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The strategy of nitrite and immunoassay human IgG biosensors based on ZnO@ZIF-8 and ionic liquid composite film

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ABSTRACT

The strategy of bifunctional electrochemistry platform based on heterogeneous composite ZnO@ZIF-8 and ionic liquid (IL) composite film for nitrite (NO_2^-) and immunoassay human IgG biosensors was proposed. On the one hand, the electrocatalytic ability of myoglobin (Mb) modified electrode (ZnO@ZIF-8/IL/Mb-CPE) to NO_2^- was studied, and a linear response from 10 to 833 μM with a detection limit of 3.5 μM was achieved. On the other, a label-free immunosensor for the determination of human IgG was proposed using ZnO@ZIF-8/IL composite film as immobilization matrix. The differential pulse voltammetry (DPV) response of the developed immunosensor was found to be proportional to logarithm of human IgG concentrations in the two ranges of 0.1-10 and 10–400 ng/mL. The lower detection limit was calculated as 0.03 ng/mL. The excellent properties of ZnO@ZIF-8 were attributed to the synergistic effects of ZnO nanorods with good conductivity, biocompatibility and ZIF-8 with high porosity. Meanwhile, IL not only prevented the aggregation of ZnO@ZIF-8 nanorods, but also displayed excellent ability in facilitating the electron transfer. Both biosensors exhibited good selectivity, reproducibility and stability, indicating ZnO@ZIF-8 composite film could be a promising matrix in electrochemical biosensor design.

1. Introduction

Engineering the bioelectrochemical sensing interface is crucial for improving the stability and sensitivity of electrochemical biosensors [1,2]. Currently, many efforts have been done to modify the interface of the electrodes with various materials. For instance, Jiang et al. [3] prepared a biofunctionalized graphene-AuNP composite for immobilizing hemoglobin (Hb) to develop a NO_2^- biosensor with well performance. Mani et al. [4] achieved the direct electrochemistry of myoglobin (Mb) and successfully detected hydrogen peroxide (H_2O_2) and NO_2^- based on a novel nanobiocomposite (RGO-MWCNT-Pt/Mb). Alternatively, label-free immunosensors have attracted great research interests because of their high sensitivity, more cost effectiveness, simple preparation, and well activity preservation of antibodies and antigens [5]. Li et al. [6] constructed a biocompatible interface based on ionic liquid (IL) modified gold nanoparticles (AMPPH-AuNPs) for the immobilization of rabbit anti-IgG, and achieved a lower detection limit of IgG by DPV. Zhang et al. [7] reported a simple strategy to directly immobilize anti-IgG on dialdehyde cellulose film through the covalent bonding to detect IgG by DPV. Besides, impedimetric immunosensors were also fabricated for the detection of IgG [8,9].

Apparently, the performances of above biosensors critically depend on the properties of electrode interface which include the conductivity, structure, surface area and biocompatibility. As far as we know, there are few studies and applications of bifunctional platform for both enzymatic biosensor and immunosensor with same matrix materials. From this viewpoint, it is significant to develop **a** strategy to construct a bifunctional electrochemical platform and to explore the extensive applications of materials [10].

Currently, zeolitic imidazolate frameworks (ZIFs) materials [11–15] built by tetrahedral metal ions (such as Zn, Co and so on) bridging with imidazolate anions have been researched extensively for a variety of applications due to their facile preparation process, highly thermal stability and chemical robustness. The most interesting ZIF compound is ZIF-8 with sodalite-related structure which composed of Zn ions and 2-methylimidazolate. Abdolraouf et al. [16] fabricated Ag/ZIF-8/CPE for the electrocatalytic reduction of H_2O_2. Notably, the hybrids of pure ZIFs integrated with some functional materials exhibited great advantages due to their synergism action [17–19]. Magnetic Fe_3O_4@ZIF-8 core-shell microspheres enhanced catalytic activity for the Knoevenagel condensation reaction of ethyl cyanoacetate and benzaldehyde [20].

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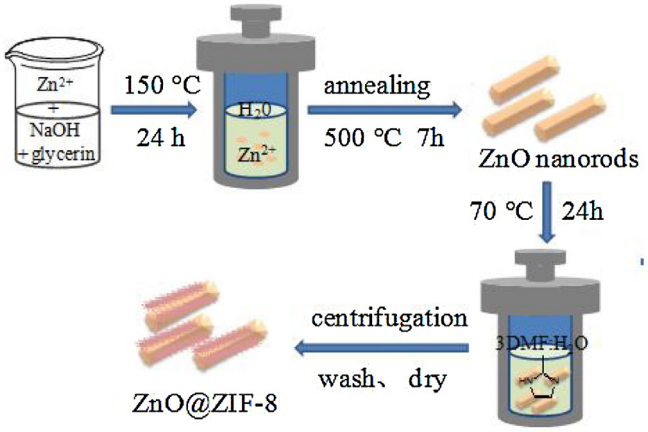

Scheme 1. The illustration of the procedure to synthesize ZnO@ZIF-8.

Especially, ZnO@ZIF-8 nanorods heterostructures displayed photoelectric response owing to the presence of ZnO nanorods core with a good photoelectric catalytic effect and ZIF-8 shell aperture [21]. Additionally, ionic liquid (IL) possessed good electrical conductivity, excellent film forming effect and well biocompatibility, which made it a useful immobilized matrix [22–24]. It can be imagined that ZnO@ZIF-8 nanorods dispersed in IL can further broaden their potential application in the construction of bifunctional electrochemical platform.

