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ORIGINAL PAPER

Poly(taurine)/MWNT-modified glassy carbon electrodes for the detection of acetaminophen

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Abstract A novel dye-polymer/CNT, poly(taurine)/MWNT-modified glassy carbon electrode was fabricated. This electrode is based on an electrochemically polymerized taurine layer coated on a MWNT film. The application of this electrode for voltammetric detection of acetaminophen is described. The electroactive surface area of the modified electrode was calculated to be 0.37 cm^2. Acetaminophen is oxidized at 0.38 V and then reduced at 0.27 V on the modified electrode. The irreversible oxidation process is due to the conversion of acetaminophen into imidogenquinone; the reduction process is ascribed to the reverse electrode reaction. The adsorption-controlled anodic peak current is proportional to the acetaminophen concentration (from 1.0 μM to 0.1 mM) with a detection limit of 0.5 μM. The detection of acetaminophen in drugs was conducted.

Keywords Carbon nanotubes (CNTs) · Chemically modified electrodes · Conducting polymers · Acetaminophen · Drug analysis

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1 Introduction

Carbon nanotube (CNT) is a new material [1] and has been widely recognized as an important nano-material for the design of electrochemical sensors and biosensors [2–7] since its discovery in 1991. CNT possesses a strong electrocatalytic effect, fast electron transfer rate, high conductance, tensile strength, good chemical stability, and excellent biocompatibility. The poor solubility of CNTs, however, partially impairs the fabrication of CNT-based electronic devices. With an aim to immobilize CNTs on electrode surfaces without dissolving the CNTs in solvents, several types of modified electrodes have been reported recently. They include CNT paste electrode [8, 9], CNT film-coated electrode [10, 11], CNT powder microelectrode [12], CNT paper electrode [13], and polymer/CNT modified electrodes [14–24]. Conducting polymer/CNT modified electrodes are of special interest because they have three-dimensional structures due to the incorporation of CNTs into conducting polymers. These three-dimensional structures show large surface areas and properties of each component with a synergistic effect [14]. Various conducting polymers (e.g., polypyrrole [15], poly(phenylene vinylene) [16], polythiophene and its derivatives [17], and polyaniline [18]) have been used. These polymer/CNT modified electrodes have

been applied successfully for electrochemical sensing [19–24]. Nevertheless, to the best of our knowledge, relatively few reports focus on the utilization of dye polymers to prepare polymer/CNT modified electrodes. Taking poly(taurine) as an example, it has been reported [25] that the functionalized CNTs dissolve in poly(taurine) suspension. Further experiments confirm [25] the formation of a novel nano-structured material, poly(taurine)/CNTs.

Acetaminophen (paracetamol, *N*-acetyl-*p*-aminophenol) is a widely used analgesic anti-pyretic drug. It is a suitable alternative for the patients who are sensitive to aspirin [26]. However, overdoses will cause liver and kidney damage [27] and finally lead to death. Several techniques [28–30] including titrimetry, spectrophotometry, and liquid chromatography (LC) have been applied for the determination of acetaminophen in pharmaceutical formulations and biological fluids. Both titrimetric and spectrophotometric methods involve a tedious extraction process prior to the determination, whereas the LC method is time-consuming. Due to the advantages of low cost, fast response, simple instrumentation, high sensitivity, facile miniaturization, and low power requirement, numerous voltammetric methods of acetaminophen have been developed [31–40].

Herein, we report about the fabrication of a novel conducting polymer/CNT modified electrode by electrochemical polymerization of taurine on the functionalized MWNT-film coated glassy carbon electrode and the application of the modified electrodes for voltammetric detection of acetaminophen in drugs. Especially, the voltammetric behavior of acetaminophen on the modified electrode was investigated and the experimental conditions for the detection of acetaminophen were optimized.

2 Experimental

2.1 Chemicals and solutions

Taurine was purchased from Shanghai No. 1 Chemical Company (Shanghai, China). Acetaminophen (analytical grade) was purchased from Sigma. Its stock solution (5.0 μM) was prepared with absolute alcohol and stored in a refrigerator at 4 °C. Other reagents were analytical grade. Double-distilled water was used in all experiments.

