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Surface modification and ratiometric fluorescence dual function enhancement for visual and fluorescent detection of glucose based on dual-emission quantum dots hybrid

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ABSTRACT

In this work, 3-aminophenylboronic acid (APBA) functionalized dual-emission quantum dots (QDs) were prepared and utilized as the ratiometric fluorescence probe for the onsite naked eye determination of glucose. The unique ratiometric fluorescence probe, which combined ratiometric fluorescence technique with boric acid functional materials into one system, has been prepared by hybridizing red-emitting CdTe QDs (r-QDs) and green-emitting CdTe QDs (g-QDs). The fluorescence of the embedded r-QDs stays constant, whereas the g-QDs functionalized with APBA can selectively bind glucose by the chemistry of boronic acid and cis diol compounds, leading to the fluorescence of g-QDs quenched due to the surface quenching states induced mechanism and resulting in continuous fluorescence color changes (from green to red) of the ratiometric fluorescence probe system. Under optimum conditions, the proposed ratiometric probe was used for selective detection of glucose in a concentration range of 0.1–2.0 mmol/L with a detection limit of 4.5 μmol/L. Moreover, the developed ratiometric fluorescence probe was successfully applied to the detection of glucose in human serum samples. The present study provides an efficient and facile ratiometric fluorescence probe for rapid, convenient, sensitive and selective visual identification of glucose in blood glucose sensing without the need of complex equipment.

1. Introduction

Blood glucose sensing has attracted much attention in recent years due to the increasing severity of the diabetes mellitus. According to the World Health Organization statistics, there are about 300 million people with diabetes in 2010, and this number will be increased to almost double in the year of 2030 [1,2]. Glucose has become a commonly tested analyte because millions of diabetics need to measure the blood glucose levels everyday [3]. To date, various methods such as electrochemical approach and fluorescence analysis have been developed for glucose sensing [4,5]. Compared with well-developed electrochemical approach, fluorescence analysis has attracted much attention due to its simplicity, good stability, low cost, high sensitivity and test rapidity [6]. Therefore, it is of great importance to develop rapid, facile, sensitive and selective fluorescence analytical methods to monitor the level of glucose in blood.

Quantum dots (QDs), also called semiconductor nanocrystals, have attracted continuous concern in recent years due to their excellent properties, such as good photostability, narrow and symmetric emission, broad absorption spectrum, and high luminescence efficiency [7–9]. Fluorescence methods based QDs have appeared as satisfactory techniques due to their low cost, rapid response, high sensitivity, and low detection limit, meanwhile, QDs are widely used as fluorescence sensors for sensing and detecting various analytes, such as ions, small molecules, and biological macromolecule [10–18]. For detecting glucose, there are two sensing systems based QDs-fluorescence method: one is the enzymatic system by using the enzyme glucose oxidases, the other is the nonenzymatic system based on the surface chemical properties of the QDs for glucose [19]. Compared with the former, the latter is even simpler, cheaper, faster and more stable. To our knowledge, the detection system based on the chemistry of boronic acid and cis diol compounds, a kind of nonenzymatic system, has been reported and successfully used as a special recognition way in sensor applica-

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tions [20–24]. However, the boronic acid modified QDs-fluorescent sensors for blood glucose sensing are very few.

Recently, the ratiometric fluorescent technique has attracted continuous concern due to its advantages including improved sensitivity and accuracy at low concentration levels of analyte, and built-in corrections for the environmental effects [25–27]. The ratiometric fluorescent methods are mainly based on the measurement of changes in the fluorescence intensity ratio of the two different wavelengths before and following optical detection [28]. In comparison with the single fluorescence probe, the color changes of the ratiometric fluorescent probe can be clearly and easily distinguished by the naked eyes [7]. Among the various ratiometric sensors, QDs-ratiometric fluorescent sensors possess many advantages as we mentioned already in the previous section. And there have been some significant reports about the QDs-ratiometric fluorescent sensors and their applications [29–36]. For example, Zhang et al. have reported a dual-emission QDs probe for visual detection of TNT particulates [29]. Yao et al. have reported a ratiometric fluorescence probe by dual-emission QDs for on-site visual determination of copper ions [30]. Wang et al. have prepared a dual-emission ratiometric fluorescence probe with desired intensity ratio for onsite naked eye determination of cysteine and homocysteine [31]. It could be found from the literatures that the ratiometric fluorescence QDs probes could achieve high sensitivity with a lower detection limit and visual signal output observed by the naked eye. More importantly, dual-emission QDs ratiometric fluorescence probes are obtained by bonding two differently sized QDs in one nanoparticle, one of the QDs as a signal response unit and another as the reference. Therefore, dual-emission QDs ratiometric fluorescence probe could be used as a powerful tool in biological and chemical sensing application.

