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Full Paper

Cyclic Voltammetry of Normal (Bulk) and Nanosized Copper Sulfate (NSCS) with Doxorubicin Using Glassy Carbon Electrode

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Abstract

The cyclic voltammetry of both normalsized and nanosized Copper sulfate (NSCS), fluids were studied using 0.1M KCl and glassy carbon working electrode. The redox behavior for both normal and nanosized copper sulfate (NSCS) was studied voltammetrically in presence and absence of Doxorubicin (DUR) using three electrode system, silver- silver chloride , platinum and glassy carbon electrodes .Various scan rates were studied for the redox behaviors for bulk(normal) and nanosized copper sulfate (NSCS) fluids alone or in presence of Doxorubicin(DR). Stability constants for the interaction of cupric ions with Doxorubicin (DR) were evaluated. All mechanisms were discussed.

Keywords: Cyclic voltammetry, normal & nanosized copper sulfate (NSCS), glassy carbon electrode, Doxorubicin.

1. Introduction

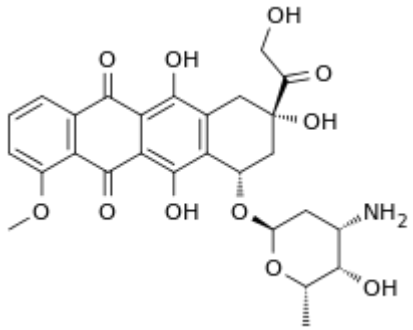
Drug doxorubicin (DUR) is used to treat certain types of bladder, lung, stomach ,breast and ovarian cancer; Hodgkin's lymphoma (H.L) and (N .H.L) Non-Hodgkin's lymphoma (cancer begins in the cells); and some types of L.K. Leukemia,. (cancer of the white blood cells), including acute lymphoblastic Leukemia (LK) and acute Myeloid Leukemia (ML). Doxorubicin (DUR) is used in combination with some other drugs for treating certain types of thyroid cancer (TCA), certain types of soft tissue or bone sarcomas (cancer that forms in bones and muscles(TBS). It is used to treat ,N.B, neuroblastoma (a cancer that begins in nerve cells and occurs in some children) and Wilms' tumor (a type of kidney cancer ,K.C., that occurs in children). Doxorubicin (DUR) is in a class of medications called anthracyclines (AC). It works by decreasing the cancer cells growth in the bodies [1, 2].

2. Experimental

2.1 Materials

Copper sulfate($CuSO_4$ .5 H_2O) and KCl provided from Al Nasr Chemicals Co., while nanosized $CuSO_4$ (NSCS)was prepared by ball milling using Retsch MM 2000 swing mill with 10 cm^3 stainless double walled tubes. Two balls stainless steel with diameters of 12 mm are used. Ball milling was performed at 20225Hz and shaking was done at room temperature 25^o for one hour, the temperature did not rise above room temperature.

2.2 Drug



Systematic (IUPAC) name

(7*S*,9*S*)-7-[(2*R*,4*S*,5*S*,6*S*)-4-amino-5-hydroxy-6-methyloxan-2-yl]oxy-6,9,11-trihydroxy-9-(2-hydroxyacetyl)-4-methoxy-8,10-dihydro-7*H*-tetracene-5,12-dione

Fig.1 Structure of Doxorubicin

2.3. Instrument

DY2000, Multichannel Potentiostat was used for voltammetry measurement. Voltammetry analyzer using three electrodes (TE) electrochemical cell to perform cyclic voltammetry (CV). Measurements were done by using glassy carbon readymade in our laboratory from pure carbon peace, polished with aluminum oxide in wool peace, as working electrode (WE) with geometrical area of 2.011 cm^2, platinum wire electrode as counter electrode and Ag/AgCl (saturated) standard electrode.

2.4. Cyclic voltammetry measurements (CV)

Cyclic voltammetry is one common technique used to study the electrochemical systems which obtained in undivided glass cell of 30 ml solution with three electrodes mentioned above. Cyclic voltammetry experiments were carried out using different concentrations of bulk (normal) and nanosized $CuSO_4$ (NSCS) solutions in water at 19.3 ^{o}C.KCl (0.1M) as transporting medium was used at different scan rates (0.1 ,0.05 , 0.02 and 0.01 V/sec). After each run, the working electrode was polished well with aluminum oxide (α alumina) , rinsed with distilled water to obtain reproducible results. The solutions nitrogen gas were passed for (10) minutes before each experiment.

