



Electrochemical sensor for epinephrine based on a glassy carbon electrode modified with graphene/gold nanocomposites

Fei Cui, Xiaoli Zhang*

School of Chemistry and Chemical Engineering, Shandong University, Jinan 250100, China

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ABSTRACT

A solution-based approach of chemical co-reduction of Au (III) and graphene oxide (GO) was used to prepare graphene/Au (GR/Au) nanocomposites. The gold nanoparticles (nano-Au) integrated in GR acted as spacers for inhibiting the aggregation of GR sheets. Scanning electron microscopy (SEM) and transmission electron microscope (TEM) results revealed that nano-Au particles were dispersed uniformly on the GR sheets. The obtained GR/Au nanocomposites modified glassy carbon electrode (GR/Au/GCE) exhibited high sensitivity in the detection of epinephrine (EP). It has been found that oxidation of EP at this modified electrode occurred at less positive potentials than on bare GCE. The anodic peak current observed were directly proportional to EP concentration between the range of 5.0×10^{-8} and 8.0×10^{-6} mol L⁻¹ (L.O.D. = 7.0×10^{-9} mol L⁻¹). In addition, the oxidation peaks of EP and ascorbic acid (AA) were separated from each other by approximately 180 mV. Therefore the GR/Au nanocomposites modified electrode successfully differentiates the signals of the two analytes. At the same time, this electrode also showed favorable electrocatalytic activity toward some other small biomolecules (such as dopamine, β -nicotinamide adenine dinucleotide, and uric acid), suggesting the potential applications of GR/Au nanocomposites for constructing biosensors.

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1. Introduction

Graphene (GR) is a novel carbon-based nanomaterial, which has captured great interest among scientists in recent years [1,2]. It is an ideal material for electrochemistry [3–5] because of its excellent electrical conductivity, high surface area and low cost. GR modified electrodes have been used in the detection of some biomolecules [6–9]. However, unless well separated from each other, GR tends to form irreversible agglomerates or even restack to form graphite through van der Waals interactions and π - π stacking [10]. Therefore, different methods have been used to improve the solvency of GR by chemical modifications or non-covalent functionalizations [11–14].

Recently, GR-based hybrids with metallic nanoparticles have shown potential applications in the area of chemical sensors, energy storage and catalysis [15,16]. The GR-based hybrids with metallic composite materials can improve electronic and thermal conductivity [17,18]. Another important feature of the adhesion of metal nanoparticles to GR is the inhibition of aggregation of GR sheets in dry state. By functioning as a spacer, the metal nanoparticles make both faces of GR accessible by increasing the distance between the GR sheets [19].

Nano-Au has been widely used as catalysts to promote various chemical reactions for their unique optical and surface properties [20]. It is expected that a hybrid composed of GR and nano-Au could become a novel functional material for application in electrochemistry. Until now, two main methods have been used to fabricate GR/Au hybrids. One is using inter-media [21–25], such as cationic polyelectrolyte poly (diallyldimethyl ammonium chloride), for the linkage of nano-Au and graphene to form graphene-media-Au hybrids. The disadvantage of the method is poor conductivity of the hybrid because of the barrier of nonconducting media between the graphene and the nano-Au. In order to overcome this, in situ growth of nano-Au on graphene has been presented. Through such a method, some researchers showed that nano-Au were uniformly distributed on GR [26,27].

Epinephrine (EP) is an importance neurotransmitter in mammalian central nervous systems [28]. Many diseases are related to the change of its concentration. Thus, a quantitative determination of EP is significant. EP is an electroactive molecule, whose electrochemical behaviors have been studied [29–35] and some methods have also been reported for its determination [36–38].

Herein, a solution-based method was used to prepare nano-Au decorated GR nanocomposites via a chemical co-reduction. The reduction of GO and the in situ deposition of nano-Au were achieved in a one-pot process. The as-prepared nanocomposites show good dispersibility and their catalytic activities were evaluated by determination of EP. This modified electrode exhibited high sensitivity

* Corresponding author. Tel.: +86 53188364446; fax: +86 53188564464.

E-mail address: zhangxl@sdu.edu.cn (X. Zhang).

and stability in detection of EP. The obtained linear range for EP was 5.0×10^{-8} – 8.0×10^{-6} mol L⁻¹. We also studied the use of GR/Au/GCE for sensing some other biomolecules, such as dopamine, β -nicotinamide adenine dinucleotide, ascorbic acid, uric acid and pyrocatechol.