MWNTs with approximately 95% purity were obtained from Shenzhen Nanotech Port (Shenzhen, China) and purified/functionalized as reported previously [9, 41, 42]. Briefly, 500 mg of MWNT were oxidized at 400 °C for 30 min to remove amorphous carbon particles. The oxidized MWNTs were dispersed in 60 ml of 6.0 M HCl for 4 h in an ultrasonic bath to eliminate metal oxide catalysts. Then the MWNTs were washed with water until the solution pH was close to 7.0. Finally, they were air-dried at room temperature. In order to generate carboxylic acid-functionalized MWNT surface, the purified MWNTs werefurther oxidized in a mixture of concentrated sulfuric and nitric acid (v/v = 3:1) with the aid of ultrasonication for 6 h at 50–60°C. The resultant solution was filtered through a poly (tetra Xuoroethylene) membrane with a 200-nm pore size. The solid powders were washed thoroughly with water to remove any residual acid and then dried at 60 °C for 2 h. The functionalized MWNTs (1.0 mg) were then dispersed in 2 mM taurine dissolved in pH 6.98 phosphate buffer. This suspension was used for the fabrication of poly(taurine)/MWNT-modified electrodes.

2.2 Electrochemical measurements

Electrochemical measurements were carried out on a CHI 760B electrochemical station (Shanghai Chenhua, China) with a conventional three-electrode system at room temperature. Either the bare or the modified glassy carbon electrode aced as the working electrode, a saturated calomel electrode (SCE) aced as the reference electrode and a platinum foil constituted the counter electrode.

Poly(taurine)/MWNT-modified electrodes were prepared as follows. Prior to the polymerization of taurine, a glassy carbon electrode (4.0 mm in diameter) was polished with emery paper and alumina slurry, cleaned in sonication bath for 10 min and thoroughly rinsed with distilled water. Then one drop (10 μL) of MWNT suspension was cast on the clean glassy carbon electrode. The electrode was air-dried at room temperature. Electrochemical polymerization of taurine on MWNT film-coated electrodes was conducted in a 2.0 mM taurine solution from −1.5 and +2.5 V at a sweep rate of 100 mV s^{-1} for 10 cycles. After washing copiously with water, the poly(taurine)/MWNT-modified electrodes were fabricated.

3 Results and discussion

Figure 1 shows cyclic voltammograms of the electrochemical polymerization of taurine on the MWNT film-coated electrode. One obvious anodic wave at 1.6 V and two cathodic waves at −0.15 and −0.77 V are seen. An increase in cycle number results in the enhancement of the peak currents and a slight shift of the peak potentials. The shift of peak potential is possibly related to the change in resistance of the electrode during polymerization. A shiny and light green color was found on the electrode surface after eight cycles. Similar colorful films have been also reported due to the formation of polymers [43–45]. These results indicate the fabrication of poly(taurine) layers on MWNT-film coated electrode. This poly(taurine)/MWNT-modified electrode was then adopted for the following investigations.

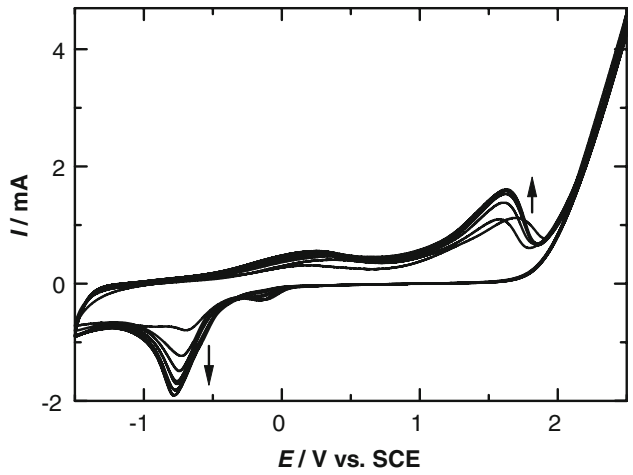

Fig. 1 Cyclic voltammograms of polymerization of taurine on the MWNTs film-coated glassy carbon electrode in the potential range from −1.5 to 2.5 V at a scan rate of 100 mV s^{-1}. The polymerization solution was 2 mM taurine in 1/15 M pH 6.98 phosphate buffer. The cycling number is 16

