Chinese Chemical Letters 26 (2015) 613–618

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Original article

Electroanalytical method for determination of shikonin based on the enhancement effect of cyclodextrin functionalized carbon nanotubes

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ARTICLE INFO

Article history:
Received 10 October 2014
Received in revised form 3 November 2014
Accepted 17 November 2014
Available online 28 November 2014

Keywords:
Shikonin
β-Cyclodextrin
Multiwalled carbon nanotubes
Modified electrode
Electrochemical detection

ABSTRACT

A simple and sensitive electroanalytical method for determination of shikonin, a widely used antitumoral agent, using β-cyclodextrin-functionalized multiwalled carbon nanotubes composite modified glassy carbon electrodes (MWCNTs/β-CD/GCE) was presented. CDs are water-soluble and environmentally friendly and can improve the dispersibility of MWCNTs/β-CD functional materials, which was confirmed by SEM. The electrochemical behaviors of shikonin on different electrodes were investigated by cyclic voltammetry (CV) and differential pulse voltammograms (DPVs). The results demonstrated that the redox peak currents of shikonin obtained at MWCNTs/β-CD/GCE were much higher than those at the β-CD/GCE and MWCNTs/GCE, which can be attributed to the combination of the excellent electrocatalytic properties of MWCNTs and the molecular recognition ability of β-CD. At MWCNTs/β-CD/GCE, the response current exhibits a linear range from 5.0 nmol/L to 10.0 μmol/L with a detection limit of 1.0 nmol/L (S/N = 3). As a practical application, the proposed method was applied to quantitatively determine shikoninin urine samples with satisfying results.

1. Introduction

Shikonin, a naphthoquinone isolated from the Chinese herbal plant *Lithospermum erythrorhizon*, has attracted considerable attention due to its interesting biological activities as an antibacterial, antifungal antimicrobial, wound healing, anti-inflammatory, antithrombotic, and antitumor agent [1,2]. Besides pharmaceutical application, shikonin is also considered as a natural colorant in the printing, textile, dye, food, and cosmetic fields due to its strong and stable coloring features as well as certain antiphlogistic, antibacterial, and antiviral properties [3–5]. Hence, a simple, economical, and efficient analytical method for the qualitative and quantitative detection of shikonin is needed.

Until now, various methods have been developed for the detection of shikonin, including thin-layer chromatography chemiluminescence [6], high performance liquid chromatography [7], capillary electrophoresis (CE) [8], and electroanalysis [9]. Among them, electrochemical methods have gained considerable interest in recent years due to their simplicity, high sensitivity, good stability, low-cost instrumentation, and on-site monitoring. However, shikonin exhibits slow electron transfer at bare glass carbon electrodes, which leads to low sensitivity [10]. So, some functional materials should be synthesized to develop a sensitive electrochemical method for its detection.

Multiwalled carbon nanotubes (MWCNTs) have been extensively used in recent years due to their low cost, good mechanical strength electrical conductivity, high surface area, and their chemical stability [11]. In particular, MWCNTs can be used as a promising material for the fabrication of electrochemical sensors and biosensors mainly because they can not only improve electrochemical properties, but also provide electrocatalytic activity as well as minimize electrode surface fouling [12,13]. Then higher sensitivities and lower detection limits can be obtained relative to traditional electrode materials. However, the intrinsic van der Waals interactions between the pristine tubes make MWCNTs bundle together on a large scale, which are insoluble in routine solvents. This limits their further application [14,15]. Thus, it is essential to design or introduce suitable functional groups that effectively disperse MWCNTs and create enhanced functions.

Cyclodextrin (CD) is a macrocyclic glucose oligomer, consisting mostly of six, seven or eight D-glucose units forming α-, β-, or γ-CD, respectively [16–18]. CD has hydrophilic outer tails and a

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http://dx.doi.org/10.1016/j.cclet.2014.11.032

hydrophobic center, which makes it readily soluble in aqueous solutions and prepares it to undergo host–guest interaction with other compounds [19–22]. In addition, CDs are water-soluble and environmentally friendly and can improve the dispersibility of functional materials [17,23,24]. Based on these, β-CD is chosen to functionalize with MWCNTs. The CD-functionalized MWCNTs composites (MWCNTs/β-CD) can simultaneously possess the properties of the individual constituent materials, such as the supramolecular recognition and enrichment capability of CD and the large surface area and high conductivity of MWCNTs, which were designed for the determination of some electroactive molecules [17,25,26], *etc.* However, the application of MWCNTs/β-CD as an electrode material for determination of shikonin has not been reported yet.

