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Study of Electrochemical Redox Reaction of CuSO₄ Salt with Amoxicillin at Different Temperatures Using Glassy Carbon Electrode

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Abstract

The redox behavior of copper sulfate in absence and presence of Amoxicillin was studied at two different temperatures (288.15 and 298.15)K. The redox behavior was studied in 0.1 M HCl electrolyte, potential range from (1.5 to -1.5)V. The copper ions concentration is small ones ranging from $(3.3 \times 10^{-4}$ to $1.67 \times 10^{-3})$M. Only one reduction and one oxidation peaks are obtained in our results indicating the reduction and oxidation of the divalent copper ions to the zero valent copper metal. All the solvation cyclic voltammetry parameters were evaluated at the two temperatures used and their values were discussed for cupric ions in presence and absence of Amoxicillin. Also, the thermodynamic parameters for the interaction of copper ions with Amoxicillin as stability constant, Gibbs free energies, enthalpies and entropies of interaction were calculated. The thermodynamic parameters indicate that the reaction between cupric ions and Amoxicillin is chemical reaction (high negative Gibbs free energies values), good spontaneous (positive entropies) and endothermic chemical reaction (valuable positive values). Energy values of interaction between Amx and 2hg6 which obtained by molecular docking calculations indicate that Amx has an anticancer activity for liver cancer treatment

Keywords: Redox reaction; Cyclic voltammetry; amoxicillin; CuSO4; Temperature; Thermodynamic parameters; Molecular docking

Introduction

Voltametric techniques are characterized by many analytical merits which include outstanding sensitivity to organic and inorganic solutions with wide range of concentrations and temperatures, determination variety of useful solvents and electrolytes, its strength in calculation kinetic and mechanistic parameters, estimation of unknown parameters, the ability to form different wave forms and measure small current [1, 2].

The work in the thesis includes one type of voltametric techniques which is called cyclic voltametry. Cyclic Voltametry is voltametric technique which is used to describe the redox behavior of the electrochemical reaction. It was first announced in 1938 and characterized by Randles [3]. A lot of researches discuss cyclic voltametry of copper with different ligand [4-6]. Copper has an important role in many biological processes inside the human and animal bodies. Copper complexes has great attention as good reagent against bacterial activity and used for humans and animals as nutritious [7, 8]. Proteins which are natural occurring materials are essential for a large number of vital functions [9]. Transition metal complexes with them and in peptides are consumed in several biological processes [10]. Both potentiometric and spectroscopic techniques take special attention, due to its accurate values for the estimation of stability constants from voltametric techniques and also on its ability to give structural information [11, 12]. However, these methods have specific condition and can critically use in concentrated solutions. The oxidation and reduction processes for *CuSO₄* and its

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interaction with Amoxicillin were done in aqueous medium and the data was analyzed using origin software.

Experimental

The chemicals used in the present study are copper sulfate salt ,$CuSO_4$ from Oxford Co. India, Amoxicillin from Merck Co, hydrochloric acid pure (HCl) from Adwic Co Company and bidestilled water with conductivity of 3 micro Siemens.
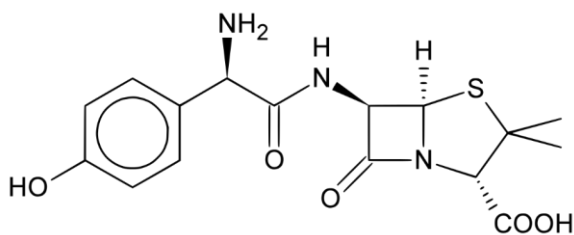
Amoxicillin (Amx)	
Synonyms	((2S,5R,6R)-{[2R-2-Amino-2-(4-hydroxy phenyl)acetyl]amino}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3,2,0] heptane-2-carboxylic acid) sodium salt
Formula	$C_{16}H_{19}N_3O_5S$
Mol. Wt.	365.4 g/mol

The cyclic voltametric studies were done by using DY2000 multichannel potentiometer, delivered from USA. It was connected to a cell of three electrodes, silver/silver chloride put in saturated KCl solution used as reference electrode, solid glassy carbon electrode (SGC) was used as working electrode and platinum wire, auxiliary electrode. The solid glassy carbon electrode (SGR) surface was polished to mirror state using 1-0.03 micro alumina powder. The SGR was washed with absolute alcohol and doubly-distilled water till removing any adhering alumina particles. Area of electrode is (5.72×10^{-2}) cm^2. The system was applied from (1.5 to -1.5)V potential window and (0.1, 0.02, 0.01)$V.s^{-1}$ scan rates at different temperatures (288.15 and 298.15)K. Passing purified N_2 was done before each experiment to insure inert atmosphere and diffusion experiment. Finally, the data was analyzed using origin software.

Results and Discussion

$CuSO_4$ reduction and oxidation behaviors in absence and presence of Amoxicillin have been examined in 0.1M HCl using cyclic voltametry at (288.15 and 298.15) K.

3.1. Electrochemical behavior of $CuSO_4$ (Cu^{2+}) in absence of Amoxicillin (Amx) at (288.15 and 298.15)K

3.1.1 Effect of different Cu^{2+} concentrations in absence of Amx at (288.15 and 298.15)K

First, the cyclic voltamogram of 30 ml HCl (0.1) M as a supporting electrolyte was measured from (1.5 to -1.5)V using DY2000 multichannel potentiometer at (288.15 and 298.15)K, **Fig.1**. Then, the redox behavior of Cu^{2+} was examined in 0.1 M HCl by adding Cu^{2+} ions solution step wisely from 1 ml (3.32×10^{-4}) M to 6 ml (16.7×10^{-4}) M as shown in **Fig.2**.

The electrochemical redox behavior of Cu^{2+} in absence of Amoxicillin using solid glassy carbon electrode was studied at the steady state current, cyclic waves were obtained and explained using the following equations [7, 24].

$$i_p = 0.4463 \ n \ F \ A \ C \ (n \ F \ D \ \nu/ \ R \ T \ )^{1/2} \quad (1)$$

i_p is the current in ampere , A is the surface area of working electrode in cm^2 , D is the diffusion coefficient in cm^2/sec , ν is the scan rate in volts/sec and C is the Cu^{2+} concentration.

ΔE_P is the peak potential difference and calculated from equation (2)

$$\Delta E_P = E_{Pa} - E_{Pc} \qquad (2)$$

If ΔE_P will close to 59/n mv (at 298.15K) the reaction is reversible where, n is the number of electrons in redox reactions

The standard heterogeneous electron transfer rate constant k_s in cm/sec were calculated by applying the following equation (3):

$$k_s = 2.18* [D_C \ \alpha n_a \ F \ \nu/RT]^{1/2} *exp \ [\alpha^2 nF \ \Delta E_P/RT] \quad (3)$$

where : α is charge transfer coefficient and n_a is the numbers of electron transfer in the rate determining step.