2. Experimental

2.1. Apparatus and reagents

A CHI 832 electrochemical analyzer (Shanghai Chenhua Instrument Company, China) was used to perform electrode characterization and voltammetric measurements. A conventional three-electrode system, including a bare or modified glassy carbon electrode (GCE, 4 mm in diameter) as working electrode, a saturated calomel electrode (SCE) as reference electrode and a platinum (Pt) plate as counter electrode was used in this work. All potentials in the text were against SCE.

EP (obtained from Wuhan GPC-China Chemistry Co. Ltd.), dopamine (DA), uric acid (UA), ascorbic acid (AA) and β -nicotinamide adenine dinucleotide (NADH), pyrocatechol and sodium citrate (obtained from Sinopharm Chemical Reagent Co. Ltd.) were used without further purification, and the stock solution was stored at -4°C away from light. H₂AuCl₄ was obtained from Shanghai Chemical Reagents Co. Ltd. Graphite oxide (GO) was got from Nanjing Xianfeng NANO Materials Tech Co. Ltd. N,N-dimethylformamide (DMF) were bought from Beijing Chemical Company. Dialysis membranes (MWCO 8000–14000) were purchased from Solarbio. Phosphate buffer solutions (PBS) with different pH values were prepared by mixing 0.1 mol L⁻¹ Na₂HPO₄ and 0.1 mol L⁻¹ NaH₂PO₄. All the chemicals used were analytical reagent grade. Doubly distilled water was used throughout the experiments.

2.2. Synthesis of GR/Au nanocomposites

Graphite oxide was suspended in water to give a brown dispersion, which was subjected to dialysis to completely remove residual salts and acids. As-purified graphite oxide suspensions were then dispersed in water to create 1 mg mL⁻¹ dispersion. Exfoliation of graphite oxide to GO was carried out by sonicating graphite oxide dispersion for 6 h.

GR/Au nanocomposites were prepared by the chemical co-reduction of Au (III) and GO with sodium citrate [26]. Briefly, the aforementioned dispersion of GO (4 mL) was added to 25 mL of H₂AuCl₄ solution (0.2 mg mL⁻¹). The resultant suspension was stirred for 1 h to promote the interaction of gold ions with the graphene surface [15,26]. After that, 940 μL of sodium citrate (0.2 mol L⁻¹) was added dropwise into the above mixture. The mixture was heated at 80°C for 2 h. The product was separated by centrifugation and thoroughly rinsing with ethanol and doubly distilled water, and vacuum-dried at room temperature.

GR was prepared through the same procedure except for only reduce GO [10]. Nano-Au was prepared by only reduce H₂AuCl₄ [39].

2.3. Preparation of modified electrode

A GCE was polished with 0.5 and 0.05 μm Al₂O₃ powder and then rinsed with water and sonicated in ethanol and doubly distilled water in turn. Then, the cleaned GCE was gently blown under a nitrogen stream. A volume of 10 μL of GR/Au or GR DMF/aqueous solution (volume ratio DMF/H₂O = 9:1) or nano-Au aqueous solution (the concentration of GR/Au or GR is 1.0 mg mL⁻¹) was added onto the clean GCE and dried at room temperature. They were respectively denoted as GR/Au/GCE, GR/GCE and nano-Au/GCE.

2.4. Analytical procedure

A 0.1 mol L⁻¹ PBS (pH 7.0) was used as the supporting electrolyte for determination of EP. Firstly, the solution was deoxygenated with N₂ and kept under N₂ blanket. Then, the voltammograms of EP were recorded from -0.8 to 0.6 V with a scan rate of 100 mV s⁻¹.

3. Results and discussion

3.1. Structure characterization

The Raman spectroscopy of GR (see Supporting information Fig. 1S) shows two characteristic peaks at 1327 cm⁻¹ (D band) and 1595 cm⁻¹ (G band) [40]. The result indicated the existence of small size of the in-plane sp² domains of GR [41,42]. Fig. 1A illustrates the typical TEM image of the prepared GR sheets. As shown in this figure, GR clearly shows the flake-like shapes. Therefore, the Raman spectrum and TEM analyzes demonstrated that GR is successfully synthesized. Fig. 1B and C are the TEM images of the prepared GR/Au nanocomposites, indicating GR/Au nanocomposites could be synthesized in one pot by chemical co-reduction. Besides, it can be seen that nano-Au is uniformly embedded on the whole surface of GR sheets with the diameter of 7–12 nm, which is close to the optimum Au particle size for catalysis [43]. In this case, nano-Au layers separate the GR sheets in the precipitate and prevent GR sheets from aggregation upon π - π stacking interaction. SEM image of external modality of GR/Au on the glassy carbon surface was shown in Fig. 1D. The GR/Au image clearly indicates a homogeneous distribution of discrete gold nanoparticles at graphene surface and its well-packed graphene films.

