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Nickel nanoparticles functionalized multi-walled carbon nanotubes at platinum electrodes for the detection of bromhexine

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ABSTRACT

Multi-walled carbon nanotubes (MWCNTs) functionalized by nickel nanoparticles were obtained using a single step chemical deposition method in an ultrasonic bath. The composite material was characterized by means of scanning electron microscopy (SEM) and energy dispersive X-ray analysis (EDX). The electroactivity of the nickel nanoparticle-functionalized MWCNTs was assessed in respect to the electrooxidation of bromhexine. Compared with a bare Pt and a bare Pt modified with MWNCTs, the nickel nanoparticle-functionalized MWCNTs modified Pt electrode exhibited a well-defined oxidation peak for bromhexine at 997 mV and a marked enhancement of the current response. The nanocomposite material modified Pt electrode has significantly improved the voltammetry of bromhexine and provided a highly reproducible detection. The modified electrode was used for the determination of bromhexine in 0.1 M phosphate buffer solution (PBS) at pH 4.0. The peak current increased linearly with the concentration of bromhexine in the range of 5.0×10^{-6} to 2.3×10^{-4} M with a correlation coefficient of 0.9999. The detection limit was 3.0×10^{-6} M ($S/N = 3$). The proposed method was successfully applied to the determination of bromhexine in pharmaceutical formulations. The nanocomposite material modified Pt electrode has several advantageous such as providing improved voltammetric behavior, long-time stability and excellent reproducibility.

1. Introduction

Bromhexine (Fig. 1) is a mucolytic drug used in the treatment of respiratory disorders [1]. It is rapidly absorbed by oral route and spreads to the tissues including the bronchial epithelium [2]. Since mucolytics may disrupt the gastric mucosal barrier, bromhexine should be used with caution in patients with a history of gastric ulceration. The quantification of bromhexine is important in many areas including clinical chemistry and pharmaceutical formulations. A number of analytical methods have been utilized for the determination of bromhexine in pharmaceuticals and biological fluids including UV–visible spectrophotometry [3,4], flow injection analysis with ion selective electrodes [5], liquid chromatography [6], inductively coupled plasma mass spectrometry [7], capillary isotachophoresis [8], electrokinetic chromatography [9], liquid-gas chromatography [10] gas chromatography with mass detection [11] and differential pulse voltammetry [12]. Spectrophotometry and chromatography are the two most widely employed techniques for the determination of bromhexine. However, these techniques are expensive and require time-consuming derivatization step. Voltammetric detection provides a highly sensitive approach to the analysis of a wide range of analytes [13–15]. The electrooxidation of bromhexine has been studied in solution using a glassy carbon electrode [12]. However, it is necessary to find an adequate surface for a reproducible and sensitive determination of bromhexine in order to overcome electrode fouling. The modification of conventional electrodes has attracted much attention in last two decades because it provides powerful means to bring new qualities to the electrode surface which exploited for electrochemical purposes [16]. Chemically modified electrodes can be obtained by either attaching molecules on electrode surfaces or by immobilizing multimolecular layers on electrodes. They found applications in various fields including electroanalysis and electrocatalysis [17–19]. Among the wide range of electrode modifiers carbon nanotubes and metal nanoparticles have been focus of attention for electrochemists because of advantageous features such as excellent long term stability, response time, increased sensitivity, resistance to surface fouling, decreased overpotentials, limits of detection, conductivity, nanometersize and providing large surface area [20–24]. Furthermore, no articles have appeared in the literature on the use of chemically modified electrodes for the determination of bromhexine.

In this study, a voltammetric nanosensor has been prepared by one-pot synthesis of multi-walled carbon nanotube-supported nickel nanoparticles in an ultrasonic bath. The nanocomposite

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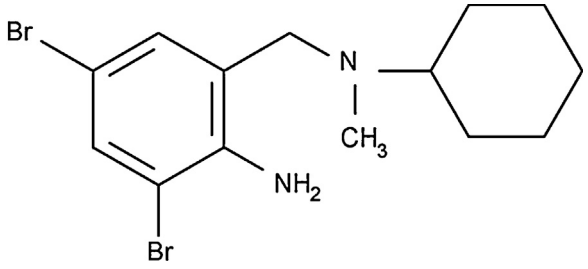

Fig. 1. Chemical structure of bromhexine.

material was immobilized on a Pt electrode surface for the detection of bromhexine. The surface modification with MWCNT and nanoparticles of nickel served to reduce the potential required to oxidize species, improve voltammetric behavior and enables a reproducible detection for bromhexine.

2. Experimental

2.1. Chemicals

Bromhexine and L-ascorbic acid were obtained from Sigma–Aldrich (St Louis, USA). Nickel (II) chloride, chloroform, acetonitrile, ortho-phosphoric acid, sodium dihydrogen phosphate, di-sodium hydrogen phosphate and potassium dihydrogen phosphate were purchased from Merck (Darmstadt, Germany). Multiwalled carbon nanotubes (MWCNTs) of 95% purity were obtained from NanoLab, USA. Stock solutions were prepared with 0.1 M phosphate buffer at pH 7.0. All solutions were prepared using ultra pure water. Oxygen-free nitrogen was bubbled through the cell prior to each experiment. All experiments were carried out at room temperature.

