



## Electrochemical studies of $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$ and its interactions with DNA

M. Zidan<sup>a\*</sup>, A. Jamil<sup>a</sup>, C.W. Yaw<sup>b</sup>

<sup>a</sup> Chemistry Department, Faculty of Science, University of Sabha, Libya.

<sup>b</sup> Department of Chemistry, Faculty of Science, Universiti Putra Malaysia, 43400 UPM, Serdang, Selangor D.E., Malaysia.

Received 17 June 2015; accepted 1 September 2015

### Keywords

copper complex;  
 $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$ ;  
electrochemistry;  
DNA.

**Abstract** Electrochemical characterization of copper complex,  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  (sar = sarcosine), has been carried out using cyclic voltammetry (CV), chronocoulometry (CC), and chronoamperometry (CA). The Cu(II) complex was found to be electroactive as shown by its well defined redox wave forms during cyclic voltammetry at room temperature. The effects of scan rate and pH have been examined by cyclic voltammetry technique. A linear plot of  $\log I$  versus  $\log$  scan rate with slope of 0.6 was obtained indicating the presence of a diffusion controlled process. The pH study showed that the original pH which is 4.2 was an optimum condition for current enhancement. The results of double potential steps chronocoulometric studies showed the presence of surface charge to be in the order of  $10^{-5} \text{ C/cm}^2$  and charge density to be  $4.314 \times 10^{-4} \text{ cm}^2/\text{sec}$ . The monotonic rising current was observed in chronoamperometric studies, providing another evidence of the diffusion controlled process. The interaction between copper complex and DNA was investigated using CV with the scan rate of 5 mV/s. The results revealed that there is a slight positive shift of 9 mV in peak potential and a significant decrease in redox peak currents of  $\text{Cu}^{2+}$  complex in the presence of DNA. These showed that the interaction between them is *via* intercalation process.

\* Corresponding Author: Mohammed Zidan.

E-mail: [zidanupm@gmail.com](mailto:zidanupm@gmail.com)

### Introduction

$[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  is blue in color and has an octahedral geometry. The Cu ion is coordinated through nitrogen atom, carbonyl oxygen atom and water molecules or the carbonyl oxygen atoms of neighbouring molecules. DNA is called as "the blue print of life" because it contains the code or instruction for building and organism and ensuring that organism function correctly. It is in double

helix formed which base pairs, Adenine(A)-Thymine(T) and Cytosine(C)-Guanine(G) attached to a sugar-phosphate backbone. The interaction between transition metal complexes with DNA has been an active field of research as an alternative way to kill cancer because of special properties of metal that attributes important for medical applications (Hong *et al.*, 2011 and Marzano *et al.*, 2009). Electrochemical studies on interaction between this copper complex with DNA have been

done using various electrochemical techniques. According to our previous researches (Yaw *et al.*, 2012; Zidan *et al.*, 2011; Ghamarian *et al.*, 2013 and Tan, *et al.*, 2008), electrochemistry is a powerful tool. It is well known that electrochemical methods are simple and inexpensive, in which analytical techniques require small amount of sample (Breithaupt *et al.*, 2001). Electrochemical devices are easy to miniaturize, simple and inexpensive compared with optical instrumentation (Mirmoghtadaie *et al.*, 2013). Indeed the use of electrochemical techniques instead of fluorescence allows for simpler and smaller detectors (Tansil *et al.*, 2005). DNA is a genetic material that acts as a form of memory storage for genetic information (Sujatha *et al.*, 2012). Barton and co-workers have studied extensively the interaction of DNA with various types of coordination complexes including  $Ru^{3+}$ ,  $Ir^{3+}$  and  $Pt^{2+}$  (Murphy *et al.*, 2009). The interaction of a

variety of transition metal complexes of 1,10-phenanthroline or polypyridine ligand with DNA has been investigated (Sasmal *et al.*, 2010; Dixit *et al.*, 2011 and Chen *et al.*, 2011). The ability of many transition metal complexes to interact with and cleave DNA has been extensively studied for their nuclease-like activity in recent years. Copper is a biologically important metal found in a number of enzymes such as superoxide dismutase, tyrosinase, B-hydroxylases, monoaminoxidase, and ascorbic acid oxidase (Pereira *et al.*, 2007; Wang *et al.*, 2012 and Frieden *et al.*, 1965).

