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Voltammetric sensor for tinidazole based on poly(carmine) film modified electrode and its application

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Abstract

A poly(carmine) film modified glassy carbon electrode (GCE) was fabricated and the electrochemical behaviors of tinidazole were investigated by electrochemical methods at this modified electrode. A well-defined reduction peak is observed at 0.606 V. Compared with that at a bare GCE, the reduction peak potential of tinidazole shifts negatively and the reduction peak current increases significantly at the modified electrode. The influences of some parameters on the reduction of tinidazole were examined and a simple and sensitive electroanalytical method was developed for the determination of tinidazole. The reduction peak current is proportional to the concentration of tinidazole from 1×10^{-7} to 5×10^{-5} M. The detection limit is about 5.0×10^{-8} M for 90 s accumulation at a constant potential of 0 V. Based on the experimental data a possible mechanism is proposed and discussed. The proposed method was applied to determine tinidazole in drugs and the result was satisfying.

Keywords: Tinidazole; Carmine; Chemically modified electrodes; Voltammetric determination

1. Introduction

Tinidazole is an anti-parasitic drug used as a treatment for a variety of amebic and parasitic infections [1]. The chemical structure is shown in Fig. 1. Because of its important role in numerous pathological processes, tinidazole has been widely studied in recent years. To date, various methods have been employed in the quantitative determination of tinidazole, such as spectrophotometric [2,3], chromatographic methods [4,5] and electrochemical method [6,7]. As far as I know, the detection of tinidazole at poly(carmine) film electrode has not been reported.

Electroactive polymeric films have acquired wide popularity, since they are easier to be modified on the electrode surface than monolayer. A number of studies indicated that polymer film modified electrodes showed an enhanced response for the determination of various important biological and clinical species. Many researches demonstrated that electropolymerization is a very convenient way to immobilize polymers on electrode surface and the thickness, permeation and charge transport characteristics of the polymeric films can be controlled by the potential and current applied. Dye molecules have been widely used as mediators to study the electrochemical reduction of nitro compounds [8,9], including methylene blue [10,11], methylene green [12] and brilliant cresyl blue [13]. In general, the derivatives of dyes formed via bonding a dye molecule to an aromatic ring covalently could decrease their proton-donor ability and improve their catalytic activity [14]. Polymerization of dyes can form a cross-linked oligomer which leads to the enhancement of its electrocatalytic ability [15].

As we know, carmine is a valuable dye obtained from the bodies of the female of insect *Coccus cacti* [16]. In this paper, carmine was used to develop a polymer film modified electrode by a constant potential technique. This modified

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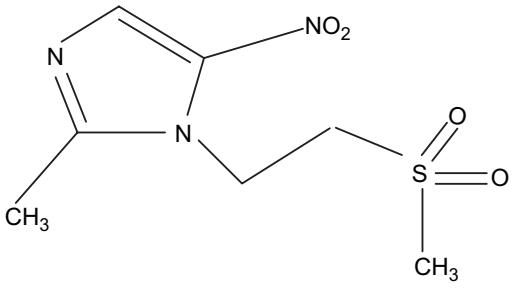

Fig. 1. Scheme of the chemical structure for tinidazole.

electrode shows excellent enhancement effects on the electrochemical reduction of tinidazole. The reduction peak current increases remarkably and peak potential shifts positively slightly at this modified electrode. The outcome of scientific experiments showed that the sensitivity for the determination of tinidazole increases markedly at poly(carmine) film-coated GCE. Furthermore, some experimental conditions were optimized and an electrochemical method for the determination of tinidazole was proposed. This method was convenient and available because of its rapid response, high sensitivity, good selectivity, low detection limit, excellent reproducibility, simplicity and low cost.

2. Experimental

2.1. Apparatus and reagents

Electrochemical data were obtained with a three-electrode system using a CHI 660A electrochemical workstation (CH Instruments, TX, USA). A three-electrode system was developed including the polymer-modified electrode as working electrode, a platinum wire counter electrode and a saturated calomel electrode (SCE) as reference electrode.

