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Journal of Pharmaceutical and Biomedical Analysis 44 (2007) 1192–1196

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

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Short communication

Catalytic action of copper (II) ion on electrochemical oxidation of metformine and voltammetric determination of metformine in pharmaceuticals

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Received 3 December 2006; received in revised form 10 April 2007; accepted 15 April 2007
Available online 20 April 2007

Abstract

The catalytic effect of Cu(II) ion toward the oxidation of metformine (MET) have been observed in $NH_3 \cdot H_2O–NH_4Cl$ buffer (pH 8.9; 0.1 M). The oxidation peak current of imino-group in guanidino-group of MET at 0.95 V at carbon paste electrode (C/PE) in the presence of 2.0×10^{-4} M Cu(II) ion was increased by about 20 times and the peak potential was unchanged compared with that in the absence of Cu(II) ion. Moreover, the oxidation peak current of MET at multiwalled carbon nanotube paste electrode (MWCNT/PE) was further increased by about three times compared with that at C/PE in the same medium. Based on the catalytic oxidation peak of MET by Cu(II) ion at MWCNT/PE, a voltammetric method for the determination of MET is developed. The peak current of the catalytic oxidation peak was proportional to MET concentration in the range of 2.0×10^{-7} to 1.0×10^{-5} M. The detection limit was 6.7×10^{-8} M.

Keywords: Metformine; Cu(II) ion; Oxidation; Carbon nanotube; Voltammetry

1. Introduction

Metformin (MET) is one of most commonly prescribed medications for type II diabetes. It is the drug of choice in obese diabetic patients [1]. Multiple pharmacological mechanisms of MET have been studied. On the one hand, through activation of tyrosine kinases and AMP-activated protein kinase, MET leads into an increase in cellular glucose transport and a decrease in hepatic glucose production, cholesterol and triglyceride synthesis [2–6]. On the other hand, MET can combine with many transition metal ions and these coordination compounds can improve or change its pharmacological function and biochemical process [7–12]. For instance, the complexes of MET with endogenous metals, Zn^{2+}, Cu^{2+}, Fe^{3+} and others, can inhibit cysteine proteases, and oxovanadium (IV)-MET coordination compounds is used as insulin-enhancing agents from a synergistic action.

In this work, the catalytic action of Cu(II) ion toward the oxidation of MET at carbon paste electrode (C/PE) was studied, and a voltammetric method for the determination of MET using multiwalled carbon nanotube paste electrode (MWCNT/PE) is proposed, and is applied to MET determination in pharmaceutical formulations.

2. Experimental

2.1. Reagents and apparatus

A 1.0×10^{-2} M stock standard aqueous solution of metformin hydrochloride (purity >98.9%, Shandong Keyuan Pharmaceutical, China) was prepared and stored under refrigeration at 4 °C. Working standard solutions of MET were prepared by diluting the stock solution with water before use. Multiwalled carbon nanotubes (MWCNT, purity ≥95%, 10–20 nm diameter, 5–15 µm length, Shenzhen Nanotech Port, China) were further purified by stirring in 2 M nitric acid for 20 h in order to remove metal ions which maybe present [13]. Graphite powder was of chemical pure grade (Beijing Chemical Reagent Factory, China). Silicon oil was of chromatographic pure grade (Chengdu Chemical Reagent Factory, China). All chemicals used were of analytical reagent grade. Twice-distilled water was used throughout.

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doi:10.1016/j.jpba.2007.04.014

A CHI 660 electrochemical workstation (CH Instrument Inc., USA) and a JP-303 polarographic analyzer (Chendu Instrument Factory, China) were used for voltammetric study and measurements. A three-electrode set-up was equipped with homemade C/PE or MWCNT/PE working electrode, a saturated calomel reference electrode (SCE) and a platinum-wire counter electrode. All the potentials quoted in this work were relative to the SCE. UV-2550 UV–vis spectrophotometry (Shimadzu Corporation Assembled, China) were used for the spectrophotometric determination of MET content in the samples. All the measurements were performed at room temperature.

2.2. *Preparation and activation of the working electrodes*

Preparation of C/PE and MWCNT/PE: the C/PE was prepared by thorough mixing graphite powder and silicon oil in a ratio of 5:2 (w/w) in a mortar. A portion of the resulting paste was packed firmly into a plastic tube (Φ 3 mm), in which a copper wire was inserted to produce the electrical connection. The MWCNT/PE was prepared in similar manner by mixing MWCNT powder and silicon oil in a ratio of 3:2 (w/w).

