

# Cyclic Voltammetry of Nano Copper Sulfate with Cefepime Using Glassy Carbon Electrode

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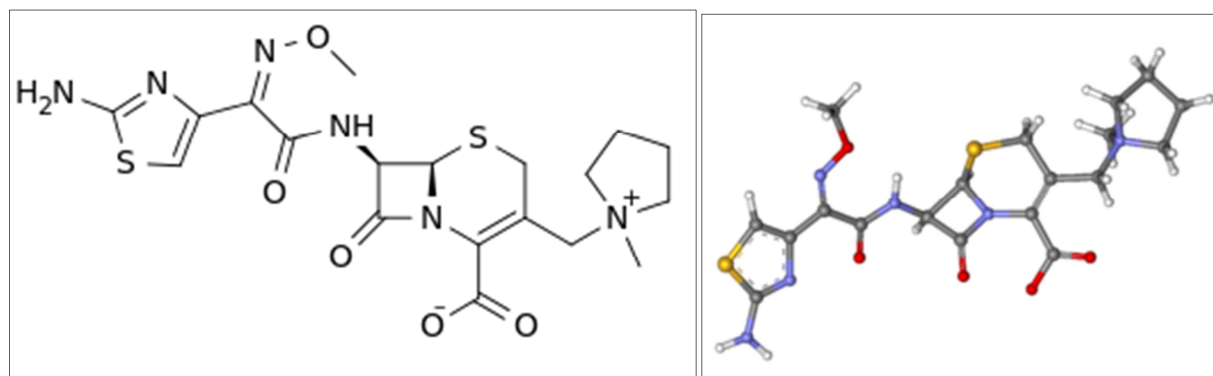
## Keywords

Cyclic Voltammetry, Copper Sulfate, Glassy Carbon Electrode, Cefepime

The nano copper sulfate was prepared by ball milling of normal  $\text{CuSO}_4$ . The redox behavior for nano copper sulfate was studied voltammetrically in presence and absence of Cefepime using glassy carbon electrodes in 0.1 M KCl supporting electrode. Scan rates were studied for the redox behaviors for  $\text{CuSO}_4$  alone or in presence of Cefepime. Stability constants for the interaction of copper ions with Cefepime were evaluated. All mechanisms were discussed.

## Introduction

Cefepime has big spectrum of activity against Gram-positive and Gram-negative bacteria, with greater activity against both types of organism than third-generation agents. This chemical compound, registered with CAS number of 88040-25-9, is a fourth-generation cephalosporin antibiotic. Analysis data was increased in people treated with Cefepime compared with other  $\beta$ -lactam antibiotics. Cefepime is a broad-spectrum cephalosporin antibiotic and used to treat bacteria responsible for causing pneumonia and infections of the skin and urinary tract [1, 2]. Some of these bacteria include *Pseudomonas*, *Escherichia*, and *Streptococcus* species. The following represents MIC susceptibility data for few microorganisms [2 - 10]. Cefepime was developed by Bristol-Myers Squibb and marketed beginning in 1994. It is now available as a generic drug and sold under a variety of trade names worldwide. Cefepime evaluation is valuable for further study. Its structure is shown in Fig. 1 [10].



**Fig. 1.** Cefepime structure, 2D and 3D.

(IUPAC) name: (6R, 7R, Z)-7-(2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetamido)-3-((1-methylpyrrolidinium-1-yl)methyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate was from "GlaxoSmithKline"

## Experimental

### Preparation of Nano Cooper Sulfate Materials

The nano  $\text{CuSO}_4$  material studied in the study was prepared by ball milling technique using a Retsch MM 2000 swing mill with  $10\text{ cm}^3$  stainless steel double walled tube. The copper sulfate ( $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ ) and KCl compounds used in the material preparation were provided from Al Nasr Chemicals Company. In the preparation, in which two balls stainless steel with diameter of 12 mm were used, the ball milling process was performed at 20225Hz and the shaking process was done usually at room temperature for one hour. The temperature was kept under  $30^\circ\text{C}$  during the material preparation.

### Experimental Measurements

DY2000, DY2000EN Multichannel Potentiostat was used for voltammetry measurement Voltammetry analyzer using conventional three - electrode 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 with are of  $0.64\text{ cm}^2$ , platinum wire electrode as counter electrode and Ag/AgCl standard electrode.