Assuming that α coefficient is equal to 0.5. Hence, αn_a will be as the shown in equation (4)

$$\alpha n_a = 1.857 \ RT / (E_{pc} - E_{pc/2}) \ F \quad (4)$$

where $E_{pc/2}$ is the half wave potential for cathodic peak

Then the surface coverage Γ (surface concentration of the electroactive species in $mol.cm^{-2}$) was evaluated by equation (5).

$$\Gamma = i_p \ 4RT \ /n^2 \ F^2 \ A \ \nu \quad (5)$$

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The quantity of charge consumed during the reduction of the adsorbed layer can be used to calculate the surface coverage by eq. (6).

$$Q = n \, FA \, \Gamma \qquad (6)$$

The calculated solvation and kinetic parameters are Ep_a (anodic peak potential), Ep_c (cathodic peak potential), Ip_a (anodic peak current), Ip_c (cathodic peak current), ΔE_P (peak potential difference), D_a (anodic diffusion coefficient), D_c (cathodic diffusion coefficient), k_s (electron transfer rate constant), Γ_a (anodic surface coverage), Γ_c (cathodic surface coverage), Q_a (anodic quantity of electricity) and Q_c (cathodic quantity of electricity) in **Table 1 (a,b)**.
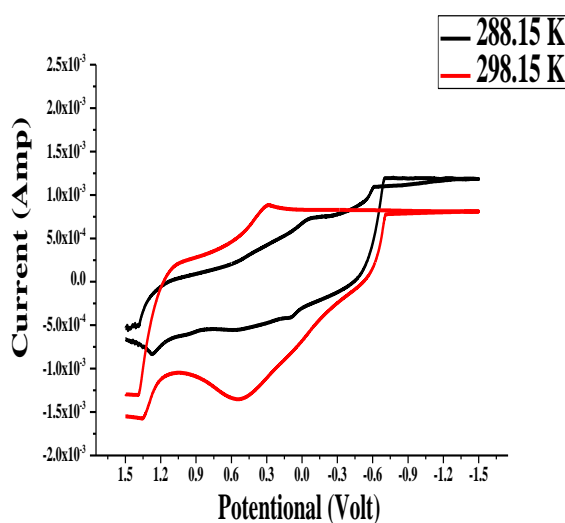
Fig.(1): Cyclic voltamogram of 30 ml HCl (0.1) M and scan rate 0.1 V/s at (288.15 and 298.15)K
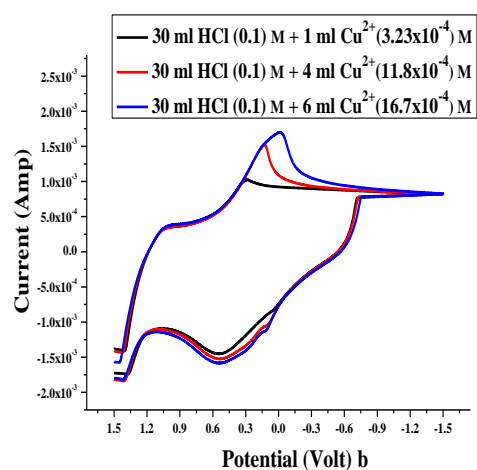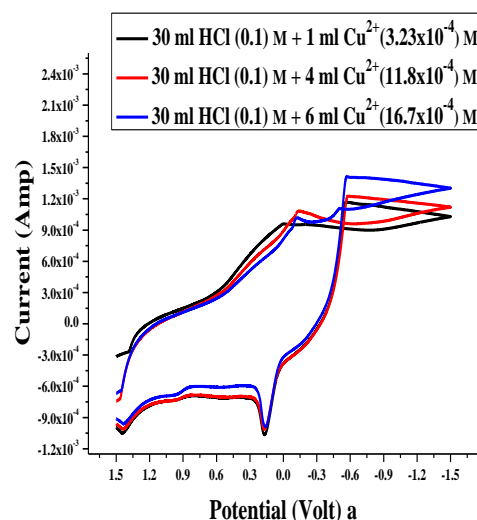
Fig.(2): Cyclic voltamogram of different Cu^{2+} concentrations in 30 ml HCl (0.1) M and scan rate 0.1 V/S at (a) 288.15K (b) 298.15K

The relation between cathodic and anodic peak current I_p against different concentrations of Cu^{2+} ions in 0.1M HCl and scan rate 0.1 V.s^{-1} were shown in **Fig.3**.

Table.1(a): Effect of different concentrations of Cu^{2+} for redox peaks at 288.15K

[M] x10^{-4}	Ep$_a$	Ep$_c$	ΔE_p x10^{-2}	(-)Ip$_a$ x10^{-4}	Ip$_c$ x10^{-4}	E$^{\circ}$	D$_a$ x10^{-9}	D$_c$ x10^{-9}	k$_s$ x10^{-4}	Γ_c x10^{-8}	(+)Q$_c$ x 10^{-4}	Γ_a x10^{-8}	(-)Q$_a$ x 10^{-4}
3.23	0.110	0.082	2.82	1.359	3.192	0.096	7.496	41.4	49.8	5.740	3.17	2.445	1.35
11.8	0.142	0.083	5.89	4.393	3.994	0.112	5.889	4.87	21.7	7.187	3.97	7.905	4.36
16.7	0.157	0.104	5.29	5.562	4.961	0.130	4.704	3.74	4.04	8.927	4.93	10.00	5.52

Table.1(b): Effect of different concentrations of Cu^{2+} for redox peaks at 298.15K

[M] x10^{-4}	Ep$_a$	Ep$_c$	ΔE_p	(-)Ip$_a$ x10^{-4}	Ip$_c$ x10^{-4}	E$^{\circ}$	D$_a$ x10^{-8}	D$_c$ x10^{-8}	k$_s$ x10^{-3}	Γ_c x10^{-8}	(+)Q$_c$ x10^{-4}	Γ_a x10^{-8}	(-)Q$_a$ x10^{-4}
3.23	0.532	0.318	0.214	3.03	4.6	0.425	3.738	8.57	6.65	8.557	4.72	5.650	3.12
11.8	0.534	0.157	0.377	3.76	9.3	0.345	0.431	2.64	14.6	17.31	9.55	7.005	3.87
16.7	0.534	0.107	0.427	4.35	9.6	0.320	0.287	1.40	16.1	17.80	9.80	8.097	4.47