3. Results and discussion

3.1 TEM Images for nano $CuSO_4$

The photogram from TEM transmission electron microscope is presented for nanosized $CuSO_4$ (NSCS) salt . TEM images are sensitive so, it was used to investigate the size and shape of the nano $CuSO_4$, (NSCS) fluids which found to be spherical in the range 11.1-24.3 nm Fig. (2).

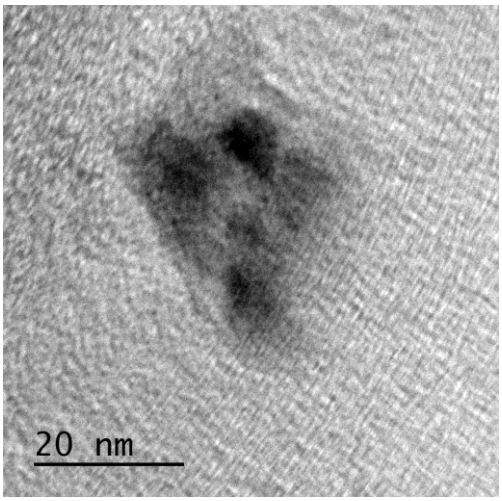


Fig. 2. TEM image of nanosized $CuSO_4$ (NSCS)

3.2. Cyclic voltammetry analysis

The interaction of bulk (normal) and Nanosized (NSCS) $CuSO_4$ with Doxorubicin (DUR) had been studied using cyclic voltammetry technique in the potential range (+1.5 to -1.5) V at different scan rates in water at 292.25K using KCl (0.1M) as conducting medium and glassy carbon as a working electrode. The study is valuable for evaluating different thermodynamic properties [3-18].

Mechanism of redox reaction:

The copper ions used show two oxidation peaks at +0.1 and +0.2 V mV and two reduction peaks at 0 and -0.5 V.These two peaks corresponding to the oxidation of copper zero valent to +1 and then the oxidation of copper +1 to divalent cupric ions [19]. The vice verse for the reduction peaks is the reduction of cupric to copper monovalent (cuprous) then the reduction of monovalent copper to zero valent one , copper metal involving two electrons in this media versus silver / silver chloride electrode as follows :

$$Cu^{+2}(aq.) + e^{-} = Cu^{+} \quad (1)$$

$$Cu^{+} + e^{-} = Cu^{o} \quad (2)$$

Adding Drug, Doxorubicin (DUR) to the copper normal and nanosized , NSCS salts both peak heights were decreased indicating the reaction between them forming complex [20-35].Also it is shown that the disportionation of the monovalent copper to divalent and zero valent ones happen [19] due to its unstable character in this medium was observed.

$$2\,Cu^{+}(aq.) = Cu^{+2} + Cu^{o} \quad (3)$$

Different scan rates were discussed for the redox reaction for 1 mM bulk (normal) and nanosized copper sulphate (NSCS) alone were done in water. Straight lines were obtained by drawing the relation between Ip,a & Ip,c against scan rate . From this relation the diffusion coefficient was obtained and found to be in the range from 0.48 to 0.5, indicating the diffusion control of the reaction .Different additions of Doxorubicin (DUR) from 1mm to 3 mM were done (Fig.5) and different scan presented by using 1 mm Cu^{2++} + 3 mM Doxorubicin (DUR).The analysis of the complex formation voltamogram was done and the diffusion coefficients were found to be within the range of diffusion reactions.

The total stability constants for the interaction of nano $CuSO_4$ with Doxorubicin (DUR) were calculated by applying DeFord-Hume equation [34-41] and their data are given in Table (1) .From the stability constants obtained we change their values into Gibbs free energies of complex parameters [20-43] and the obtained value are listed in Table (1) also .The Gibbs free energy of interaction for both bulk and nanosized (NSCS) $CuSO_4$ fluids +

Doxorubicin (DUR) given in Table (1), it was found to be in the range of -8.1 to -31.937 kJ/mole indicating specific complex formed.

