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Electrochemical sensor for dopamine based on imprinted silica matrix-poly(aniline boronic acid) hybrid as recognition element

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ABSTRACT

A novel imprinted silica matrix-poly(aniline boronic acid) hybrid for electrochemical detection of dopamine (DA) was developed. Boronic acid functionalized conducting polymer was electrochemically prepared on Au electrode. The number of covalent binding sites toward DA templates was controlled by potential cycles. A precursory sol solution of ammonium fluorosilicate (as cross-linking monomer) containing DA was spin-coated on the polymer modified electrode. Under NH_3 atmosphere, the hydroxyl ions were generated in the solution and catalyzed the hydrolysis of fluorosilicate to form silica matrix. After this aqueous sol-gel process, an inorganic framework around the DA template was formed and the imprinted hybrid for DA was also produced. As revealed by scanning electron microscopy, UV-vis spectroscopy and cyclic voltammetry characterization, DA was embedded in the imprinted hybrid successfully. The affinity and selectivity of the imprinted hybrid were also characterized by cyclic voltammetry. The imprinted hybrid showed higher affinity for DA than that for epinephrine, and little or no affinity for ascorbic acid and uric acid due to the combined effects of covalent interaction, cavities matching and electrostatic repulsion. The imprinted hybrid sensor exhibited a quick response (within 5 min) to DA in the concentration range from 0.05 to 500 $\mu mol\,L^{-1}$ with a detection limit of 0.018 $\mu mol\,L^{-1}$. The prepared sensor was also applied to detect DA in real samples with a satisfactory result.

1. Introduction

Molecular imprinting polymer (MIP) is fabricated based on covalent or non-covalent interaction between functional monomer and template molecule, then formed by polymerization. Subsequently, removal of the template can induce the formation of imprinted cavities that are complementary in size and shape to the target analyte (original template) [1–3]. Particularly, these synthesized MIP as recognition unit for biomimetic sensor have attracted much attention. Integration of MIP and different transduction unit can be used to produce various sensors, especially electrochemical sensor [4]. The distinctive advantages of MIP sensors are including stability, reusability, ease of preparation and low cost [5–7].

Dopamine (DA) is one of the most important neurotransmitters in human body. The detection of DA has been a concerned issue in analytical science, since it is an important biomaker for schizophrenia and Parkinson's disease. Electrochemical detection of DA is a promising method for its simple process, high sensitivity and fast response. The major weakness of electrochemical detection is the electroactive interference such as ascorbic acid (AA), uric acid (UA), epinephrine (EP) and norepinephrine (NE), which usually coexist with DA in biofluids [8–12]. Especially, the concentrations of AA and UA are several orders of magnitude higher than that of DA in biofluids [13,14]. Therefore, special focus has been concentrated on developing MIP with excellent binding properties to DA via electropolymerization. The electroactive substances such as pristine and derivative pyrrole [15,16], o-phenylenediamine [17–19] and o-aminophenol [20] have been acted as functional monomers to noncovalently interact with DA. Compared with non-covalent interaction, more homogeneous population of binding sites and more imprinting efficiency are conceivably obtained owing to the stability of covalent interaction [2].

Boronic acid is well known to create stable cyclic esters with diols by covalent interactions in an alkaline aqueous solution. Conversely, the boronate esters dissociate in an acidic environment [21]. As the recognition element, artificial receptors of boronic acids have been generally used in the development of determination of cis-diol compound including catechol [22], saccharides [23–25], or even glycoproteins [26,27]. 3-acrylamido [28] and pyrrole [29] substituted phenylboronic acid were acted as functional monomers for imprinted DA sensor by

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electropolymerization. On the other hand, the boronic acid functionalized nano-poly(aniline-co-anthranilic acid) was used as support material for in-situ polymerization of imprinted thin films, then suspensions of the corresponding MIP in DMF and chitosan were casted on the electrode for detection of DA [30].

Molecular imprinting in sol-gel materials exhibits several conspicuous advantages for sensor technology due to their controllable pore sizes, structural rigidities, thermal stabilities and enhanced recognition properties [31,32]. The sol-gel process has been used to produce porous, thin, selective silicate materials for electrochemical detection of DA. The conventional procedures were mixing template with tetramethoxysilane and other organosilanes in organic solvent, then an inorganic framework was formed around template via the hydrolysis and condensation by chemical and electrochemical method [33–35]. Nano-sized imprinted materials have been further developed by coating imprinted silica on the surface of carbon nanotube [36], gold nanoparticles [37] and graphene oxide [38], respectively, resulting in higher binding capacity and faster binding kinetics. These methods above commonly focused on non-covalent interactions. Meanwhile, the previous sol-gel processes for MIP sensor have several weaknesses, such as the hydrogen bonding becoming much weaker in aqueous system, the organic solvents unsuitable for hydrosoluble molecules, especially for biomacromolecule [39], the lack of a direct electrical conduction from the recognition sites within insulating materials to the electrode [40]. The insertion of conducting polymers within the silica is result in a hybrid material with both electrical conductivity and electrochemical activity [41,42]. In this case, the integration of a conducting polymer containing covalent binding sites to DA, and imprinted silica matrix to form hybrid materials can be considered as a potential way to improve the imprinting efficiency of MIP. Moreover, it allows easy electrical conduction from recognition sites within silica matrix to the electrode.