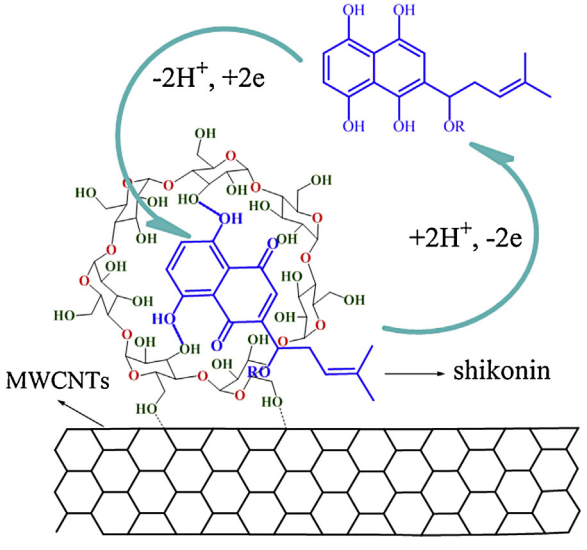
In this paper, we demonstrated a novel electrochemical method based on a glassy carbon electrode (GCE) modified with MWCNTs/β-CD composites. The electrochemical redox behavior of shikonin was investigated. MWCNTs/β-CD/GCE exhibited excellent enhancement effect on the electrochemical redox reactions of shikonin compared with bare GCE, β-CD/GCE and MWCNTs/GCE, which was attributed to the synergistic effect of β-CD and MWCNTs. Consequently, a voltammetric method for shikonin was developed based on MWCNTs/β-CD/GCE and used for the detection of shikonin in urine samples with satisfactory results (Scheme 1).

2. Experimental

Chemicals and reagents: MWCNTs (purity > 95%) were purchased from Shenzhen Nanotech Port Co., Ltd. β-CD was obtained from Aladdin Reagent Co., Ltd. Shikonin was purchased from Biopurify. Shikonin stock solution (0.01 mol/L) prepared with absolute ethyl alcohol was stored at 278–281 K. Lithium perchlorate ($LiClO_4$), disodium hydrogen phosphate (Na_2HPO_4), and sodium dihydrogen phosphate dehydrate (NaH_2PO_4) were obtained from Sinopharm chemical reagent Co., Ltd. All other reagents were of analytical grade, and double distilled water was used throughout the experiment.

2.1. Apparatus

The cyclic voltammetric and electrochemical impedance spectroscopy measurements were carried out on a CHI660D electrochemical workstation (Shanghai, China). A three-electrode cell (5 mL) was used with the modified glassy carbon electrode (GCE) as the working electrode, a saturated calomel electrode (SCE) as the reference electrode and a platinum foil electrode as the counter electrode. All potentials were measured and reported *vs.* the SCE and all experiments were carried out at room temperature. The differential pulse voltammetry (DPV) was carried out in a potential range from 0.35 V to 0.75 V with the parameters of an increment potential of 0.004 V, a pulse amplitude of 0.05 V, a pulse width of 0.2 s, a sample width of 0.02 s, a pulse period of 0.5 s, and a quiet time of 20 s.



Scheme 1. The redox mechanism of shikonin at the MWCNTs/β-CD modified electrode.

2.2. Preparation of different modified electrodes

Prior to modification, the GCEs were polished with chamois leather containing 0.05 μm Al_2O_3 slurry, rinsed thoroughly with double distilled water, then washed successively with double distilled water, anhydrous ethanol, and acetone in an ultrasonic bath, and dried under N_2 before use. The β-CD suspension (1.0 wt%) was prepared by adding 10 mg β-CD powder into 1 mL deionized water. Then, 1 mg MWCNTs were added into the as-prepared β-CD solution and stable MWCNTs/β-CD suspensions (1 mg/mL) were obtained by sonicating for 1 h. To obtain MWCNTs/β-CD modified GCE (MWCNTs/β-CD/GCE), 5 μL dispersion was dropped onto the clean GCE surface and dried at room temperature. For the sake of comparison, MWCNTs/GCE and β-CD/GCE were fabricated in a similar method.

3. Results and discussion

3.1. Surface morphologies of the MWCNTs and MWCNTs/β-CD films

Fig. 1 shows scanning electron microscope (SEM) images of MWCNTs (A) and MWCNTs/β-CD (B). From Fig. 1A, it can be seen that the MWCNTs could not be well dispersed and they always formed badly ordered agglomerates. However, after modification with β-CD, they could be dispersed uniformly due to the van der Waals forces between MWCNTs and β-CD and the hydrogen-bonding interaction between adjacent β-CD molecules [27,28]. Meanwhile, a number of porous interspaces were also obtained from the surface morphology of MWCNTs/β-CD film, which was beneficial to maintain a large electroactive area on the electrode surface.

3.2. Electrochemical characterization of the modified electrodes

In electrochemical impedance spectroscopy measurements, the semicircle diameter of the impedance equals the electron-transfer resistance (Ret), which controls the electron-transfer kinetics of the redox probe at the electrode interface and is an important parameter. Fig. 2 presents the representative impedance spectrum of the bare GCE (a), MWCNTs/GCE (b), β-CD/GCE (c) and MWCNTs/β-CD/GCE (d) in 5.0 mmol/L $K_3Fe(CN)_6$/$K_4Fe(CN)_6$ (1:1) containing 0.1 mol/L KCl. Compared with bare GCE (curve a), the semicircle of MWCNTs/GCE (curve b) decreased distinctively, which was ascribed to the significantly improved electrical conductivity of MWCNTs [27,28]. While the Rct increased dramatically at β-CD (curves c), indicating that β-CD layer hindered the electron transfer and made the interfacial charge transfer difficult. For the MWCNTs/β-CD/GCE, the semicircle of MWCNTs/β-CD/GCE was larger than that of MWCNTs/GCE but smaller than that of β-CD/GCE, indicating β-CD on the surface of MWCNTs cannot recognize ion and block the electron transfer between electrode and $Fe(CN)_6^{3-/4-}$. The result was consistent with that reported in literatures [23,29].