3.2. Electrochemical behaviors of GR/Au modified electrode

Potassium ferrocyanide solution was first used to evaluate the electrochemical behavior of GR/Au nanocomposites modified electrodes. Fig. 2A displays the CV curves of bare GCE (dash line) and GR/Au/GCE (solid line) in 0.5 mol L⁻¹ KCl containing 0.01 mol L⁻¹ [Fe(CN)₆]^{3-/4-} aqueous solution. The voltammogram obtained at the GR/Au/GCE exhibited a redox peak pair smaller than that of bare GCE. This observation proved that the presence of negative charges on nanocomposites of GR and nano-Au repels the negatively charged Fe(CN)₆^{3-/4-} ions, thereby resulting in a lower current signal.

To further investigate the charge on the modified electrodes, a cyclic voltammetric study for the above electrodes was performed utilizing a positively charged redox probe, Ru(bpy)₃²⁺ (shown in Fig. 2B). Contrary to the negatively charged redox probe [Fe(CN)₆]^{3-/4-}, the electron-transfer reaction involving Ru(bpy)₃²⁺ at the negatively charged electrode surface was enhanced because of the attractive electrostatic forces. The response of 1.0×10^{-3} mol L⁻¹ Ru(bpy)₃²⁺ in 0.2 mol L⁻¹ Na₂SO₄ at GR/Au/GCE (solid line) was increased 3-fold compared with that of the bare GCE (dash line). The results further exhibited the presence of negatively charged on the surface of modified electrode.

3.3. Optimization of experimental condition

To optimize the experimental condition, the cyclic voltammetric curves in the presence of 5.0×10^{-5} mol L⁻¹ EP were recorded. Based on the peak height for EP detection, the influence of experimental conditions was examined.

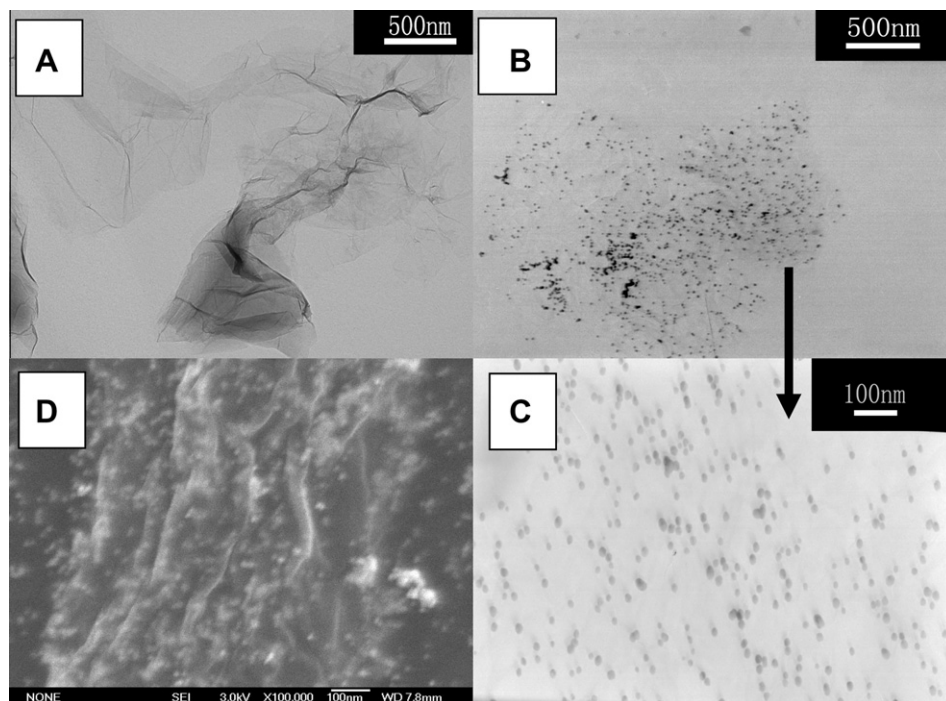


Fig. 1. TEM images of the prepared GR (A) and GR/Au (B) nanocomposites. (C) High-resolution TEM of GR/Au nanocomposites. (D) SEM image of GR/Au nanocomposites on the glassy carbon.

