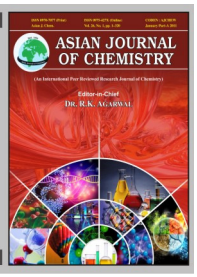
Asian Journal of Chemistry; Vol. 26, No. 1 (2014), 261-263

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2014.15862



Synthesis and Properties of Copper(II)-Ferrocene Formylated Curcumin

QIYONG HUAI[1,2,*], JUNQIANG YU[3], XIUSHANG XU[2], JINLAI MIAO[1] and ZONGLING WANG[1,*]

[1]The First Institute of Oceanography, State Oceanic Administration, Qingdao 266061, P.R. China
[2]Shandong University (Weihai), Marine College, Weihai 264209, P.R. China
[3]Rongcheng Entry-Exit Insepection and Quarantine Bureau, Weihai 264300, P.R. China

*Corresponding authors: E-mail: huaiqy01@163.com; wangzl@fio.org.cn

Received: 4 June 2013; *Accepted*: 24 September 2013; *Published online*: 26 December 2013; AJC-14519

A mononuclear (1:1) copper complex of ferrocene formylated curcumin was synthesized. The complex was characterized by elemental analysis, IR and UV-visible spectra. The copper atom is coordinated through the keto-enol group of ferrocene formylated curcumin along with one acetate group and one water molecule. Its electrochemical property was examined by cyclic voltammogram and antibacterial activities to *Staphylococcus aureus* was detected by bacteriostatic experiment. Cyclic voltammetric studies of complex showed a reversible Cu^{2+}/Cu^{+} couple redox wave at oxidation potential 0.142 V and at reduction potential 0.116 V, respectively, appearing from -1 to 1 V. The peak separation (ΔP) is 26 mV and the peak current ratio (I_{pa}/I_{pc}) is 1.01, which expected to show superoxide dismutase activity. Bacteriostatic experiment showed the antibacterial activity of complex is stronger than that of curcumin.

Keywords: Copper(II)-ferrocene formylated curcumin, Cyclic voltammetry, Antibacterial activities.

INTRODUCTION

Curcumin [1,7-*bis*-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-di-one] is an important natural product found in the rhizomes of turmeric, having been known for its medicinal properties since ancient time. It possesses antioxidant and anticancer effects, enhancing wound healing[1]. Due to its structure of keto-enol, curcumin has strong ability to coordinate to metal ion. The complex could show special electrochemical property. The coordination between Ni^{2+} and curcumin modified glassy carbon bonds with electrode, improving the electron transfer[2]. The Al(III)-curcumin complex could reduce the binding affinity of Al^{3+} to DNA and be applied for treatment of brain disease[3]. A mononuclear (1:1) copper complex of curcumin has been synthesized, showing excellent scavenger of superoxide radicals[4]. Curcumin could also coordinate with rare earth element, such as Sm, Eu, Dy, enhancing antioxidant activity. Zn(II)-curcumin has potent gastroprotective activity against pylorus-ligation-induced lesions in rats[5]. By now the field of metal-curcumin complex research is still relatively active.

Cooper(II)-curcumin has been synthesized and examined for its scavenger of superoxide radicals. However, the potential for the Cu^{2+}/Cu^{+} couple in the complex was determined to be 0.160 *vs.* SCE and 0.402 V *vs.* NHE, showing the worse effect of electron transfer[6]. Ferrocene formylated curcumin has been synthesized and found that curcumin had a larger impact on the reversibility of the ferrocene through the ester changing in the oxidation peak position. Ferrocene is a rich electron-donating group, if it was bonding to macromolecule through a conjugated group, a bigger conjugated system would be formed which is easy for electron transfer. With this background it can be predicted that copper complex of ferrocene formylated curcumin can be found special electrochemical properties.

In this paper, a mononuclear (1:1) copper(II) complex of ferrocene formylated curcumin was synthesized and examined for its electrochemical properties by use of cyclic voltammogram. Electrochemical properties of the compound have been improved obviously. Antibacterial activity towards *Staphylococcus aureus* was also been tested.