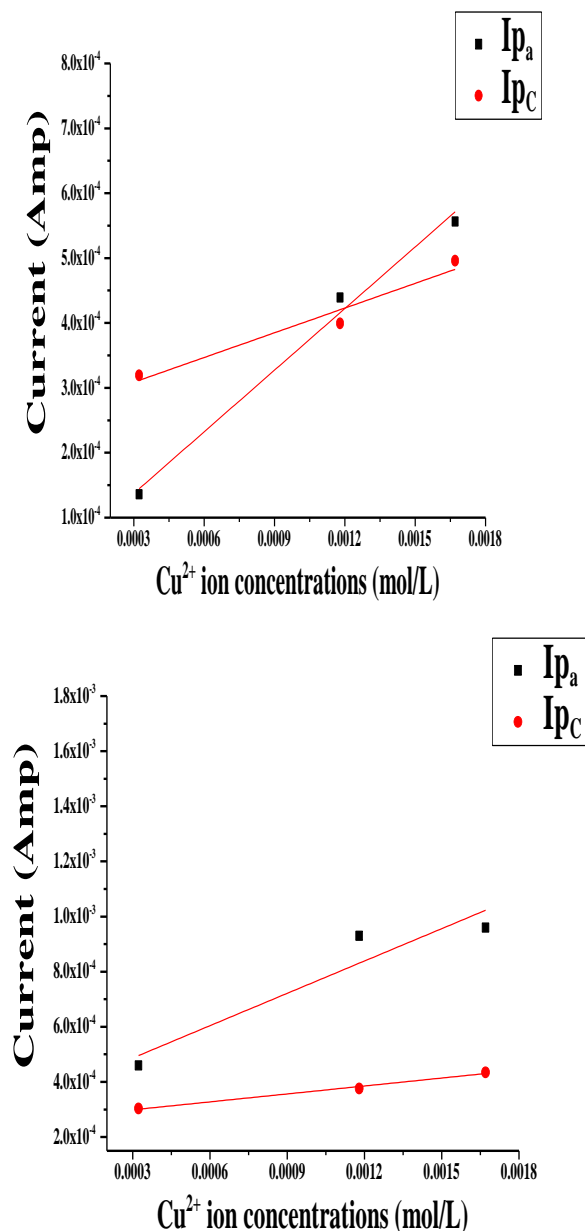**Fig.(3):** The relation between peak current Ip (Ip_C – Ip_a) against different concentrations of Cu²⁺ ions at (a) 288.15K (b) 298.15K and scan rate 0.1 V.s⁻¹

Fig.(4): Cyclic voltamogram of different scan rates of (16.7x10⁻⁴) M CuSO₄ in (0.1)M HCl at (a) 288.15K (b) 298.15K

Effect of different scan rates

Cyclic voltamogram of Cu²⁺ ions in 0.1 M HCl was studied at different scan rates (0.1, 0.02 and 0.01)(V.s⁻¹) and temperatures (288.15 and 298.15)K, **Fig.4**. **Table.2 (a,b)** illustrate the calculated solvation and kinetic parameters (Ep, Ip, ΔE_P, E ½, D, k_S, Γ and Q) of different scan rates**.**

The reduction peak of cupric ions from divalent into zero valent metal was shown in all our cyclic voltamograms for copper sulfate alone indicating the use of two electron reduction mechanism at approximately -0.3V. The oxidation process is the opposite direction of the above discussed mechanism in this range of concentration at approximatly 0.1V [1,3].

Randless Sevicek equation [24-28] was used to apply the relation between cathodic and anodic peak current I_p against the square root of scan rate in 0.1M HCl which gives straight lines indicating diffusion process as shown in **Fig.5**.
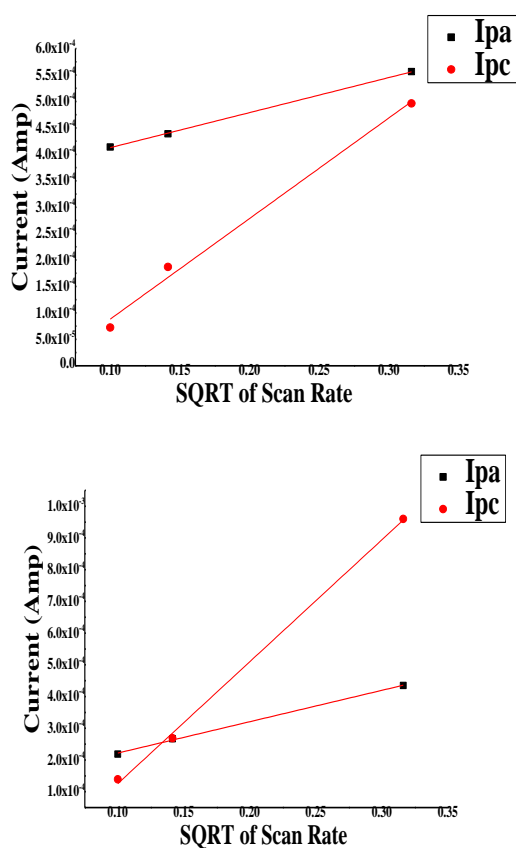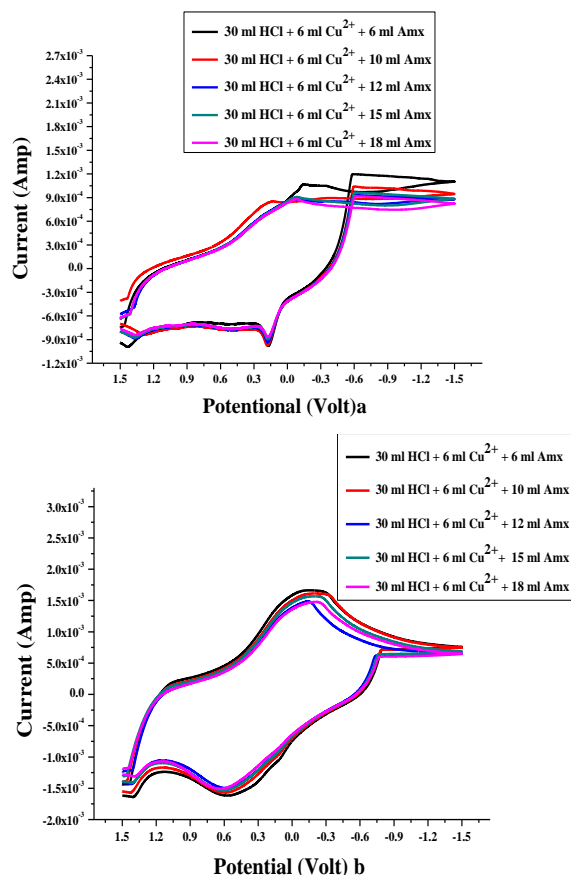
Fig.(5): The relation between peak current Ip (ipₐ - ip_c) against the square root of different scan rates for (16.7x 10^{-04}) M CuSO₄ at (a) 288.15K (b) 298.15K.

of interaction of (16.7x 10^{-04})M Cu²⁺ ions and different concentrations of Amx at (288.15 and 298.15)K and scan rate 0.1 V.s⁻¹ were presented in **Table.3 (a,b)**.


