Electrochemical sensor for terbutaline sulfate based on a glassy carbon electrode modified with grapheme and multi-walled carbon nanotubes

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Abstract. A glass carbon electrode was prepared that coated with a composite film containing grapheme and multi-walled carbon nanotubes. It was used to study the electrochemical response of terbutaline sulfate. Under the optimized conditions, the oxidation peak current was found to be proportional to its concentration in the range of 0.2-5 μmol·L⁻¹ and 5-40 μmol·L⁻¹. Compared with the bare GC electrode, the GN-MWNTs-modified GC (GN-MWNTs/GC) had many advantages such as relatively high sensitivity, good stability and long life time. The modified electrode was used to determine the TES tablets with satisfactory results.

1. Introduction
Terbutaline sulfate [(±)-α-[(tert-butylamino) methyl]-3,5-dihydroxybenzyl alcohol sulfate] is a synthetic β₂-adrenoceptor that has been widely used as a bronchodilator for treatment of bronchial asthma, chronic bronchitis, and emphysema. Many analytical methods have been developed for determination of terbutaline sulfate in a variety of substrates; these include Spectrophotometry [1], chemiluminescence [2], capillary electrophoresis [3], HPLC [4], electrochemical method [5]. There is, however, a lack of information about electrochemical method of terbutaline sulfate in the public literature.

In this paper, the glass carbon electrode was prepared that coated with a composite film containing grapheme and multi-walled carbon nanotubes. It was used to study the electrochemical response of terbutaline sulfate. Compared with the bare GC electrode, the GN-MWNTs-modified GC (GN-MWNTs/GC) had many advantages such as relatively high sensitivity, good stability and long-life time.

2. Experimental
2.1. Instruments and reagents
CHI 600C electrochemical workstation (Chenhua Instrumental Co., Shanghai, China). A conventional three-electrode system was employed, including a MWNTs/GCE or bare GCE working electrode, an Ag/AgCl reference electrode and a platinum wire counter electrode. All of the used electrodes were
purchased from CHI Co. QT-2060 ultrasonic cleaning device (Ruipu electronic instrument Co., Tianjin, China). PuXiKe P4-036 Pen type acidity meter (Leqingdacang electronic instrument Co., Leqing, China).

Graphene dispersion (0.5 mg/ml, Nanjing Xianfeng nanomaterials technology co., LTD), Multi-walled carbon nanotubes (Φ 8~15 nm, Chengdu institute of organic chemistry, Chinese academy of sciences), terbutaline sulfate (Aladdin reagent co., LTD). All other reagents were analytical pure. Secondary distilled water was employed throughout the experiments.

2.2. Preparation of GN-MWNTs/GC
The bare GCE was polished with 1.0, 0.3, and 0.05 μm Gamma alumina powder (γ-Al₂O₃) on chamois leather, and then washed ultrasonically in water, HNO₃ (1:1) and ethanol, respectively. After ultrasonic, the electrode was rinsed with double-distilled water and allowed to dry at room temperature. 2.5 mg MWNTs was added to 10mL DMF, and the mixture was ultrasonicated to form a homogeneous solution. Then 4mL graphene dispersion was added to 1mL MWNTs dispersion above. The mixture was ultrasonicated for 15 min to form GN-MWNTs solution. About 6 μL GN-MWNTs solution was dropped on the pre-treated GCE surface and dried at room temperature to form GN-MWNTs modified GCE [6].

3. Results and discussion

3.1. Electrochemical response of TES on the GN/MWNTs/GCE
The bare GCE and the GN-MWNTs/GCE were respectively deposited by cyclic sweeping for 2 cycles in pH 7.2 BR buffer solution containing 1.0×10⁻⁵ mol·L⁻¹ TES solution (shown in Fig. 1). For the bare GCE (Fig.1-a), the oxidative peak current of TES was relatively weak with peak potential of 0.6-0.7 V, which indicated that TES irreversible oxidation was near the high voltage of 0.7 V. Compared with the bare GCE, oxidation peak current and background current of the GN-MWNTs/GCE(Fig1-b) was large, this is because the modification of graphene and carbon nanotubes had increased the electrode surface and the surface area or the micro microscopic capacitance per unit area.

![Figure 1. Cyclic voltammograms of a glassy carbon electrode (a) and GN/MWNTs electrode (b).](image)

In order to investigate the effective surface area of the modified electrodes, the bare glassy carbon electrode and GN / MWNTs / GCE was studied in 5×10⁻⁴ mol/L K₃[Fe(CN)]₆ by chronocoulometry, respectively (shown in Fig. 2). According to Anson [7] and the slope of the Q·t⁻¹/² linear relationship (shown in Fig. 2B), the effective surface area of bare GCE and GN / MWNTs / GCE were 0.06989 cm² and 0.2002 cm². The experimental data confirmed that the graphene and carbon nanotubes increased the microscopic surface area of the glassy carbon electrode.
3.2. The reaction mechanism of TES in GN/MWNTs/GCE

The electrochemical mechanism of 1.0×10⁻⁵ mol/L TES was studied in modified electrode surface. The effect of scan rate on the voltammetry response for the TES on the GN/MWNTs/GCE was investigated from 20 to 200 mV·s⁻¹. The cyclic voltammetry result indicated that with the increase of the scan rate the peak potential was also increased. The linear regression equation was $E_p = 0.0267 \ln v + 0.5817$ ($R^2 = 0.9939$). According Laviron [8], the slope is $RT/αnF$ (T=298 K), the electron number is 2. The oxidation process of TES is two electronic processes.

