

Voltammetric Sensing of Promethazine on a Multi-Walled Carbon Nanotubes Coated Gold Electrode

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The voltammetric study of promethazine on multi-walled carbon nanotubes (MWNTs) coated gold electrode (MWNTs/Au) has been carried out. Promethazine can cause a sensitive anodic peak on it. In pH=4.0 phosphate buffer solution, the peak potential is 0.66 V (vs. SCE). The electrode process is adsorption-controlled, the adsorption amount is about 9.9×10^{-10} mol·cm⁻² (for 1.0×10^{-6} M promethazine), and the electron-transfer coefficient (α) is about 0.79. The influence of various experimental parameters on the voltammetric behavior of promethazine has been examined. Under the optimized conditions, the anodic peak current is linear to promethazine concentration in the range from 5.0×10^{-8} to 1.0×10^{-5} M. After 120 s accumulation, the detection limit is 1.0×10^{-8} M (S/N=3). This method has been successfully applied to the determination of promethazine in medicine sample (i.e. Compound Reserpine) and the recovery is 97.6-101.8%. The electrode can be regenerated by successively repeating potential scan in a blank solution, and exhibits good reproducibility.

Keywords: promethazine, multi-walled carbon nanotubes, voltammetry, compound reserpine

1. INTRODUCTION

Promethazine is an important compound in the large group of phenothiazine derivatives. It is widely used as therapeutic agent for treating various mental disorders or for enhancing the analgesic, anesthetic and sedative effect with other medicines. The characteristics and determination of promethazine were studied by using many methods including electrophoresis [1], spectrophotometry [2], flow injection analysis [3], and chromatography [4]. Based on the electroactivity of promethazine, it also was investigated and detected electrochemically [5-9]. Uslu et al studied the electrochemical oxidation of promethazine on platinum and glassy carbon electrodes by linear sweep and cyclic voltammetry and developed a voltammetric method for its determination [5]. Khodari et al. reported the determination of promethazine at lipid-modified graphite paste electrodes [6]. The presence of lipid

made the response more sensitive and the detection limit was down to 1.0×10^{-9} M after 5 minutes accumulation by using differential pulse voltammetry. Ni et al. studied the voltammetric behavior of promethazine hydrochloride and chlorpromazine hydrochloride at a glassy carbon electrode in Britton-Robinson buffer of pH 9.0 [7]. They proposed a method for the simultaneous determination of them, which is based on their oxidation at a glassy carbon electrode and a multivariate calibration method.

Carbon nanotubes (CNTs) can promote electron-transfer reactions and improve sensitivity, so CNTs based electrodes are widely used in electrochemistry field [10-13]. Some phenothiazine derivatives were studied and determined with CNTs -based electrodes. For example, Zeng et al. fabricated a multi-walled carbon nanotubes/(3-mercaptopropyl)trimethoxysilane bilayer modified gold electrode for fluphenazine determination and got a satisfactory result [14]. But the electrode preparation was more complicated. To our knowledge, there are no reports on the detection of promethazine with a multi-walled carbon nanotubes coated electrode. The purpose of this work is to explore the voltammetric behavior of promethazine on MWNTs/Au electrodes and the feasibility to detect it with a simple CNTs-based electrode.

2. EXPERIMENTS

2.1. Apparatus

Electrochemical experiments were performed on a CHI 660B electrochemical workstation (CH Instrumental Company, Shanghai, China) with a conventional three-electrode cell. A gold electrode or a MWNTs/Au electrode served as working electrode, a saturated calomel electrode (SCE) and a platinum wire served as reference and auxiliary electrode, respectively. The pH values of solutions were measured with a PHS-3C pH meter (Shanghai, China).

2.2. Chemicals

Promethazine was purchased from Jiufu Pharmaceutical Company (Shanghai, China) and used as received. The stock solution of promethazine (5.0 mM) was prepared with ethanol. The multi-walled carbon nanotubes (Diameter: <10 nm; Length: 1-2 μm) was obtained from Shenzhen Nanotech Port Co. Ltd (Shenzhen, China). The medicine sample came from Changzhou Pharmaceutical Company (Jiangsu, China). Prior to determination, it was ground into powder, dissolved in ethanol and then filtered into a container. A standard addition method was used to assay it. Other reagents used were analytical or reagent grade, and water used was redistilled.

2.3. Preparation of MWNTs modified electrode

Prior to modification, the gold electrode was polished with 0.3 and 0.05 μm alumina slurries, rinsed with double distilled water, and then ultrasonicated for 3 min in a water bath. The multi-walled carbon nanotubes was dispersed in N, N-Dimethylformamide (DMF) with the aid of ultrasonic agitation to prepare 1.0 mg mL⁻¹ MWNTs suspension. The MWNTs/Au electrode was fabricated by dropping 5.0 μL MWNTs suspension on the Au electrode surface and evaporating the solvent.

