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Graphene-based hybrid for enantioselective sensing applications

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ABSTRACT

Chirality is a major field of research of chemical biology and is essential in pharmacology. Accordingly, approaches for distinguishing between different chiral forms of a compound are of great interest. We report on an efficient and generic enantioselective sensor that is achieved by coupling reduced graphene oxide with γ-cyclodextrin (*rGO/γ-CD*). The enantioselective sensing capability of the resulting structure was operated in both electrical and optical mode for of tryptophan enantiomers (*D*-/*L*-Trp). In this sense, voltammetric and photoluminescence measurements were conducted and the experimental results were compared to molecular docking method. We gain insight into the occurring recognition mechanism with selectivity toward *D*- and *L*-Trp as shown in voltammetric, photoluminescence and molecular docking responses. As an enantioselective solid phase on an electrochemical transducer, thanks to the different dimensional interaction of enantiomers with hybrid material, a discrepancy occurs in the Gibbs free energy leading to a difference in oxidation peak potential as observed in electrochemical measurements. The optical sensing principle is based on the energy transfer phenomenon that occurs between photo-excited *D*-/*L*-Trp enantiomers and *rGO/γ-CD* giving rise to an enantioselective photoluminescence quenching due to the tendency of chiral enantiomers to form complexes with *γ-CD* in different molecular orientations as demonstrated by molecular docking studies. The approach, which is the first demonstration of applicability of molecular docking to show both enantioselective electrochemical and photoluminescence quenching capabilities of a graphene-related hybrid material, is truly new and may have broad interest in combination of experimental and computational methods for enantiosensing of chiral molecules.

1. Introduction

Chirality is a prominent characteristic of natural systems, and artificial enantioselective sensing and discrimination of biologically important chiral species is a crucial challenge in various applications related to sensors, catalysis, biomedicine and biotechnology (Wattanakit et al., 2014). During the past decade, chiral discrimination has become of increasing importance and many efforts have been devoted to the goal of understanding biochemical processes in biological phenomena involving artificial systems (Zor et al., 2013). Great success has been attained in the development of specific chiral selectors that enable enantioselective discrimination by high performance liquid chromatography (Bobbitt and Linder, 2001), NMR (Ema et al., 2007), chemiluminescence (Wang et al., 2008) and circular dichroism (Cao et al., 2013) techniques. Apart from the conventional application of these techniques, in recent years, electrochemical sensors have been frequently reported for discriminative sensing of bioactive compounds due to their advantages such as high stability and sensitivity, and they are easy to be integrated in various sensing platforms for advanced intelligent sensing (Trojanowicz, 2014).

The key step to produce an electrochemical chiral sensor is to build molecular architectures consisting of enantioselective sensing sites which exhibits different binding affinity for enantiomers

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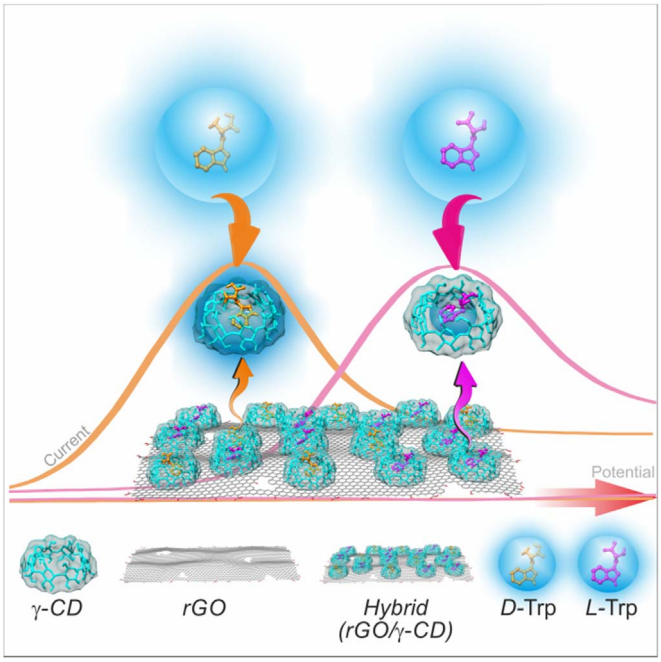
(Kaminker et al., 2013). In addition to their host-guest properties with interest in sensing (Alarcón-Angeles et al., 2008) cyclodextrins (CDs) have been widely used for enantioselective extraction of bioactive compounds, various methods using these cyclic polysaccharides composed of glucose molecules have been reported as electrochemical chiral biosensors (Guo et al., 2010; Zor et al., 2015). However, the requirement for an electrochemical chiral sensor for discrimination of enantiomers is not only recognition of enantiomers but also a material enhancing and distinguishing the analytical signal (ex. electrical current) resulted by the interaction on the electrode surface. The unification of enantioselectivity with electrical conductivity endows conjugated materials with various fascinating characteristics to serve as a sensing platform (Sannicolò et al., 2014).

