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An inner filter effect fluorescent sensor based on g-C_3N_4 nanosheets/chromogenic probe for simple detection of glutathione

Chunlei Yang[a], Xiu Wang[a], Haiyun Liu[a], Shenguang Ge[b], Mei Yan[a,*], Jinghua Yu[a], Xianrang Song[c]

[a] School of Chemistry and Chemical Engineering, University of Jinan, Jinan 250022, PR China
[b] Shandong Provincial Key Laboratory of Preparation and Measurement of Building Materials, University of Jinan, Jinan 250022, China
[c] Shangdong Provincial Key Laboratory of Radiation Oncology, Shandong Cancer Hospital and Institute, Jinan 250117, China

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ABSTRACT

A fluorescent sensor for the determination of glutathione (GSH) has been developed, which is based on the absorption of a newly designed thiols-specific chromogenic probe (CP) coupled with the use of a thiols-independent fluorophore g-C_3N_4 nanosheets. It was operated on the inner filter effect (IFE). To construct an efficient IFE system, the CP molecules were adsorbed on the surface of g-C_3N_4 nanosheets via π–π stacking interaction. When the biothiol introduced the systems, the weak fluorescence would be restored because of "IFE off". The novel IFE sensor was established for GSH and regarded it as a model target analyte. The IFE sensor had a sensitive response for GSH in a linear range of 0.05 μM L^{-1} to 1.0 μM L^{-1} and the limit of detection was 0.01 μM. The sensor was successfully applied for the quantitative detection of biothiols in human serum. Additionally, the proposed sensor shows high specificity and sensitivity.

1. Introduction

Graphitic carbon nitride (g-C_3N_4), a typical semiconductor and the most stable allotrope of carbon nitride with a stacked two-dimensional (2D) structure, is known for its applications in sensing [1,2], drug delivery and bioimaging [3,4], the oxygen reduction reaction [5,6], peroxidase-like catalysis of hydrogen peroxide [7] and photoelectrocatalysis [8–10]. Different from bulk materials, the g-C_3N_4 nanosheets of nanometer scale process a graphite-like lamellar structure and high surface area, which facilitates the charge transfer and greatly promotes their photoresponse and electroresponse [11]. In order to prepare high performance atomic-scale-thickness g-C_3N_4 nanosheets, various methods have been performed, such as liquid phase exfoliation [12], chemical oxidation [13] and hydrothermal methods [14]. These approaches have been widely used in the fluorescence detection of a variety of ions and biological molecules [15,16]. We obtained it by a green liquid exfoliation route from bulk g-C_3N_4 in water. The as-obtained g-C_3N_4 nanosheets solution possesses excellent properties, such as high quantum yields, high stability, good biocompatibility and nontoxicity. Compared with carbon dots and graphene QDs, the g-C_3N_4 nanosheets are much easier for integrating with other functional materials because of its merits, such as thick two-dimensional structure and high specific surface area. For example, Xie et al. synthesized photoresponsive ultrathin graphitic-phase C_3N_4 nanosheets, which was a promising candidate for bioimaging application [17].

Glutathione (γ-glutamylcysteinylglycine, GSH), the most abundant cellular thiol and nucleophilic tripeptide, is of great interest due to its roles in various enzymatic and nonenzymatic detoxification mechanisms [18]. The level of GSH has been reported to associate with various human diseases, such as cancer, liver damage, AIDS, aging, and diabetes [19–21]. The level of blood GSH is directly related with cellular damage and some diseases, such as leucocyte loss, psoriasis, liver damage and cancer [22]. Therefore, the quantification and detection of GSH have attractive interest on account of its biological and clinical significance. Various analytical methods have been developed for GSH detection, including electrochemistry, electrogenerated chemiluminescence [23], luminescence analysis [24], colorimetry [25], high-performance liquid chromatography (HPLC) [26], surface-enhanced Raman scattering (SERS) [27], mass spectrometry [28] and fluorometry [29,30]. Compared with other techniques, fluorescence technique holds significant advantages for its simplicity, high sensitivity and non-destructive properties [31].

On the basis of different photophysical processes, conventional sensing mechanisms including photoinduced electron transfer (PET), intramolecular charge transfer (ICT), twisted intramolecular

* Corresponding author.
E-mail address: chm_yanm@126.com (M. Yan).

