Biosensors and Bioelectronics 86 (2016) 748–755

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: www.elsevier.com/locate/bios

A dual-channel fluorescent chemosensor for discriminative detection of glutathione based on functionalized carbon quantum dots

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ARTICLE INFO

Article history:
Received 18 May 2016
Received in revised form
23 July 2016
Accepted 23 July 2016
Available online 25 July 2016

Keywords:
Carbon quantum dots
Chemosensor
Fluorometric assay
Glutathione detection

ABSTRACT

A convenient, fluorescent dual-channel chemosensor on the basis of bis(3-pyridylmethyl)amine-functionalized carbon quantum dots (BPMA-CQDs) nanoprobe was constructed, and it can discriminatively detect glutathione from its analogues cysteine and homocysteine based on two distinctive strategies. Two distinct fluorescence responses of BPMA-CQDs probe to Cu(II) and Ag(I) were identified and further employed to achieve selective detection of Cu(II) and Ag(I) respectively. Based on the BPMA-CQDs/Cu(II) conjugate, discriminative detection of GSH was achieved in terms of correlation between the amounts of GSH and fluorescence recovery. The addition of GSH into BPMA-CQDs/Cu(II) system induces the reduction of Cu(II) to Cu(I), which could efficiently block PET process resulting in the following fluorescence recovery. Based on the BPMA-CQDs/Ag(I) conjugate, GSH assay could also be established on the basis of fluorescence response to GSH. The introduction of GSH into the preceding system triggers the competitive coordination to Ag(I) between BPMA and GSH, and silver ions are finally taken away by GSH from the probe, where the fluorescence is restored to its original weak state. Both of the detection strategies can achieve discriminative detection of GSH from Cys and Hcy. The assays showed good stability and repeatability, and covered a broad linear range of up to 13.3 μM with a lowest detection limit of 42.0 nM. Moreover, both of them were utilized to monitor GSH level in live cells.

1. Introduction

Glutathione (γ-L-glutamyl-L-cysteinylglycine, GSH), a thiol-containing tripeptide, is renowned for a requisite endogenous antioxidant, and plays a vital role in defending cellular components against reactive oxygen species (ROS) and toxins (Lu, 1999). If cells are under the oxidized circumstances, it will break the balance between GSH and its oxidized form, glutathione disulfide (GSSG). Under the effect of GSH reductase, GSSG then is promptly transformed into GSH to relieve the oxidative stress of cells. Previous research indicated that intracellular GSH can be served as a crucial clinical biomarker for the reason that enormous clinical diseases are correlated with the alternation of the intracellular redox status (ratio GSSG of to GSH) (Armstrong et al., 2002). Meanwhile, an abnormally descending level of GSH is directly associated with retarded growth of children, dermatosis, hepatic impairment, and even some diseases such as Alzheimer disease, AIDS, cancer, cardiovascular disease, diabetes mellitus, and others (Dennany et al., 2011). Therefore, the development of highly simple, rapid, sensitive and selective detection assays of GSH is in urgent demand for practical application in clinical diagnosis.

In recent decades, a host of detection approaches are utilized to monitor or quantify the variations of GSH in previous literatures, involving high performance liquid chromatography (Bayram et al., 2014; Janes et al., 2010), surface-enhanced Raman scattering (Huang et al., 2009; Saha and Jana, 2013), electrochemistry (Pacsial-Ong et al., 2006; Safavi et al., 2009), electrogenerated chemiluminescence (Niu et al., 2015; Wang et al., 2009), colorimetry (Hu et al., 2013; Li et al., 2011; Xianyu et al., 2015) and fluorescence spectroscopy (Huang et al., 2013; Ju et al., 2014; Xu et al., 2015). In comparison with other analytical methods which usually suffer from their own non-negligible intrinsic shortcomings such as lengthy operation process, expensive instrument and apparatus, intricate extraction systems (Yuan et al., 2013), fluorometric approach is the most widespread, convenient and promising detection approach due to its operational simplicity, inexpensive cost, high sensitivity and real time monitoring (Yang et al., 2013; Zhang

