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Circular dichroism sensor based on cadmium sulfide quantum dots for chiral identification and detection of penicillamine

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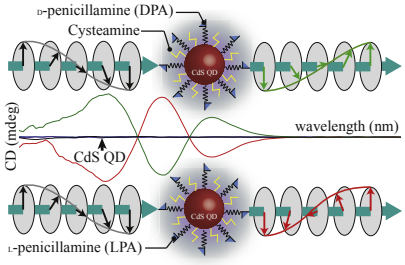
HIGHLIGHTS

- This paper demonstrates a new CD sensor based on cadmium sulfide quantum dots.
- Achiral quantum dots are used for the detection and chiral identification of thiol-chiral containing compounds.
- The sensor show highest selectivity towards penicillamine.
- The detection limits of the sensor less than 1 μM.
- The sensor can potentially be used in physiological urine samples.

GRAPHICAL ABSTRACT



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ABSTRACT

A new chemical sensor based on the measuring of circular dichroism signal (CD) was fabricated from cysteamine capped cadmium sulfide quantum dots (Cys-CdS QDs). The chiral-thiol molecules, D-penicillamine (DPA) and L-penicillamine (LPA), were used to evaluate potentials of this sensor. Basically, DPA and LPA provide very low CD signals. However, the CD signals of DPA and LPA can be enhanced in the presence of Cys-CdS QDs. The CD spectra of DPA and LPA exhibited a mirror image profile. Parameters affecting the determination of DPA and LPA were thoroughly investigated in details. Under the optimized condition, the CD signals of DPA and LPA displayed a linear relationship with the concentrations of both enantiomers, ranging from 1 to 35 μM. Detection limits of this sensor were 0.49 and 0.74 μM for DPA and LPA, respectively. To demonstrate a potential application of this sensor, the proposed sensor was used to determine DPA and LPA in real urine samples. It was confirmed that the proposed detection technique was reliable and could be utilized in a broad range of applications.

1. Introduction

Penicillamine (PA) is a sulfur-containing amino acid which is generally considered to be in a family of aminothiols [1]. It is a pharmaceutically essential chiral compound which is a degradation product of penicillin [2]. It can typically be classified into two forms including D-penicillamine (DPA) and L-penicillamine (LPA). The pharmaceutical form is DPA whereas LPA is clinically toxic since it inhibits the action of pyridoxine [3]. DPA is therefore favorable in the treatment of clinical pathology [4]. Due to the toxicity of the LPA form, various analytical techniques, including high performance

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liquid chromatography [5], chemiluminescence, flow injection analysis [6,7], capillary electrophoresis [8], electrochemistry [9], spectrophotometry [10], and fluorometry [11] have been reported for identification of DPA in both pharmaceutical preparations and biological samples. All of these methods, however, cannot make an effective discrimination between D- and L-isomers. Consequently, the development of methods for analytical identification of DPA and LPA is in an early state and still a challenging issue to pursue.

Recently, chemical sensing based upon tailored nanoparticles (NPs) has attracted more and more attentions due to their unique size-dependent optical properties. Optical NPs have been widely used in a wide spectrum of practical applications such as biosensors [12], biomarkers [13], biomedical imaging [14] and optical sensors [15,16]. Recently, nanocrystalline semiconductors or quantum dots (QDs) have been efficiently used for optical sensors. The detection technique is primarily relied upon the fluorescence properties of QDs [17]. They can be designed and modified for selective fluorescence sensors by using appropriate core materials and capping molecules [18–23]. In addition to the direct sensing onto the QD surface, other indirect approaches could be used for electrochemical sensors [24].

In order to modify the fluorescence properties of QDs, various capping molecules are modified onto the QDs surface. The use of stereospecific chiral molecules as a capping agent is capable of providing a new strategy for chemical sensors [25]. Basically, chiroptical activity of QDs can be induced by a chiral environment via binding of chiral organic ligands to the QDs surface [26]. The chiroptical properties of QDs can be modified by using different types of core and capping molecules. Chiroptical properties of many tailored QDs structures have been reported, for example D- and L-penicillamine capped on the CdS QDs [27], CdS nano-tetrapods [28] or CdSe QDs [26,29] and chiral thiols capped CdTe QDs [30]. The distinctive properties of the surface-modified QDs can lead to the potential applications in fluorescence sensors.