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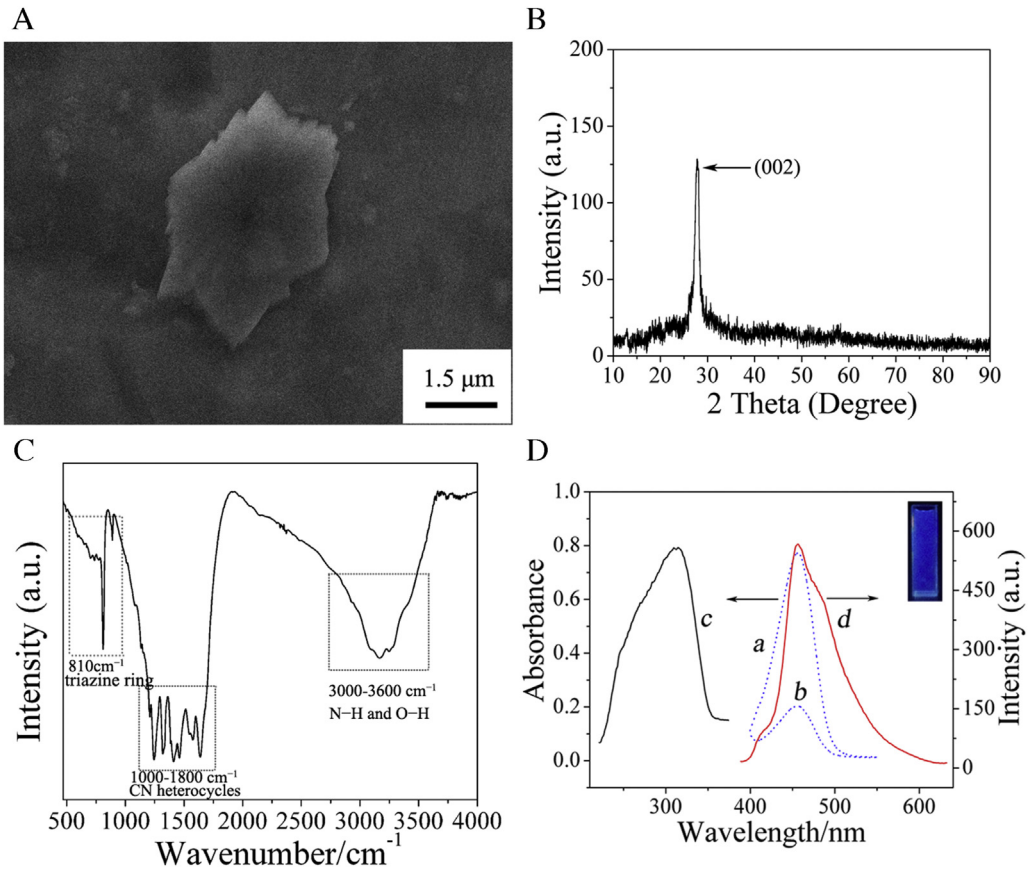

Fig. 1. (A) SEM image of the g-C_3N_4 nanosheets. (B) XRD patterns of the g-C_3N_4 nanosheets. (C) FT-IR spectrum of the g-C_3N_4 nanosheets. (D) Absorption spectra of 100 μM CP in the absence (a) and presence (b) of 10 mM GSH, and fluorescence excitation (λex = 305 nm (c)) and emission spectra (λem = 433 nm (d)) of g-C_3N_4 nanosheets, Inset: the photograph of g-C_3N_4 suspension under UV light (365 nm).

charge transfer (TICT), metal–ligand charge transfer (MLCT), electronic energy transfer (EET), and fluorescence resonance energy transfer (FRET) are employed for the fluorescent chemosensor [32]. It only works when they are at a particular distance or have a complementary geometry. These methods are complicated and time-consuming, leading to restricting further practical applications. There is an alternative way to be useful for designing a fluorescent sensor based on inner filter effect (IFE), which is known to result from the absorption of the exciting and/or emitted light by absorbers in the detection system. The IFE has been used as a smart approach to design fluorescent sensors, which are characterized by the simplicity and flexibility with high sensitivity. How to improve the performances of IFE-based fluorescent sensors is highly desirable but remains an unsatisfied challenge. The integration of functionalized nanomaterial and technology with biology and chemistry is the current trend for opening new horizons of novel sensor protocols that employ electronic and optical signal transductions [33]. Based on above, we choose g-C_3N_4 nanosheets as the fluorophore and solid substrate, which has a high surface area and could load much probe molecules.

Following this line of thought, in this work, we designed a nanomaterial-assisted IFE sensing system. There were few reports about the research on the g-C_3N_4 nanosheets-based nanosensor via IFE. A fluorescent sensor for biothiols was developed employing a newly designed thiols-specific chromogenic probe (CP), operative on the IFE on g-C_3N_4 nanosheets. The CP molecules were adsorbed on the surface of g-C_3N_4 nanosheets via π–π stacking interaction. Biological thiols include cysteine (Cys), homocysteine (Hcy) and glutathione (GSH). The sensor we designed has an obvious fluorescence response for GSH than others. Although direct detection of biothiols by CP could realize, it still exist some inherent limitations, such as probable biologic toxicity, poor photostability and susceptibility to the organic dyes [34]. Therefore, it is necessary for us to improve sensing performances in term of sensitivity and analysis speed. The proposed sensor CP/g-C_3N_4 nanosheets possesses several remarkable advantages, including high response sensitivity for GSH, short response time and suitability for complicated biological environment, which possesses promising applications. In this way, a quantitative detection of biothiols in human serum was realized via the simple and convenient strategy with the proposed sensor.

2. Materials and methods

2.1. Chemicals and reagents

All reagents were of analytical-reagent grade or the highest purity available and directly used for the following experiments without further purification. 4-(diethylamino)benzaldehyde ($C_{11}H_{15}NO$) and 3,3-diethoxypropanenitrile ($C_7H_{13}NO_2$) were purchased from Aladdin Co., Ltd (Shanghai, China). Ferric chloride hexahydrate ($FeCl_3{\cdot}6H_2O$), melamine ($C_3H_6N_6$) and nitric acid (HNO_3) were purchased from Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). Ethanol (C_2H_5OH), acetic acid ethyl acetate ($CH_3COOC_2H_5$) and petroleum were purchased from Shanghai Chemical Reagent Company (Shanghai, China). Glutathione (GSH) and other biomolecules were bought from Shanghai Boao Bio-Technology Co., Ltd (Shanghai, China). Human serum samples were obtained from healthy volunteers at a local hospital and stored at −20 °C until further analysis.