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Circular dichroism glucose biosensor based on chiral cadmium sulfide quantum dots

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ABSTRACT

A new approach to the fabrication of a glucose biosensor based on circular dichroism spectroscopy (CD) using cadmium sulfide quantum dots (CdS QDs) as a sensor probe was successfully developed and showed excellent selectivity and sensitivity. The chiral CdS QDs (DPA/Cys-CdS QDs) can be simply prepared by mixing cysteamine-capped CdS QDs (Cys-CdS QDs; achiral QDs) with **D**-penicillamine (DPA). The as-prepared DPA/Cys-CdS QDs are active in circular dichroism spectroscopy due to the chirality of DPA. The principle of glucose detection is based on the destruction of chiral QDs by the H_2O_2 generated in situ from the enzymatic reaction of glucose oxidase (GOx) and glucose in the presence of dissolved oxygen. In the presence of the generated H_2O_2, the DPA/Cys-CdS QDs were etched, and the CD signal decreased as a linear function of the glucose concentration. This sensor provided excellent selectivity for the detection of glucose over other possible interfering compounds because of the combination of the enzymatic reaction and the circular dichroism measurement. Parameters that might affect the detection sensitivity of the sensor were investigated and optimized. Under the optimized conditions, the linear working concentration range was found to be 50–250 μM with a limit of detection (LOD) of 31 μM.

1. Introduction

Circular dichroism spectroscopy (CD) is an important technique used to examine the absolute chirality of molecules. The detection principle of CD is based on measuring the difference in absorption between left- and right-handed circularly polarized light [1]. Recently, circular dichroism sensors based on chiral nanomaterials have been proposed [2–4]. This approach can provide excellent selectivity due to the specific interaction/reaction between the sensor probe and the target analyte. Moreover, good selectivity can be obtained by the measurement of the circular dichroism phenomenon, which is subject to fewer interfering species than other techniques. For these reasons, the development of chemical sensors based on circular dichroism spectroscopy is currently of interest. Several types of interaction/reaction with chiral nanomaterials have been introduced, such as the formation of a chiral complex [2] and the in situ generation of chiral nanomaterials from achiral nanomaterials [5,6].

Several types of chiral nanomaterials have been reported, such as gold nanorods [7,8], silver nanoparticles [9,10], and quantum dots [11–13]. Most reports on the subject have described the synthesis and chiroptical properties of the as-prepared compounds. However, applications of the synthesized chiral nanomaterials in the fabrication of circular dichroism sensors have rarely been reported. Chiral quantum dots are among the most interesting chiral nanomaterials. Basically, chiral molecules provide a strong CD signal in the UV range but essentially no signal in the visible region [14]. Chirality in semiconductor quantum dots can be obtained by ligand-induced chirality of the QD surface [12], by electronic coupling between chiral capping ligands and achiral QDs, or by the formation of chiral assemblies of achiral QDs [6].

Accordingly, the optical chirality of nanosystems is an interesting area of research that has received much attention [15]. Many researchers are interested in the utilization of specific chiral molecules as capping agents for the fabrication of new sensing probes [2,4,16–18]. Very recently, the fabrication of the circular dichroism sensors based on the chiroptical properties of chiral quantum dots have been reported by our research group. **L**-cysteine-capped cadmium sulfide quantum dots (L-Cyst-CdS QDs) were proposed as chiral quantum dots to be used as sensor probes for the selective determination of Ni^{2+} and Co^{2+} by monitoring the circular dichroism signals [2]. This report is the first to state that CD spectroscopy can be used for the determination of trace metal ions. Another report describes the fabrication of a sensor for the chiral identification and quantitative analysis of penicillamine by using

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quantum dots as a sensor probe and monitoring by CD spectroscopy [6].

Glucose is an important source of energy for biological processes. The detection of glucose is therefore of great importance in food analysis as well as in the identification of metabolites [19]. It is well known that glucose can be oxidized by oxygen (O_2) in the presence of glucose oxidase (GOx), resulting in the generation of hydrogen peroxide (H_2O_2). Many glucose biosensors are based on the detection of the H_2O_2 generated by this reaction by using several detection principles, including both direct and indirect approaches, such as electrochemical sensors [20,21], colorimetric sensors [22,23], fluorescence sensors [24,25], and conductance glucose biosensors [26]. Various nanomaterials have been proposed for the fabrication of sensor probes to detect the H_2O_2 generated from the enzymatic reaction of glucose [26–28]. The generated H_2O_2 can cause oxidative stress through the oxidation of the fluorescent nanomaterials. In the literature, most reports of the utilization of nanomaterials to detect the H_2O_2 generated from the enzymatic reaction of glucose are based on the measurement of the fluorescence quenching. However, there have not been any reports on the utilization of circular dichroism spectroscopy to detect the H_2O_2 generated from the enzymatic reaction for glucose determination.

In this work, we have proposed for the first time a circular dichroism biosensor for the detection of glucose by the facile in situ generation of chiral quantum dots (DPA/Cys-CdS QDs) from achiral quantum dots (Cys-CdS QDs). The chiral sensor probe is responsible for the detection of H_2O_2 generated from the enzymatic reaction of GOx and glucose. By coupling the enzymatic reaction with specific detection by the circular dichroism activity of the sensor probe, a highly sensitive and selective biosensor for the detection of glucose can be obtained. Moreover, the feasibility of the proposed sensor in practical application is demonstrated by the determination of the glucose content in coconut water samples and comparison of the results obtained by the proposed sensor and by HPLC.