Fig.(6): Cyclic voltamograms for the interaction of (16.7x 10^{-04})M CuSO₄ and different concentrations of Amx and scan rate 0.1 V.s⁻¹ at (a) 288.15K (b) 298.15K

Electrochemical behavior of CuSO₄ (Cu²⁺) in presence of Amoxicillin (Amx) at (288.15 and 298.15)K

Effect of different Cu²⁺ concentrations in presence of Amx at (288.15 and 298.15)K

The electrochemical behavior of the complexation between Amx and Cu²⁺ ions was studied in 0.1M HCl and scan rate 0.1 V.s⁻¹ at (288.15 and 298.15)K, **Fig.6**. The solvation and kinetic parameters (Eₚ, Ip, ΔEₚ, E½, D, k_S, Γ and Q)

Table.2(a): Effect of different scan rate on (16.7x10⁻⁰⁴)M of Cu²⁺ for redox peak at 288.15K

υ	Epₐ	Ep_c	ΔEₚ	(-)Ipₐ x10⁻⁴	Ip_c x10⁻⁴	E°	Dₐ x10⁻⁹	D_c x10⁻⁹	k_s x10⁻⁴	Γ_c x10⁻⁷	(+)Q_c x10⁻⁴	Γ_a x10⁻⁷	(-)Qₐ x10⁻⁴
0.1	0.157	0.104	0.052	5.56	4.96	0.026	4.70	3.742	4.04	0.89	4.93	1.000	5.52
0.02	0.132	0.040	0.092	4.39	1.87	0.080	14.6	2.650	2.59	1.68	9.27	3.948	21.8
0.01	0.132	0.024	0.107	4.14	0.72	0.078	26	0.798	1.17	1.30	7.20	7.444	41.1

Table.2(b): Effect of different scan rate on (16.7x10⁻⁰⁴)M of Cu²⁺ for redox at 298.15K

| υ	Epₐ	Ep_c	ΔEₚ	(-)Ipₐ x10⁻⁴	Ip_c x10⁻⁴	E°	Dₐ x10⁻⁹	D_c x10⁻⁹	k_s x10⁻⁵	Γ_c x10⁻⁷	(+)Q_c x10⁻⁴	Γ_a x10⁻⁷	(-)Qₐ x10⁻⁴
0.1	0.533	0.107	0.426	4.35	9.60	0.320	2.88	14.00	1610	1.787	9.86	8.097	4.47
0.02	0.200	0.260	0.060	2.67	2.69	0.230	5.42	5.492	4.46	2.502	13.8	24.85	13.7
0.01	0.204	0.311	0.106	2.19	1.39	0.258	7.26	2.926	1.73	2.583	14.3	40.68	22.5
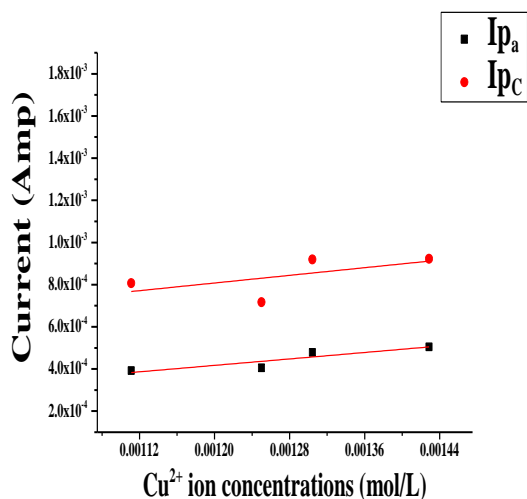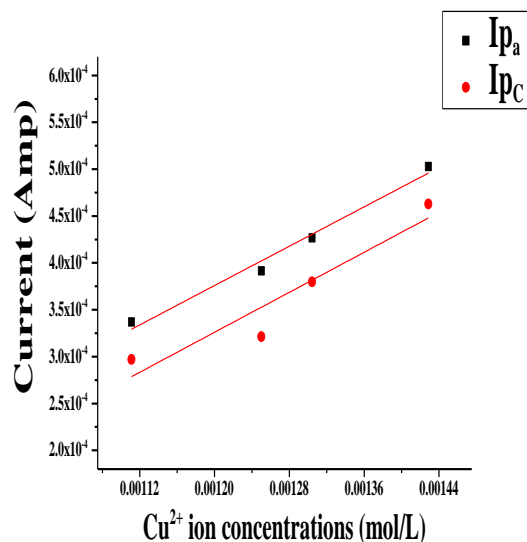
Fig.(7): The relation between peak current Ip (Ip$_C$ – Ip$_a$) against different concentrations of Cu^{2+} ions in the presence of Amx at (a) 288.15K (b) 298.15K and scan rate 0.1 V.s^{-1}

All the cyclic voltametric data obtained (D$_a$, D$_C$, k$_S$, Γ$_a$, Γ$_C$, Q$_a$ and Q$_C$) are increased by increasing the Amoxicillin concentration which indicate the diffusion control of the reaction between Amoxicillin and cupric ions and also increased by increasing temperature

Effect of different scan rates

Effect of different scan rates on the interaction between Cu^{2+} ions and Amx was studied in (0.1, 0.02 and 0.01) V.s^{-1}, **Fig.8**.
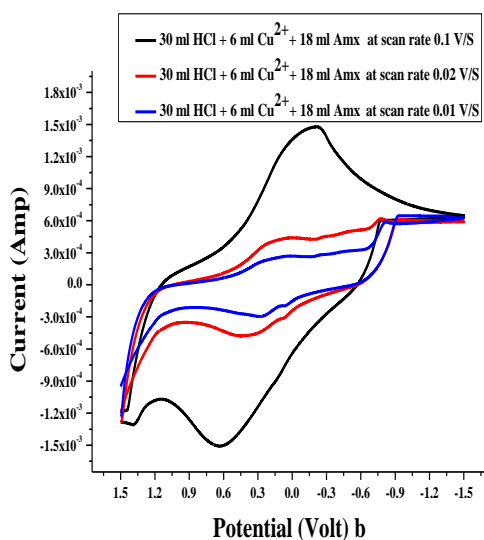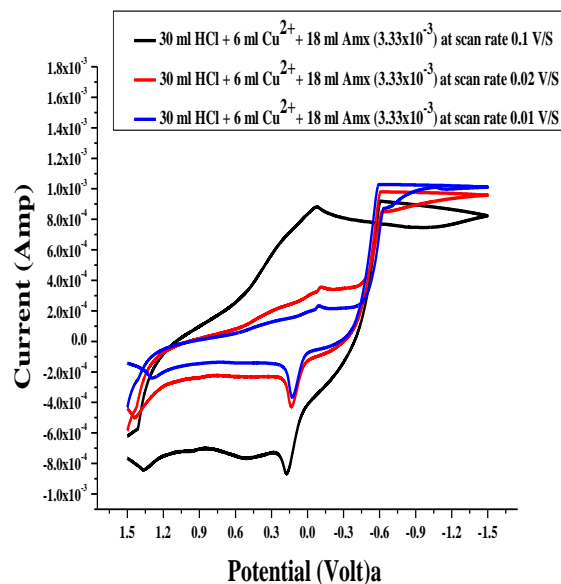
Fig.(8): Cyclic voltamogram of different scan rate of (1.11x 10^{-3})M Cu^{2+} with (3.33x 10^{-3})M Amx at (a) 288.15K (b) 298.15K

