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Direct electrochemical reduction of hematite decorated graphene oxide (α-Fe_2O_3@erGO) nanocomposite for selective detection of Parkinson's disease biomarker

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ABSTRACT

An unusual approach is reported herein to fabricate magnetic hematite (α-Fe_2O_3) decorated electrochemically reduced graphene oxide (α-Fe_2O_3@erGO) nanocomposite. The method utilizes direct electrochemical reduction of self-assembled, ex-situ synthesized α-Fe_2O_3 anchored GO to erGO (α-Fe_2O_3@erGO) on glassy carbon electrode (GCE) for selective detection dopamine (DA), an important biomarker of Parkinson's disease. The formation of α-Fe_2O_3@erGO/GCE has been confirmed by XPS and Raman spectroscopy. α-Fe_2O_3@erGO modified GCE exhibits synergistic catalytic activity nearly 2.2 and 5 fold higher than α-Fe_2O_3@GO and other modified electrodes, respectively towards oxidation of DA. The fabricated sensor exhibited linear dynamic ranges over 0.25 − 100 μM in response to DA with a LOD of 0.024 μM (S/N = 3), LOQ of 0.08 μM (S/N = 10), and a sensitivity of 12.56 μA μM^{-1} cm^{-2}. Finally, the practical analytical application of the proposed α-Fe_2O_3@erGO/GCE was investigated for the determination of DA in commercially available pharmaceutical formulation and human serum samples, and showed satisfactory recovery results towards DA.

1. Introduction

Dopamine (3,4-dihydroxyphenyl ethylamine, DA) belongs to the class of catechol amines is an influential neurotransmitter present in the central nervous system (CNS) of the human body and regulates numerous cognitive functions like movement, stress, reward-related behavior, attention and mood (Biswas et al., 2016; Liu et al., 2017). Abnormal metabolism of DA in the body may lead to neurological disorders including: (i) Parkinson's diseases (PD) (Sansuk et al., 2013) and (ii) impulsivity that are reported to be induced by the low and high concentration of DA, respectively (Birtwistle and Baldwin, 1998). Duan et al. asserted that DA is an important biomarker for the diagnosis and treatment of Parkinson's disease (Duan et al., 2015). The existing techniques for the detection of dopamine include chemiluminescence (Sun et al., 2018), capillary electrophoresis with laser-induced native fluorescence (Park et al., 1999), flow injection analytical methods (Li et al., 2011), high-performance liquid chromatography-mass spectroscopy (HPLC-MS) (Carrera et al., 2007) and electrochemical approaches. However, most of these methods have their own constraints such as being expensive, associated with complicated sample pretreatment, required prolong time, limited to detect one compound, etc. and therefore does not meet the requirement for point-of-care (POC) diagnostics.

Lately, fabrication of electrochemical sensor is considered as the most convenient and affordable alternate to achieve highly selective and sensitive detection of DA with a low detection limit. However, the main difficulty in the electrochemical detection of DA is the presence of co-existing interferences like ascorbic acid (AA) and uric acid (UA) in the body fluid, which have close oxidation potentials to that of DA (Chang et al., 2017). Resulting, an overlapping of voltammetric response and poor resolution in detection of DA. To circumvent these obstacles, chemical modification of the electrode using different metal or metal oxide nanoparticles (Farka et al., 2017; Lakhera et al., 2018; Solanki et al., 2011), carbon-based materials particularly GO and their composites have been employed instead of bare electrode (Gao et al., 2016; Tiwari et al., 2016).