Since the electroactive surface area is the key issue to demonstrate the efficiency of the electrodes towards analytes in solutions, the electroactive surface area of the modified electrodes was first estimated by cyclic voltammetry using $Fe(CN)_6^{3-/4-}$ as probe molecules. Figure 2 shows cyclic voltammograms of (a) a bare, (b) MWNT modified, (c) poly(taurine)-film modified, and (d) poly(taurine)/MWNT-modified glassy carbon electrode in 10 mM $Fe(CN)_6^{3-/4-}$ solution containing 0.1 M KCl at a scan rate of 50 mV s^{-1}. Well-defined oxidation and reduction peaks are observed without significant difference in separation of peak-to-peak potentials on these electrodes. The biggest peak current is noticed on the poly(taurine)/MWNT-modified electrode, indicating the highest electroactive surface area.

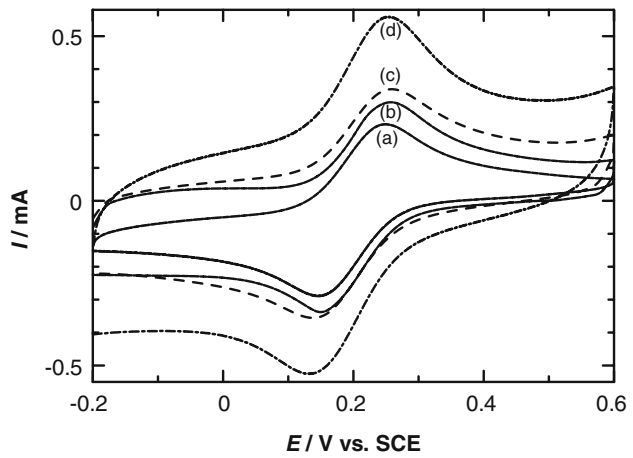

Fig. 2 Cyclic voltammograms of 10 mM $Fe(CN)_6^{3-/4-}$ in 0.1 M KCl on (a) bare, (b) the MWNTs film-modified, (c) the poly(taurine) film-modified, and (d) the poly(taurine)/MWNTs-modified glassy carbon electrode at a scan rate of 50 mV s^{-1}

The electroactive surface area was calculated according to the Randles–Sevcik equation [46],

$$I_p = 2.69 \times 10^5 A D^{1/2} n^{3/2} \nu^{1/2} c \quad (1)$$

where n (=1) is the number of electrons participating in the redox reaction, A is the area of the electroactive surface area (cm^2), D (=6.70 (±0.02) × 10^{-6} cm^2 s^{-1}) is the diffusion coefficient of $Fe(CN)_6^{3-/4-}$ in solution (cm^2 s^{-1}) [46], c (=10 mM) corresponds to the concentration of the redox probe ($Fe(CN)_6^{3-/4-}$, M), and v is the scan rate of the potential perturbation (V s^{-1}). The calculated electroactive surface area for the poly(taurine)/MWNT-modified electrode is 0.37 cm^2, while the surface areas for poly(taurine) film-coated and MWNT-modified electrodes are 0.22 and 0.19 cm^2, respectively. The significant increase in electroactive surface area suggests that the poly(taurine)/MWNT-modified electrode is promising for electrochemical sensing and bio-sensing.

Figure 3 shows cyclic voltammograms of 0.45 mM acetaminophen dissolving in pH 7.38 phosphate buffer solution at (a) a bare, (b) the MWNT film-coated, (c) the poly(taurine) film-coated, and (d) poly(taurine)/MWNTs-modified glassy carbon electrode. On the bare glassy carbon electrode, acetaminophen is oxidized irreversibly at 0.36 V with a small anodic peak current. No obvious reduction peak is observed. The anodic peak current of acetaminophen at the MWNT film-coated electrode increases and the oxidative peak potential shifts 15 mV negatively. However, on the poly(taurine) film-modified electrode and poly(taurine)/MWNT-modified electrodes, a pair of well-defined redox waves are observed at 0.37 and 0.27 V for the anodic and cathodic process, respectively.