No new peaks was appeared on adding Amoxicillin to cupric ions indicating the effect is only decease in cupric peak hights and shift of the cathodic potentials to more negative values and the anodic potential to more positive values indicating the interaction between cupric ions and Amoxicillin.

The solvation and kinetic parameters (Ep, Ip, ΔE$_P$, E $_{½}$, D, k$_S$, Γ and Q) of different scan rates of Cu^{2+} ions in the presence of Amx were presented in **Table.4.(a,b)**.

Table.3(a): Effect of different concentrations of Amx for redox peak at 288.15K

[Amx] x10^{-3}	Epa	Epc	ΔEp	(-)Ipa x10^{-4}	Ipc x10^{-4}	E°	Da x10^{-9}	Dc x10^{-9}	ks x10^{-4}	Γc x10^{-8}	(+)Qc x10^{-4}	Γa x10^{-8}	(-)Qa x10^{-4}
1.43	0.176	0.146	0.030	5.03	4.63	0.161	5.233	4.43	2.36	8.328	4.60	9.049	4.99
2.17	0.198	0.133	0.065	4.27	3.80	0.166	4.520	3.58	2.41	6.83	3.77	7.679	4.24
2.50	0.176	0.058	0.117	3.91	3.21	0.117	4.140	2.79	5.11	5.779	3.19	7.042	3.89
2.94	0.173	0.078	0.094	3.57	3.08	0.125	3.898	2.9	6.37	5.544	3.06	6.430	3.55
3.33	0.181	0.078	0.103	3.37	2.97	0.130	3.880	3.02	5.69	5.344	2.95	6.060	3.35

Table.3(b): Effect of different concentrations of Amx for redox peak at 298.15K

[Amx] x10^{-3}	Epa	Epc	ΔEp	(-)Ipa x10^{-4}	Ipc x10^{-4}	E°	Da x10^{-9}	Dc x10^{-9}	ks x10^{-2}	Γc x10^{-8}	(+)Qc x10^{-4}	Γa x10^{-8}	(-)Qa x10^{-4}
1.43	0.545	0.1206	0.4249	5.05	9.23	0.3331	5.268	17.62	2.632	17.18	9.481	9.395	5.185
2.17	0.566	0.0774	0.4892	4.79	9.19	0.3220	5.684	20.97	4.437	17.11	9.444	8.910	4.917
2.50	0.568	0.0576	0.5107	4.06	7.16	0.3130	4.449	13.86	4.082	13.33	7.359	7.554	4.169
2.8	0.589	0.0585	0.5308	4.24	8.51	0.3239	5.267	21.23	6.611	15.84	8.742	7.890	4.355
3.33	0.589	0.0774	0.5119	3.92	8.07	0.3334	5.249	22.26	5.959	15.02	8.290	7.293	4.025

Table.4(a): Effect of different scan rate of (1:3) complex for redox peak at 288.15K

υ	Epa	Epc	ΔEp	(-)Ipa x10^{-4}	Ipc x10^{-4}	E°	Da x10^{-9}	Dc x10^{-9}	ks x10^{-5}	Γc x10^{-8}	(+)Qc x10^{-4}	Γa x10^{-8}	(-)Qa x10^{-4}
0.1	0.181	0.078	0.103	3.37	2.97	0.130	3.881	3.018	56.9	5.340	2.95	6.061	3.35
0.02	0.137	0.112	0.024	2.73	1.59	0.125	12.70	4.343	6.65	14.30	7.91	24.52	13.5
0.01	0.130	0.095	0.034	2.68	1.11	0.112	24.52	4.204	5.13	19.94	11	48.18	26.6

Table.4(b): Effect of different scan rate of (1:3) complex for redox peak at 298.15K

υ	Epa	Epc	ΔEp	(-)Ipa x10^{-4}	Ipc x10^{-4}	E°	Da x10^{-9}	Dc x10^{-9}	ks x10^{-5}	Γc x10^{-7}	(+)Qc x10^{-4}	Γa x10^{-7}	(-)Qa x10^{-4}
0.1	0.5893	0.0774	0.6667	3.92	8.07	0.2559	5.248	22.263	177	1.502	8.29	1.328	7.33
0.02	0.4054	0.1234	0.282	2.32	2.47	0.2644	9.206	10.47	1.47	2.303	12.7	3.934	21.7
0.01	0.2646	0.1196	0.14492	1.80	1.54	0.1921	11.069	8.1366	0.232	2.87	15.8	6.1013	33.7

The relation between cathodic and anodic peak current I_p against the square root of scan rate in 0.1M HCl were shown in **Fig.9**.
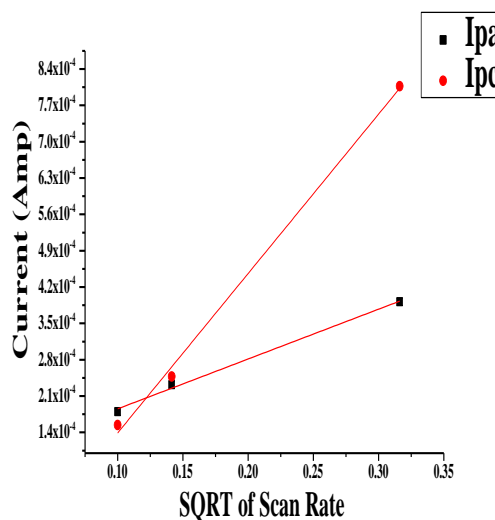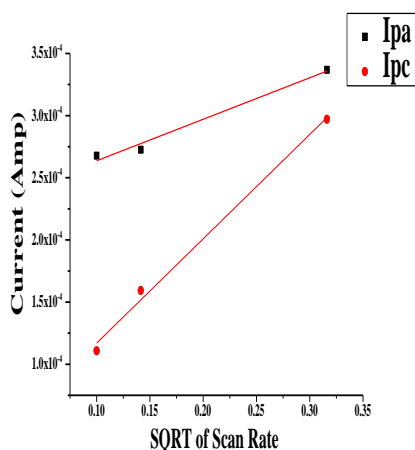
Fig.(9): The relation between peak current Ip (ip_a - ip_c) against different scan rates of Cu^{2+} in presence of Amx at (a) 288.15K (b) 298.15K

Electrochemical behavior of the complexation between Cu²⁺ ions and Amx.