Among the low cost and biocompatible metal oxides, hematite (α-Fe_2O_3) nanoparticles (NPs) is considered as one of the promising

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candidates for biosensing applications with n-type semiconducting properties (band gap ca. 2.2 eV) and is also reported as the most thermodynamically favourable phase of iron oxide. Nonetheless, the high electron-hole recombination rate of α-Fe_2O_3 is often associated with the low electrocatalytic and poor cycling performance, which severely hinders its practical applications to a certain extent (Yang et al., 2016). On the contrary, conductive supporting materials comprising of α-Fe_2O_3 can be introduced to enhance its electrocatalytic efficiency. Recently, GO supported nanomaterials have been emerged as a promising electrocatalyst for diverse applications (Manivel et al., 2013; Babu et al., 2015). Conventionally, to accomplish the reduced-GO/Fe_2O_3 nanocomposite, chemical reduction of GO to rGO followed by one step synthesis of α-Fe_2O_3 onto rGO materials are performed (Teymourian et al., 2013). However, lack of control over uniform dimensions, anchoring strength and dispersion of the α-Fe_2O_3 onto rGO, loss of dielectric and magnetic of the composites, etc. often limits their applications. According to Wang et al., direct anchoring of α-Fe_2O_3 on rGO could enhance the charge transfer between the α-Fe_2O_3 and rGO resulting in an increased sensitivity (Wang et al., 2014).

Herein, we demonstrate a novel approach to fabricate electrochemically reduced α-Fe_2O_3@erGO nanocomposite as an electrode material without adding any reducing or toxic agents. The method utilizes self-assembly of ex-situ synthesized magnetic α-Fe_2O_3 NPs and GO to form α-Fe_2O_3@GO, and followed by electrochemical reduction of GO in α-Fe_2O_3@GO (α-Fe_2O_3@erGO). The self-assembling method is driven by the mutual electrostatic interaction between the positively charged α-Fe_2O_3 NPs and negatively charged GO. The unique nanocomposite has the potential to (i) reduce the aggregation of α-Fe_2O_3 NPs, (ii) prevent the stacking of GO, (iii) enhance the active surface area, and (iv) accelerate the electrocatalytic performance of the overall electrode. Finally, α-Fe_2O_3@erGO modified electrochemical sensor was investigated for detection of dopamine in pharmaceutical formulations as well as human serum samples. To the best of our knowledge, no such procedure has been documented on dopamine biosensor so far.

2. Experimental

2.1. Reagents and materials

All the chemicals in this experiment were used as received without any further purification (Section 1; Supporting information).

2.2. Fabrication of α-Fe_2O_3@erGO/GCE

Ex-situ synthesized α-Fe_2O_3 and GO were used to design the self-assembled α-Fe_2O_3@GO nanocomposite (Sections 2, 3, and 4; Supporting information). Prior to fabrication, GCE was polished repeatedly with 1.0, 0.3, and 0.05 μM alumina/water slurries and mild sonicated with ethanol/water (3:1 v/v) for 2 min until shows mirror-like surface. Fabrication of α-Fe_2O_3@erGO/GCE was achieved via a simple two-step process: drop casting of self-assembled α-Fe_2O_3@GO nanocomposite followed by electrochemical reduction of α-Fe_2O_3@GO to α-Fe_2O_3@erGO. Briefly, 6 μL aqueous dispersion of the as-prepared α-Fe_2O_3@GO nanocomposite (3 mg mL^{-1}) was directly drop-casted on to the polished working GCE surface and allowed for subsequent evaporation of the solvent at room temperature. The well-dried α-Fe_2O_3@GO/GCE was then transferred to an electrochemical cell containing 10 mL of 0.1 M PBS (pH 7.0). The electrochemical reduction of α-Fe_2O_3@GO to α-Fe_2O_3@erGO was performed in the potential range of 0 to −1.2 V and at a scan rate of 50 mV s^{-1} using 15 successive cycles of cyclic voltammograms where Na_2HPO_4/NaH_2PO_4 in PBS acts as a supporting electrolyte. Thus, α-Fe_2O_3 anchored electrochemically reduced GO modified electrode (α-Fe_2O_3@erGO/GCE) was fabricated for DA detection as shown in Scheme 1.

2.3. Materials characterization

As-synthesized α-Fe_2O_3, GO, α-Fe_2O_3@GO, and α-Fe_2O_3@erGO were analytically and electrochemically characterized using various instrumental techniques (Section 5; Supporting information).

