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Carbon dots based photoelectrochemical sensors for ultrasensitive detection of glutathione and its applications in probing of myocardial infarction

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ABSTRACT

In this work, photoelectrochemical (PEC) sensors based on carbon dots (CDs) were developed for ultrasensitive detection of glutathione (GSH) without additional catalysts. In this PEC sensing system, CDs exhibited both photoelectric and catalytic properties. Silver nanoparticles (AgNPs), graphene oxide (GO), and mesoporous silica (MS) were introduced in order to enhance the sensing properties of CDs for GSH. Among the different hybrid nanocomposites, CDs@MS based PEC sensors exhibited the best sensing properties: the sensitivity and limit of detection (LOD) for GSH were found to be 57.6 nA μM^{-1} and 6.2 nM (S/N = 3), respectively, in the linear range 0.02–4 μM. In addition, the developed PEC sensors showed a high selectivity for GSH even with interferences of other biological thiols and amino acids. The PEC sensor was successfully applied for GSH detection in human serum and probing of myocardial infarction (MI) conditions by estimating the amount of GSH in the myocardial cells of mice, which had been treated with different ischemia/ischemia-reperfusion times. These results indicated that the CDs based hybrid nanocomposites are promising candidates for the development of PEC biosensors with enhanced sensing performances.

1. Introduction

Glutathione (GSH, γ-glutamyl-cysteinyl-glycine) is an important tripeptide thiol, which acts as an antioxidant and whose intracellular concentration is an indicator of oxidative stress. It is well known that abnormal levels of GSH are closely related to ailments, such as cancer, liver damage, AIDS, and cardiovascular disease (Han et al., 2008; Mills et al., 2000; Townsend et al., 2003; Vairetti et al., 2007). As the changes in cellular concentration of GSH are normally very small, a highly sensitive and selective detection of GSH in biological samples is of great importance for the early diagnoses of the above mentioned diseases (Hao et al., 2015). Myocardial infarction (MI), a common heart disease, is induced by continuous myocardial ischemia and hypoxia, which can trigger free radical production. The substantial production of free radicals following myocardial ischemia usually leads to the depletion of GSH. Therefore, it may be concluded that heart healthy is closely associated with the level of GSH, which can be used for indirect diagnosis of acute myocardial infarction in its early stages (Li et al., 2009).

Compared to bulk materials, nanomaterials exhibit unique physical and chemical properties because of their small size, and can be used for the detection of biological substances such as GSH with better sensing performances. Among the different analytical methods available for this purpose, PEC sensors based on fluorescent nanomaterials are excellent detection tools because of their significant advantages such as lower limits of detection, lower potential consumption, easier operation, and easier extension to light-addressable sensors for multichannel detections (Yue et al., 2013; Zhang et al., 2013; Zhao et al., 2014; W.W. Zhao et al., 2016). However, most fluorescent nanomaterials that are currently used are quantum dots (QDs) and these often contain Cd or Pb heavy metal ions. Thus, the applications of QDs based PEC sensors are limited because of their toxicity in fabrication processes and biological detections, especially in cell detections. Moreover, owing to complex fabrication processes and limitation of material properties, these nanomaterials based PEC sensors do not exhibit good enough sensing performances, and the limit of detection is also not very high (Yue et al., 2013). Therefore, new fluorescent nanomaterials with lower