From difference of peak potential for copper cyclicvolatmograms in presence and absence of Doxorubicn (DUR),it is observed that the complex is formed due to both anodic and cathodic peak decrease and potential shifts their position to more lower values. Due to precipitating the complex during the process, no peak is appeared. A stability constant is a measure of the strength of the interaction between the reagents that come together to form complex. The stability constant (β_{MX}) for bulk (normal) and nanosized $CuSO_4$complexes in 0.1 M KCl for oxidation peaks , current 1mA and scan rate 0.1V/S in water was calculated [18-34] by applying equation (4). The Gibbs free energy of interaction for bulk (normal) and nanosized $CuSO_4$ with Doxorubicin (DUR) were calculated [34-41] from stability constant (β_{MX}) using equation (5).

Ill developed waves were observed on using bulk (normal) and nanosized (NSCS) $CuSO_4$ indicating less solvation behaviours in case of using nano salt and the reduction , oxidation processes proceed through one step only as shown in Fig.(4).

$$(E_p)_M + (E_P)_C = 2.303\frac{RT}{nF} Log\beta_{MX} + 2.303\frac{RT}{nF} LogC_X \quad (4)$$

Where $(E_p)_M$ is the peak potential of metal at final adding in absence of ligand, $(E_p)_C$ is the peak potential of metal complex, R is a gas constant (8.314 $J.mol^{-1}.degree^{-1}$), T is the absolute temperature and C_x is the concentration of metal in the presence of ligand.

$$\Delta G = -2.303RTLog\beta_{MX} \quad (5)$$

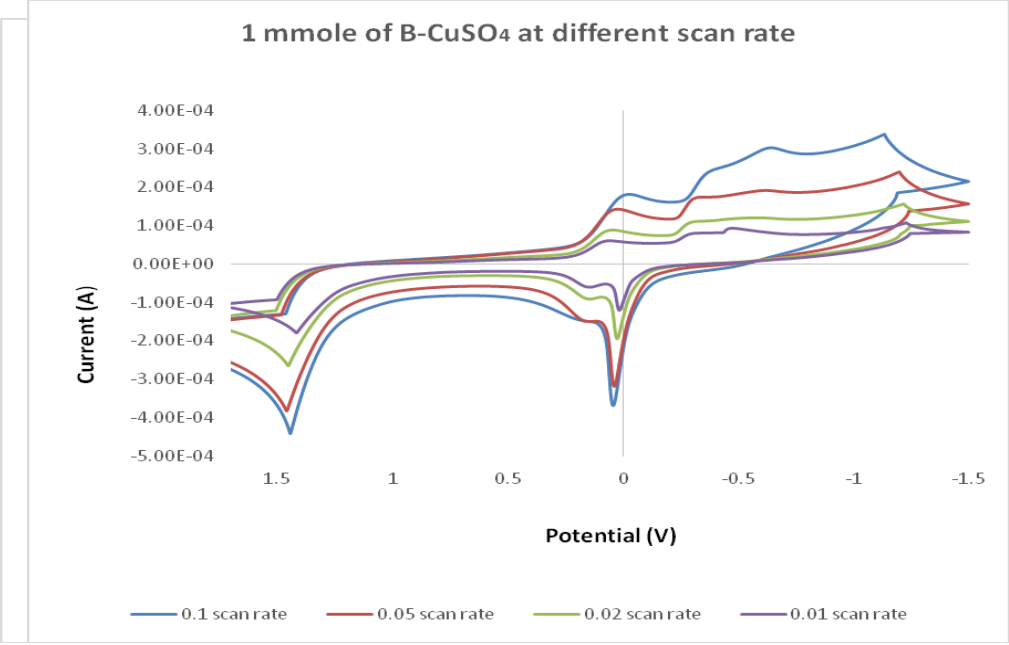


Fig. 3. Effect of different scan rate on the cyclic voltammetry of bulk (normal) $CuSO_4$ in 0.1M KCl solution.

Different scan rates were studied for 1:1 complex formed from the interaction of drug doxorubicin on the voltamogram of both bulk and nano $MnSO_4$ on using KCl as supporting electrode at rates 0.1,0.05,0.02 1nd 0.01 v/s shown in Figs.(5) and (6) indicate the redox processes happened are controlled by diffusion .