Tinidazole (obtained from Sigma Chemical Company) was dissolved in ethanol to form 1.0×10^{-3} M standard solution and stored at 277.15 K in dark to avoid any decomposition. Carmine was purchased from Flyka. Other chemicals used were analytical reagents. All the chemicals were used without further purification and all the solutions were prepared with doubly distilled water.

2.2. Preparation of modified electrode

Electropolymerization of carmine was carried out in 1 mol L^{-1} H_2SO_4 solution containing 1.0×10^{-3} mol L^{-1} carmine at a constant potential of 1.6 V for 20 min. The modified electrode was washed with ethanol and distilled water in turn.

2.3. Analytical procedure

A certain volume of phosphate buffer solution (PBS, pH 5.7) was used as the supporting electrolyte. After addition of tinidazole standard solutions the solution was deoxidized with pure nitrogen for 10 min. The accumulation was carried out at 0 V via stirring the solution for 90 s. The voltammograms were recorded by linear sweep voltammograms (LSV) from 0.0 to −1.0 V. The reduction peak current was measured at 0.606 V. After each measurement the modified electrode was refreshed by successive cyclic voltammetric scan in phosphate buffer solution (pH 5.5) between 0.0 and 1.0 V at 100 mV/s to get a reproducible electrode surface.

2.4. Sample preparation

Tinidazole tablet (10 mg, obtained from Guangzhou Qiaoguang Pharmaceutical Co., Ltd., China No 40060) was weighed accurately and dissolved in ethanol, then stirred magnetically for 15 min to dissolve completely. The extract was filtered, and filtrate was diluted to 10 ml with ethanol and stored at 277.15 K in dark. The standard addition method was used to evaluate the content of tinidazole in the tablet.

The suitable content of one ampoule [1 ml of solution contains 4 mg tinidazole and 8.5 mg sodium chloride] was diluted with doubly distilled water to 50 ml and stored at 277.15 K in dark.

3. Results and discussion

3.1. Electrochemical behaviors of tinidazole

Fig. 2 shows cyclic voltammograms of 1×10^{-4} mol L^{-1} tinidazole at the poly(carmine) film modified GCE in 0.1 mol L^{-1} phosphate buffer solution (pH 5.7). A well-defined reduction peak appears at 0.606 V when potential initially sweeps from 0.2 to −1.2 V and no peak is observed in the reversal scan, revealing that the electrode reaction of tinidazole is a totally irreversible process. According to the accepted mechanism [17], the cathodic response is attributed to four-electron reduction of the nitro group via the derivation of the hydroxylamine. However, the reduction peak current decreases remarkably in the second scan. During following

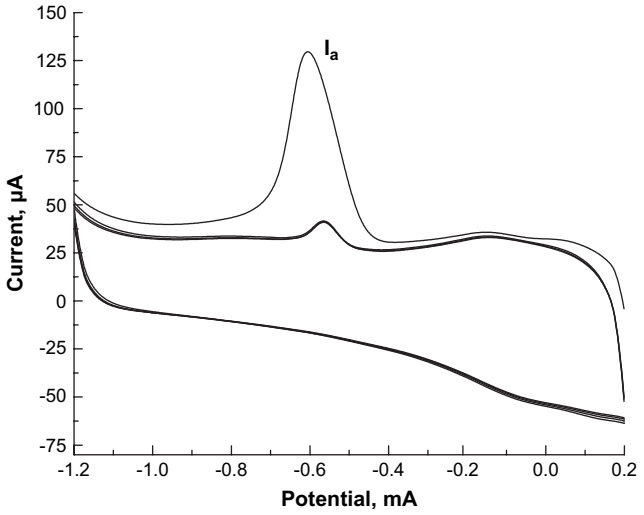

Fig. 2. Cyclic voltammograms of 1×10^{-4} mol L^{-1} tinidazole at the poly(carmine) film modified GCE in 0.01 mol L^{-1} phosphate buffer solution (pH 5.7). Scan rate, 100 mV s^{-1}.

successive cyclic scans, the reduction peak current decreases continuously with the increase of scan number, resulting from the fact that the electrode surface is blocked by the strong adsorption of the reaction products.