### Experimental

Cu(II) phenanthroline *c*-methylaniline nitrate,  $[Cu(sar)(c-mala)]NO_3$ , is synthesized (Skladanowski *et al.*, 2001) and its structure is shown below:

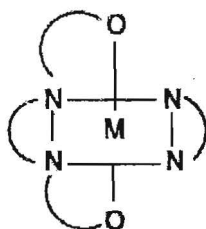


Fig. 1: Molecular structure of metal complex

Experiments of electrochemical were carried out using a BAS (Bioanalytical Systems, West Lafayette, IN, USA): CV-50W electrochemical workstation.  $[Cu(phen)(c-mala)]NO_3$  (1 mM) is characterized by electrochemical techniques using 0.1M of potassium dihydrogen orthophosphate ( $KH_2PO_4$ ) as supporting electrolyte. Cu(II) complex is dissolved into the supporting electrolyte and place into an electrochemical cell. To remove the dissolved oxygen from the solution the cell was purged with nitrogen gas for 10 minutes. A conventional three electrode potentiostated system was used with 3 mm diameter glassy carbon (GC) as working electrode, Ag/AgCl (3 M NaCl) as reference electrode, and 1 mm diameter platinum wire as counter electrode. The three electrodes were immersed into the solution at temperature (25

$\pm 2$  °C). A rotating (carbon) disk electrode (RDE) and model: BAS-100A voltammetric workstation was used for hydrodynamic voltammetry.

### Results

#### Cyclic voltammetry (CV) of $[Cu(phen)(c-mala)].NO_3$

Cyclic voltammogram of the Cu(II) complex,  $[Cu(sar)_2].2H_2O$  (Figure 1), shows a a quasi-reversible redox reaction involving the Cu(II)/Cu(0) couple with presence of DNA caused suppression of current and positive shift about 9 mV. This indicates that the Cu (II) complex molecule binds to DNA via intercalation.

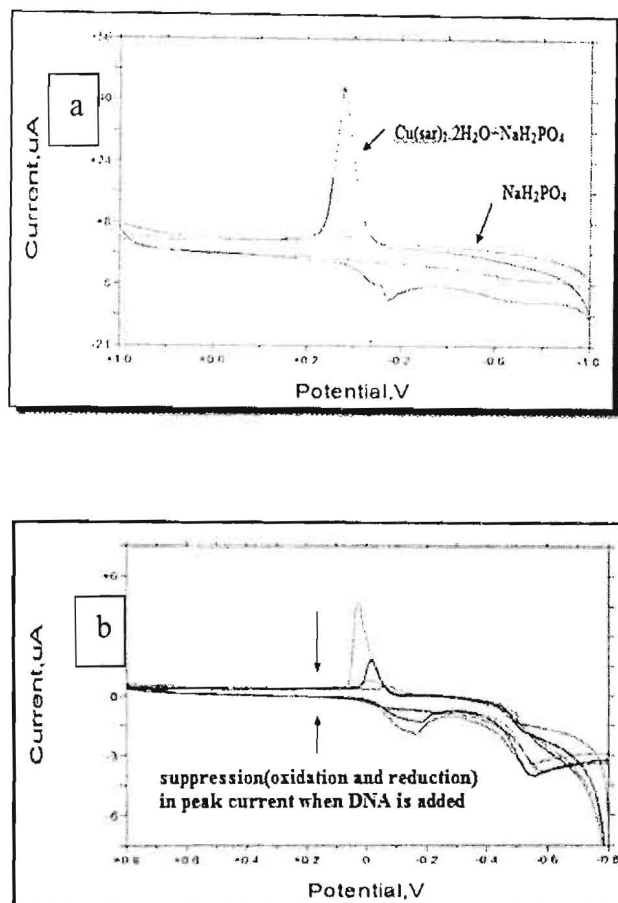


Fig. 2: CV curve of (a) 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  in 0.1M  $\text{NaH}_2\text{PO}_4$  and (b) 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  in 0.1M  $\text{NaH}_2\text{PO}_4$  solution with  $1.475 \times 10^{-12}$  M to  $4.425 \times 10^{-12}$  M DNA at pH 4.2, respectively.

