β_2 = Overall formation constant or Overall stability constant for 1:1 & 1:2 Cu(II)- Isoniazid complexes at 30°C.

Figure-2



Concentration of Isoniazid→ [Cu(II)-Isoniazid system at 30°C]

Table (3): Stability constant for Cu(II)-Isoniazid

System	Composition of complex	Stability constants	
		20°C	30°C
$[Cu(Isoniazid)]^{2+}$	1:1	2.9365	2.7679
$[Cu(Isoniazid)_2]^{2+}$	1:2	6.3711	6.3655

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

System	Composition of complex	Thermodynamic parameters		
		ΔG° Kcal/mole	ΔH° Kcal/mole	ΔS° cal/degree/mole
$[Cu(Isoniazid)]^{2+}$	1:1	-3.92242	-6.82439	-0.0099
$[Cu(Isoniazid)_2]^{2+}$	1:2	-8.5101	-0.22583	0.028274

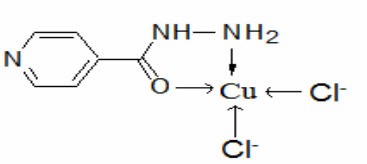
ΔG° = Standard Gibb's free energy change.
ΔH° = Standard enthalpy change.
ΔH° = Standard entropy change.

The thermodynamic parameters[11-12] like free energy change (ΔG), enthalpy change (ΔH), and entropy change (ΔS) of interaction are important to interpret the binding mode[13]. The kind of complex species that can be measured with a mercury electrode depends on thermodynamic aspect[14].

As we know from chemical thermodynamics that the complex which have less value of Gibb's free energy change is more stable, here for $[Cu(Isoniazid)_2]^{2+}$ Gibb's free energy change is more negative and entropy change is positive, which suggest that $[Cu(Isoniazid)_2]^{2+}$ complex is more stable than $[Cu(Isoniazid)]^{2+}$(Entropy change is negative for 1:1 complex). The Enthalpy change in 1:1 complex is more negative which suggest that the formation of than $[Cu(Isoniazid)]^{2+}$ complex accompanied with release of more energy in comparison of than $[Cu(Isoniazid)_2]^{2+}$. Positive value of entropy in ratio 1:2 reveals the formation of comparatively disordered complex[15].

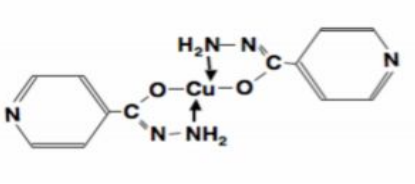
Gibb's free energy change, Enthalpy change and Entropy change are listed in Table-4 for 1:1 and 1:2 Cu(II)-INH complexes.

Proposed structure of the complexes-
The geometry of Cu(II)- INH complex in both 1:1 and 1:2 ratio is square planer.
In 1:1 ratio Cu^{2+} bounded with the isoniazid carbonyl oxygen and hydrazid amino nitrogen atoms and two chlorines occupying coordination positions as:



[Cu(II)- INH complex in 1:1 ratio]

In 1:2 ratio Cu^{2+} bounded with the two isoniazid molecule as:



[Cu(II)- INH complex in 1:2 ratio]

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