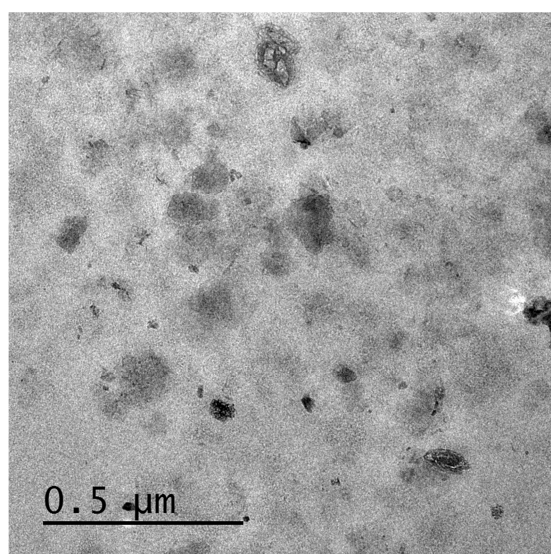
### Cyclic Voltammetry Measurements (CV)

Cyclic voltammetry is the most common technique used to study the electrochemical systems obtained in undivided glass cell of 30 ml solution by utilizing the three electrodes mentioned above. Cyclic voltammetry experiments were carried out using different concentrations of CEF and different nano  $\text{CuSO}_4$  solutions in water at  $19.3^\circ\text{C}$ . KCl (0.1M) as supporting electrolyte was used at different scan rates. After each run, the working electrode was polished with aluminum oxide ( $\alpha$  alumina), rinsed with distilled water to obtain reproducible results. The solutions were purged with purified nitrogen gas for (10) min before each experiment.

## Results and Discussion

### TEM Images for Nano $\text{CuSO}_4$

The photogram from TEM transmission electron microscope is presented for nano  $\text{CuSO}_4$  salt. The image in Fig. 2, which show the crystalline forms of nano  $\text{CuSO}_4$ , indicate that nano  $\text{CuSO}_4$  is either in the form of irregular spheres or in the form of deformed spheres. In this image, boundaries ranging from 20 to 40 nm were observed.



*Fig. 2. Tem image of nano Cu SO<sub>4</sub>.*

## Cyclic Voltammetry Analysis

The interaction of nano  $\text{CuSO}_4$  with Cefepime (CEF) had been studied using cyclic voltammetry technique in the potential range (+1.5 to -1.0) V at different scan rates in water at 292.25K using KCl (0.1M) as supporting 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 0.02 and 0.06 V mV and two reduction peaks at 0 and -0.45 V. These two peaks corresponding to the oxidation of copper zero valent (uncharged) to monovalent ( $\text{Cu}^+$ ) and then the oxidation of copper monovalent ( $\text{Cu}^+$ ) to divalent cupric ions ( $\text{Cu}^{2+}$ ) [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:

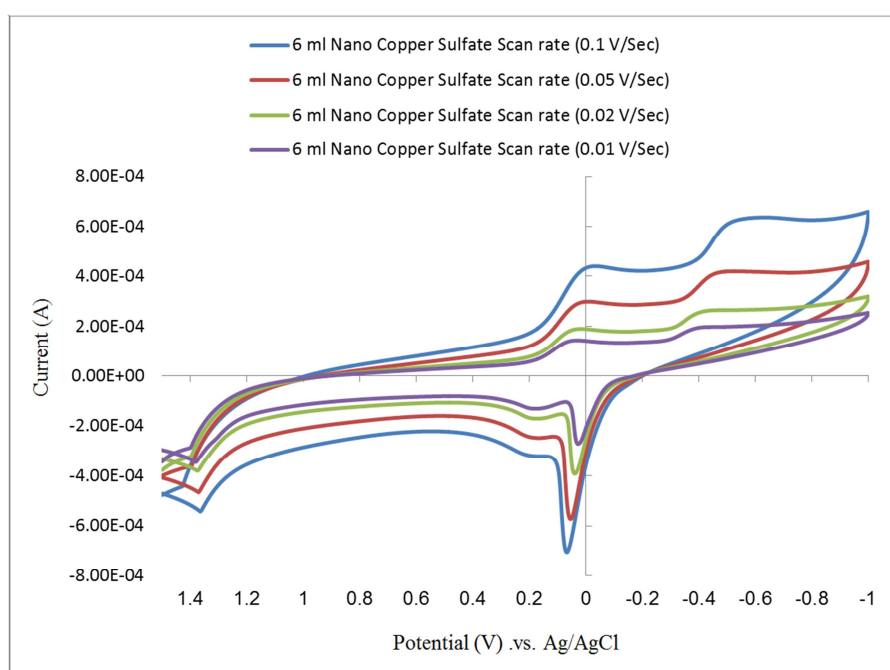


It was determined that adding drug Cefepime caused decreases in both peak heights, which indicate the reaction between the cooper nano salt and CFE [20-35]. Also, it was shown that the disproportionation of the monovalent copper to divalent and zero valent ones occurred as a result of its unstable character in this medium [19]; in the measurements only one reduction peak at -0.7 V was observed.



