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A cholylglycine sensor based on 1,2-naphthoquinone-4-sulphonic acid sodium (NQS)/β-cyclodextrin-graphene oxide modified electrode

Bo Fu, Tailin Liu, Jincheng Chen, Kang Li*

School of Pharmacy, Guangdong Pharmaceutical University, Guangzhou 510006, China

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ABSTRACT

In this paper, a novel, simple and sensitive cholylglycine (CG) electrochemical sensor was prepared based on the specific recognition of 1, 2-naphthoquinone-4-sulphonic acid sodium salt (NQS) to CG for the first time. It was constructed with β-cyclodextrin-graphene oxide (β-CD-GO) on glassy carbon electrode (GCE) and modified with NQS to obtain NQS/β-CD-GO/GCE. A decrease of the oxidation peak current of NQS arising from the specific binding of CG and NQS through a nucleophilic substitution reaction was used for indirect detection of CG. The performances of the proposed sensor were investigated by cyclic voltammetry (CV), differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS). The difference of the oxidation peak current was linear with the CG concentration in the range of 0.2-60.0 μM and the detection limit of CG was 0.061 μM. Moreover, the CG sensor showed good repeatability and high stability and has been applied to the determination of CG in human serum with satisfactory recoveries. So, a new method has been provided for detecting electrochemically inert material CG.

1. Introduction

Liver disease is an important killer for human health, among which hepatitis, cirrhosis and liver cancer are widely concerned by the medical community due to their widespread epidemic, long duration and high mortality rate [1,2]. Cholylglycine (CG) is a combination of cholic acid and glycine, which is one of the main components of bile acids. The normal metabolic pathway of CG in serum is enterohepatic circulation [3]. Under normal circumstances, whether fasting or postprandial, the CG content in the blood are kept at a low level. When human liver cell has damage or cholestasis occurs, it will cause a disorder of CG metabolism. As a result, the ability of liver cells for taking up CG is reduced, which can lead to a elevated CG blood level [4,5]. Therefore, the concentration of CG in serum has been a sensitive and specific indicator of liver disease [6–8].

Currently, some methods used for determination of CG mainly are enzyme-linked immunosorbent assay (ELISA) [9], gas chromatography (GC) [10], high performance liquid chromatography (HPLC) [11,12]. However, these methods require cumbersome preconditioning, expensive equipment and trained personnel, which increase the analysis cost and time cost and is not suitable for clinical diagnosis. The electrochemical sensors have arisen as a promising analytical tool based on its relative technical simplicity, rapid response, low-cost and easy miniaturization. But, for CG, due to the poor electrochemical property, it is still a big challenge for direct electrochemical detection of CG. Therefore, it is very significant to develop a simple and effective electrochemical method for detection of CG.

1,2-Naphthoquinone-4-sulphonic acid sodium salt (NQS) is widely used as a chromogenic reagent in the spectrophotometric determination of amines and amino acids [13]. On the application of NQS, several papers have been reported [14,15], which is based on the ability of NQS to react with primary and secondary amino groups under basic and neutral conditions to yield spectrophotometrically detectable derivatives. In this work, for detection of CG (an amine derivatives), NQS was used as a redox indicator because it can react with amino groups through a nucleophilic substitution reaction. β-Cyclodextrin (β-CD) is a cyclic oligosaccharides formed through the combination of seven D-glucopyranose units by 1,4-glycosidic bonds [16]. Due to the moderate molecular cavity and low production cost, it is the most widely used cyclodextrin in the industry [17]. β-CD has a hydrophilic outer cavity and a hydrophobic lumen, providing a hydrophobic binding site to form inclusion complexes with guest molecules for specific recognition of guest molecule [18]. The high selectivity, recognition, catalysis and enrichment performances of β-CD make it become an ideal material for electrochemical sensor [19–21]. Graphene oxide (GO) has a large surface area, excellent conductivity, good water-soluble and easy functionalization as the supporting nanomaterial [22]. In this work, to obtain the β-CD-GO composite, we use the hydrogen bond between the

* Corresponding author.
E-mail address: likang229@aliyun.com (K. Li).