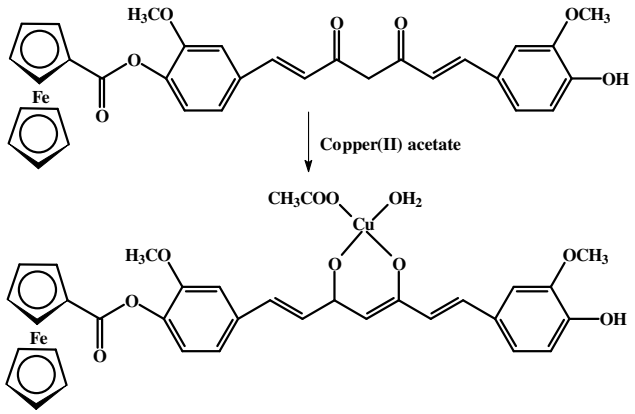
EXPERIMENTAL

Curcumin (Sinopharm Chemical Reagent AR); Ferrocenecarboxylate (Suzhou Highfine, Biotechnology Co., Ltd. AR); column chromatography silica gel (Qingdao Marine Chemical Factory, 200 μm); chemical reagents were of analytical grade (twice distilled, no water).

Elemental analysis was carried out by using C, H and N analyzer and copper, iron were estimated by an atomic absorption spectrometer. IR data was got from AVATAR360

Fourier transform infrared spectrometer (Nicolet). UV-visible absorption spectrum data was known from UV-254.

Synthesis of copper(II)-ferrocene formylated curcumin: Under a nitrogen atmosphere, copper acetate 0.05 g (0.25 mmol) was dissolved in dry ethanol and was heated at 60 °C. Ferrocene formylated curcumin (It was synthesized according to method Xu and Kong[7] dissolved in dry ethanol and added slowly and refluxed for 6 h, under a nitrogen atmosphere. The system of reaction was observed darker significantly, appearing solid. The precipitation was washed by cold ethanol and water several times to remove unreacted ferrocene formylated curcumin and copper acetate. The separated solid was dried in vacuum to get dry dark brown powder.



Scheme-I: Synthesis of Ferrocene Formylated Curcumin-copper(II) complex

Elemental analysis (%) showed that the complex contain C 57.45 (57.11), H 4.65 (4.93), Cu 8.95 (8.63), Fe 7.19 (7.59). The values in parentheses indicated the calculated ones.

IR (ν_{max}, cm^{-1}): 3565-3000 (O-H), 1709 (ester), 1621 (C=O, curcumin), 1532, 1392 (acetate). The differences between ν_{asym} and ν_{sym} bands for acetate in the complex appear at 1532 cm^{-1} and 1392 cm^{-1}, respectively. The C=O ferequency in curcumin appears at 1630 cm^{-1} and changes 10 cm^{-1} on copper complexation, showing its involvement in complexation[5].

UV-visible absorption spectrum: The UV-visible absorption spectrum of complex in DMSO showed absorption maximum at 426 nm, which are attributed to the destroying the keto-enol of copper. Comparing to curcumin, it has been shifted. Another weak nonfeatured *d-d* transition is observed at 500-600 nm[6].

Electrochemical experiment: Glassy carbon electrode as working electrode, saturated calomel electrode as the reference electrode, platinum wire electrode as the counter electrode, the compound dissolve in DMSO making 0.1 mmol/L of solution; adding saturated KCl as the supporting electrolyte, cyclic voltammetry, scans rate of 10 mV s^{-1} scan range of -1 to 1 V.

Inhibition experiment: In the sterile bench, first, every dish was added 10^8 CFU/mL of *Staphylococcus aureus* 0.1 mL. Then, prepare 10 mg/mL of complex in DMSO. Finally, dip in an equal amount of the same concentration of curcumin, the complex A1and A2, DMSO respectively by 6 mm sterile filter paper. Under optimal incubation temperature, measure the diameter of each zone of inhibition after a growth cycle of *Staphylococcus aureus*. The inhibition zone diameter is the average of each bacteriostatic circle diameter measured in three groups of parallel experiments.

RESULTS AND DISCUSSION

Cyclic voltammetric studies of Cu(II)-ferrocene formylated curcumin: The compound was dissolved in DMSO with potassium chloride as supporting electrolyte. The voltammogram is given in Fig. 1, where we could find that Cu^{2+}/Cu^{+} couple redox wave at oxidation potential 0.142 V and at reduction potential 0.116V, respectively, appearing at rang of -1 to 1 V. The peak separation (ΔP) is 26 mV and the peak current ratio (I_{pa}/I_{pc}) is 1.01. The redox potential of Fe^{2+}/Fe^{3+} correspond to 0.711 V and 0.620 V. These date showed that Cu(II)-ferrocene formylated curcumin has the good ability to transfer electron in the solvent of DMSO. After copper(II) reacting with the keto-enol of ferrocene formylated curcumin, the compound could form a large conjugated system, which is easy to stabilize Cu^{2+}. Therefore, Cu^{2+}/Cu^{+} redox process occurs in low potential. This value is within the range of compounds that are expected to show superoxide dismutase activity. This indicates that the copper complex is capable of removing free radicals[6].