The voltammetric responses of 1×10^{-4} mol L^{-1} tinidazole at different electrodes are illustrated in Fig. 3 in phosphate buffer solution (pH 5.7) for 90 s accumulation at 0 V. A flat reduction peak appears at −0.649 V at the bare glassy carbon electrode (Fig. 3c). The reduction peak current of tinidazole at the modified electrode increases significantly and the reduction peak potential shifts positively for 40 mV (Fig. 3a). This remarkable enhancement is undoubtedly attributed to the extraordinary properties of polymer, such as high aspect ratio and strong adsorption ability.

3.2. Effect of scan rate on the peak current

The influences of scan rate on the electrochemical behavior of tinidazole at the poly(carmine) film modified GCE in phosphate buffer solution (pH 5.7) were researched and the data are demonstrated in Fig. 4. Moreover, the electrochemical behaviors of tinidazole at different scan rates from 20 to 240 mV/s were investigated by cyclic voltammetry. The reduction peak current i_p of tinidazole increases with increasing scan rate and exhibits a linear relation with the scan rate. The corresponding linear regression equation is expressed as follows i_p (10 μA) = 2.7760 + 0.0700v (mV/s) (R = 0.9929). The result indicates that the electrode process of reduction of tinidazole at this modified electrode is controlled by the adsorption step. The reduction peak is corresponding to the four-electron reduction of nitro group to the corresponding hydroxylamine according to the currently accepted mechanism for the electroreduction of aromatic and heteroaromatic nitro compounds [18].

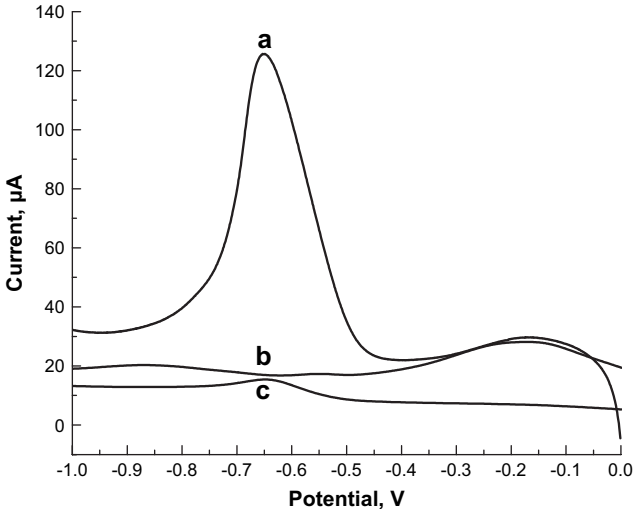

Fig. 3. Linear sweep voltammograms of 1×10^{-4} mol L^{-1} tinidazole at the poly(carmine)film modified GCE (a); bare GCE (c). Curve (b) presents the voltammograms at the modified electrode in phosphate buffer solution without tinidazole. Scan rate: 100 mV s^{-1}; accumulation potential, 0 V; accumulation time, 90 s.

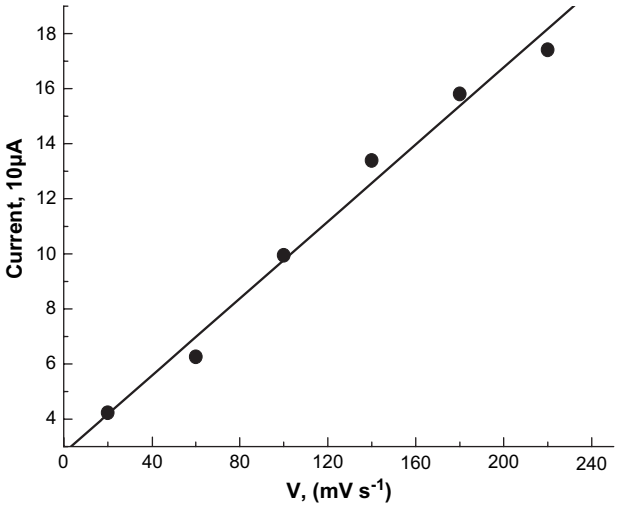

Fig. 4. Effect of scan rates on the reduction peak current of 1×10^{-4} mol L^{-1} tinidazole. Other conditions are the same as in Fig. 1.