Activation of the C/PE and MWCNT/PE: to obtain a more sensitive and stable voltammetric responds, the working electrodes were activated by cyclically scanning in the potential range of −0.2 to 1.2 V at 0.1 V s^{-1} for 16 times until a stable background current was obtained.

2.3. *Procedure*

$NH_3 \cdot H_2O$–NH_4Cl (pH 8.9; 0.1 M; 10 mL) buffer containing 2.0×10^{-4} M Cu(II) ion and appropriate amount of MET was transferred into a voltammetric cell, and the second-order derivative linear sweep voltammogram was recorded by applying an anode-going potential scan from 0.6 to 1.2 V at 0.1 V s^{-1} and the second-order derivative peak current of the catalytic oxidation peak of MET at 0.95 V was measured. The calibration curve was obtained by plotting the second-order derivative peak current versus MET concentration. Cyclic voltammetry was conducted in the same medium.

After each measurement, the C/PE and MWCNT/PE were cleaned in $NH_3 \cdot H_2O$–NH_4Cl (pH 8.9; 0.1 M) buffer by potential linearly scanning from 0.6 to 1.2 V until a stable background current was obtained to remove the residuary MET and Cu(II) ion, the electrodes were then used to the next measurement after washing with water. If necessary, the electrode surfaces were renewed by cutting a part of the graphite or multiwalled carbon nanotubes paste (a thickness of 2–3 mm), then polishing and washing with water.

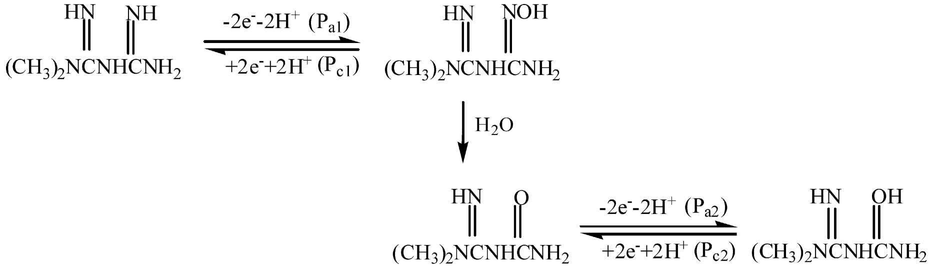
2.4. *Analysis of drug samples*

Ten tablets of metformin hydrochloride tablets (Shenzhen Zhonglian Pharmaceutical Co. Ltd., China) were weighed and powdered in a mortar. A portion of the powder was accurately weighed and dissolved into 100 mL volumetric flask using water. The sample solution was stored under refrigerator at 4 °C until it became clear. The supernatant liquid of the sample solution was properly diluted with water to obtain suitable final concentrations of MET. The determination of MET in the obtained samples were performed according to the experimental procedure described above. The MET content of the samples was calculated according to the calibration curve.

3. Results and discussion

3.1. *Voltammetric behavior of MET in the presence of Cu(II) ion at C/PE*

Cyclic voltammograms of MET in $NH_3 \cdot H_2O$–NH_4Cl buffer (pH 8.9; 0.1 M) at C/PE was shown in Fig. 1 by curve a. Over the potential range of −0.2–1.2 V, MET exhibited two pairs of redox peaks P_1 and P_2, respectively. The oxidation peak P_{a1} appeared at 0.95 V, the corresponding reduction peak P_{c1} did at 0.81 V. And the oxidation peak P_{a2} appeared at 0.18 V, the corresponding reduction peak P_{c2} did at 0.17 V. From this, the voltammetric behavior of MET at C/PE in this work was similar to that at the paste electrode prepared from molecular wires containing copper(II) and multiwalled carbon nanotubes in pH 7.2 Britton–Robinson buffer reported in our previous work [14]. The electrode process for MET can be described as:



The electrochemical oxidation of an imino-group in guanidino-group to a *N*-hydroxy imino-group produced the oxidation peak P_{a1}. Then most of the *N*-hydroxy imino-group fast hydrolyzed to a carbonyl imino-group, the reduction of the residuary *N*-hydroxy imino-group after hydrolyzing produced the reduction peak P_{c1}. Reversible redox reaction of the carbonyl imino-group produced the pair of the peak P_2.

The experiments showed that the peak current of the oxidation peak P_{a1} at 0.95 V was obviously increased and the peak potential was unchanged when Cu(II) ion was present. Cyclic voltammograms of MET in $NH_3 \cdot H_2O$–NH_4Cl buffer (pH 8.9; 0.1 M) containing 2.0×10^{-4} M Cu(II) ion at C/PE was shown in Fig. 1 by curve b. A pair of reversible redox peaks of Cu(II)/Cu(0) couple appeared at about 0 V and overlaped the peaks P_{a2} and