From **Fig.6**, it is observed that the complex is formed as a result of decreasing in the anodic and cathodic peak current beside the potential shifts to new values. A stability constant is a measure of the strength of the interaction between the reagents that come together to form the complex.

The stability constants (β_{MX}) for $CuSO_4$ complexes for each addition are calculated by applying the following equations [19-33]:

$$\Delta E° = E°_C - E°_M = 2.303\ (RT/nF) * (\log \beta_{MX} + j \log C_x)\quad (7)$$

Where $E°_M$ is the formal peak potential of metal at finally adding in the absence of Amx, $E°_C$ is the formal peak potential of metal complex after each addition of Amx, R is a gas constant (8.314 $J.mol^{-1}.degree^{-1}$), T is the absolute temperature, j is the coordination number of the stoichiometric complex and C_x is the concentration of Amx in the solution.

The formal potential E° can be found as the midway between the two cyclic voltametric peaks comprising the voltamogram by Eq.(8).

$$E° = (E_{pa} + E_{pc})/2\quad (8)$$

where both E_{pa} and E_{pc} are anodic peak potential and cathodic peak potential, respectively.

The Gibbs free energy of interaction for Cu²⁺ ions with Amx were calculated from stability constant (β_{MX}) using Eq.(9)[20-33].

$$\Delta G = -2.303\ RT \log \beta_{MX}\quad (9)$$

The relation between Gibbs free energy against stability constant of $CuSO_4$ complexes with Amox were shown in **Fig.10**.

All equilibrium constants vary with temperature, so the enthalpy (ΔH) of interaction for $CuSO_4$ with Amox was calculated by using Van't Hoff Eq. (10)

$$\log \frac{\beta MX\ at\ (T_2)}{\beta MX\ at\ (T_1)} = \frac{\Delta H}{2.303}\left(\frac{T_2\ T_1}{T_2 - T_1}\right)\quad (10)$$

where β_{MX} is the stability constant at different temperature, both T_2 and T_1 are 298.15 K and 288.15 K, respectively.

The entropy (ΔS) for $CuSO_4$ complexes in 0.1 M HCl at (1.5 to -1.5)V potential windows and scan rate 0.1 V.s⁻¹ at different temperatures (288.15, 298.15 K) are calculated by using Eq. (11)

$$\Delta S = \frac{\Delta H - \Delta G}{T}\quad (11)$$

The calculated values of β_{MX}, ΔG, ΔH, and ΔS for $CuSO_4$ complexes are estimated and collected in **Table.5**.
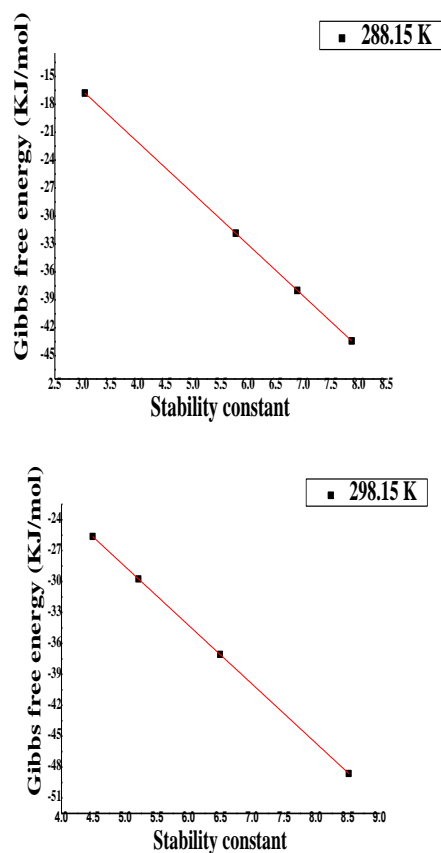

Fig.(10): The relation between Gibbs free energy and stability constant for $CuSO_4$ complex at (a) 288.15K (b) 298.15K

All the thermodynamic parameters given in Table.5 indicate the complexation interaction between Amoxicillin and cupric ions at the two temperatures used indicating high stability constant and high Gibbs free energies of complexation. Positive enthalpic data indicate that the reaction process is endothermic one and positive entropies indicate the spontaneous character of the reaction between cupric ions and Amoxicillin.

Computational studies

Molecular docking of Amoxicillin (Amx)

Table.5: The stability constant, Gibbs free energy, enthalpy and entropy of interaction for $CuSO_4$ Complex at (288.15 and 298.15)K

[M]x10⁻³	[L]x10⁻³	j	log βj		ΔG (KJ/mol)		ΔH (KJ/mol)	ΔS (KJ/mol)
			288.15K	298.15	288.15K	298.15		
1.43	1.43	1	3.04	4.48	-16.79	-25.62	278.94	1.018
1.30	2.17	1.67	6.88	5.89	-37.98	-33.65	124.48	0.563
1.25	2.50	2	5.77	6.49	-31.85	-37.07	185.02	0.752
1.11	3.33	3	7.87	8.518	-43.43	-48.62	178.03	0.768

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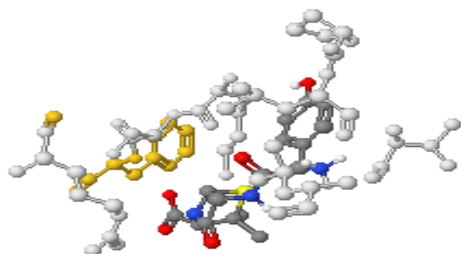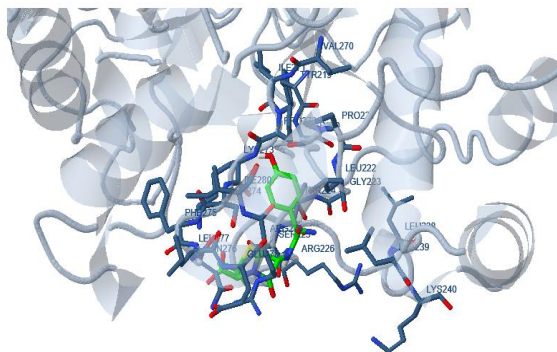**Table.6 : Energy values for Amoxicillin alone**

Free Energy of Binding (Kcal/mol)	Inhibition const, K_i (uM)	vdW+Hbond+desolv Energy (Kcal/mol)	Electrostatic Energy (Kcal/mol)	Total Intermolec. Energy (Kcal/mol)	Frequency %	Interact. Surface
-6.06	36.12	-6.02	-1.44	-7.46	30	697.969

was done to show its affinity with receptors. It was done with protein 2hg6 which is responsible for liver cancer, **Figs. [11-13]**.