3. Results and discussion

3.1. Analytical characterization

The morphological features, surface chemistry, magnetic property of the as-prepared α-Fe_2O_3, GO, and self-assembled α-Fe_2O_3@GO nanocomposite were characterized using FESEM, DLS, zeta potential and Raman analysis. Fig. 1a represents the FESEM image of ex-situ synthesized α-Fe_2O_3 NPs. It can be obviously seen that the α-Fe_2O_3 NPs was predominantly spherical in shape within 65.15–267.18 nm with little or no aggregation. DLS analysis reveals that hydrodynamic diameter of the average α-Fe_2O_3 NPs is 141.73 nm (Fig. 1b). Inset of Fig. 1a-i shows a negative electrokinetic zeta potential of –7.02 ± 1.45 mV due to the adsorption of citrate anions onto the surface. This observation suggests that α-Fe_2O_3 NPs are stabilized by steric repulsion forces. Eventually, in addition of low concentration of NaCl (0.02 M), negative zeta potential of α-Fe_2O_3 have been observed to switch towards positive potential of + 6.25 ± 3.2 mV (Inset of Fig. 1a-ii), indicates the charge screening or charge neutralization effects of NaCl (Huynh and Chen, 2011). Fig. 1c depicts transparent, wrinkled, and 2-dimensional planar structure of GO that comprises a few monolayer carbon structure. Zeta potential measurments shows that GO had surface charge of ca. –19.63 ± 4.8 mV due to the presence of carboxylic and phenolic hydroxy groups (Inset of Fig. 1c). Finally, the self-assembly of α-Fe_2O_3 with GO is evidenced from FESEM micrograph (Fig. 1d). It can be noticed that α-Fe_2O_3 are evenly distributed around the surface of GO layer and the estimated zeta potential measurments of the α-Fe_2O_3@GO nanocomposite is found to be –36.44 ± 3.1 mV (Inset of Fig. 1d). This result is expected due to the electrostatic coupling of low positively charged surface of α-Fe_2O_3 and high negatively charged surface of GO, which is beneficial to fabricate efficient α-Fe_2O_3@GO nanocomposite with enhanced active surface area for electrocatalysis. It is noteworthy to observe that α-Fe_2O_3 are also seen to aggregate around the GO layer due to the high magnetic and adsorption properties. The magnetic properties of α-Fe_2O_3 and α-Fe_2O_3@GO were analyzed using vibrating sample magnetometer (VSM) applying external magnetic field within ± 15,000 G at room temperature (Fig. 1e). The reversible S-like magnetization hysteresis loop and coercivity tending to zero Oe indicate the superparamagnetic behavior of α-Fe_2O_3. The estimated magnetic saturation (*Ms*) values of α-Fe_2O_3 and α-Fe_2O_3@GO were observed to be 151.70 and 79.06 emu g^{-1}, respectively. The lower *Ms* of α-Fe_2O_3@GO compared to α-Fe_2O_3 may be attributed to the presence of GO in α-Fe_2O_3@GO nanocomposite. These characteristic properties may be desirable to develop recyclable catalyst and fabricate magnetically controlled electrochemical sensor. Furthermore, the successful self-assembly of α-Fe_2O_3 and GO, and the electrochemical reduction of GO to erGO in the composite were ascertained by FT-Raman analysis (Fig. 1f). Raman spectrum of pristine GO exhibit two distinct peaks centered at 1349 and 1590 cm^{-1} corresponding to D and G band, respectively. The D band is considered to be a disordered band originating due to partial edge defects, structural defects, and dangling sp^2 carbon bonds that lost symmetry, while the G band attributes in-plane stretching vibration between sp^2 carbon atoms. The intensity ratio of the D and G bands i.e. (I_D/I_G ratio) provides a parameter to quantify the partial defects of GO, where a higher I_D/I_G ratio ensures more defects on GO. As shown in Fig. 1f, compared with pristine GO, additional characteristics bands observed at 213, 298, 369, 494 cm^{-1} for the α-Fe_2O_3@GO composite are due to the existence of α-Fe_2O_3 (Wang et al., 2015). The bands at 213 and 494 cm^{-1} are attributed to A_{1g} mode and those at 298 and 369 cm^{-1} are attributed to E_g