3.3. Effect of pH on the peak current and peak potential of tinidazole

The effects of pH of solution on the tinidazole reduction at the poly(carmine) film modified GCE were investigated by cyclic voltammetry and the result is shown in Fig. 5. The reduction peak potential of tinidazole shifts negatively with the increase of pH. The slope for the linear regression equation is −0.061, suggesting that the number of the electron transferred in the reduction of tinidazole equals to that of proton. The peak current increases with the increase of pH and gets to utmost at pH 5.5, and then decreases.

3.4. Optimization of accumulation conditions

The reduction peak current of 1×10^{-4} mol L^{-1} tinidazole remained almost unchanged as the accumulation potential shifted from 0.4 to 0.0 V. However, the peak current increased gradually when accumulation potential shifted negatively in the range of 0.0 to −0.5 V. Thus, an accumulation potential of 0.0 V was employed.

The accumulation time significantly affects the reduction peak current of 1.0×10^{-4} mol L^{-1} tinidazole as shown in Fig. 3. The reduction peak current enhances greatly with the increase of the accumulation time within first 90 s and then remains stable. This may be attributed to the saturated adsorption of tinidazole on the poly(carmine) film modified GCE surface.

3.5. Calibration graph

Under these optimized experimental conditions, the calibration curve for tinidazole in 0.01 mol L^{-1} phosphate buffer solution (pH 5.7) at the poly(carmine) film modified GCE was characterized by LSV, and the linear range comprised between 1.0×10^{-7} and 5.0×10^{-5} mol L^{-1} in terms of the relationship between tinidazole concentration and the reduction peak

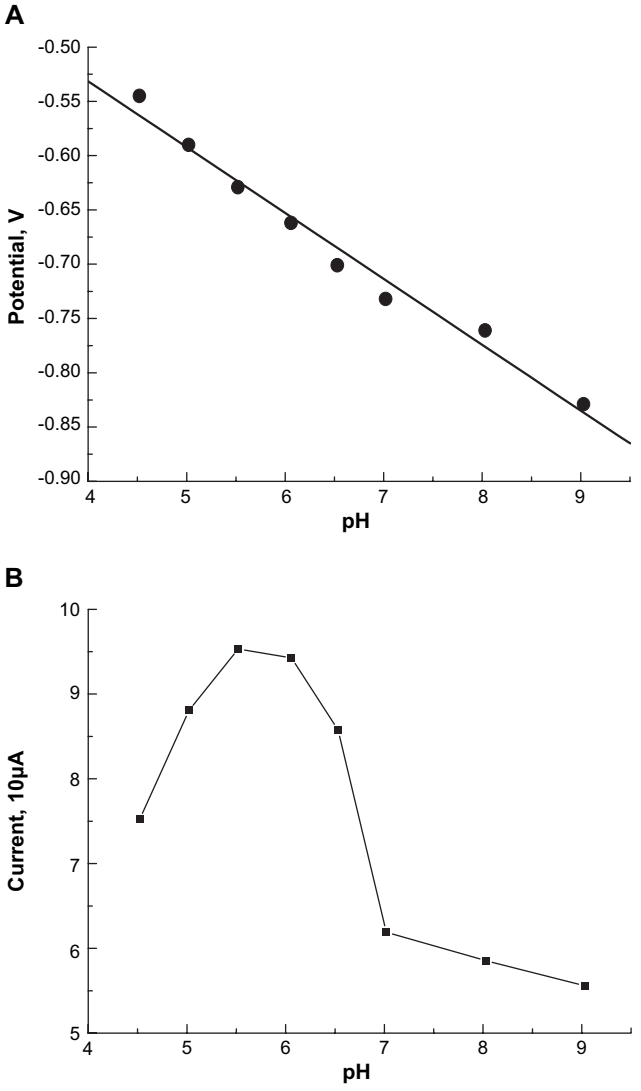

Fig. 5. Effects of pH on the peak potentials (A) and peak currents (B) of 1×10^{-4} mol L^{-1} tinidazole reduction at the poly(carmine) film modified GCE. Scan rate: 100 mV s^{-1}.