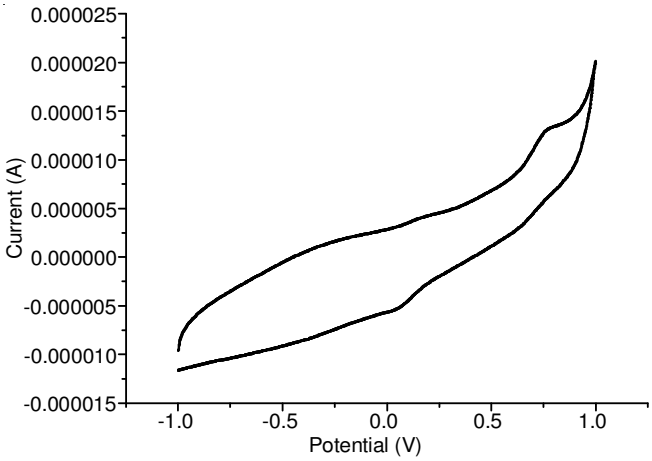


Fig.1. Cyclic voltammogram of complex (scan rate was 10 mV/s)

Antibacterial activities: The inhibition zone diameters (cm) with filter paper for compound A1, A2 and curcumin have been measured respectively and the results were summarized in the below table.

According to the literature[8], the minimum inhibitory concentration of curcumin was 10 mg/mL. It is concluded that the complex has significant antibacterial activities according to the size of the inhibition zone. However, copper(II) occurs with curcumin carbonyl ligand, which does not make the activity of the compound changed greatly. The antibacterial mechanism of these compounds needs to be explored. Table-1 showed that the compound antibacterial activity showed the following sequence: Compound A1 > Compound A2 > curcumin.

Conclusion

A mononuclear (1:1) copper complex of ferrocene formylated curcumin was synthesized and examined for its electrochemical properties by use of cyclic voltammogram. The complex was characterized by elemental analysis, IR and

TABLE-1
INHIBITION ZONE DIAMETERS (cm) WITH FILTER PAPER FOR COMPOUND A1, A2 AND CURRUMIN

Compound	DMSO	Curcumin	Compound A1	Compound A2
Ferrocene formylated curcumin	0.71	0.81	1.11	0.98
Copper(II) complex	0.68	0.82	1.08	1.01
Curcuin	0.70	0.79	1.09	0.99
Average	0.69	0.81	1.09	0.99

UV-visible from which we could find that a copper atom is coordinated through the keto-enol group of ferrocene formylated curcumin along with one acetate group and one water molecule, which expected to show superoxide dismutase activity. The complex has stronger antibacterial activity than curcumin. This study will emphasize the application of natural product of curcumin in electrochemistry and also in design and synthesis of antibacterial agents.

ACKNOWLEDGEMENTS

The authors thank Postdoctoral Innovation Fund Project of Shandong Province (No. 2011020070), Natural Science Foundation of Shandong Province (No. ZR2010BM021), Science and technology plan of The State General Administration of Quality Supervision, Inspection and Quarantine of P.R. China (No. 2012IK181) and Open Research Fund of State Key Laboratory of Biological Fermentation Engineering of Beer (No. K2012007) for funding.

REFERENCES

1. R.K. Maheshwari, A.K. Singh, J. Gaddipati and R.C. Srimal, *Life Sci*., **78**, 2081 (2006).
2. R. Ojani, J.-B. Raoof and S. Zamani, *Bioelectrochem.*, **85**, 44 (2012).
3. F. Ahmadi, A.A. Alizadeh, N. Shahabadi and M. Rahimi-Nasrabadi, *Spectrochim. Acta A*, **79**, 1466 (2011).
4. A. Barik, B. Mishra, L. Shen, H. Mohan, R.M. Kadam, S. Dutta, H.-Y. Zhang and K.I. Priyadarsini, *Free Radic. Biol. Med*., **39**, 811 (2005).
5. X. Mei, X. Luo, S. Xu, D. Xu, Y. Zheng, S. Xu and J. Lv, *Chem. Biol. Interact*., **181**, 316 (2009).
6. A. Barik, B. Mishra, A. Kunwar, R.M. Kadam, L. Shen, S. Dutta, S. Padhye, A.K. Satpati, H.-Y. Zhang and K. Indira Priyadarsini, *Eur. J. Med. Chem*., **42**, 431 (2007).
7. X.-S. Xu, L.-K. Kong and Q.-Y. Huai, *Asian J. Chem*., **25**, 7637 (2013).
8. S. Manju and K. Sreenivasan, *Indian J. Med. Res.*, **359**, 318 (2011).