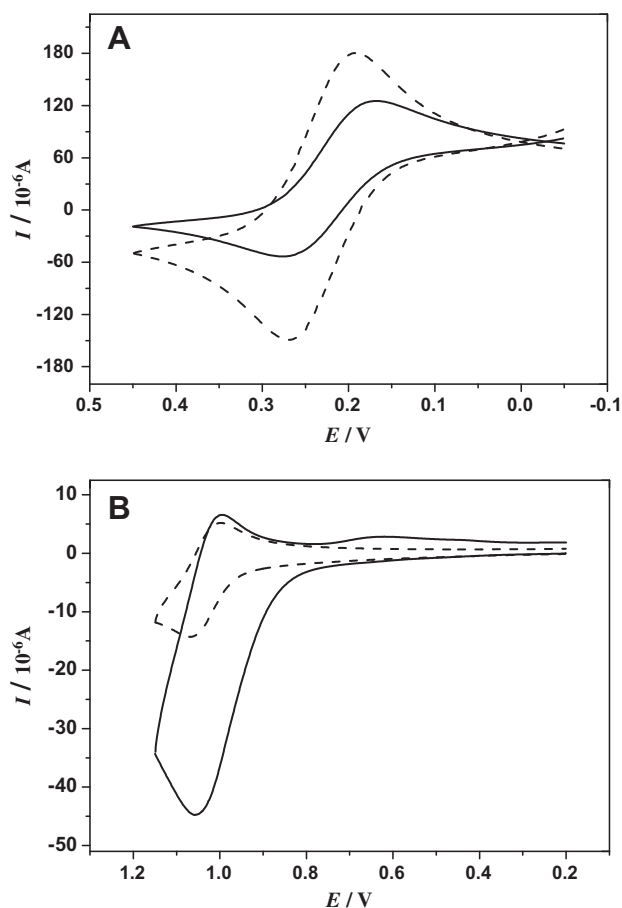


Fig. 2. (A) Cyclic voltammograms obtained at a bare GCE (dash line) and GR/Au/GCE (solid line) in 0.5 mol L^{-1} KCl with 0.01 mol L^{-1} $[\text{Fe}(\text{CN})_6]^{3-/4-}$. (B) Cyclic voltammograms obtained at a bare GCE (dash line) and GR/Au/GCE (solid line) in 0.2 mol L^{-1} Na_2SO_4 with $1.0 \times 10^{-3} \text{ mol L}^{-1}$ $\text{Ru}(\text{bpy})_3^{2+}$. Scan rate: 50 mV s^{-1} .

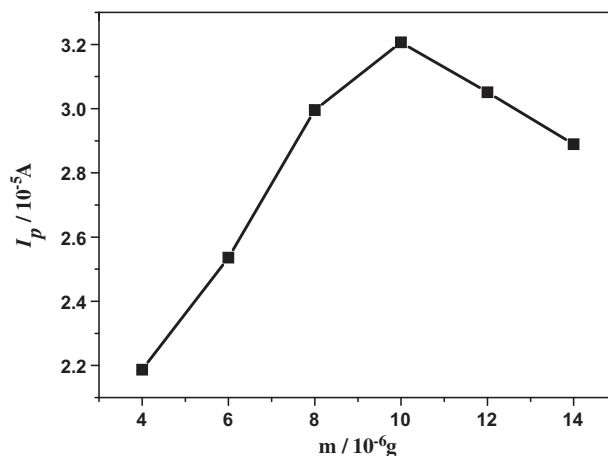


Fig. 3. Plot of anodic peak current of $5 \times 10^{-5} \text{ mol L}^{-1}$ EP in 0.1 mol L^{-1} PBS (pH 7.0) recorded at GR/Au/GCE according to amounts of modified GR/Au nanocomposites. Scan rate is 100 mV s^{-1} . Accumulation time: 2 min (on open circuit).

3.3.1. Effect of amounts of modification

Firstly, the effect of amounts of modification was examined (Fig. 3). As seen that the anodic peak current of $5.0 \times 10^{-5} \text{ mol L}^{-1}$ EP at GR/Au/GCE changed with the amounts of GR/Au modification. High loading of GR/Au nanocomposites increased peak current. However, excessive loading of GR/Au nanocomposites induced the large increase in the capacitive background current which may lead to the diminution of peak current. In our experiments, $10 \mu\text{g}$ GR/Au nanocomposites ($10 \mu\text{L}$ drop of 1.0 mg mL^{-1} GR/Au suspension) was the optimized value for the modification of GR/Au on GCE.