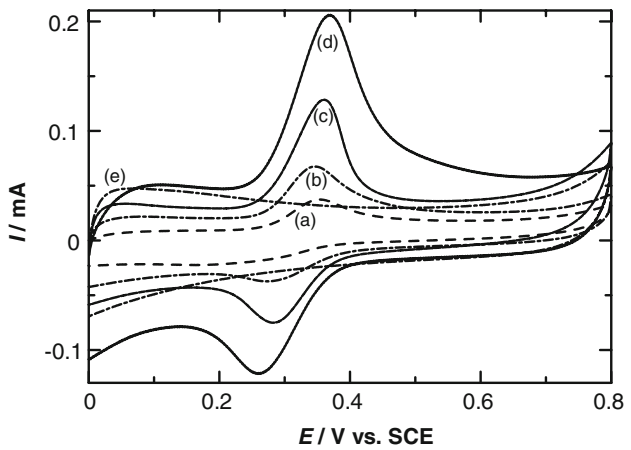

Fig. 3 Cyclic voltammograms of 0.45 mM acetaminophen in pH 7.38 PBS on (a) bare, (b) the MWNTs film-modified, (c) the poly(taurine)film-modified, and (d) the poly(taurine)/MWNTs-modified glassy carbon electrode at a scan rate of 50 mV s^{-1}. The curve (e) is the cyclic voltammograms on the poly(taurine)/MWNTs-modified electrode in pH 7.38 phosphate buffer without acetaminophen

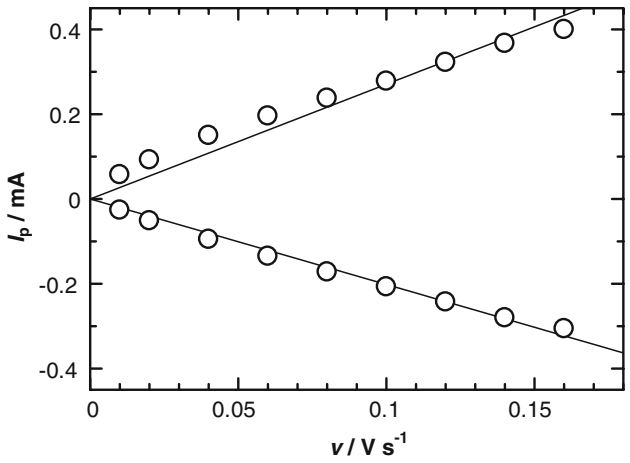

Fig. 4 Peak currents of 0.45 mM acetaminophen on the poly(taurine)/MWNTs-modified electrode, I_p, as a function of scan rate, v

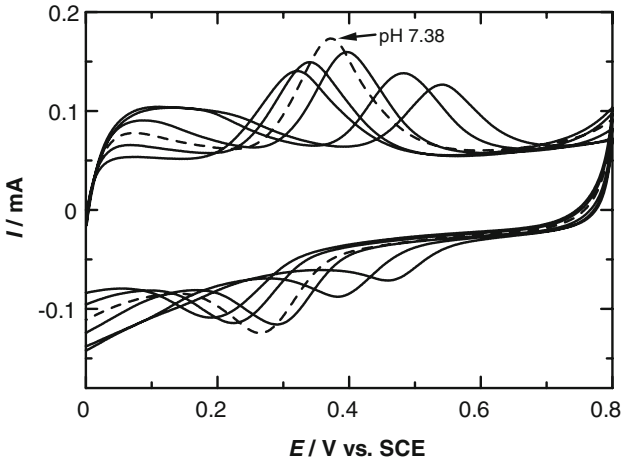

Fig. 5 Cyclic voltammograms of 0.45 mM acetaminophen on the poly(taurine)/MWNTs-modified electrode in phosphate buffer with different pH values. From right to left, the pH values are 4.4, 5.4, 6.2, 6.98, 7.38, 7.9, and 8.3, respectively

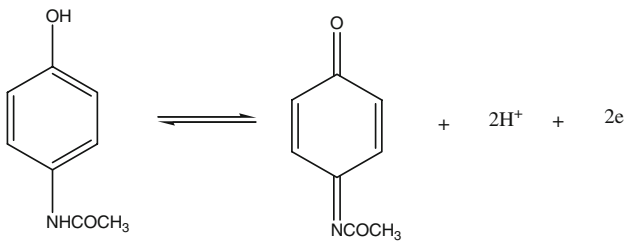

Fig. 6 Possible redox mechanism of acetaminophen on the poly(taurine)/MWNTs-modified electrode