Energy values of interaction between Amx and 2hg6 which obtained by docking calculations indicate that Amx can act as a good anticancer drug, **Tables. (6,7)**. The interaction between almost all atoms of Amx and amino residue of enzyme predict their anticancer action.

Free energy of binding, inhibition constant, Van der Waals forces, hydrogen bonding, dessolvation energy, total intermolecular energy are indicated for different ranks and gave better results than that of Amx alone.

The redox behaviour of copper sulfate in absence and presence of Amoxicillin was studies at two different temperatures. The solvation cyclic voltametry data was obtained and their values were compared. The different thermodynamic parameter, stability constant, Gibbs free energies of solvation, entropies and enthalpies of solvation indicate the complexation of cupric ions and Amoxicillin.

Fig. (13): The 3D docking pose of monomer Amoxicillin at active 2hg6 and active site showing the hydrogen bonding in blue

Conclusion

The redox behavior of copper sulfate in absence and presence of Amoxicillin was studies at two different temperatures. The solvation cyclic voltammetry data was obtained and their values were compared. The different thermodynamic parameter, stability constant, Gibbs free energies of solvation, entropies and enthalpies of solvation indicate the complexation of cupric ions and Amoxicillin.

Molecular Docking interaction between Amoxicillin and amino acid residue 2hq6 was detected and proved that Amx has an anticancer activity for liver cancer treatment.

Fig. (11): The 3D structure of Amoxicillin with 2hg6 isomerase enzyme

Fig. (12): The 3D active sites of docking of Amoxicillin into 2hg6 isomerase enzyme

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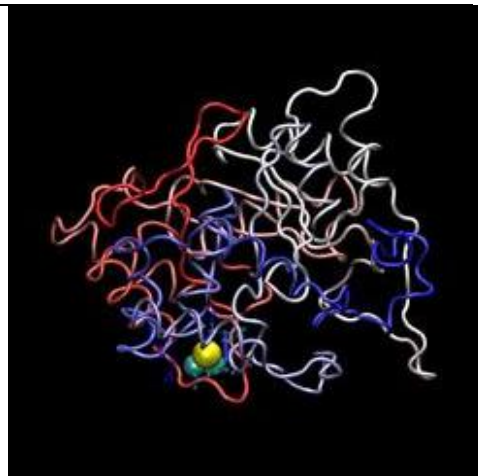**Table.7: Energy values for Amoxicillin with 2hq6 enzyme**

Rank	Free Energy of Binding (Kcal/mol)	Inhibition const, K_i (uM)	vdW+Hbond+desolv Energy (Kcal/mol)	Electrostatic Energy (Kcal/mol)	Total Intermolec. Energy (Kcal/mol)	Frequency %	Interact. Surface
1	-7.32	4.28	-8.29	-1.10	-9.39	10	769.202
2	-6.78	10.74	-6.50	-1.02	-7.52	20	739.104
3	-6.06	36.12	-6.02	-1.44	-7.46	30	697.969
4	-5.65	72.37	-5.80	-0.89	-6.69	10	667.231
5	-5.07	192.45	-5.54	-0.55	-6.09	10	705.126
6	-4.92	248.30	-5.39	-0.60	-5.99	10	699.786
7	-4.79	308.44	-6.58	-0.01	-6.59	10	805.752

References

1- Wei Y., Chan C., Tian J., Jang G. and Hsueh K.F, Electrochemical Polymerization of Thiophenes in the Presence of Bithiophene or Terthiophene: Kinetics and Mechanism of the Polymerization, *Chem. Mater.*, **3**, 888–897(1991).

2- Haier S.N. and Park S., Electrochemistry of Conductive Polymers, *J. Electrochem. Soc.,* **140**, 2454–2463(1993).

3- Randles J.E.B., A cathode ray polarograph. Part II. The current-voltage curves, *Trans. Faraday. Soc.*, **44**, 327–338(1948).

4- Gomaa E.A., Negm A. and Tahoon M.A., Study of redox behavior of Cu (II) with lysine in the aqueous medium using cyclic voltametry, *Eur. J. Chem.,* **7**, 341-346(2016).

5- Gomaa E.A., Diab M., Elsonbati A., Abulenader H.M. and Helmy A., Interaction Parameters for CuCl$_2$ Plus Orange G (OG) at 19.1C Using Carbon Glassy Electrode (CGE) in KCl Aqueous Solutions, *Asia. J. Nano Sci. & Mat*, **1**, 172-293(2018).

6- Gomaa E.A., Negm A.E. and Abu Qarn A.E, Cyclic Voltametry of Nano Copper Sulphate with Cefepime Using Glassy Carbon Electrode, AASCIT, 3, 177-183(2016).

7- Iqbal M.Z., Khurshid S. and Iqbal M.S., Antibacterial activity of copper amino acid complexes, *J. Pak. Med. Assoc.*, **40**, 221-222(1990).

8- Gomaa E.A. and Tahoon M.A., Ion association and solvation behavior of copper sulfate in binary aqueous-methanol mixtures at different temperatures, *J. Mol. liq.*, **214**, 19-23(2016).

9- Gomaa E.A., Zaky R.R. and Shokr A., Estimated the physical parameters of lanthanum chloride in water N,N-dimethyl formamaide using different techniques, *Chem. Data. Collec*., **242**, 67-76(2017).

10- Voet D. and Voet J., Biochemistry, Wiely, New York, (1993).

11- Husain A. and Ajmal M., Synthesis of novel 1,3,4-oxadiazole derivatives and their biological properties, *Acta Pharm.*, **59**, 223-233(2009).

12- Pogni R., Baratto M.C., Diaz A. and Basosi R., EPR characterization of mono(thiosemicarbazones) copper(II) complexes. Note II, *J. Inorg. Biochem.,* **79**, 1-4(2000).

13- Brownson D.A.C. and Banks C.E., The Handbook Of Graphene Electrochemistry, Springer-Verlag London Ltd, (2014).

14- Gosser D.K., Cyclic voltaametry: Simulation and analysis of reaction mechanisms, 1993, New York, VCH, (1993).

15- Bamford C.H. and Compton R.G., Electrode Kinetics: Principles and Methodology, Vol. **26**, 1st Edition, Elsevier Science, London, (1986).