3.3.2. Influence of scan rate

The CV curves of EP at the GR/Au/GCE were investigated at different scan rate (shown in Fig. 4). With the increased of scan rate, the

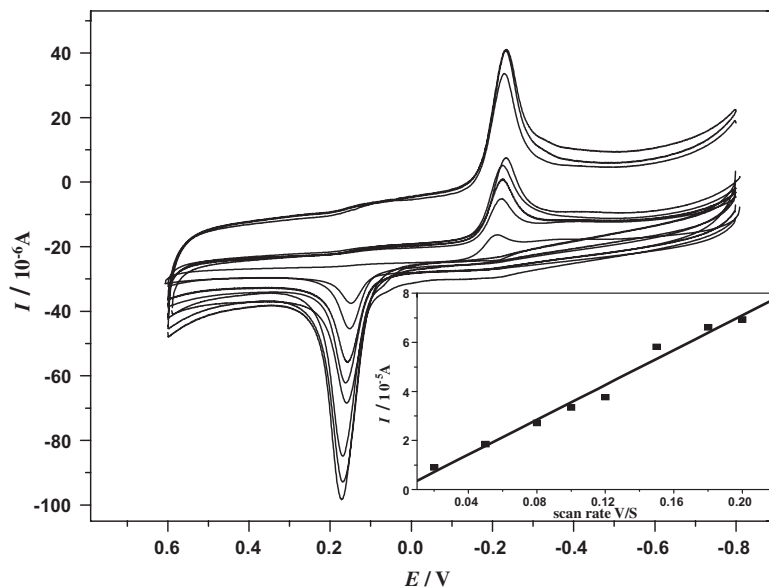


Fig. 4. Voltammetric responses of GR/Au/GCE in 0.1 mol L⁻¹ PBS (pH 7.0) containing 5.0×10^{-5} mol L⁻¹ EP at different scan rate. Scan rate: 20, 50, 80, 100, 120, 150, 180 and 200 mV s⁻¹. Inset: the plot of peak currents (I_{pa}) versus scan rate. Experimental conditions were same as in Fig. 3, except for the scan rate.

peak current of EP increased. The inset of Fig. 4 shows a linear response of the anodic peak current versus the scan rate ($R = 0.992$) which implies a surface absorption-controlled process.

3.3.3. Effect of accumulation time

A further adsorption experiment was made. Fig. 5 illustrates the influence of accumulation time on the oxidation peak height of EP. When the accumulation time increased from 0 s to 180 s, the peak height of 1.0×10^{-6} mol L⁻¹ EP increased greatly (curve a). As improving the accumulation time, more and more EP was accumulated at the modified electrode surface owing to the adsorption ability of GR/Au. Without a doubt, the peak height of EP should remarkably increase. Further increase in accumulation time did not increase the amount of EP at the electrode surface owing to surface adsorption equilibrium, and the peak height remained constant. The same performance was observed for 1.0×10^{-7} mol L⁻¹ EP (curve b). It was clear that the peak current of EP increased remarkably within the first 4 min and then enhanced slowly. Fur-

ther increase in accumulation time did not increase the peak current owing to surface adsorption equilibrium. At both experiments, peak current increased with time first, and then stable signals were observed, which has been suggested the film to be apparent accumulation of the positively charged EP.

3.3.4. Effect of solution pH

In most cases, the solution pH is an important influence factor to the electrochemical reaction. Cyclic voltammetry was carried out to characterize influence of solution pH on electrochemical behavior of EP at the GR/Au/GCE. Fig. 6A showed the dependence of anodic peak current of EP on solution pH in the range of 3.0–9.0. The large anodic peak current was obtained in the range of pH 6.5–7.5. Hence, the pH 7.0 was chose in the electrochemical detection of EP experiments. In addition, we explored the relationship between peak potential of EP and pH (shown in Fig. 6B). It can be found that peak potential shifted negatively with the increase of solution pH. The anodic peak potential (E_{pa}) was proportional with the solution pH in the range of 3.0–9.0. The linear regression equation (with $R = 0.994$) is described in Eq. (1), whose slope indicates that the electron transfer step is preceded by a protonation with the same number of protons involved in the EP oxidation mechanism [44,45].

$$E_{pa} = 0.6270 - 0.06738 \text{ pH} \quad (1)$$

3.4. Comparison of response to epinephrine

The electrochemical response of EP at bare GCE, GR/GCE, nano-Au/GCE and GR/Au/GCE, respectively, was investigated. Fig. 7 illustrates the CV curves of 5.0×10^{-5} mol L⁻¹ EP at the above four electrodes. As can be seen, at bare GCE (curve a), EP produced a broad and insensitive anodic peak at 0.196 V, the anodic peak current (I_{pa}) was found to be 4.964 μ A. By contrast, the GR/Au/GCE produced a sensitive anodic peak at 0.163 V, I_{pa} was found to be 32.08 μ A, around 6.5-fold higher than observed at the bare GCE, indicating a much larger active area and catalytical ability. The GR/GCE (anodic peak at 0.203 V) and nano-Au/GCE (anodic peak at 0.181 V) also showed an increase of 1.8-fold and 2.7-fold, respectively. Especially, the electrochemical response of GR/Au/