A major advance in the last few years is the discovery of graphene, defined as a single layer of carbon atoms patterned in a 2D honeycomb network, which is the rising star of nanomaterials received fascinating research attention in (bio)sensors (Novoselov et al., 2012). Due to the fact that graphene surface can acquire various functionalities through the creation of different receptor units and bioactive scaffolds (Gravagnuolo et al., 2015), graphene-based enantioselective sensors have attracted widespread attention in electrochemical chiral sensing and discrimination platform for bioactive molecules such as naproxen (Guo et al., 2014), cystine (Zor et al., 2015).

Herein, novel platform based on graphene and cyclodextrin (*rGO/γ-CD*) with high sensing capability toward enantiomers thanks to their complex formation (due to the chiral selector behavior) and different molecular orientations is reported. The peculiarity of this platform stands in its enantioselective capability while operating in either electrochemical or optical detection mode. Sensing behavior of *rGO/γ-CD* for Trp enantiomers, an essential amino acid that is a precursor for a variety of biologically active compounds, in addition of being an important metabolite in human and animals and consequently utilized as a pharmaceutical antidepressant agent (Baytak and Aslanoglu, 2015), was studied and demonstrated *via* electrochemical, photoluminescence and computational methods. The results show that Trp enantiomers exhibit different affinity towards *rGO/γ-CD* and the obtained sensor gives higher sensitivity towards *L*-Trp. The results ensure that the proposed enantioselective sensor can be used as an effective tool to estimate the enantiomeric quantity of *D*- and *L*-Trp.

Graphene-related materials can be integrated as the core of bio/sensing platforms due to their excellent abilities for direct interaction with bio/molecules, electrical conductivity, their applicability in solution and the capability to be used as highly efficient long-range quenchers (Morales-Narváez and Merkoçi, 2012). After surface modification with selective groups, antibodies, aptamers and etc. for target materials, unprecedented bio/sensing strategies can be developed (Morales-Narváez et al., 2013). Here we propose the use of a hybrid material such as *rGO/γ-CD* that can operate in both electrical and optical biosensing with interest for enantioselective sensing of *D*- and *L*-Trp (See Scheme 1). The operation principle of such platform and its efficiency to be used in such an important field are clarified and demonstrated through a series of spectroscopic characterizations of the involved materials, electrical and optical behaviors in addition to molecular docking responses as shown in the following sections.



Scheme 1. Schematic, not in scale, of the graphene-based hybrid for enantioselective sensing applications operating through both optical (photoluminescent quenching) and electrochemical generated signals.

2. Material and methods

2.1. Reagent and apparatus

Graphite powder (99.99%), concentrated H_2SO_4 and H_3PO_4, H_2O_2 (30%), $KMnO_4$ (99%), $K_2S_2O_8$, P_2O_5, γ-cyclodextrin, *D*- and *L*-Trp (tryptophan) were purchased from Sigma-Aldrich. All reagents were used with regard to the material safety guide recommended by the suppliers and used as received without further purification.

Transmission Electron Microscopy (TEM) images were acquired using JEOL JEM 2100F HR-TEM operating at 20 kV. AFM micrographs were obtained using a Park XE7 instrument. Fourier transformed infrared (FTIR) spectra were recorded on an FTIR spectrophotometer equipped with an attenuated total reflectance (ATR) accessory (Perkin Elmer 100 FTIR) in the 550–4000 cm^{-1} range in ambient air at room temperature. Thermogravimetric analysis (TGA) of the materials (10–15 mg) was performed on a Setaram thermal gravimetric analyzer at a heating ramp of 10 °C min^{-1} over the temperature range of 25–1200 °C under inert gas atmosphere. Raman spectra were recorded on a Renishaw inVia Reflex equipped with CCD detector. X-ray photoelectron spectroscopy (XPS) measurements were performed using a PHI 5000 VersaProbe analyzer/spectrometer. Photoluminescence experiments were recorded with PTI QuantaMaster™ 40 steady state spectrofluorometer system (QM40) using a high intensity continuous Xe lamp. For the electrochemical measurements, a computer-controlled IVIUM-CompactStat potentiostat was used. A BAS/C3 electrochemical cell stand consisting of three electrode configuration cell was combined to potentiostat. A bare or modified GCE was used as working electrode, the reference and counter electrode were Ag/AgCl electrode and a platinum wire, respectively. A Sonorex Super RK 106 was used to exfoliate materials and to clean electrode surfaces.

2.2. Production of γ-cyclodextrin decorated graphene (rGO/γ-CD) hybrid and overall procedure

Production of γ-cyclodextrin decorated graphene (*rGO/γ-CD*) hybrid and overall procedure for measurements were given as Supplementary material file.