The cyclic voltammogram (e) of the poly(taurine)/MWNT-modified electrode in pH 7.38 phosphate buffer without acetaminophen is featureless. Based on the electrochemical behavior of acetaminophen on the modified electrodes reported previously [31–40] and our experimental results, the anodic wave at 0.37 V may result from the oxidation of acetaminophen to imidogenquinone, while that at 0.27 V is from the reduction of imidogenquinone to acetaminophen. The peak currents on poly(taurine)/MWNT-modified electrodes (d) are much larger than those on (a) a bare, (b) MWNT film-coated, or (c) poly(taurine) film-coated electrode. The largest peak current is due to the largest electroactive surface area of poly(taurine)/MWNT-modified electrode, which has been demonstrated in the previous section. The peak current of acetaminophen on the poly(taurine)/MWNT-modified electrode is proportional to the concentration of acetaminophen, and hence the peak current is adopted as the parameter for the detection of acetaminophen in the next sections.

Mass transfer of acetaminophen on the poly(taurine)/MWNT-modified electrode was investigated. Figure 4 shows the peak currents as a function of scan rate, indicating proportionality. The effects of the accumulation potential and time on anodic peak current were examined. The oxidation peak currents of acetaminophen remain quite stable after 1 min accumulation at different potentials from −0.50 to 0.30 V. This reveals that the accumulation potential does not affect the oxidation remarkably. In contrast, accumulation time strongly influences the anodic peak current. The oxidative peak currents increase remarkably with longer accumulation time and reach maxima with an accumulation time of 30 s. The peak currents then remain constant even for longer accumulation times than 30 s. After the accumulation of acetaminophen, the resultant electrode still shows a voltammetric response when it is scanned in pH 7.38 phosphate buffer without acetaminophen. These results demonstrate an adsorption-controlled electrode process of acetaminophen on the poly(taurine)/MWNT-modified electrode.

The effect of pH on the voltammetric behavior of acetaminophen on the poly(taurine)/MWNT-modified electrode was examined. Figure 5 shows cyclic voltammograms of 0.45 mM acetaminophen in phosphate buffer with different pH values ranging from 4.4 to 8.3 at a scan rate of 50 mV s^{-1}. The anodic peak potential, $E_{p,a}$, and the anodic peak current change with pH. The anodic peak current increases when the buffer pH alters from 4.4 to 7.38. It reaches a maximum value when the buffer pH is 7.38 and then the anodic peak current drops when the buffer pH is higher than 7.38. When pH increases, the peak potential shifts negatively with a linear relationship of $E_{p,a}$ (V) = 0.79033–0.057 pH, (R = 0.999), indicating that the loss of electrons is accompanied by the loss of an equal number of protons [47]. The electrons transferred (n) during acetaminophen oxidation has been shown to be 2 [32]. Therefore, the oxidation and reduction of acetaminophen on the poly(taurine)/MWNT-modified electrode should be as shown in Fig. 6.

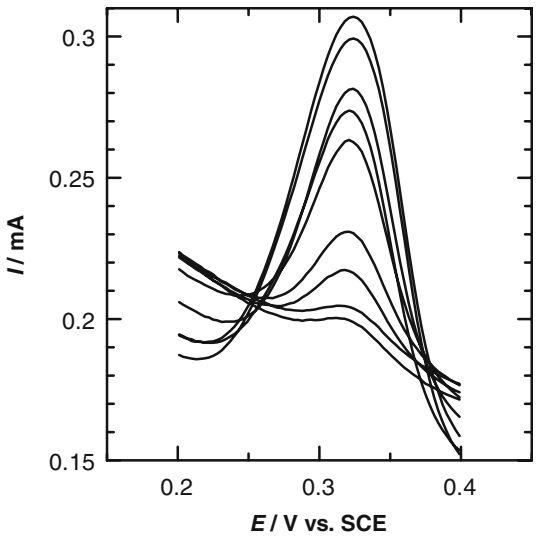

Fig. 7 Differential pulse voltammograms of acetaminophen on the poly(taurine)/MWNTs-modified electrode with different concentrations. From bottom to up, the concentrations are 1.0; 5.0; 15, 30, 50, 60, 70, 90, and 100 μM, respectively. The scan rate is 100 mV s^{-1} and the amplitude is 2.5 mV