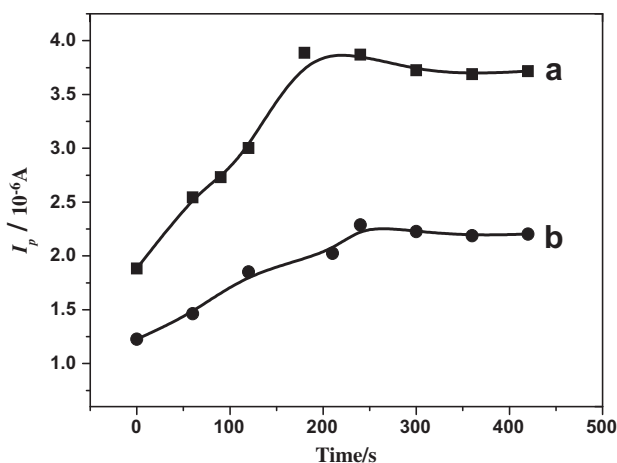


Fig. 5. The influence of accumulation time on the peak height of (a) 1.0×10^{-6} mol L⁻¹ EP; (b) 1.0×10^{-7} mol L⁻¹ EP in 0.1 mol L⁻¹ PBS (pH 7.0). Scan rate: 100 mV s⁻¹.

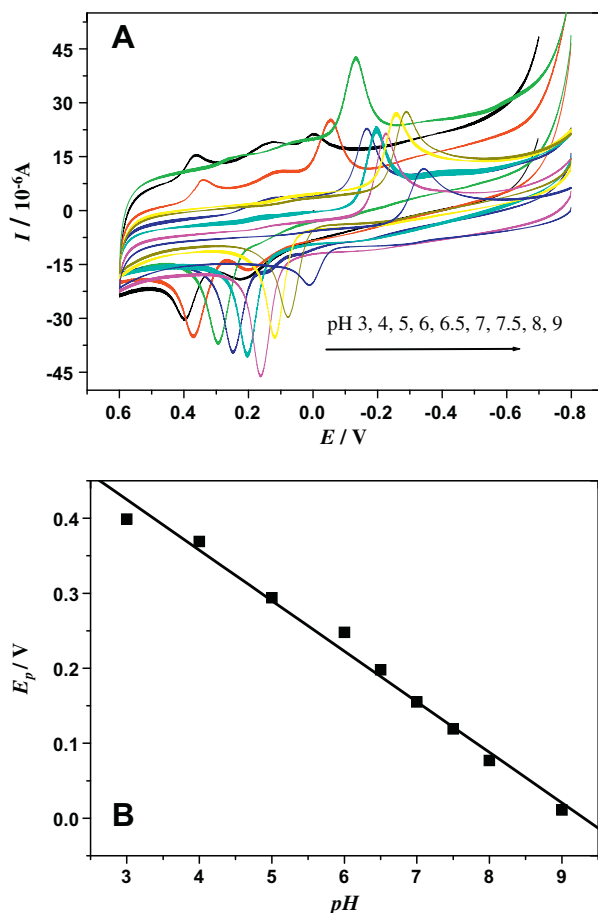


Fig. 6. (A) Effects of solution pH at the GR/Au/GCE on the cyclic voltammetric response. (B) The influence of solution pH on the anodic peak potential of EP. Scan rate is 100 mV s^{-1} . Accumulation time: 2 min (on open circuit).

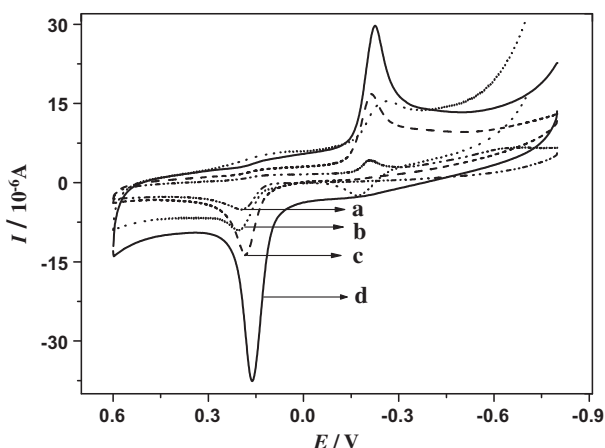


Fig. 7. Cyclic voltammograms of $5 \times 10^{-5} \text{ mol L}^{-1}$ EP in 0.1 mol L^{-1} PBS (pH 7.0) recorded at the bare GCE (a), GR/GCE (b), nano-Au/GCE (c) and GR/Au/GCE (d). Scan rate is 100 mV s^{-1} . Accumulation time: 2 min (on open circuit).