Different scan rates were discussed for the redox reaction for 2 mM nano copper sulphate alone were done in water and the obtained results are shown in Fig. 3. Straight lines were obtained by drawing the relation between  $I_{p,a}$  &  $I_{p,c}$  against scan rate Fig. 4. From this relation the diffusion coefficient was obtained and found to be in the range from 0.47 to 0.5, indicating the diffusion control of the reaction. Different additions of Cefepime from 1mm to 6 mM were done (Fig. 5) and different scan presented by using 2 mM  $\text{Cu}^{2+}$  + 6mM Cefepime. The analysis of the complex formation voltamogram was done and the diffusion coefficients were estimated and found to be within the range of diffusion reactions.

The total stability constants for the interaction of nano  $\text{CuSO}_4$  with Cefepime were calculated by applying DeFord-Hume equation [34-37]. These calculation data together with the Gibbs free energies obtained for the complex formation of  $\text{CuSO}_4$  and Cefepime [20-49] have been presented in Table 1. The Gibbs free energy of interaction for  $\text{CuSO}_4$  + Cefepime given in Table 1 was found to be in the range of 26 to 29 kJ/mole indicating specific complex formed.



**Fig. 3.** Effect of different scan rate for nano  $\text{CuSO}_4$  at Concentration 2 mM (6 ml from the stock solution). The scan rates were maintained at 0.1, 0.05, 0.02, 0.01 (V/Sec), Sens (A/V) =  $1 \times 10^{-3}$ , initial E (V) = 1.5, High E (V) = 1.5 and Low E (V) = -1.

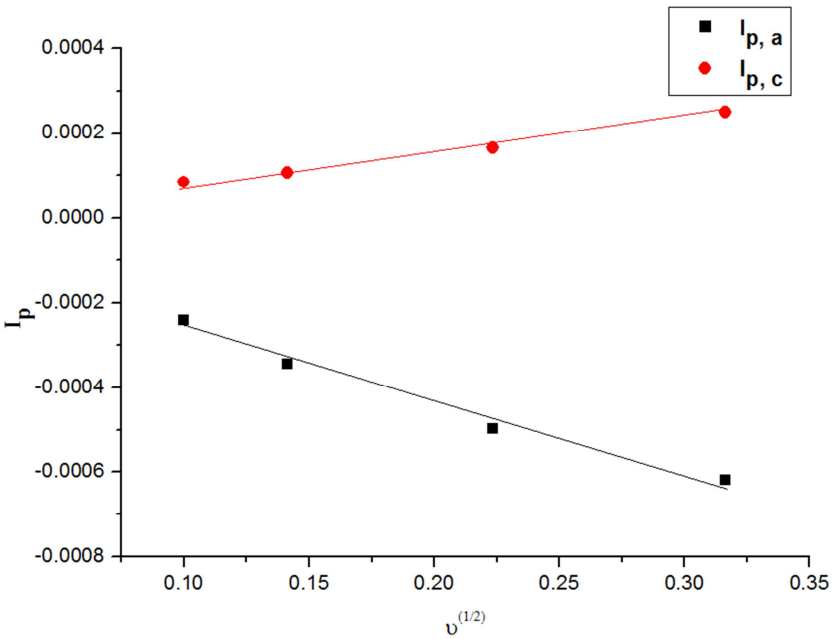


Fig. 4. The relation between  $I_{p,c}$ ,  $I_{p,a}$  and  $v^{1/2}$  for 2mM of  $\text{CuSO}_4$  in 30 ml  $\text{KCl}$  (0.1 M).