2.4. Procedure

A 10 mL of phosphate buffer solution (0.10 M, pH=4.0) with proper amount of promethazine was transferred into a cell, and then the electrode system was immersed into the solution. After accumulation at 0.2 V for 120 s, the potential scan between 0.2 and 0.8 V was triggered, and the anodic peak was measured. The electrode was regenerated by successive potential scan between 0.2 and 0.8 V in a blank solution for reuse. All experiments were carried out at room temperature.

3. RESULTS AND DISCUSSION

3.1. Estimation of electrode area

$K_3Fe(CN)_6$ could exhibit a pair of reversible peaks at the MWNTs/Au electrode. When scan rate changed from 50 to 500 $mV \cdot s^{-1}$, the anodic peak current was linear to its square root. The regression equation was $i_p = 4.13 + 108 v^{1/2}$ ($r = 0.999$). For a reversible system, the peak current should follow Randles-Sevcik equation [15]: $i_p = 2.69 \times 10^5 n^{3/2} AD^{1/2} C_0 v^{1/2}$. Supposed the diffusion coefficient (D) of $K_3Fe(CN)_6$ was $6.5 \times 10^{-6} cm^2 \cdot s^{-1}$ in this case [16], the electrode area of MWNTs/Au was estimated and it was about $0.079 cm^2$. It was larger than the effective area of the bare gold electrode (ca. $0.0533 cm^2$). Therefore, in comparison with the bare gold electrode, the MWNTs/Au could give more sensitive response to electroactive species.

3.2. Cyclic voltammograms of promethazine

Promethazine can produce a pair of voltammetric peaks on the MWNTs/Au in phosphate buffer solutions (Fig. 1). At $100 mV s^{-1}$, their peak potentials are 0.40 and 0.66 V, respectively.

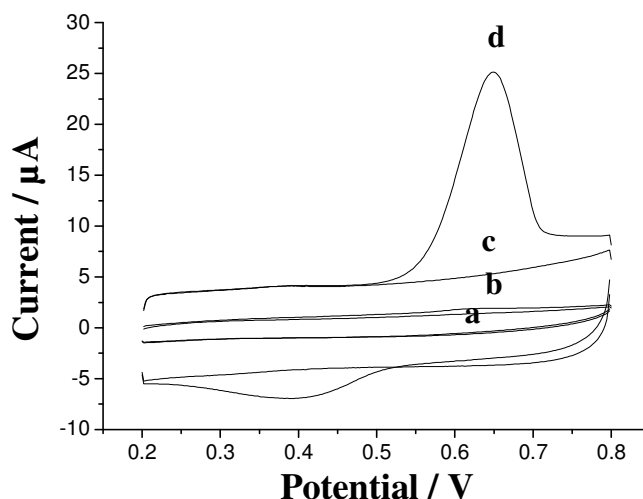


Figure 1. Cyclic voltammograms of Au electrode (a, b) and MWNTs/Au electrode (c, d) in solution containing 0 (a, c) or 5.0×10^{-6} M promethazine (b, d). Supporting electrolyte: 0.10 M phosphate buffer (pH=4.0); scan rate: $100 mV s^{-1}$; accumulation under open circuit for 60 s.

The anodic peak is much higher than the cathodic peak and the peak separation is quite large, meaning the electrochemical process is irreversible. For the anodic peak, in this case the signal to background current ratio is about 2.3, which is greater than on a bare glassy carbon electrode, platinum electrode and graphite paste electrode, but smaller than on a carbon nanotubes paste electrode. However, a carbon nanotubes paste electrode shows poor reproducibility as promethazine can enter in the paste. As can be seen, promethazine does not generate voltammetric peak on the bare gold electrode, thus the voltammetric response of promethazine on MWNTs/Au should be ascribed to the effect of MWNTs, which can promote the electron transfer and enhance the accumulation of promethazine. The corresponding hydrodynamic voltammograms of promethazine are shown in Fig. 2.