current. The corresponding linear regression equation can be expressed as follows: i_p (μA) $= 2.7494 + 0.9286c$ ($R = 0.9969$) and the detection limit was 5.0×10^{-8} mol L^{-1}.

The stability of the modified electrode was evaluated by the current responses of 1.0×10^{-5} mol L^{-1} tinidazole at room temperature. During measurements, the modified electrode was kept at 4 °C. The experimental results indicate that the sensitivity maintains 96.84% of that of initial modified electrode after 2 weeks, suggesting good stability.

3.6. Interference

Under optimized experimental conditions described above, the effects of some compounds on the current responses of 1×10^{-5} mol L^{-1} tinidazole have been evaluated. The results showed that 500-fold of Cd^{2+}, Pb^{2+}, Cu^{2+}, Hg^{2+}, K^{+}, Zn^{2+}, Mg^{2+}, Ca^{2+}, Fe^{3+}, Fe^{2+} and Al^{3+} does not interfere with the determination of tinidazole. Some organic molecules such as 10-fold of dopamine, ascorbic acid, acetaminophen, tyrosine, vitamin B, glucose, cholesterol have almost no influences on the current responses of 1×10^{-5} mol L^{-1} tinidazole (signal change below 6%) (error < 5%). However, some compounds containing a nitro group, such as nitrofurantoin, azathioprien and nitrophenols, have serious influences on the determination of tinidazole, because they contain the same electroactive groups as inidazole and affect their reduction peak current of tinidazole.

Table 1
Determination of tinidazole in commercial available tablets ($n = 7$)

Codeine-tablet	Original detected value (μM)	Spike (μM)	Detected value after spike (μM)	Recovery (%)
#1	17.77 ± 0.12	15.00	32.53 ± 0.07	98.4
#2	7.461 ± 0.21	15.00	22.14 ± 0.03	97.9
#3	27.49 ± 0.17	10.00	37.94 ± 0.11	107.5

3.7. Tinidazole assay in pharmaceutical formulation

The proposed method was applied to determination of tinidazole in tablets by LSV. The data are shown in Table 1. The recoveries in this method were investigated and the value is between 98.4 and 107.5%, which indicates that the determination of tinidazole using the poly(carmine) film modified GCE is effective and sensitive.

3.8. Determination of tinidazole in pharmaceutical formulation

Standard addition method was used for the determination of tinidazole in a tinidazole tablets and ampoule. The analytical procedure was the same as that described above. The results are shown in Tables 1 and 2. The recoveries were in the range of 95.7–107.5%, which can be considered to be good. These results were consistent with that obtained by HPLC.

4. Conclusion

Carmine is easy to be cast onto the surface of glassy carbon electrode to form modified electrode. The modified electrode displays a strongly electrocatalytic activity towards the reduction of tinidazole. Based on this property, the concentration of tinidazole in solution could be determined directly by voltammetry with excellent sensitivity. Sufficient experimental results demonstrated that the poly(carmine) modified electrodes are good electrochemical sensors for direct measurements of tinidazole.

Table 2
Determination of tinidazole in commercial available ampoule ($n = 7$)

Codeine-ampoule	Original detected value (μM)	Spike (μM)	Detected value after spike (μM)	Recovery (%)
#1	4.99 ± 0.16	15.00	19.34 ± 0.04	95.7
#2	1.16 ± 0.03	15.00	16.17 ± 0.09	100.1
#3	3.11 ± 0.11	10.00	13.24 ± 0.06	101.3

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