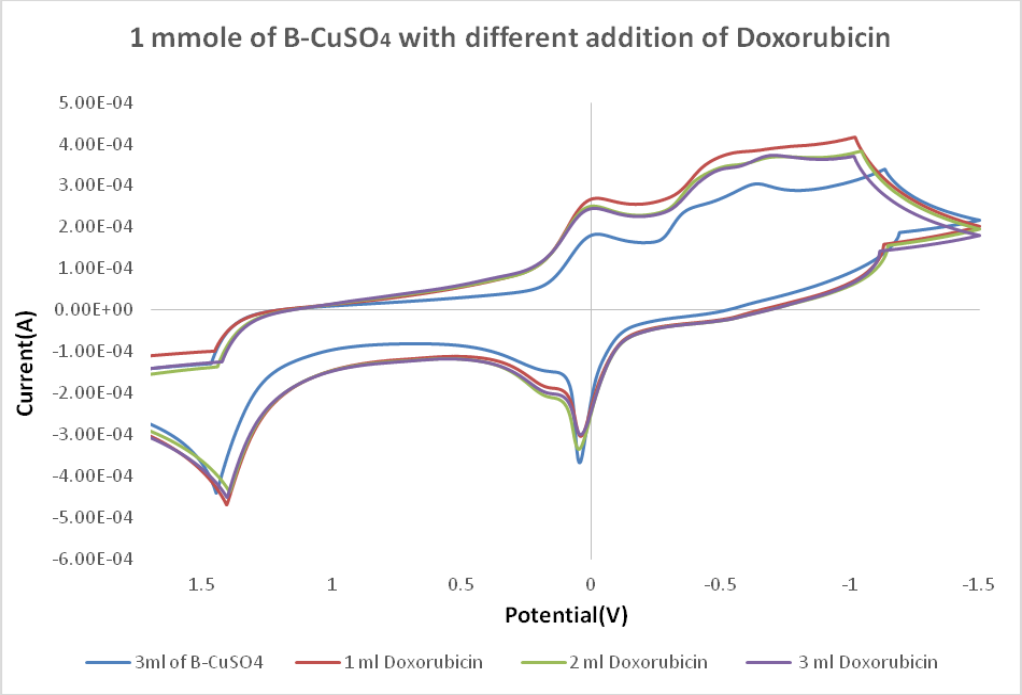


Fig. 4. Effect of different concentration of Doxorubicin (DUR) on Bulk (normal) $CuSO_4$ voltamogram.

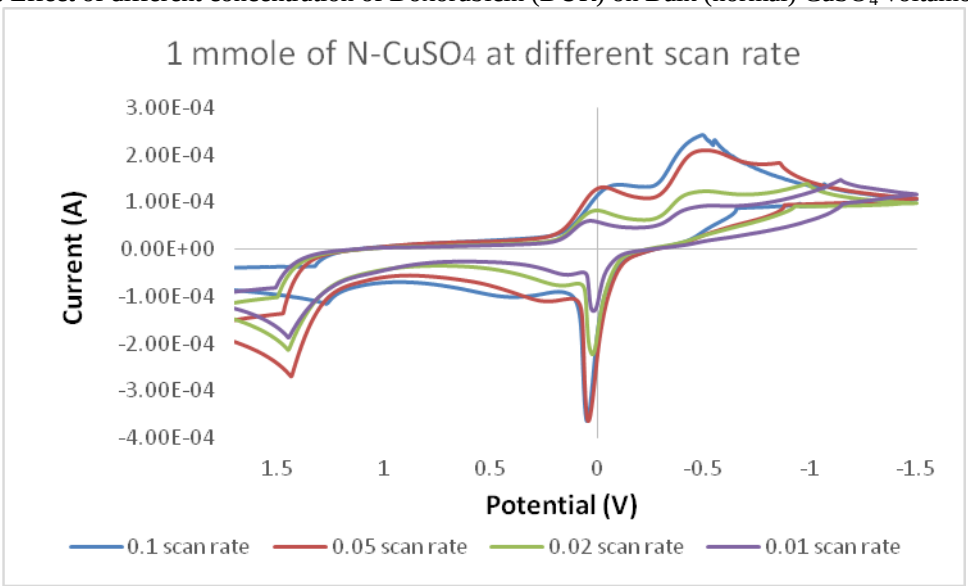


Fig. 5. Effect of different scan rate on the voltamogram of 1 mmole Nanosized CuSO4 (NSCS) .

The analysis of the complexes formed were done and the diffusion coefficients were estimated and found to be within the range of diffusion reactions.

The ovelall stability and complexing constants for the interaction of both bulk and nano CuSO4 with Doxorubicin (DUR) were calculated by applying DeFord-Hume equation [34-37] and their data are given in Table (1) .From the stability constants obtained we change their values into Gibbs free energies of complex parameters [20-41] and the obtained value are listed in Tables (1) and (2).