In the current work, poly(aniline boronic acid) and the synthetic imprinted silica matrix were combined in order to enhance the affinity of the resulting hybrid material. The boronic acid functionalized conducting polymer on the electrode provided amounts of covalent binding sites toward DA. An aqueous hydrolysis of ammonium fluorosilicate was used to obtain imprinted silica matrix. Subsequently, the templates were removed by washing with an acidic solution to disrupt the covalent interaction. The affinity and selectivity of the imprinted hybrid were studied by electrochemical methods. Simultaneously, the imprinted hybrid based sensor was applied to detect DA in injected samples and human serum samples.

2. Experimental section

2.1. Materials

3-aminophenylboronic acid (98%) was obtained from Beijing J & K Technology Co., Ltd. (Beijing, China). Aniline (99.5%), dopamine hydrochloride (DA, 98%), ascorbic acid (AA, 98%), uric acid (UA, 99%) and epinephrine hydrochloride (EP, 98%) were purchased from Aladdin Chemistry Co., Ltd. (Shanghai, China). Ammonium fluorosilicate ($(NH_4)_2SiF_6$, 98%) was provided by Alfa Aesar Co., Ltd. (Shanghai, China). DA hydrochloride injection samples (2 mL: 20.0 mg) were purchased from Yabang Johnson & Johnson Pharmaceutical Co., Ltd. (Jiangsu, China) and Jingxi Pharmaceutical Co., Ltd. (Shaanxi, China). Human serum samples were obtained from the local hospital. Indium tin oxide (ITO) glass was got from Beijing Tsinghua Engineering Research Center of Liquid Crystal Technology. Phosphate buffer saline (PBS) was employed as the supporting electrolyte containing 0.1 mol L^{-1} KCl, Na_2HPO_4 and KH_2PO_4. Other chemicals and reagents were of analytical reagent grade.

2.2. Apparatus

Electrochemical experiments were recorded by a CHI 660 electrochemical workstation (Shanghai Chenhua Instrument Co. Ltd., China). Electrochemical measurements were using a traditional three-electrode system with an Au electrode (radius 1.0 mm) as the working electrode, an Ag/AgCl (3 mol L^{-1} KCl) electrode as the reference electrode and a Pt wire as the auxiliary electrode. All the electrochemical tests were performed at room temperature (about 25 °C). The surface morphology of modified electrode was detailed using a scanning electron microscope (Hitachi SEM-TM3000, Japan) at a 20 kV accelerating voltage. UV-vis spectroscopy was recorded by a UV-2550 (Shimadzu, Japan).

2.3. Fabrication of poly(aniline boronic acid)(PABA) modified electrode

The Au electrode was treated with 1.0, 0.3 and 0.05 μm alumina powders repeatedly to get mirror face and then sonicated in double distilled water and ethanol for each 5 min. The electrode was pretreated by cycling the potential from −0.2 to +1.6 V at the scan rate of 0.10 V s^{-1} to get a stable voltammogram in a 0.1 mol L^{-1} H_2SO_4 solution. The clean Au electrode was treated to repeat potential scanning from −0.2 to 1.0 V in 0.5 mol L^{-1} HCl solution with 40 mmol L^{-1} 3-aminophenylboronic acid and 200 mmol L^{-1} NaF. In the course of the potential scanning, a deep bluish-green PABA were formed by the electropolymerization of 3-aminophenylboronic acid. The prepared modified electrode was washed using double distilled water and subjected in a 0.1 mol L^{-1} H_2SO_4 solution to demonstrate its redox performance by cyclic voltammetry. For comparison, polyaniline modified electrode was prepared via the electropolymerization of aniline and treated in exactly the same way. Each ITO electrode was approached with freshly prepared piranha solution (a 3:1 mixed solution of concentrated H_2SO_4 and 30% H_2O_2) and then was washed with pure ethanol and double distilled water, and was permitted to dry by nitrogen prior to use. PABA was formed on an ITO electrode through the above mentioned process.

2.4. Preparation of imprinted hybrid modified electrode

The process of imprinted hybrid modified electrode is illustrated in Scheme 1. First, the precursory sol solution containing 0.15 mol L^{-1} $(NH_4)_2SiF_6$ and 1 mmol L^{-1} DA was adjusted to pH of 6.8 by incrementally adding small amounts 1 mol L^{-1} NaOH, and was sonicated for 20 min. Second, spin coating was carried out through putting 5 μL of the mixture onto PABA modified electrode and spinning for 30 s at 3000 revolutions per minute. Third, the precursory sol solution covered electrode was placed in NH_3 atmosphere for 30 min to get the imprinted hybrid modified electrode. After that, the modified electrode was dried at room temperature for an hour and then rinsed using double distilled water. Subsequently, the removal of DA was performed by immersing above electrode into 80 mmol L^{-1} acetic acid solution for 30 min. As a control, non-imprinted hybrid was produced and treated identically except for the omitting of DA. The imprinted hybrid and non-imprinted hybrid were produced on ITO electrodes identically for the characterization by UV-vis spectroscopy.