2. Experimental

2.1. Chemicals

All reagents were of analytical grade and used without further purification. Cysteamine hydrochloride was purchased from Sigma. Glucose oxidase from *Aspergillus niger* (GOx, EC 1.1.3.4, 173.5 U mg^{-1}), glucose, L-penicillamine (LPA) and D-penicillamine (DPA) were purchased from Aldrich. Sodium sulfide was obtained from BDH. Cadmium chloride ($CdCl_2{\cdot}H_2O$), potassium dihydrogen orthophosphate and dipotassium hydrogen orthophosphate were obtained from UNIVAR. All aqueous solutions were prepared with deionized water with a specific resistivity of 18.2 MΩ cm obtained from a $RiO_s^{™}$ Type I Simplicity 185 (Millipore Water). The cysteamine-capped CdS quantum dots (Cys-CdS QDs) were synthesized and characterized using the procedure published previously [29] as detailed in the electronic supporting materials (ESI).

2.2. Instrumentation

Circular dichroism spectra were recorded with a Jasco-815 CD spectropolarimeter (JASCO, Japan) using a 1 cm quartz cell cuvette with a scanning rate of 200 nm min^{-1}. The fluorescence spectra were recorded by using a Shimadzu RF-5301PC spectrofluorometer. Excitation and emission spectra were recorded using a slit width of 5 nm. Absorption spectra were measured using an Agilent HP 8453 spectrophotometer. The pH of solutions was determined by using a UB-10 UltraBasic pH meter (Denver Instrument). Transmission electron microscopy (TEM) images were recorded with a JEOL JEM 1230 TEM (JEOL Ltd., Tokyo, Japan) under an accelerating voltage of 100 kV. Transmission electron microscope (TEM) micrographs were recorded by operating at a 100 kV accelerating voltage.

2.3. Circular dichroism (CD) measurements

In a 10.00 mL volumetric flask containing a solution of glucose at the given concentration, 75 µL of 15 mg mL^{-1} Cys-CdS QDs (to obtain a final concentration of 112.5 µg mL^{-1}) was mixed with 100 µL of 10.0 mM DPA (to obtain a final concentration of 100 µM), 200 µL of 150 U mL^{-1} GOx (to obtain a final concentration of 3.0 U mL^{-1}) and 500 µL of 1.0 M Tris-HCl buffer solution pH 8.5. The mixture was then brought to a final volume of 10.00 mL with deionized water. The resulting solution mixture was then incubated at room temperature for 60 min. The CD signal at a wavelength of 253 nm was used for quantitative analysis.

2.4. Selectivity of the sensor

To evaluate the selectivity of the proposed sensors, the following procedure was carried out. In a 10.00 mL volumetric flask containing different types of individual sugar solution at a final concentration of − 200 µM, 75 µL of 15 mg mL^{-1} Cys-CdS QDs was mixed with 100 µL of 10.0 mM DPA, 200 µL of 150 U mL^{-1} GOx and 500 µL of 1.0 M Tris-HCl buffer solution pH 8.5. The mixture was then brought to a final volume of 10.00 mL with deionized water. The solution was mixed thoroughly and allowed to stand for 60 min before recording the CD spectra.

2.5. Application to real samples

To show the feasibility of the proposed method and the applicability of the proposed sensor in real samples, a coconut water sample was used. The coconut water samples were filtered through filter paper (11 µm pore size) to remove particulate matter and diluted 20 fold with 50 mM Tris-HCl buffer pH 8.5. In a 10.00 mL volumetric flask, 75 µL of 15 mg mL^{-1} Cyst-CdS QDs was mixed with 100 µL of 10.0 mM DPA, 200 µL of 150 U mL^{-1} GOx and 500 µL of 1.0 M Tris-HCl buffer solution pH 8.5. The mixture was then brought to a final volume of 10.00 mL with the diluted sample and equilibrated for 60 min at room temperature. The accuracy and precision of the measurement were evaluated by spiking the sample solution with a standard glucose solution at 50 and 100 µM before measuring the concentration of glucose by the proposed method.

2.6. Determination of glucose in coconut water sample by HPLC

To evaluate the accuracy of the proposed method, the glucose concentrations in the real samples and the corresponding spiked samples were also determined by HPLC. The HPLC (LC20 A, Shimadzu, Japan) experiments were performed using the following conditions. An Inertsil ODS-3 250 × 4.60 mm column (GL Science Inc., Japan) was equipped with an LC-20AD pump system and a refractive index detector. The mobile phase was 100% water. The flow rate of the mobile phase was 1.0 mL min^{-1}, and the injection volume was 20 µL. The glucose in the samples and the corresponding spiked samples was identified by comparison with the retention time of standards, and the concentrations of glucose were determined using the external standard method.

3. Results and discussion

This work aims to demonstrate a new strategy for the fabrication of an enzyme biosensor by using the special optical property of the chiral cadmium sulfide quantum dots shown in Scheme 1 . The change in the chiral cadmium sulfide quantum dots based on the enzymatic reaction was recorded by circular dichroism spectroscopy. Excellence selectivity can be expected for this strategy because of the combination of the excellent properties of CD spectroscopy and the bio-enzymatic reaction. The sensitivity of the sensor was studied, optimized and discussed in detail.