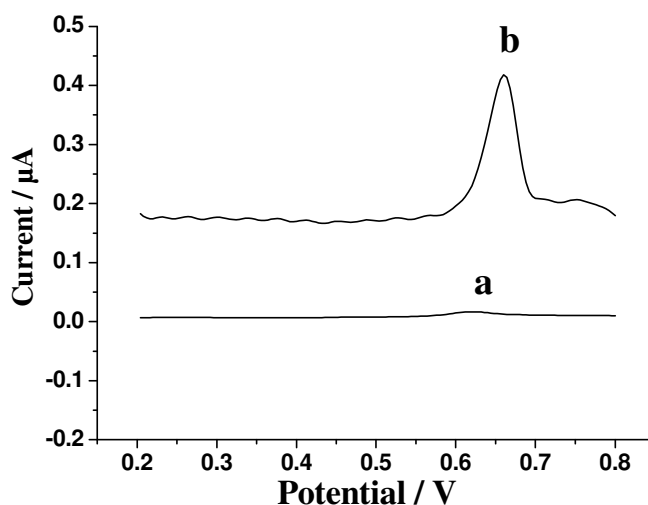


Figure 2. Hydrodynamic voltammograms of promethazine at bare gold electrode (a) and MWNTs/Au (b). Other conditions as in Fig. 1

Promethazine does not exhibit discernible peaks at the bare gold electrode in the potential range. But on the MWNTs/Au, a sharp peak is observable, which starts at 0.60 V and reaches a maximum value at 0.66 V. This illustrates that the MWNTs/Au is favorable for the accumulation and redox of promethazine. If a MWNTs/Au was immersed in a 1.0×10^{-6} M promethazine solution for 2 min, then rinsed with water and transferred into a blank buffer solution for voltammetric measurement, a pair of redox peaks was observable. The peaks were a little smaller than those without such treatment. Hence, the influence of some coexist species can be expected to be eliminated by measurement in a blank solution after the accumulation step.

3.3. Influence of pH

The influence of solution pH on the peak current and potential was investigated from 2.5 to 9.0. With increasing pH, the peak current increased and attained a maximum value at about pH 4.0 (Fig. 3). Further increase in solution pH would make the peak height decrease. Part of this can be attributed to

the change of electrostatic interaction between MWNT and promethazine, which depends on their protonization. In addition, it is also related to the change of electrochemical reaction rate as it involves proton-transfer. The peak potential shifts negatively with pH rising at a rate of about 26 mV/ pH, which suggests that the number of electron-transferred is two times as many as that of proton-transferred in the electrochemical reaction. This is different from what reported in literature [7]. It must be related to the protonization of promethazine in acidic solutions. In this work, pH 4.0 phosphate buffer solution is chosen.

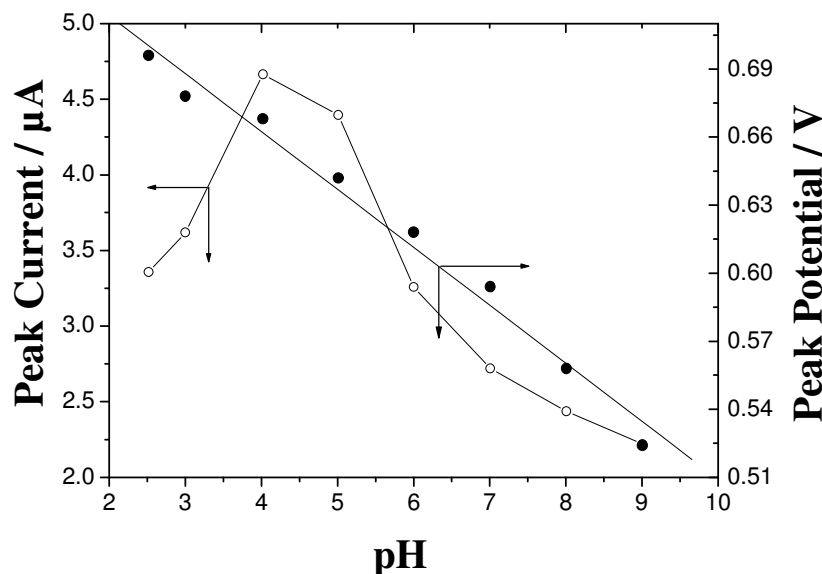


Figure 3. Influence of solution pH on anodic peak current and peak potential. Promethazine concentration: 1.0×10^{-6} M; other conditions as in Fig. 1