As shown in Fig.5, the linear relationship between the oxidation peak current and scan rates is $I_p = 0.0674 v - 0.1915$, $R^2 = 0.9919$, when the scan rates were from 20 mV·s⁻¹ to 120 mV·s⁻¹. When the scan rate was increased to 140 mV·s⁻¹, the peak current decreased significantly. But with the scan rate continue increase, the peak current was also can continue increased. However, the peak current did not exceed the peak current that in the scan rate of 100 mV·s⁻¹ and 120 mV·s⁻¹. Because the electrode processes may be affected by diffusion, when the scan rate was lager, the speed of TES adsorbed to the surface of the electrode was slower than the scan rate.

3.3. Effect of buffer solution and pH

Respectively, using BR, HAc- NaAc, KNO₃, NaCl, Na₂HPO₄-NaH₂PO₄ was respectively studied its effects on the modified electrode as the supporting electrolyte. The results showed that GN/MWNTs/GCE had good electrochemical behaviour in the BR buffer solution. So the BR buffer solution was chosen as the supporting electrolyte.

The pH of buffer solution has an important influence on the electrochemical response of TES. The voltammetry behaviour of TES was examined in BR buffer with different pH values. The results show that, when the pH was 7.2, the peak current was the greatest, so we chose pH 7.2 BR buffer solution.

3.4. Effects of enrichment time

For the electrode process controlled by adsorption, pre-enrichment process could improve the detection sensitivity significantly. Therefore, we also investigated the enrichment time ($t_{acc}$) of 1.0 × 10⁻⁵ mol·L⁻¹ TES in the system. The results showed that the peak current was increased with the extension of the accumulation time within 20 s. And the peak current tended to decrease, when the accumulation time exceeded 20 s. The longer the accumulation time was, the lower the limit of detection was, but the narrower the linear range was. Considered the experiment, 20 s was chosen as the enrichment time.
3.5. Working curve, Detection limit, Reproducibility and Stability

The results showed that the oxidation peak current was proportional to TES concentrations in the range 0.2 μmol·L⁻¹ to 5 μmol·L⁻¹ and 5μmol·L⁻¹ to 40 μmol·L⁻¹, respectively. Linear equations were shown as following, respectively:

\[ I_p (\mu A) = 1.904 \log C_{TES} (\mu mol\cdot L^{-1}) + 1.746, R^2 = 0.9915 \ (0.2 \sim 5 \mu mol\cdot L^{-1}) \]

\[ I_p (\mu A) = 10.91 \log C_{TES} (\mu mol\cdot L^{-1}) - 4.252, R^2 = 0.9945 \ (5 \sim 40 \mu mol\cdot L^{-1}) \]

Notably, the two-linear range also can have proved that the reaction of TES in the GN / MWNTs / GCE surface was controlled by shift from adsorption to diffusion gradually with the increasing concentration of TES.

The TES of 1.0×10⁻⁵ mol·L⁻¹ was determined repeatedly with the same electrode for ten times. The relative standard deviation (RSD) of current peak was 2.6 %, which indicated that the modified electrode possessed a good reproducibility. Stability tests were carried out at room temperature. The current response had been decreased 16 % after a period of 10 days of exposed the GN/MWNTs/GCE in air, which showed that GN/MWNTs/GCE had good long-time stability for the determination of PCT.

3.6. Analysis of real samples

In order to fit into the linear range of the method, TES tablet was accurately diluted with the supporting electrolyte. Under optimum conditions, the TES tablets were measured. The recovery experiments were measured after TES standard solution added to the sample, the RSD and average recoveries were 3.5 % and 96.6 % (shown in Table 1). The results showed that GN / MWNTs / GCE had better accuracy for measuring TES.

| Sample | Terbutaline sulfate tablets |
|--------|----------------------------|
| Measured values (μmol·L⁻¹) | 3.50 | 3.57 | 3.38 | 3.56 | 3.72 |
| RSD (%) | 3.5 |
| Standard added (μmol·L⁻¹) | 1.0 | 1.5 | 2.5 | 3.5 | 7.0 |
| Measured values (μmol·L⁻¹) | 4.37 | 4.92 | 6.24 | 7.11 | 10.58 |
| Recovery (%) | 82.0 | 91.3 | 107.6 | 101.7 | 100.4 |

4. Conclusion

In this work, a novel GN/MWNTs composite film modified electrode was fabricated for the determination of TES. The electrochemical behaviors of TES at the GN/MWNTs/GCE were investigated, and an irreversible oxidative peak was obtained. From the electrochemical analysis, it was clearly demonstrated that the GN-MWNTs-modified GC (GN-MWNTs/GC) was with relatively high sensitivity, stability and life time compared with the bare GC electrode. The modified electrode was used to determine the TES tablets with satisfactory results.

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