The total Gibbs free energy of interaction for bulk (normal) and nanosized $CuSO_4$ (NSCS) + Doxorubicin (DUR) given in Tables (1) and (2) were found to be in the range of -8.1 to -31.637 kJ/mole indicating specific complex formed.The parameters given in Tables 1 and 2 are the molar concentration of copper metal salt [M],drug concentration [L],acivity coeffients, $\gamma_{\pm}$,salt peak potential $(E_{p,a})_M$,complex peak potentials $(E_{p,a})_C$,difference in half wave potentials $\Delta E_{1/2}$,number of electrons n, anodic diffusion coeffiecient D_a ,stability constants β_{MX} and Gibbs free energies of complexation ΔG,respectively.

The total stability constants are greater for the interaction of Doxorubicin (DUR) with bulk (normal) $CuSO_4$ than that of nanosized $CuSO_4$ (NSCS) giving greater values for the mean Gibbs free energy of interaction of -26.4164 kJ in case of normal (bulk)-$CuSO_4$ than the mean value of -16.8440 kJ in case of nanosized $CuSO_4$ (NSCS).

Table 1: Solvation parameters for interaction of Doxorubicin (DUR) with bulk (normal) $CuSO_4$ in 0.1M KCl

[M] $*10^3$	[L] $*10^3$	log γ±	γ±	$(E_{p,a})_M$	$E_{p,}$ $(_a)_C$	$I_{p,a}$ $*10^4$	$\Delta E_{1/2}$	n	D_a*10^{12}	β_{MX}	ΔG(kJ -mol^{-1})
1	0.556	0.9508	-0.0219	0.043	0.039	-2.48	0.082	1	2.94	77032.48	-27.4288
1	0.833	0.9597	-0.0179	0.043	0.039	-2.48	0.082	1	2.56	38516.24	-25.7391
1	1	0.9508	-0.0219	0.043	0.039	-2.40	0.082	1	1.51	25677.49	-24.7508
1	2	0.9434	-0.0253	0.043	0.037	-2.30	0.080	1	1.39	17792.4	-23.8565
1	2.5	0.9370	-0.0283	0.043	0.013	-3.33	0.056	2	0.255	50511.92	-26.4001
1	3	0.9311	-0.0310	0.043	0.015	-3.47	0.058	3	0.138	489747.2	-31.9377
1	3.5	0.9258	-0.0335	0.043	0.014	-3.38	0.057	3	0.231	372783	-31.2725
1	4	0.9209	-0.0358	0.043	0.013	-3.28	0.056	2	0.437	31569.95	-25.2544
1	5	0.9163	-0.0380	0.043	0.029	-2.97	0.072	1	6.72	5761.489	-21.1078

Table 2: Solvation parameters for interaction of Doxorubicin (DUR) with Nanosized (NSCS) $CuSO_4$ in 0.1M KCl.

log γ±	γ±	$(E_{p,a})_M$	$(E_{p,a})_C$	$I_{p,a}$ *10^4	$\Delta E_{1/2}$	n	D_a*10^{11}	β_{MX}	ΔG(kJ -mol^{-1})
0.9508	-0.0219	0.049	-0.1	-4.01	-0.051	1	10.8	398.5183	-14.5963
0.9597	-0.0179	0.049	-0.1 2	-3.79	-0.073	1	0.299	83.41528	-10.7839
0.9508	-0.0219	0.049	-0.139	-3.77	-0.09	1	0.246	28.37462	-8.15527
0.9434	-0.0253	0.049	0.024	-4.05	0.073	1	3.17	13486.74	-23.1811
0.9370	-0.0283	0.049	0.022	-3.81	0.071	1	1.33	9968.219	-22.4442
0.9311	-0.0310	0.049	0.021	-3.74	0.07	1	1.33	7984.48	-21.9033

4. Conclusion

From cyclic voltammetry measurements it is noticed that addition of Doxorubicin (DUR) to copper both normal and nanosized ions decreased the amount of deposited copper during the cathodic reaction. The redox mechanism was presented .The stability constant and Gibbs free energy of interaction between both normal (bulk) $CuSO_4$ and Nanosized $CuSO_4$ (NSCS) with (DUR) was estimated.

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