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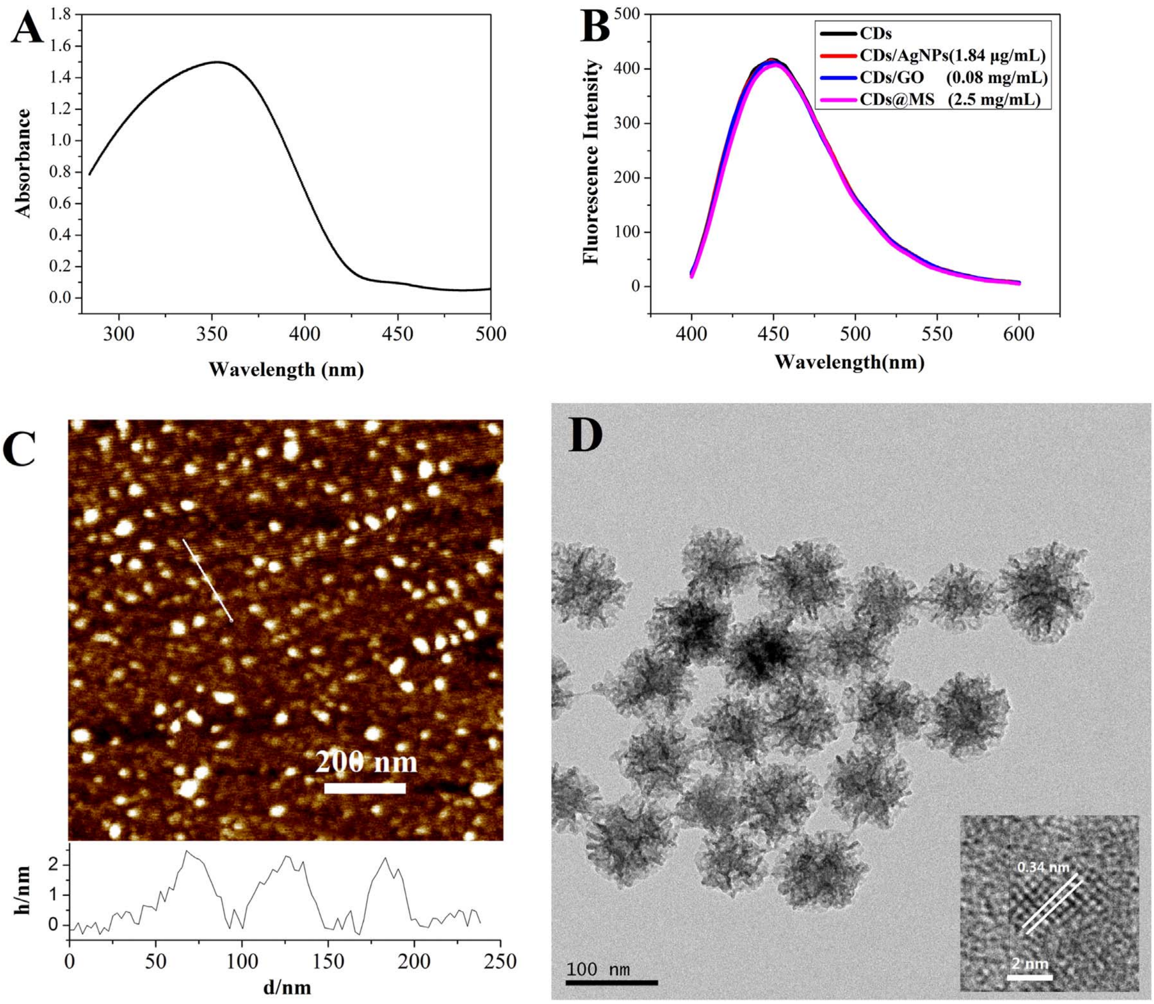

Fig. 1. (A) Absorption spectrum of CDs. (B) Fluorescence spectra of CDs, CDs/AgNPs, CDs/GO, and CDs@MS with optimized concentrations of AgNPs, GO, and MS, respectively. (C) AFM topography image of CDs with the height profile. (D) HRTEM image of the CDs@MS nanocomposite. The inset shows the HRTEM image of individual carbon dots on the surface of MS.

toxicity and better sensing properties are required for developing PEC sensors for GSH detection in cells.

Carbon dots (CDs) are "green" fluorescent nanomaterials and have been utilized in this work to build a PEC sensor for ultrasensitive GSH detection. CDs display unique optical properties, high chemical stability, low environmental risk, and excellent biocompatibility. Owing to these advantages, CDs based nanomaterials are now being used to develop biosensors for different analytical methods (Zuo et al., 2015; Wang and Qiu, 2016). To date, several CDs based optical sensors, such as fluorescent, electrochemiluminescent, and colorimetric sensors, for the detection of GSH have been developed (Cai et al., 2015; Niu et al., 2015; Shi et al., 2014; Y. Xu et al., 2016). All these sensors follow the same sensing mechanism: MnO_2, gold nanoparticles, or other metal ions either affect or quench the fluorescence intensity of CDs. After GSH is added to the test solution, it either reacts or competes with these nanomaterials, leading to a change of fluorescence intensity of CDs. The concentration of GSH can be determined by measuring the changes in optical properties of the CDs. In these detection systems, CDs were only used as optical probes, which implies that the photoelectric and catalytic properties of CDs were not utilized efficiently. However, to the best of our knowledge, there are only a limited number of studies that have used CDs for building PEC sensors, besides a PEC cytosensor that utilizes gold nanoparticle-enhanced CDs (CDs-AuNPs-Cys/chitosan/folic acid/bovine serum albumin) for the detection of Hela cells (Liu et al., 2015). In this PEC biosensor, CDs played the role of fluorescent materials to provide photoelectric properties. The sensing mechanism on Hela cells was mainly due to folic acid rather than CDs. Moreover, no CDs based PEC sensors have been reported for the detection of GSH. Therefore, by combining the advantages of CDs and PEC, CDs based PEC sensors were developed for ultrasensitive detection of GSH with a better limit of detection (LOD) and higher selectivity. This is the first report where CDs exhibit both photoelectric and catalytic properties in a PEC sensing system. Moreover, silver nanoparticles (AgNPs), graphene oxide (GO), and mesoporous silica (MS) were introduced as hybrid nanocomposites in order to enhance the catalytic properties of CDs and obtain better GSH sensing performances. It has been previously shown that these three nanomaterials can improve the catalytic properties of other nanomaterials (Liang et al., 2014; Zhao et al., 2017; Fang et al., 2013).

Finally, the practicality of our PEC sensors was proven by the estimation of GSH concentration in human serum and in myocardial cells of mice, which had been treated with different ischemia/ischemia-reperfusion times.

2. Materials and methods

2.1. Reagents and apparatus

All chemicals were of analytical grade and are listed in the Supplementary Information (SI). All aqueous solutions were prepared using ultrapure water with electrical resistance of 18.2 MΩ cm (25 °C).

The absorption and fluorescence measurements of the different