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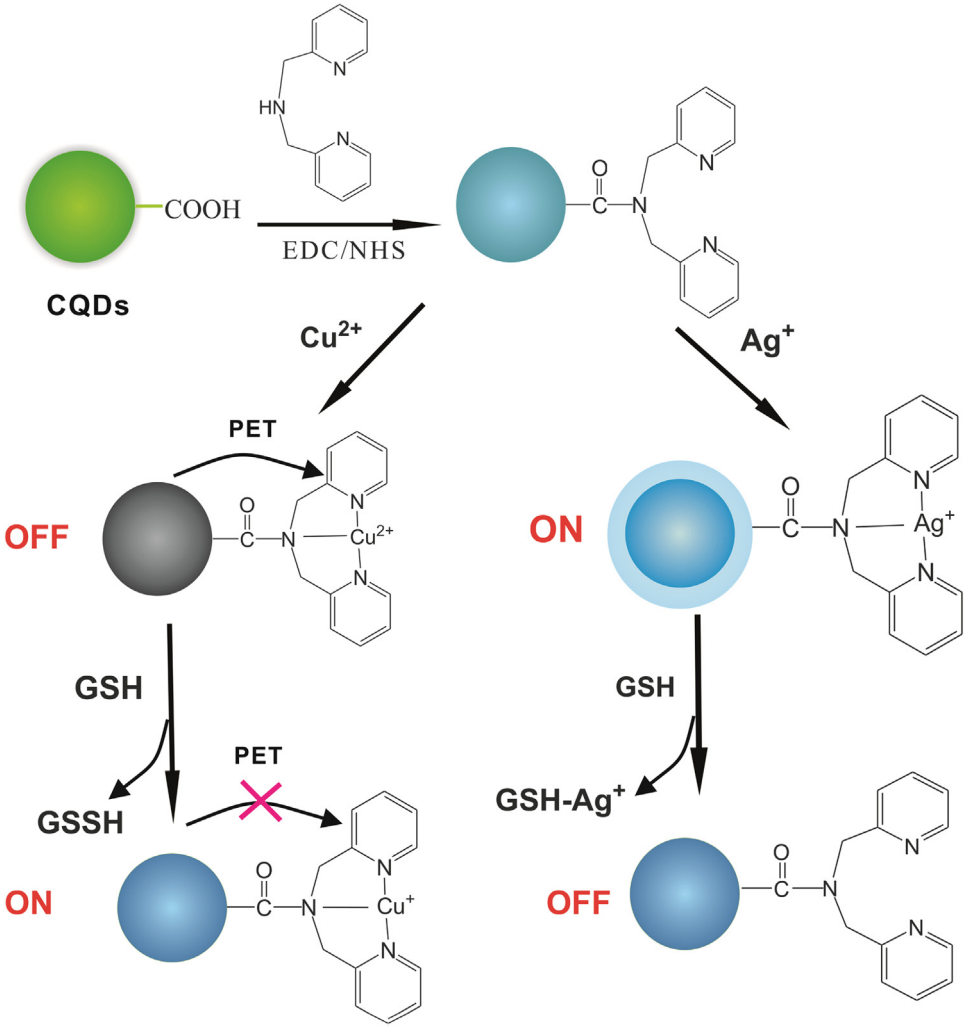
http://dx.doi.org/10.1016/j.bios.2016.07.081
0956-5663/

et al., 2014). Currently, the assays based on molecular probes often have some deficiencies including tedious synthesis and instability to light (Niu et al., 2012; Samarasinghe et al., 2014; Yin et al., 2014), while those based on semiconductor quantum dots have been concerned about the environmental hazard and potential toxicity (Liu et al., 2010). Carbon quantum dots (CQDs) as a new rising fluorescent nanomaterial, have shown great potential in biosensor and bioimaging (Baker and Baker, 2010; Lim et al., 2015; Shen et al., 2012; Zhao et al., 2015; Zheng et al., 2015). Recent advances of CQDs in analysis and sensing promise its practical application in detection of chemical/biological target of interest (Du and Guo, 2016; Jahanbakhshi and Habibi, 2016; Tang et al., 2016). Up to date, several papers have reported fluorescent detection of GSH based on CQDs. One kind of them exploited FRET strategy to detect GSH using carbon quantum dots and MnO_2 nanosheet (Cai et al., 2015; He et al., 2015; Wang et al., 2015; Yang et al., 2015), and the others utilized the disaggregation mechanism to quantify GSH (Gu et al., 2015; Hou et al., 2015; Shi et al., 2014). In general, cysteine (Cys) and homocysteine (Hcy) can seriously interfere with detection of GSH among common biological species because they possess similar chemical behavior. From the previous reports, it can be seen that discriminative detection of GSH from Cys and Hcy was achieved in only two papers (Shi et al., 2014; Wang et al., 2015). Therefore, it is in great demand to develop novel discriminative assays of GSH based on biocompatible CQDs.

In this study, we constructed a convenient fluorescence turn-on/off chemosensor on the basis of bis(3-pyridylmethyl)amine-functionalized carbon quantum dots (BPMA-CQDs) which can discriminatively detect GSH from its analogues Cys and Hcy. On the basis of BPMA-CQDs probe, a dual-channel fluorescent chemosensor was constructed in two different routes, and both of them can discriminatively assay GSH with high selectivity. One route is based on BPMA-CQDs/Cu(II) system in terms of the facts that the coordination of Cu(II) to BPMA site of the probe leads to severe quenching of the fluorescence, and the following addition of GSH into BPMA-CQDs/Cu(II) system induces the fluorescence recovery of the probe. The other route is based on BPMA-CQDs/Ag (I) conjugate according to the facts that fluorescence enhancement of the probe takes place due to the attachment of a vast number of Ag(I) on the surface of BPMA-CQDs; the following introduction of GSH into the preceding system triggers the competitive coordination to Ag(I) between BPMA and GSH, where the fluorescence is restored to its original weak state. The two distinctive fluorescence responses to GSH of BPMA-CQDs/Cu(II) and BPMA-CQDs/Ag(I) are readily used to establish fluorescence turn-ON/OFF detection strategies for GSH. More importantly, both of them can achieve discriminative detection of GSH from Cys and Hcy. Intracellular detection of GSH using the assay was also conducted, and positive results were achieved.



Scheme 1. Schematic illustration of the dual-channel detection strategy for GSH based on BPMA-CQDs probe.

Please cite this article as: Huang, Y., et al., Biosensors and Bioelectronics (2016), http://dx.doi.org/10.1016/j.bios.2016.07.081