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Pb^{2+}-modified graphene quantum dots as a fluorescent probe for biological aminothiols mediated by an inner filter effect

Dajun Yu [1], Xiaomeng Zhang [1], Yanxia Qi, Shushu Ding, Sumei Cao, Anwei Zhu *, Guoyue Shi

School of Chemistry and Molecular Engineering, East China Normal University, 500 Dongchuan Road, Shanghai 200241, PR China

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ABSTRACT

A simple, yet efficient fluorescent method for detecting biological aminothiols has been developed based on the inner filter effect principle that utilizes graphene quantum dots (GQDs) as the donor and aminothiol-Pb^{2+} complex as the absorber. Well-defined diethanol amine modified graphene quantum dots (GQD-DEA) were first synthesized by a "synthesis-modification integration" strategy. Then, the addition of aminothiols can bind with Pb^{2+} and displace it from the surface of preformed GQD-DEA-Pb^{2+}, leading to the formation of aminothiol-Pb^{2+} complex. Due to the complementary overlap between the excitation band of GQD-DEA and the absorption band of aminothiol-Pb^{2+} complex, the fluorescence of GQDs was quenched, thereby a turn-off fluorescent assay for the determination of aminothiols via the inner filter effect was constructed. This strategy enabled cost-effective and selective detection of aminothiols with theoretical simplicity and low technical demands. Moreover, the fluorescent probe offered high selectivity for aminothiol due to the strong binding of aminothiol with Pb^{2+} in comparison with other amino acids and the inner filter effect provided by thiol-Pb^{2+} complex. Under the optimum conditions, the linear concentration ranges were 5×10^{-5}–6×10^{-4} M for cysteine, 5×10^{-5}–1×10^{-3} M for homocysteine, 1×10^{-4}–2×10^{-3} M for glutathione, respectively.

1. Introduction

Biological aminothiols, such as cysteine (Cys), homocysteine (Hcy), and glutathione (GSH), play a critical role in cellular functions, protein synthesis, detoxification and metabolism [1–3]. Besides this, aminothiols concentration in biological fluids is of importance since altered levels of aminothiols have been implicated in a number of pathological conditions including Alzheimer's and Parkinson's disease, as well as autoimmune deficiency syndrome [4–6]. Consequently, great efforts have been devoted to the development of analytical methods for the detection of aminothiols, including chromatography [7], electrochemistry [8,9], mass spectrometry [10], colorimetry and fluorescence method [11–19]. Among the various analytical methods available, fluorescent assay has its own advantages over other techniques in its high sensitivity and simplicity for implementation. However, it remains a challenging work to create a fluorescent probe that possesses an appropriate combination of facile synthesis, low cost, high selectivity and photostability [20–22].

Inner filter effect (IFE)-based fluorescent assay has gained increasing interest for applications in the detection of environmentally or biologically important analytes [23–31]. The IFE, which results from the absorption of the excitation and/or emission light of fluorophores by absorbers, does not require the linking between the absorbers and the fluorophores, making the IFE-based fluorescent assay comparatively simple and flexible. Moreover, an improved detection sensitivity may be obtained compared with the absorbance or fluorescence intensity alone because the varying absorbance of an absorber results in exponential variance in the luminescence of fluorophores. With the advantages of high extinction coefficient and tunable surface plasmon resonance absorption, gold nanoparticles (AuNPs) have been frequently adopted as an absorber unit in the IFE-based detection system [23,24,27–31]. However, the surface plasmon resonance of AuNPs is very sensitive to dielectric constants of both the metal and the surrounding medium [32,33]. Without rational design of the surface chemistry of AuNPs, they often tend to aggregate in complex samples to generate false positive signals, due to the interference from salt [34], metal ions [35], small molecules [36], etc.

* Corresponding author.
E-mail address: awzhu@chem.ecnu.edu.cn (A. Zhu).
[1] These authors contributed equally to this work.

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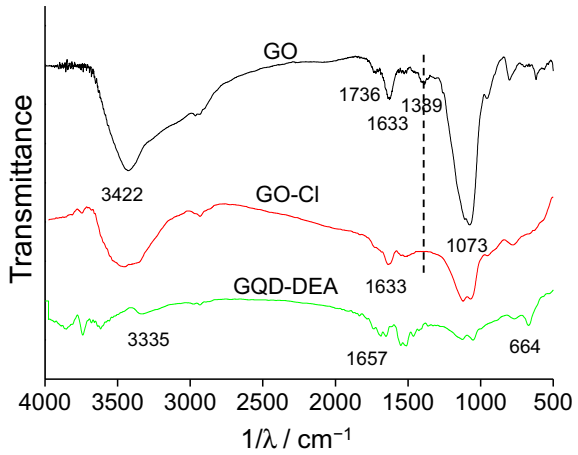

Fig. 1. FT-IR spectra of as-prepared (a) GO, (b) GO-Cl and (c) GQD-DEA.

Very recently, graphene quantum dots (GQDs), which possess favourable attributes of simple synthesis, low cost, and good chemical/photo stability, emerge as an attractive alternative to semiconductor quantum dots and organic fluorophore for fluorescent imaging and sensing [37–39]. However, no research about applications of GQDs as fluorophore in the IFE-based fluorescent assay has been reported so far. On the other hand, GQDs-based sensors are routinely fabricated by at least two steps, namely GQDs synthesis and surface functionalization by conjugation technique. Indubitably, the conjugation process is often tedious and uncontrollable for such small sized GQDs (often less than 10 nm), and even detrimental to their fluorescence. Therefore, a GQDs-based sensing platform, which gets rid of surface modification, will exhibit great promise in the development of simple but effective fluorescent sensor.