16- Masuda H. and Ayabe Y.Z., The theory of the cathode-ray polarography of Randles-Sevcik, Zeitschrift für Elektrochmie and Angewandte Physikalische, **59**, 494-503(1955).

17- Nicholson R.S. and Shain I., Theory and Application of Cyclic Voltametry for Measurement of Electrode Reaction Kinetics, *Anal. Chem.*, **37**, 1351-1355(1965).

18- Nicholson R.S. and Shain I., Theory of Stationary Electrode Polarography Single Scan and Cyclic Methods Applied to Reversible, Irreversible, and Kinetic Systems, *Anal. Chem.*, **36**, 706-723(1964).

19- Mabbott G.A., An Introduction to Cyclic Voltametry, *J. Chem. Educ.*, **60**, 697-702(1983).

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20- Zanello, P., Inorganic Electrochemistry Theory, Practice and Application, The Royal Society of Chemistry, London, (2003).

21- Conway B.E., electrolyte solutions; solvation and structural aspects, *Ann. Rev. Phys. Chem.*, **17**, 481-528(1966).

22- El-Khouly A.A., Gomaa E.A. and Abou El-leef S., Conductivity and solubility studies of (Cd-Kryptofix-22) complexes in various hydroorganic solvents, *Bull. Electrochem.*, **19**, 153-164(2003).

23- Gomaa E.A., Abou Elleef E.M. and Mahmoud M.H., Gibbs free energies for solvation of KClO$_3$ in mixed DMF-H$_2$O solvents at 301.15K, 2013, *Eur. Chem. Bull.*, **2**, 732-735(2013).

24- El-Defrawy M.M., Gomaa E.A., Salem S.E. and Abdel Razek, F.M., *Prog. Chem. Biochem. Res.*, **1**, 11-18(2018).

25- Gomaa E.A. and Salem S.E., Cyclic voltametry study of copper chloride salt with ceftazidime antibiotic, *Am. Assoc. Sci. Technol. Commun.*, **3**, 169-176(2016).

26- Gomaa E.A., Solubility and solvation parameters of barium sulphate in mixed ethanol-water mixtures at 301.15K, *Int. J. Mater. Chem.*, **2**, 16-18(2012).

27- Gomaa, E.A., Molal solubility, dissociation and solvation parameters for saturated benzoic acid solutions in various solvents at 298.15 K., *Phy. Chem. Liq.*, **50**, 279-283(2012).

28- Gomaa E.A., The microscopic free energies of solvation for K$^+$, Rb$^+$ and Cs$^+$ in mixed methanol (MeOH)-dimethylformamide(DMFA) solvents at 298.15K, *Int. J. Theor. Math. Phys.*, **2**, 1-4(2012).

29- Gomaa E.A., Thermodynamic and polarization parameters of dibenzo-18-crown-6 in mixed methanol water solvents, *Am. J. Polymer Sci.*, **2**, 5-38(2012).

30- Gomaa E.A., Mahmoud M.H., Mousa M.G. and El-Dahshan E.M., Cyclic voltametery for the interaction between bismuth nitrate and methyl red in potassium nitrate solutions, *Chem. Methodol.*, **3**, 1-11(2018).

31- Gomaa E.A., Zaky R.R., Negm A.A. and Rashad R.T., Cyclic voltametry of nano cadmium chloride (NCCl) with glycine using glassy carbon electrode, *Assiut Univ. J. Chem.*, **47**, 21-28(2018).

32- Killa H.M. and Robert H., Effects of low ligand concentration on forms and potentials of linear scan and cyclic voltamograms for the reduction of complexes, *J. Electroanal. Chem. and Interf, Electrochem.*, 1984, **175**, 223-228(1984).

33- Killa H.M. and Zaky M., Studies on Mixed Complexes of Cd(II) With Trimethylenediamine and Succinate Using Differential Pulse Polarography, *Anal. Lett.*, 1985, **18**, 167-179(1985).

34- Gomaa E.A., Mousa M.A., and El-Khouly A.A., Association, dissociation and hydrogen bonding of salicylic acid in water-N, N-dimethylformamide mixtures, *Thermochim. Acta*, **89**, 133-139(1985).

35- Long, L.H. and well, B.H., Antioxidant and prooxidant abilities of foods and beverages, *Methods Enzymol.*, **335**, 181-190(2001).

36- Roy S., Sadhukhan R., Ghosh, U. and Das T.K., Interaction studies between biosynthesized silver nanoparticle with calf thymus DNA and cytotoxicity of silver nanoparticles, *Spectrochim. Acta A*, **142**, 176-185(2015).

37- Mauceri H.J., Hanna N.N., Beckett M.A., Gorski D.H., Staba M.J., Stellato K.A., Bigelow K., Heimann R., Gately S., Dhanabal M., Soff, M.G., Sukhatme V.P., Kufe D.W. and Weichselbaum R.R., Combined Effects of Angiostatin and Ionizing Radiation in Antitumaur Therapy, *Nature*, **394,** 287-291(1998).

38- Killa H.M., Abd El Wahed M.G. and Dessouki H.A., A study of mixed ligand complexes using differential pulse polarography, *Polyhedron.*, **4**, 1219-1222(1985).

الملخص العربي

تم دراسة سلوك الأكسدة والاختزال في كبريتات النحاس في غياب وجود الأموكسيسيلين عند درجتي حرارة مختلفتين (288.15 و 298.15) ك. وتم دراسة سلوك الأكسدة والاختزال في 0.1مولاري من حمض الهيدروكلوريك باستخدام الفولتامترية الدائرية وتحت جهد يتراوح من (1.5 إلى -1.5) فولت بتركيزصغير من أيونات النحاس. تم الحصول على قمه للاختزال واحدة وأكسدة واحدة فقط في نتائجنا مما يشير إلى اختزال أيونات النحاس ثنائية التكافؤ إلى المعدن النحاسي ذي التكافؤ الصفري. تم تقييم جميع نتائج الفولتميترية الدائرية في اثنين من درجات الحرارة المستخدمة وتم المقارنه بين قيمهم في وجود وغياب أموكسيسيلين. أيضا تم حساب معلمات الديناميكية الحرارية لتفاعل أيونات النحاس مع أموكسيسيلين كثبات ثابت ، والطاقه الحره لغيبس وامحتوي الحراري والإنتروبيا. تشير المعلمات الديناميكية الحرارية إلى أن التفاعل بين أيونات النحاس والأموكسيسيلين تفاعل الكيميائي (القيم العاليه السالبة للطاقه الحره) ، التفاعل تلقائي (قيم موجبه للإنتروبيا) والتفاعل الكيميائي ماص للحرارة. تشير قيم طاقة التفاعل بين الأموكسيسيلين و البروتين اثبت ان الأموكسيسيلين له نشاط مضاد للسرطان لعلاج سرطان الكبد.