GCE is much stronger than those of the single GR or single nano-Au modified electrode. This enhanced sensitivity at GR/Au/GCE was attributed to the congenerous influence of GR and nano-Au on the electron transfer rate and effective electrode area, as well as the accumulation effects of the positively charged EP.

To verify the reproducibility of the modified electrode, repetitive measurements were done for EP. The relative standard deviation

(RSDs) less than 3.1% for five times parallel detections of $5.0 \times 10^{-5} \text{ mol L}^{-1}$ EP suggested a good reproducibility of GR/Au/GCE. The stability of the GR/Au/GCE was tested by measuring cyclic voltammetry. Without renewing the electrode surface, the modified electrode can be used consecutively for 12 times with 1 min accumulation after each measurement. After the 12 determinations the electrode retained 91% of its initial activity.

3.5. Determination of EP and interference study

Under the optimum conditions described previously, the linear relationships between the peak height and the concentration of EP were obtained. Fig. 8 shows the results of cyclic voltammograms of EP at the GR/Au/GCE. The result demonstrates that the oxidation peaks for EP can be clearly identified at about 0.163 V with a linear relation between the peak currents versus the concentrations. The results showed that I_{pa} was proportional to concentration of EP in the range of 5.0×10^{-8} – $8 \times 10^{-6} \text{ mol L}^{-1}$. In addition, the detection limit of EP could reach as low as $7.0 \times 10^{-9} \text{ mol L}^{-1}$ ($S/N = 3$).

Ascorbic acid (AA), which is electro-active and largely coexists with EP in biological system, could be oxidized at similar potentials as EP on most solid electrodes. In Fig. 9A, at bare GCE, a peak of AA and EP oxidation appears at 0.208 V and 0.196 V, respectively. This minute difference in peak potentials of AA and EP leads to the difficult discrimination of the two species. Therefore, two peaks which are partly overlapped are observed in the PBS containing $3.0 \times 10^{-3} \text{ mol L}^{-1}$ AA and $5 \times 10^{-4} \text{ mol L}^{-1}$ EP. The anodic peak current (I_{pa}) of AA and EP were found to be $1.135 \times 10^{-4} \text{ A}$ and $3.81 \times 10^{-5} \text{ A}$ respectively. While, at the GR/Au/GCE electrode, the oxidation peaks of AA and EP appear at about -0.017 V and 0.163 V , respectively (Fig. 9B). The difference between the two peak potentials is about 180 mV, which is enough to distinguishing EP from AA. Besides, the anodic peak current (I_{pa}) of AA found to be almost the same as bare GCE. While, the anodic peak current (I_{pa}) of EP was found to be $1.327 \times 10^{-4} \text{ A}$, around 3.5-fold higher than obtained at bare GCE (after accumulation, a more greater on amplification of peak current could be obtained, see Section 3.3.3. effect of accumulation time). Thus, the GR/Au films not only increase the sensitivity to EP but also successfully differentiate the signals of the two analytes.

3.6. Analytical application

The epinephrine hydrochloride injection samples (standard content of EP 1 mg mL^{-1} , 1 mL per injection) were purchased from a local pharmacy, and diluted to $1.0 \times 10^{-6} \text{ mol L}^{-1}$ using PBS (pH 7.0). The content of EP was obtained by the standard addition method, and the results are shown in Table 1. In order to testify the accuracy of this method, standard EP solution was spiked in the sample and the analytical procedure repeated. The recovery values were acceptable, revealing that this method is accurate and effective.

3.7. Response of small biomolecules at GR/Au-based electrode

The wide potential window and high electrochemically accessible area of GR/Au nanocomposites showed potential application in detection of small biomolecules. The response of some biomolecules at GR/Au-based electrode was investigated. In all cases, modified electrode provided better reversibility with substantial decreased overpotential, better defined peak shape, and high sensitivity compared with unmodified GCE. A comparison of the bare GCE and GR/Au/GCE for some biomolecules was shown in Fig. 2S and listed in Table 2.