In this work, we first present a "synthesis-modification integration" strategy for facile fabrication of diethanol amine (DEA)-functionalized GQDs (GQD-DEA), avoiding tedious and uncontrollable surface modification. Then, by exploiting the competition between DEA and aminothiols for $Pb^{2+}$and the complementary overlap between the excitation band of GQDs and the absorption band of aminothiol-Pb^{2+} complex, an IFE-based fluorescent assay for aminothiols was constructed. Such sensing platform would greatly decrease the assay cost, simplify assay procedure, exhibit stability against high salt solution, and overcome potential interferences in body fluids. On this basis, an effective sensing method based on the designed GQD probe was further developed for the detection of aminothiols in blood serum. Moreover, to the best of our knowledge, this is the first application of GQDs as fluorophore in the IFE-based fluorescent assay.

2. Experimental

2.1. Reagents and chemicals

Diethanol amine (DEA), alanine (Ala), asparaginate (Asn), aspartic acid (Asp), arginine (Arg), cysteine (Cys), glutamate (Glu), glutamine (Gln), glutathione (GSH), glycine (Gly), histidine (His), isoleucine (Ile), leucine (Leu), lysine (Lys), methionine (Met), phenylalanine (Phe), proline (Pro), serine (Ser), threonine (Thr), tryptophan (Trp), tyrosine (Tyr) and Valine (Val) were obtained from Sigma-Aldrich. All other reagents were of analytical grade and purchased from Sinopharm Chemical Reagent Co., Ltd. Aqueous solutions were prepared from deionized water (18 MΩ cm, Hitech science tool laboratory water purification system).

2.2. Apparatus

Transmission electron microscopy (TEM) images were obtained with a JEOL JEM-2100 microscope. Infrared (IR) spectrum was taken on a Thermo Scientific Nicolet iS50 spectrometer. Fluorescence emission spectra was measured on a Hitachi F-7000 fluorescence spectrophotometer with a 150 W xenon lamp. UV–vis absorption

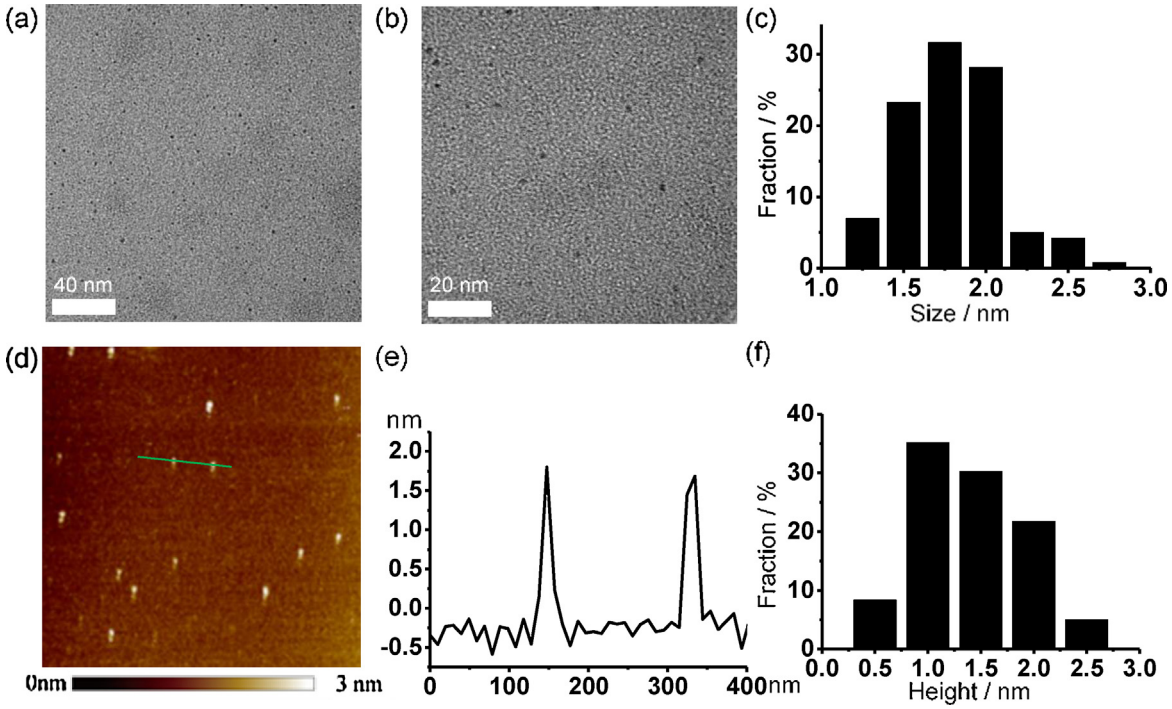

Fig. 2. (a,b) TEM images of the GQD-DEA with different magnifications. (c) The size distribution of GQD-DEA. (d) AFM topography image of GQD-DEA on a silicon substrate, with (e) the height profile along the line in the topographic image. (f) The height distribution of GQD-DEA.