3.4. Influence of scan rate

Fig. 4 illustrates the influence of scan rate on the cyclic voltammogram of promethazine. In the range of 20 to 500 $\text{mV} \cdot \text{s}^{-1}$, the peak current and scan rate show a linear relationship. The regression equation is: $i_{\text{pa}} (\mu\text{A}) = 1.06 + 30.7 v$ (v : $\text{V} \cdot \text{s}^{-1}$, $r = 0.999$). This indicates that the electrode process is controlled by adsorption. In addition, the peak potential is linear to $\ln v$, and the regression equation is $E_{\text{pa}} = 0.698 + 0.0299 \ln v$ (E_{pa} : V, $r = 0.996$), which suggests that the electrochemical process is irreversible. For an irreversible adsorbed system, it should satisfy the equation $i_{\text{p}} = n^2 F^2 v A \Gamma_0^* / 4RT$ [17]. According to the slope of the $i_{\text{p}}-v$ plot, the surface concentration of promethazine on the MWNTs/Au is estimated to be $9.9 \times 10^{-10} \text{ mol} \cdot \text{cm}^{-2}$ ($n=2$ [7]) under this condition. On the other hand, the E_{pa} and $\ln v$ satisfy following equation [18]:

$$E_{\text{pa}} = E_0' + m [0.78 + \ln(D^{1/2} k_s^{-1}) - 0.5 \ln m] + (m/2) \ln v, \quad m = RT / [(1-\alpha) n_a F]$$

Thus the electron transfer coefficient α can be calculated and it is 0.79, which is greater than on a glassy carbon electrode.

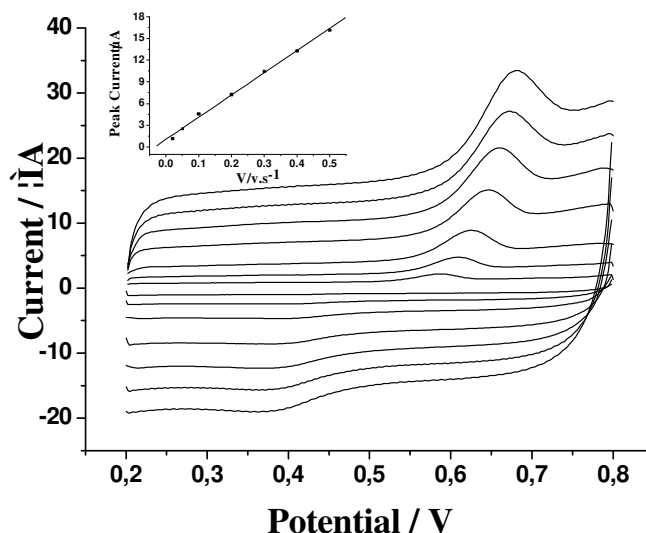


Figure 4. Influence of scan rate on the anodic peak. Scan rate: 20, 50, 100, 200, 300, 400, 500 $\text{mV} \cdot \text{s}^{-1}$ (from inner to outer); other conditions as in Fig. 3; Insert is the plot of anodic peak current versus scan rate.

3.5. Influence of accumulation potential and accumulation time

When the accumulation potential varies from -0.6 V to 0.4 V, the peak current increases until it is up to 0.2 V, then decreases. This indicates that the accumulation of promethazine involves the contribution of electrostatic effect. When the accumulation time is prolonged, the peak current increases rapidly at first, and then it keeps nearly unchanged (Fig. 5). This is a typical feature of an adsorption system, and means that a saturation accumulation is reached. Herein, 0.2 V is selected as accumulation potential and 120 s as accumulation time.

3.6. Calibration curve

Under the selected experiment conditions (i.e. $t_a=120$ s, $E_a=0.2$ V, $\text{pH}=4.0$), the variation of peak current with promethazine concentration was investigated. The results show that when the concentration changes from 5.0×10^{-8} to 1.0×10^{-5} M, the anodic peak current is linear to it. The regression equation is: $i_p (\mu\text{A}) = 1.96 + 1.67 c (\mu\text{M})$ ($r=0.992$). When the concentration exceeds 5.0×10^{-5} M, the increase in peak current slows down. When the accumulation time is 120 s the detection limit is 1.0×10^{-8} M ($S/N=3$). Therefore, the electrode is quite sensitive to promethazine although it is easily prepared. The peak currents of promethazine decrease rapidly when the potential scan is successively repeated. Thus the modified electrode is regenerated after a determination through repeating potential scan in a 0.10 M blank buffer solution. As an example, a 5.0×10^{-7} M promethazine solution was

measured for eight times with an electrode generated by such method; the relative standard deviation (RSD) of peak current was 1.53%, indicating that the modified electrode had good reproducibility.