### Effect of varying scan rate

Fig. 3 shows the graph of  $\log I_p$  vs  $\log v$  for (a) 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  in 0.1M  $\text{NaH}_2\text{PO}_4$  and (b) 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  in 0.1M  $\text{NaH}_2\text{PO}_4$  solution with  $1.475 \times 10^{-12}$  M DNA at pH 4.2, respectively. Peak current increased as scan rate increased. Slopes obtained for (a)  $I_{pa}$  is 0.6 and  $I_{pc}$  is 0.2 (b)  $I_{pa}$  is 0.3 and  $I_{pc}$  is 0.6. These indicate that for both reactions, the diffusion controlled and surface process had to be considered as the values are between 0.1-0.6.  $\log I$  versus  $\log v$  plot (Fig. 4a) is plotted and one linear graph

was obtained. Only one linear graph has plotted and it has correlation value of at least 0.95. the equation of the linear graph is;  $y = 0.574x + 6.543$  (oxidation)  
 $R^2 = 0.957$

According to theory, current is dependent on scan rate by a power of half if the current obtained diffusion controlled. Since the scan rate study of copper(II) complex provide 0.53 (oxidation) of power dependent of current on scan rate, diffusion controlled process at complex surface process probably it is a nucleation and growth controlled process.

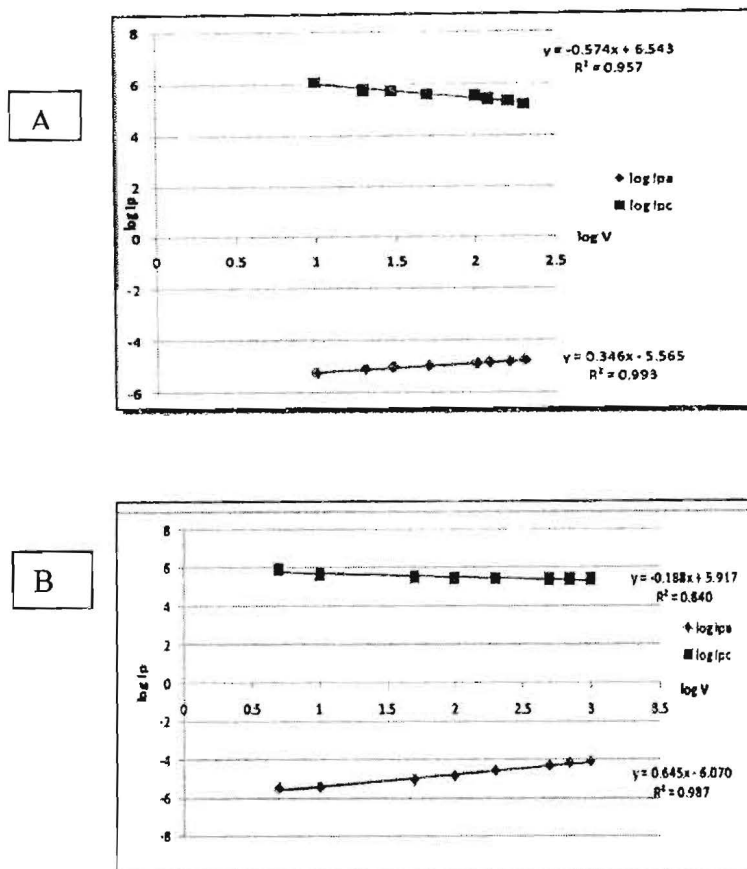


Fig. 3: Relation between  $\log I_p$  vs  $\log v$  for (a) 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  in 0.1M  $\text{NaH}_2\text{PO}_4$  and (b) 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  in 0.1 M  $\text{NaH}_2\text{PO}_4$  solution with  $1.475 \times 10^{-12}$  M DNA at pH 4.2, respectively.

#### Effect of varying pH

Fig.4 shows the graph of  $\log I_p$  vs  $\log \text{pH}$  for 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  in 0.1M  $\text{NaH}_2\text{PO}_4$ . Peak current increased at acidic medium then

decreased gradually as pH increases due to the precipitation process. Maximum current was observed at pH 4.2 which is the original pH. This pH was also used for the interactions of Cu(II) complex with DNA