The effects of the amount of MWNTs and the thickness of the polymer film on the voltammetric response of acetaminophen were investigated. An increase in the amount of MWNTs on the electrode results in a peak current enhancement. However, too high MWNT concentration results in a large background current, high noise level, low stability and poor reproducibility. In our work, a MWNT concentration of 1 mg mL^{-1} was chosen for the fabrication of poly(taurine)/MWNT-modified electrode. The polymer film thickness was varied by altering the scanning cycles during the electrochemical polymerization. Thicker films are found to exclude the interferences, but the analytes are also excluded. Longer response time is also required. If too thin a film is used the electrode is susceptible to the interferences. The best response of acetaminophen was obtained with eight cycles.

Figure 7 shows differential pulse voltammograms of acetaminophen on the poly(taurine)/MWNT-modified electrode under different concentrations. The oxidative peak current, $I_{p,a}$, is linear with the acetaminophen concentration, c, in the range 1.0×10^{-6}–1.0×10^{-4} M and the linear regression equation is $I_{p,a}$ (A) $= 1.23c$(M) $+ 2.00 \times 10^{-4}$ ($R = 0.9984$). The calculated detection limit is 5×10^{-7} M (S/N = 3). The electrode was continuously used for the detection of acetaminophen over 30 days, indicating a good stability. The relative standard derivation was <2.1% for the detection of 0.45 mM acetaminophen for 10 runs, indicating the electrode is sensitive for monitoring.

Possible interferences for acetaminophen detection were investigated by addition of various ions to the buffer solution in the presence of 50 μM acetaminophen. Ions such as Na^+, K^+, Fe^{3+}, Cu^{2+}, Al^{3+}, Cl^-, NO^{3-}, $CO_3{}^{2-}$, and $SO_4{}^{2-}$ showed no interference. As for the common interferences in biological samples for the determination of acetaminophen, 30-fold lysine, ascorbic acid, tyrosine, cysteine, and Vitamin B_6 have no effect.

Table 1 Determination results of acetaminophen in injection samples

Determined ($\times 10^{-5}$ M)	Added ($\times 10^{-5}$ M)	Found ($\times 10^{-5}$ M)	Recovery (%)
3.00	1.50	4.48	99.6
3.00	2.50	5.52	100.4
3.00	3.50	6.66	102.4
3.00	4.50	7.58	101.1
3.00	5.50	8.37	98.5

The method was also applied to determine acetaminophen in Composite Chlorzoxazone Tablets (Shiguibao Pharmaceutical Group Corporation, Shanghai, China). Powdered tablets were dissolved in 125 mL distilled water. The suspension was stirred and centrifuged at 3500 rpm for 10 min. The 5 mL supernatant was diluted 50-fold with phosphate buffer. A portion of the resultant solution (10 mL) was then taken out and served as the sample for the detection of acetaminophen concentration. The concentration of acetaminophen was calculated using the standard addition method. The results obtained are listed in Table 1. The relative standard deviation of five parallel detections for each sample is <5%. In addition, the recoveries of acetaminophen using this method are between 98.5 and 102.4%. These results indicate that the determination of acetaminophen using poly(taurine)/MWNT-modified electrode is effective and sensitive. The proposed method does not show higher detection limit than that reported in the literature using single-walled carbon nanotubes [40]. This might result from the different properties of carbon nanotubes and/or different types and numbers of terminal functional groups on the surface of the carbon nanotubes. We are currently working on this topic and will report these results elsewhere.

4 Conclusions

In summary, we prepared a new type of polymer/CNT-modified electrode by electrochemical polymerization of a dye on a MWNT film-coated electrode. This provides a new way to construct nanostructured electrodes. The prepared polymer/MWNT-modified electrode shows a large and controllable electroactive area which is efficient for electrochemical sensing. These sensors exhibit high stability, excellent sensitivity and selectivity for the detection of acetaminophen. The proposed method has the potential

of being used as an official way of monitoring the concentration of acetaminophen in injections, drugs and pharmaceuticals.

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