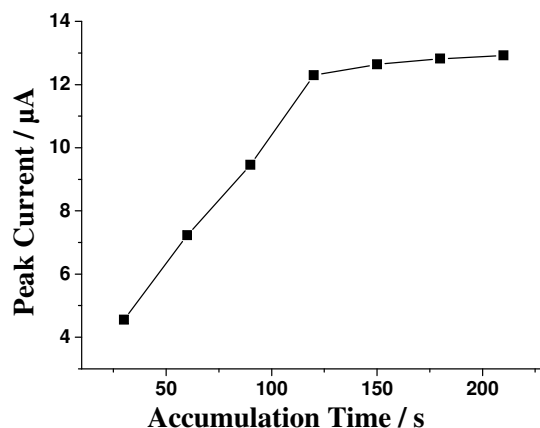


Figure 5. Variation of peak current with accumulation time. Accumulation potential: 0.2 V; other conditions as in Fig.3

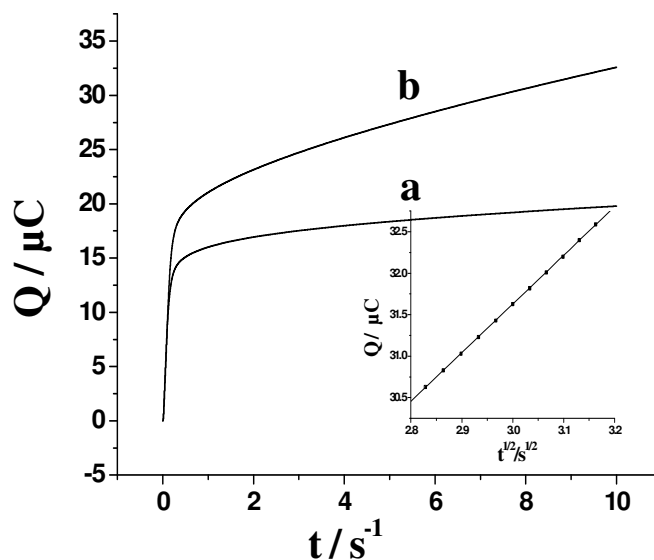


Figure 6. Chronocoulometric response of MWNTs/Au in 0.10 M phosphate buffer solution (pH=4.0) without (a) and with 5.0×10^{-5} M promethazine (b). Inset is the Q vs $t^{1/2}$ plot.

3.7. Chronocoulometric response

Fig. 6 shows the chronocoulograms of MWNTs/Au in a promethazine solution. According to the curves, a Q vs $t^{1/2}$ plot is made, and it shows a good linear relationship. The regression equation is $Q = 1.77 + 3.14 t^{1/2}$ (Q : μC ; t : s; $r = 0.999$). According to the equation [19]: $Q = (2nFAD^{1/2}C_0 t^{1/2}) / \pi^{1/2} + Q_{dl} + nFA_0$, the diffusion coefficient of promethazine is calculated to be $1.33 \times 10^{-5} \text{ cm}^2 \cdot \text{s}^{-1}$. It is smaller,

thus the diffusion current component is very small at lower concentration. The peak current should mainly be ascribed to the oxidation of accumulated promethazine.

3.8. Influence of some foreign species

The influence of some heavy metal ions and organic compounds was tested. The results showed that 100-fold of Cu^{2+} , Zn^{2+} , Fe^{3+} , Pb^{2+} , hypoxanthine, VB_1 , glucose, ascorbic acid, amino acetic acid and L-cysteine, 50-fold epinephrine and uric acid did not interfere with the determination of promethazine, while Ag^+ , folic acid and sulfocarbamide interfered severely. As mentioned above, the influence of some coexist species can be eliminated by performing voltammetric measurement in a blank solution after accumulation step. Therefore, the MWNTs casting film coated gold electrode has potential application.

3.9. Application

This method was applied to the determination of promethazine in medicine sample (i.e. Compound Reserpine). The pretreatment and determination procedure was as described in Section 2. The analytical results are shown in Table 1 and the recovery is 97.6-101.8%. The promethazine content is calculated and it is 2.04 mg per tablet. It is in agreement with the declared content of promethazine in the tablet (2.1 mg per tablet).

Table 1 Measurement results of promethazine in Compound Reserpine tablet

No.	Added (μM)	Expected (μM)	Found (μM)	Recovery (%)
	—	—	1.37	—
1	1.0	2.37	2.36	99.6
2	2.0	3.37	3.29	97.6
3	3.0	4.37	4.45	101.8

4. CONCLUSIONS

Promethazine can be adsorbed on an MWNT/Au electrode and cause a sensitive anodic peak when the potential is made to move. Under optimized conditions, the anodic peak current is linear to the concentration of promethazine in certain range and can be used for the determination of promethazine in some samples. The modified electrode can be regenerated by repeating potential scan in a blank solution and shows good reproducibility. This electrode has advantages with regard to sensitivity and simplicity in comparison with other electrodes.

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