In this work, we demonstrate a new concept to use the 3-aminophenylboronic acid (APBA) functionalized dual-emission QDs as the ratiometric fluorescence probe for the onsite naked eye determination of glucose. Firstly, thioglycollic acid (TGA)-capped CdTe QDs were directly synthesized with desired size via a conventional reflux method. Then the red-emitting CdTe QDs (r-QDs) were embedded in the silica nanoparticle by the reverse microemulsion method while the green-emitting CdTe QDs (g-QDs) were attached to the surface of the silica nanoparticle. Finally, APBA was covalently linked to the g-QDs and the APBA functionalized dual-emission QDs were obtained. The morphology, characteristic, optical stability, fluorescence property and selective recognition of r-QDs@SiO_2@g-QDs@APBA ratiometric fluorescence probe was investigated. Further, the proposed ratiometric fluorescent probe was demonstrated as an efficient and simple detecting system for selective detection of glucose in real blood samples. Notably, the APBA functionalized dual-emission QDs-based ratiometric fluorescence probe constructed in this work has several features for the determination of glucose: (1) the r-QDs were entrapped in the SiO_2, which could provide a stable luminescent core and a reliable reference signal; (2) the g-QDs were modified by the APBA which could reacted with the glucose molecule by the covalent interaction, hence making the highly selective detection of glucose possible; (3) due to the variations of the intensity ratios of the dual-emission QDs, continuous color changes from green to red could be clearly and easily observed by naked eye. To the best of our knowledge, the boric acid functional QDs-ratiometric fluorescent probe for sensing glucose has not been reported to date.

2. Experimental

2.1. Reagents and materials

$NaBH_4$ (99%), tellurium powder (~100 mesh, 99.99%), thioglycolic acid (TGA) (98%), $CdCl_2{\cdot}2.5H_2O$ (99.99%), Triton X-100, hexyl alcohol, tetraethoxysilane (TEOS), ammonia solution (25–28%), *N*-hydroxysuccinimide (NHS), poly (diallyldi-methyl-ammonium chloride) (PDDA), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC), APBA, glucose, fructose, galactose, and mannose were all purchased from Aladdin reagent Co., Ltd. (Shanghai, China). Cyclohexane, acetone, ethanol, and sodium hydroxide were obtained from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Double distilled water was used throughout.

2.2. Characterization

The morphological evaluation was carried out by a transmission electron microscope (TEM, JEOL, JEM-2100). The fluorescence spectra were obtained by a Cary Eclipse spectrofluorometer (USA) equipped with a plotter unit and a quartz cell.

2.3. Synthesis of CdTe QDs and r-QDs@SiO_2 nanospheres

The CdTe QDs in aqueous phase were synthesized according to previous reports [37]. Intially, 0.06 g of $NaBH_4$ and 0.051 g of tellurium powder were added to 3.0 mL of ultrapure water in a centrifuge tube under the ultrasonic condition to produce a clear NaHTe solution. Then, the fresh NaHTe solution was transferred into a mixed solution of $CdCl_2$ and TGA at pH 11.2 under N_2 atmosphere. The Cd^{2+}/TGA/HTe^- solution, which mole ratio was 1:2.4:0.5, was refluxed at 100 °C under open-air conditions. The two differently colored CdTe QDs were synthesized at different refluxing times, and the sizes of them were about 2.3 nm and 4.8 nm, respectively. All the QDs used in this work were synthesized using this method and capped by TGA. In addition, the concentration of the CdTe QDs solution was 8.0 mmol L^{-1} (according to Cd^{2+}).

The r-QDs were entrapped in the silica nanospheres by a modified reverse microemulsion method [38]. Briefly, 800 μL r-QDs were added to a mixed solution including 15 mL of cyclohexane, 3.6 mL of *n*-hexanol, and 3.6 mL of triton X–100. After stirring for 30 min, 200 μL of ammonia and 120 μL of PDDA solution (0.075% v/v) were added and stirred for another 30 min. Then, 200 μL of TEOS was introduced to the microemulsion system, and the mixture was stirred for 24 h. Finally, the microemulsion system was broken by adding a certain volume of acetone. After removal of the supernatant, the r-QDs@SiO_2 was obtained following washing, centrifugation, and drying.

2.4. Preparation of r-QDs@SiO_2@g-QDs@APBA ratiometric fluorescence probe

First of all, a certain amount of r-QDs@SiO_2, 10 mL of water and 20 mL of PDDA solution (1%, v/v) were added to a 100 mL flask. After stirring for 1 h at room temperature, the r-QDs@SiO_2-PDDA nanoparticles were obtained. After centrifugation and washing, the r-QDs@SiO_2-PDDA nanoparticles were redispersed in 20 mL of water, and then 2.0 mL of the g-QDs were added to the solution. After stirring for 2 h and being purified, the r-QDs@SiO_2@g-QDs was obtained and redispersed in 10 mL of Tris-HCl buffer. Subsequently, 10 mL of EDC/NHS (4 mg/L for each) was added to the r-QDs@SiO_2@g-QDs solution and stirred for 15 min, and then 20 mg of APBA was added to the mixture solution. After vigorously stirring for 6 h at room temperature in the dark and being purified, the r-QDs@SiO_2@g-QDs@APBA was obtained.

2.5. Fluorescent and visual detection of glucose

The excitation wavelength was set at 330 nm with photomultiplier tube voltage at 800 V. The slit widths of the excitation and emission were both 5 nm. The fluorescence spectra were recorded with a recording emission range of 450–750 nm. The