2.2. Apparatus

Electrochemical experiments were performed using an Eco-Chemie Autolab PGSTAT 12 potentiostat/galvanostat (Utrect, The Netherlands) with the electrochemical software package 4.9. A three-electrode system was used: a Pt electrode as working electrode [1.6 mm in diameter (Bioanalytical Systems, Lafayette, USA)], a Pt wire counter electrode and a Ag/AgCl reference electrode (Metrohm, Switzerland).

2.3. Ultrasonic synthesis of nickel nanoparticles on MWCNTs

Multiwalled carbon nanotubes were sonicated in concentrated $HClO_4 + HNO_3$ (3:7, v:v) for 7 h in order to oxidize their surface, they were then filtered and extensively washed with deionized water to pH 7, and dried in air. Then, 2.9 mg $NiCl_2$ and 2.0 mg oxidized MWCNTs were added to 60 mL of acetonitrile in an airtight glass flask. The mixture was sonicated for 1 h. 4.0 mg of L-ascorbic acid was then added in the flask and the pH was adjusted to 5.2 using 1 M NaOH. The reaction was allowed to proceed for 5–6 min at 65 °C under sonication. Finally, the products were separated by centrifugation, washed with acetonitrile and deionized water to remove any unreacted species. The multi-walled carbon nanotubes functionalized with nickel nanoparticles (NiNPs/MWCNTs) were allowed to air-dry for 24 h prior to use.

2.4. Voltammetric assay of bromhexine in tablets

Five bromhexine tablets were weighed and crushed to a fine powder in a mortar. A mass of powder equivalent to the average mass of one tablet was dissolved in 25 ml of 0.1 M PBS at pH 4.0. It was then introduced to an ultrasonic bath for 10 min, filtered and diluted with 0.1 M PBS in a calibrated 100 ml flask. Appropriate dilutions were made from the supernatant solution with 0.1 M PBS. Then the tablet solution was subjected to square wave voltammetry. The content of drug was determined referring to the regression equation.

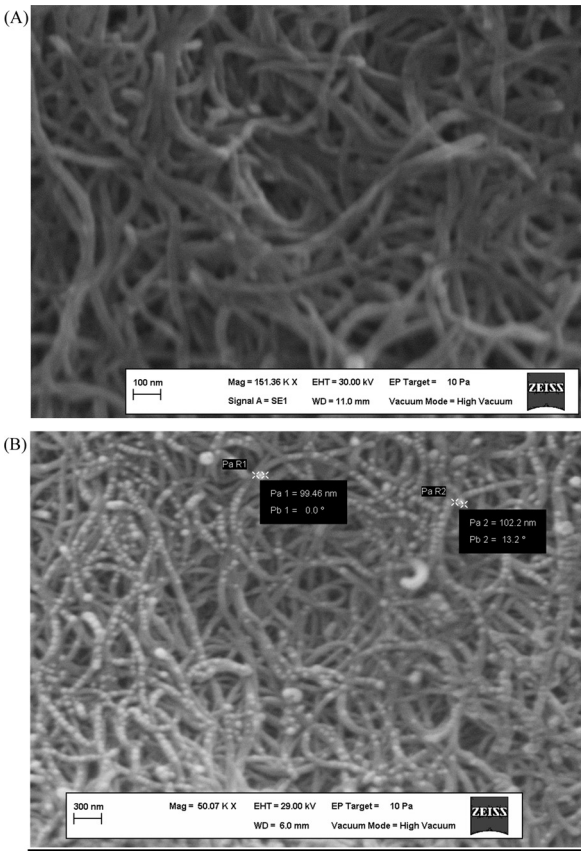

Fig. 2. SEM images of MWCNT/Pt (A) and NiNPs/MWCNT/Pt (B).

3. Results and discussion

3.1. Characterization of modified electrode

The surface morphology of the NiNPs/MWCNT/GCE was characterized by SEM. As shown in Fig. 2A, a MWCNT layer without aggregation was observed on the electrode surface, indicating that the MWCNTs were homogeneously dispersed on the surface of Pt electrode. As can be seen in Fig. 2B, the NiNPs deposited on the MWCNTs were spherical and well distributed. The average size of nickel nanoparticles was *ca.* 100 nm. The EDX results exhibited in Fig. 3 show that Ni, C and Au were the major elements on the electrode surface. The Au was obtained from the gold coating of the NiNPs/MWCNT/Pt during SEM analysis. The EDX results clearly show that Ni is electrodeposited on the surface of MWCNT layer. The surface loading has been calculated to be 6.2 ng using the table obtained from the EDX measurement as provided under Fig. 3. The cyclic voltammograms of the modified electrode are given in Fig. 4 in which nickel is clearly seen in the cathodic region. Also, no waves are observed in the potential region where bromhexine undergoes oxidation.