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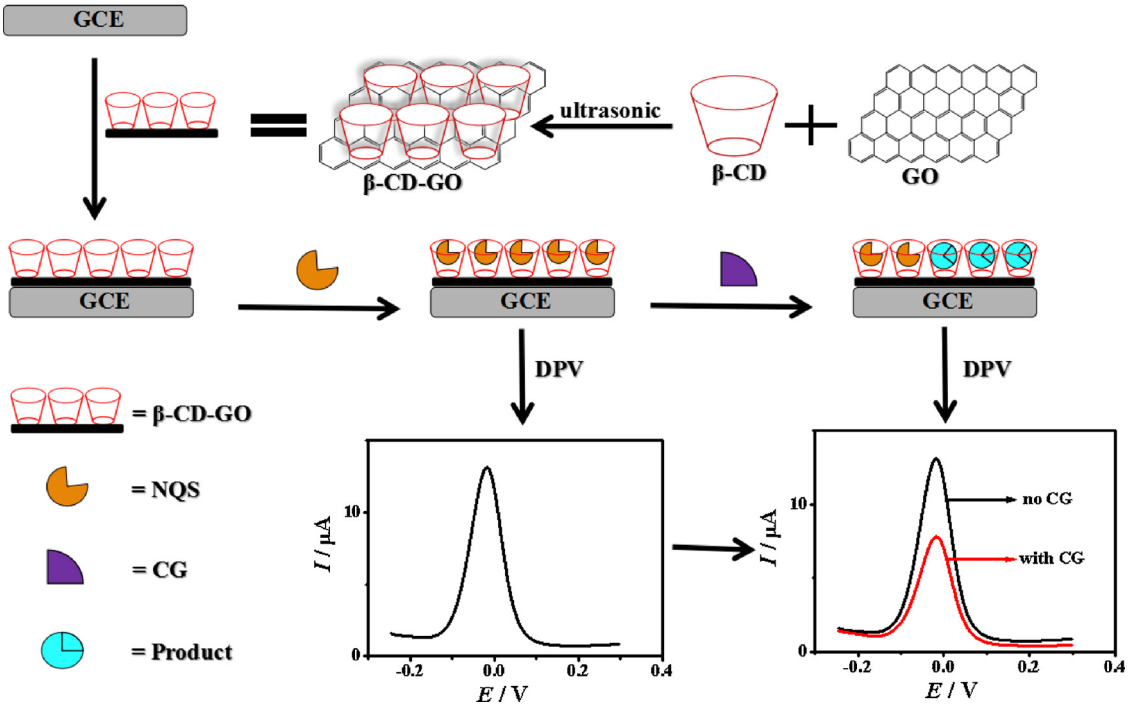

Fig. 1. Schematic illustration for the electrochemical CG assay based on NQS and β-CD-GO.

hydroxyl of the β-CD and GO to combine them [23], which exhibits high selectivity and sensitivity for CG.

In this study, a novel CG electrochemical sensor was prepared based on the specific recognition of NQS for CG. As shown in Fig. 1, β-CD-GO composite material prepared by hydrogen bond between β-CD and GO was first modified on the surface of glassy carbon electrode. NQS, as a redox indicator, can enter the β-CD lumen through host-guest action. It is observed that NQS/β-CD-GO/GCE has a significant oxidation peak. The amine group (-NH-) in the CG structure can bind to NQS specifically by a nucleophilic substitution reaction, resulting in a decrease of the electrochemical signal of NQS. The difference of oxidation peak current can be used to electrochemically quantitatively detect CG indirectly. So, a new method has been provided for detecting electrochemically inert material CG.

2. Experimental

2.1. Reagents

Graphene oxide powder (> 99%) was purchased from Nanjing Pioneer Nano Material Science and Technology Co., Ltd. (China). β-Cyclodextrin (β-CD), 1,2-naphthoquinone-4-sulphonic acid sodium salt sodium (NQS), glycocholate hydrate (cholylglycine, CG), L-lysine, L-cysteine, L-valine and cholesterol were purchased from Shanghai Macklin Biochemical Technology Co., Ltd. (China). All other chemical reagents were of analytical grade. All the experimental water was redistilled water.

2.2. Apparatus

Electrochemical experiments were performed on a CHI660E electrochemical workstation (Shanghai Chenhua Co., Ltd, China) with a conventional three-electrode system. A bare or modified CG electrode (3 mm diameter, CHI) was used as working electrode, a silver/silver chloride electrode and platinum wire were used as reference electrode and auxiliary electrode, respectively. A Zeiss Ultra55 field emission scanning electron microscope (SEM, Germany) was employed to analyze the surface appearance of the modified electrode.

2.3. Preparation of NQS/β-CD–GO/GCE

3.0 mg GO was dispersed in 3 ml aqueous solution, and then 30.0 mg β-CD was added in it. Followed by ultrasonic for 60 mins, a uniform black suspension was obtained, the pH was adjusted to 9.5 with a 5 wt% sodium carbonate solution, and then stirred for 5 h to obtain a β-CD-GO composite. 5 μl β-CD-GO composite was added to the surface of the GCE and dried under infrared light to obtain β-CD-GO/GCE. Then the β-CD-GO/GCE was immersed into 0.1 M KCl solution containing 5 mM NQS and suffered by CV scan for 20 cycles with a sweep rate of 100 mV s^{-1} within the potential range of −0.40 to 0.20 V. So, the NQS/β-CD-GO/GCE was constructed. Current measurements were made using DPV at a potential range of −0.25–0.3 V. All of the electrochemical detections were under the same conditions.

3. Results and discussion

3.1. Scanning electron microscopic characterization

The surface morphology of the modified electrode was characterized by SEM image. Fig. 2A shows the SEM image of GO/GCE and the wrinkle lamellar structure of graphene oxide nanosheets can be clearly observed. In Fig. 2B, on β-CD-GO/GCE, in addition to the pleated structure, the phenomenon of reunion can be found out. This is due to the aggregation of the polymer caused by the cross-linking between β-CD and GO[24]. The SEM image of NQS/β-CD-GO/GCE is shown in Fig. 2C, the significant change takes place on the surface of the electrode after the modification of NQS on β-CD-GO/GCE. The wrinkled layered structure of graphene oxide are masked and covered with many particulate materials, indicating that the NQS has been successfully modified on the electrode surface.

3.2. Electrochemical characteristics

CV and EIS were used to characterize the modified electrode in $[Fe(CN)_6]^{3-/4-}$ solution. The electrochemical characteristics of GCE, GO/GCE, β-CD-GO/GCE and NQS/β-CD-GO/GCE in 0.1 M KCl solution containing 5.0 mM $[Fe(CN)_6]^{3-/4-}$ were investigated by CV and EIS.