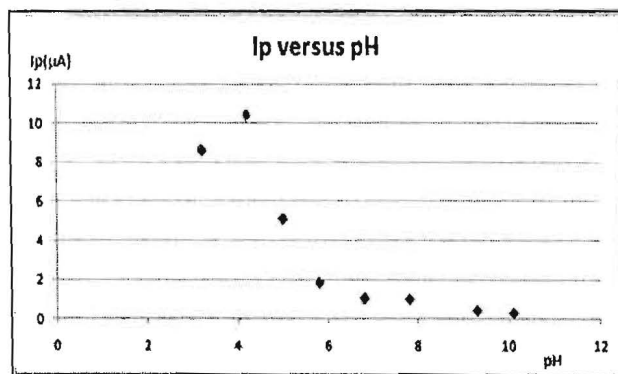


Fig. 4: shows the graph of  $\log I_p$  vs  $\log \text{pH}$  for 0.02 mM  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  solution with glassy carbon electrode as working electrode and 0.1 M  $\text{KH}_2\text{PO}_4$  as supporting electrolyte at 26 °C.

### Chronocoulometry (CA) and chronocoulometry (CC)

Amount of surface charges and diffusion coefficient,  $D$  of the reaction were determined

Charges decrease due to the interaction of  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  complex with DNA as less amount of  $\text{Cu}^{2+}$  complex undergoing electrolysis as shown in Table 1.

**Table 1:** Relation between the surface charge and diffusion coefficient.

Complex	Surface Charges (C/cm <sup>2</sup> )	Diffusion Coefficient, $D$ (cm <sup>2</sup> /sec)
$[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$	$2.92 \times 10^{-5}$	$1.29 \times 10^{-5}$
$[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O} + \text{DNA}$	$8.96 \times 10^{-6}$	$2.37 \times 10^{-6}$

### Conclusion

$[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  complex is successfully studied and characterized using electrochemical measurements. Evident of interaction with DNA can be seen in the compression of peak current and shifting of peak potential. The interaction is optimum at pH 4.2 since the suppression of current is very significant at this condition. Studies show that this complex interacts with DNA through intercalation since peak potential is 9 mV positively shifted. The diffusion coefficient,  $D$  is  $1.29 \times 10^{-5}$  cm<sup>2</sup>/sec and in the presence of DNA,  $D$  is  $2.37 \times 10^{-6}$  cm<sup>2</sup>/sec due to size effect.

### Aknowledgement

The authors wish to thank Universiti Putra Malaysia for providing research facility and financial support for the accomplishment of this work.

### References

- Breithaupt, D.E., Determination of folic acid by ion-pair RP-HPLC in vitamin-fortified fruit juices after solid-phase extraction. *Food Chemistry*, (2001), 74(4), 521-525.
- Chen, F.J., et al., Synthesis, DNA binding and cleavage activities of copper (II) thiocyanate complex with 4-(N,N-dimethylamino)pyridine and N,N-

dimethylformamide. *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy*, (2011), 81(1), 21-27.

- Cristina Marzano, Maura Pellei, Francesco Tisato and Carlo Santini, , Copper Complexes as Anticancer Agents, *Anti-Cancer Agents in Medical Chemistry* (2009), 9,185-211.
- Dixit, N., et al., One pot synthesis of Cu(II) 2,2'-bipyridyl complexes of 5-hydroxy-hydurilic acid and alloxanic acid: Synthesis, crystal structure, chemical nuclease activity and cytotoxicity. *Journal of Inorganic Biochemistry*, (2011), 105(2), 256-267.
- Frieden, E., S. Osaki, and H. Kobayashi, Copper proteins and oxygen. Correlations between structure and function of the copper oxidases. *Journal of General Physiology*, (1965), 49(1), 213-252.
- Ghamarian, N., et al., Pulse Electrochemical Deposition and Photo-electrochemical Characterization of CuInSe<sub>2</sub> Thin Films. *Int. J. Electrochem. Sci*, 2013, 8. 312-322.
- Hong-Ke Liu and Peter J.Sadler, , Metal Complexes as DNA Intercalators (2011), 5, 349- 359).
- Liu, H., et al., Synthesis, structure and DNA cleavage of mononuclear Fe(III) complexes with 1,2,4-triazole-base ligand. *Applied Organometallic Chemistry*, (2010), 24(9), 636-640.