Herein, we successfully fabricated ZnO@ZIF-8 nanorod heterostructures with core-shell, and dispersed it with 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIm]BF_4) IL to form ZnO@ZIF-8/IL composite film. On one hand, ZnO@ZIF-8/IL/Mb-CPE was prepared, and its electrocatalytic ability to NO_2^- was investigated. On the other hand, the electrochemical immunosensor of ZnO@ZIF-8/IL/GA/anti-IgG/BSA/IgG-CPE was fabricated through layer-by-layer assembly method and its electrochemical properties were also explored.

2. Experimental section

2.1. Materials and apparatus

Myoglobin (Mb, MW. 17,800) was purchased from Sigma Chemical Company. [BMIm]BF_4 was purchased from Hangzhou Chemer Chemical Limited Company. Human IgG and goat anti-IgG were both purchased from Beijing Dingguo Changsheng Biotechnology Limited Company. Bovine serum albumin (BSA, >98%) was purchased from Beijing Aoboxing Biotechnology Company. Glutaraldehyde (GA) solution (50%) was received from Tianjin Fuchen Chemical Reagent Corporation. All other reagents were of analytical grade and used without further purification. Phosphate buffer solutions (PBS) containing 1.0% (w/v) BSA was used as blocking solution.

The part of apparatus was put in the supporting information.

2.2. Preparation of znO@ZIF-8

ZnO and ZnO@ZIF-8 nanorods were prepared through a hydrothermal route reported previously [21]. In the preparation of rod ZnO and its core-shell material, pH values have an important effect on its morphology [25,26], and the pH value of precursor solution was usually controlled in the range of 11–12. The detailed description of synthesis process was depicted in the supporting information. The schematic illustration of the process to synthesize ZnO@ZIF-8 nanorods was shown in Scheme 1.

2.3. Fabrication of modified electrodes

The Mb modified electrode was fabricated based on the following procedure: Firstly, 5 mg ZnO@ZIF-8 and 10 μL IL were homogeneously dispersed into 1 mL PBS by sonication. A 5 μL aliquot of this dispersion was casted on a freshly polished CPE and evaporated at the ambient temperature to obtain ZnO@ZIF-8/IL-CPE. Then Mb solution (5 mg/mL) was casted onto the surface of ZnO@ZIF-8/IL-CPE and dried at 4 °C in a refrigerator to obtain ZnO@ZIF-8/IL/Mb-CPE.

The IgG immunosensor was prepared as follows: The first step for the fabrication of ZnO@ZIF-8/IL-CPE was nearly the same as above procedure except that the volume was 10 μL. Then 5 μL of freshly prepared GA solution at 2.5% was coated onto the electrode surface as a cross-linker. Then, 10 μL of anti-IgG solution (1 mg/mL) was dropped on the surface of the modified electrode and stored at 4 °C overnight. Subsequently, a drop of 5 μL 1.0 wt% BSA was coated on above electrode surface to block the nonspecific binding sites. Finally, the ZnO@ZIF-8/IL/GA/anti-IgG/BSA-CPE was incubated with various concentration of IgG to immunoassay. The fabrication process of the both biosensors was shown in Scheme 2.

2.4. Electrochemical measurements

All electrochemical measurements were carried out with a CHI660d electrochemical workstation (Shanghai Chenhua Co.) controlled by a microcomputer with CHI660 software. A three-electrodes system was used, where a saturated calomel electrode (SCE) served as the reference electrode, a platinum wire electrode as the auxiliary electrode and a modified CPE as the working electrode. All the potentials given in this paper were referred to the SCE. The oxidation current was set to negative.

The electrochemical measurements for Mb modified electrode: CV measurements were carried out in an undivided electrochemical teflon cell in pH 7.0 0.1 M PBS. EIS measurements were carried out in 5.0 mM $K_3Fe(CN)_6/K_4Fe(CN)_6$ (1:1) containing 0.1 M KCl, while the applied perturbation amplitude was 0.005 V, the frequencies swept from 10^5 to 10^{-2} Hz. Amperometric experiments were performed in a constantly stirred cell with the successive addition of NO_2^- substrate into 20.0 mL PBS supporting electrolyte while the electrode potential was set at 0.8 V.

The measurements for immunosensor: CV and EIS measurements were performed in 0.01 M pH 7.0 PBS containing 5 mM $K_3Fe(CN)_6/K_4Fe(CN)_6$ (1:1) and 0.1 M KCl. DPV measurements were taken under the following: The potential range was from −0.6 to 0.2 V, pulse amplitude was 0.05 V, pulse width was 0.06 s, and sample width was 0.02 s.

3. Results and discussion

3.1. Characterization of ZnO@ZIF-8

SEM images of synthesized ZnO and ZnO@ZIF-8 were obtained. As seen in Fig. 1A, ZnO appeared to be rod-like structure. After a typical ZnO@ZIF-8 product was synthesized by using ZnO nanorods as the template, it could be observed in Fig. 1B that ZIF-8 was coated on the ZnO nanorods, indicating the formation of a core-shell structure.

FT-IR spectra of ZnO@ZIF-8 was recorded and shown in Fig. 1C. The bands at 1350–1500 cm^{-1} were associated with the imidazole ring stretching. The peak at 1584 cm^{-1} can be assigned as the C=N stretching vibration. The most interesting Zn-N bond was observed at 421 cm^{-1}, which demonstrated that Zn^{2+} was coordinated with N atom in the imidazole ring and the framework material was achieved [27].