However, the study on the detection of enantiomeric compounds by using fluorescence QDs is still in the early state. Very little progress has been recently reported. This is probably due to the difficulty of design of specific interactions between each isomer and the chiral probe to obtain different signals. The core/shell structure QDs, a promising candidate, has been proposed for specific enantiomeric sensors using fluorescence spectroscopy. To illustrate, cyclodextrin capped CdSe/ZnS core/shell QDs were used as chiral recognition of amino acids [31]. Chiral cysteine-capped CdSe/ZnS core/shell QDs were also proposed as a selective fluorescence sensor for quantification of carnitine enantiomers [32]. Additionally, CdSe/ZnS core/shell QDs passivated by *N*-acetyl-L-cysteine methyl ester were used as a fluorescence sensor to recognize the chirality of the non-steroidal anti-inflammatory drugs, 2-arylpropionic acid, based on the cooperative action between the QDs and their organic capping molecules [33]. To the best of our knowledge, no experimental work has so far been published on the analysis of the QDs as a sensor for the quantitative determination of DPA and LPA.

Circular dichroism (CD) spectroscopy has been widely used to analyze chiral molecules of all types and sizes [34]. It is an essential technique to elucidate the secondary structure or conformation of macromolecules, particularly proteins. This technique can be used to observe the change of the protein secondary structure caused by the environmental changes due to interactions of amino acids. CD spectroscopy can also be used to detect interactions between QDs and biomolecules such as enzyme [35] or protein [36,37]. Nonetheless, this technique is infrequently used to observe the interactions between QDs and small chemical compounds. More specifically, this technique is seldom used as a sensor for quantitative analysis. Recently, our group demonstrated the potential application of the CD technique to detect heavy metal ions by using chiral QDs as a sensor probe [38]. The detection principle was based on the measurement of the degree of the CD signal which depends upon the formation of chiral complex on the QD surface. The proposed sensor can be utilized for the selective detection of Ni^{2+} and Co^{2+}. It was also found that the CD sensor based on chiral QDs provided superior sensor characteristics, compared to measuring QDs fluorescence property.

In the present work, a new CD sensor based upon cysteamine capped cadmium sulfide QDs (Cys-CdS QDs) has been proposed for detection and chiral identification of DPA and LPA. The Cys-CdS QDs are not optically active in the CD signal (achiral probe). In contrast, the CD data can be detected once Cys-CdS QDs react with DPA or LPA, resulting in a formation of chiral QDs. This phenomenon provides the possibility to apply Cys-CdS QDs as optical detection of chiral-thiol containing compounds. Interestingly, compared to the direct detection of chiral-thiol containing compounds by CD, this sensor is capable of detecting at relatively low concentration levels. Besides the capability of detecting at low concentrations, a progressive spectral change has been observed with increasing concentrations of the DPA or LPA. Thus, the quantitative analysis can also be addressed. The selectivity of the proposed sensor was comparatively observed among various forms of chiral-thiol containing compounds. Moreover, the feasibility of the proposed sensor in a practical application was demonstrated by determination of DPA and LPA in urine samples.

2. Materials and methods

2.1. Chemicals

Chemical reagents used in the current work were all at least of analytical grade and used as receive. Both DPA and LPA were purchased from Aldrich. Cysteamine hydrochloride was obtained from Sigma. Sodium sulfide (Na_2S) was obtained from BDH. Cadmium chloride ($CdCl_2 \cdot H_2O$), potassium dihydrogen orthophosphate (KH_2PO_4) and dipotassium hydrogen orthophosphate (K_2HPO_4) were purchased from UNIVAR. Deionized water (DI) was used for all dilutions with a specific resistivity of 18.2 MΩ cm (Millipore water). Cys-CdS QDs used in this work were prepared and characterized as previously described in our recent report [20] (see the electronic supporting information (ESI) for more information).

2.2. Instrumentations

The detection and chiral identification of DPA and LPA were carried out using circular dichroism spectroscopy recorded on a Jasco-815 CD spectropolarimeter (JASCO, Japan) using a 1 cm quartz cell cuvette, with a scanning rate at 200 nm min^{-1}. The fluorescence spectra data were collected on a Shimadzu RF-5301PC spectrofluorometer. Excitation and emission spectra were recorded with a slit width of 5 nm. Absorption spectra were investigated using an Agilent HP 8453 spectrophotometer. The pH of solutions was measured with a UB-10 UltraBasic pH meter (Denver Instrument). The transmission electron microscope (TEM) micrograph was recorded on Tecnai G^2-20 (FEI, Netherlands) operating at a 200 kV accelerating voltage.

2.3. Circular dichroism measurements

The CD spectrum of PA in the presence of Cys-CdS QDs was obtained by the following procedures. DPA or LPA was dissolved in water to obtain a 10 mM stock solution. Subsequently, 100 μL of the Cys-CdS QDs (0.04 mg mL^{-1}) were blended with the stock solution to obtain concentrations in a range of 0–40 μM. The mixed solution