- Maamor, N.A.M., W.T. Tan, and N.A. Yusof, Voltammetric Studies of Nono Zirconium Dioxide/Carbon Nanotubes/Chitosan-Modified Glassy Carbon Electrodes. *Solid State Science and Technology*, (2009), 17(1), 1-11.
- Mirmoghtadaie, L., et al., Highly selective electrochemical biosensor for the determination of folic acid based on DNA modified-pencil graphite electrode using response surface methodology. *Materials Science and Engineering: C*, (2013), 33(3), 1753-1758.
- Murphy, C.J., et al., Long-range photoinduced electron transfer through a DNA helix. *Science*, (1993), 262 (5136), 1025-1029.
- Pereira, R.M.S., et al., Synthesis and characterization of a metal complex containing naringin and Cu, and its antioxidant, antimicrobial, antiinflammatory and tumor cell cytotoxicity. *Molecules*, (2007), 12(7), 1352-1366.
- Pratviel, G., J. Bernadou, and B. Meunier, Carbon—Hydrogen Bonds of DNA Sugar Units as Targets for Chemical Nucleases and Drugs. *Angewandte Chemie International Edition in English*, (1995), 34(7), 746-769.
- Robertazzi, A., et al., Copper-1,10-Phenanthroline Complexes Binding to DNA: Structural Predictions from Molecular Simulations. *The Journal of Physical Chemistry B*, (2009), 113(31), 10881-10890.
- Sarma, B. and D.K. Das, Synthesis, Spectroscopy, Thermal Analysis, Electrochemistry and Superoxide Scavenging Activity of a New Bimetallic Copper(II) Complex. *Journal of Chemistry*, 2013. 2013: p. 5.
- Sasmal, P.K., et al., Photocytotoxicity and DNA cleavage activity of l-arg and l-lys Schiff base oxovanadium(IV) complexes having phenanthroline bases. *Dalton Transactions*, (2010), 39(30), 7104-7113.
- Skladanowski, A., M. Koba, and J. Konopa, Does the antitumor cyclopropylpyrroloindole antibiotic CC-1065 cross-link DNA in tumor cells? *Biochemical pharmacology*, 2001. 61(1): p. 67-72.
- Sujatha, S., et al., Synthesis, characterization and DNA interaction of hexaaza macrotricyclic copper(II) complexes. *Inorganica Chimica Acta*, (2012), 386(0), 109-115.
- Tan, W., et al., Voltammetric Studies of Cadmium Ion at the Mercury Electrode in the Presence of Glutathione. *The Pacific Journal of Science and Technology*, (2008), 9(2), 480-486.
- Tansil, N.C., et al., An ultrasensitive nucleic acid biosensor based on the catalytic oxidation of guanine by a novel redox threading intercalator. *Chemical Communications*, (2005), 8, 1064-1066.
- Yaw, C., et al., Electrochemical Studies of Cu (phen) edda Interaction with DNA. *Int. J. Electrochem. Sci*, (2012), 7, 4692-4701.
- Wang, Z.-g., et al., Synthesis, magnetic properties, DNA binding and cleavage activity of a new oxalato bridged copper(II) complex. *Applied Organometallic Chemistry*, (2012), 26(10), 511-517.
- Zidan, M., et al., Electrocatalytic Oxidation of Ascorbic Acid Mediated by Lithium doped Microparticles Bi<sub>2</sub>O<sub>3</sub>/MWCNT Modified Glassy Carbon Electrode. *Int. J. Electrochem. Sci*, (2010), 5(4), 501-508.
- Zidan, M., et al., Electrochemical Oxidation of Paracetamol Mediated by Nanoparticles Bismuth Oxide Modified Glassy Carbon Electrode. *Int. J. Electrochem. Sci*, (2011), 6, 279-288.

دراسات كهروكيميائية للمترابك  $[\text{Cu}(\text{sar})_2] \cdot 2\text{H}_2\text{O}$  وتفاعله مع د.ن. أ.

أ محمد زيدان،<sup>1</sup> إصلاح جميل،<sup>ب</sup> شونج ياو

أ قسم الكيمياء-كلية العلوم- جامعة سيها- ليبيا

ب قسم الكيمياء-كلية العلوم- جامعة بوترا ماليزيا-ماليزيا

من خلال التحليل الكهروكيميائي والكلولومتري لمترابك النحاس إتضح انها تتميز بخاصية التوصيل الكهربي عند درجات حرارة الغرفة حيث يعتمد التوصيل علي درجات الحموضة وأفضل درجة حموضة هي ٢,٤ كذلك إتضح من خلال دراسة السطوح لمترابك النحاس بقيم المساحة والكثافة من التجارب المعملية.