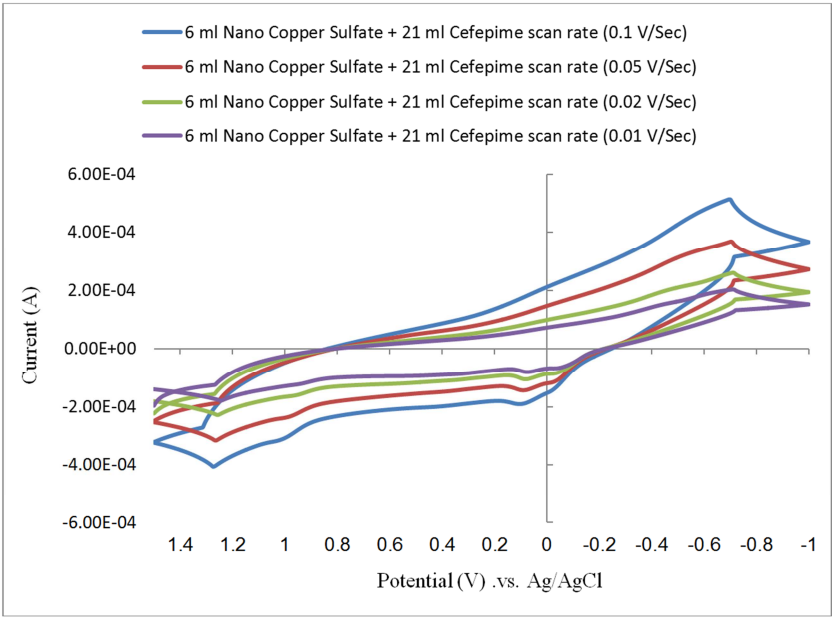


Fig. 5. Effect of different scan rate for nano  $\text{CuSO}_4$  ( $2.10^{-3}$ , 2 mM = 6 ml of stock solution added) with Cefepime ( $6.10^{-3}$ , 6 mM). The scan rates were maintained at 0.1, 0.05, 0.02, 0.01 (V/Sec), Sens (A/V) =  $1 \times 10^{-3}$ , initial E (V) = 1.5, High E (V) = 1.5 and Low E (V) = -1.

Table 1. Analysis parameters, total stability constants and Gibbs free energy of complex formation for the interaction of Cefepime with nano  $\text{CuSO}_4$  in water at 19.3°C.

[M] *10 <sup>3</sup>	[L] *10 <sup>3</sup>	log $\gamma_{\pm}$	$\gamma_{\pm}$	( $E_{p,a}$ ) <sub>M</sub>	( $E_{p,a}$ ) <sub>C</sub>	$I_{p,a}$ *10 <sup>4</sup>	$\Delta E_{1/2}$	n	$D_c$	$\beta_{MX}$	$\Delta G(\text{kJ mol}^{-1})$ -
2	0.556	-0.01633	0.9631	0.067	0.052	-7.94	0.119	1	2.78E-11	220589	-29.3796
2	0.833	-0.02001	0.9549	0.067	0.057	-6.76	0.124	0	4.89E-11	179985	-28.8938
2	1	-0.02191	0.9508	0.067	0.052	-5.98	0.119	0	5.23E-11	122549	-27.9761
2	2	-0.03099	0.9311	0.067	0.058	-5.19	0.125	1	2.19E-12	78086	-26.8999
2	2.5	-0.03503	0.9225	0.067	0.072	-4.62	0.139	1	3.32E-12	107598	-27.6654
2	3	-0.03796	0.9163	0.067	0.08	-4.4	0.147	1	4.12E-12	126636	-28.0544
2	3.5	-0.04132	0.9092	0.067	0.087	-4.26	0.154	1	4.97E-12	141779	-28.3241
2	4	-0.04383	0.904	0.067	0.092	-4.09	0.159	1	5.42E-12	154243	-28.5253
2	5	-0.049	0.8933	0.067	0.098	-3.91	0.165	1	6.00E-12	157249	-28.5714
2	5.8	-0.05293	0.8853	0.067	0.105	-3.86	0.172	1	7.17E-12	178848	-28.8787
2	6	-0.05368	0.8837	0.067	0.115	-3	0.172	1	5.70E-12	260458	-29.7763

## Conclusion

From cyclic voltammetry measurements it is worth noticing that addition of Cefepime (CEF) to nano Cu ions not only decreased the amount of deposited Cu during the cathodic scan. The redox mechanism was presented. Nano copper sulfate ions show two oxidation peaks alone in 0.1 M supporting electrolyte at 0.02 and 0.06 V mV and two reduction peaks at 0 and -0.45 V. These two peaks corresponding to the oxidation of copper zero valent to monovalent and then the oxidation of copper monovalent to divalent cupric ions. 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. Adding Cefepime (CEF) to the copper nano salt both peak heights were decreased indicating the reaction between them forming complexes. Also it is observed that the disproportionation of the monovalent copper to divalent and zero valent ones happen and only one reduction peak at -0.7 V was observed. The stability constant and Gibbs free energy of interaction between Cu and (CEF) was estimated having mean values of -28.44 kJ for total Gibbs free energies of complexation. ■

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