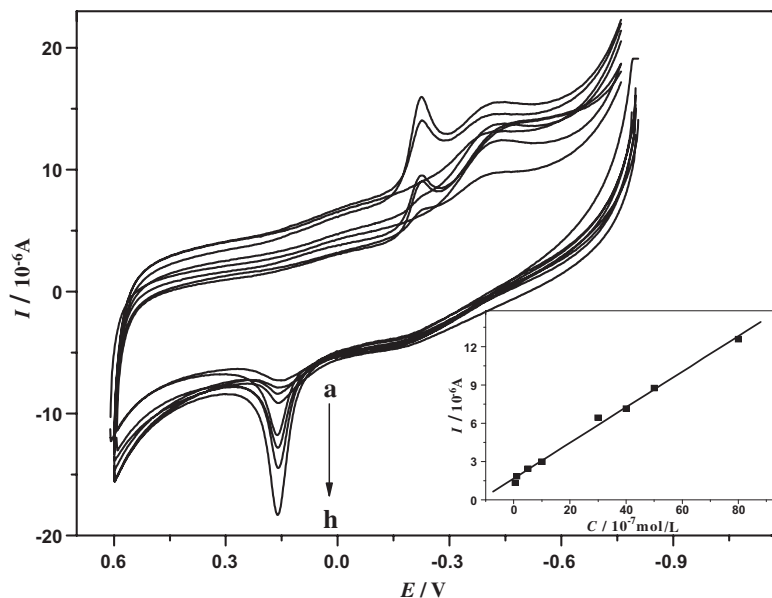


Fig. 8. The voltammetric responses of 0.05, 0.1, 0.5, 1, 3, 4, 5, 8 $\mu\text{mol L}^{-1}$ EP (from a to h) at GR/Au/GCE in the 0.1 mol L^{-1} PBS (pH 7.0). Inset: the relation between the anodic peak currents and the concentrations of EP. Scan rate: 100 mV s^{-1} . Accumulation time: 2 min (on open circuit).

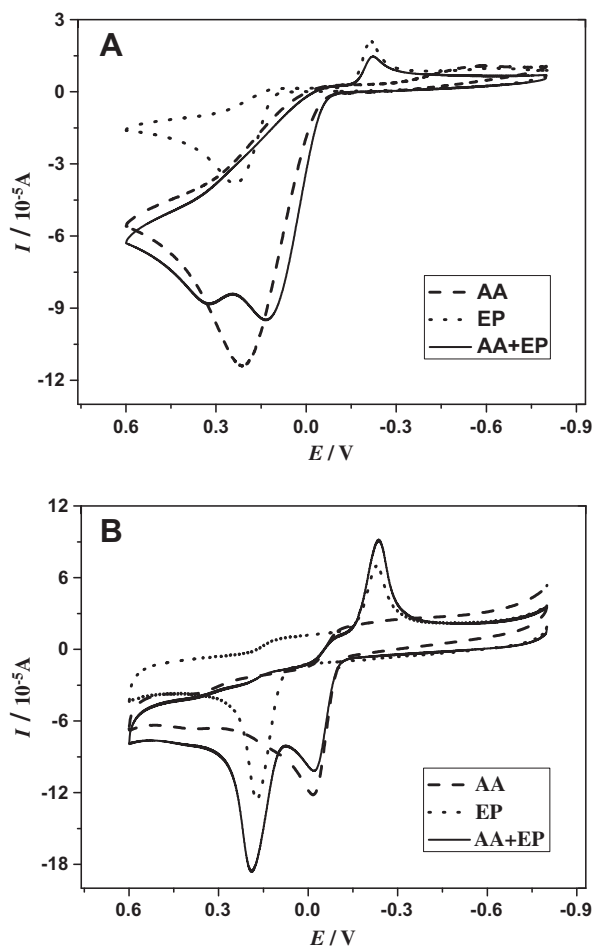


Fig. 9. Cyclic voltammograms recorded at the bare GCE (A) and GR/Au/GCE (B), respectively, in $3.0 \times 10^{-3} \text{ mol L}^{-1}$ AA (dash line), $5.0 \times 10^{-4} \text{ mol L}^{-1}$ EP (dot line), mixed solution of $3.0 \times 10^{-3} \text{ mol L}^{-1}$ AA and $5.0 \times 10^{-4} \text{ mol L}^{-1}$ EP (solid line). Scan rate: 100 mV s^{-1} .

Table 1

Selective determination of EP in injection ($n = 3$).

EP injection	Recommended (mg)	Found (mg)	Added (μg)	Recovery (%)	RSD (%), $n = 3$
I	1.0	0.98	4.0	98	2.1
II	1.0	1.05	4.0	105	3.0

Table 2

Cyclic voltammetric data at bare GCE and GR/Au/GCE.

Sample	Bare GCE		GR/Au/GCE		$I'_{\text{pa}}/I_{\text{pa}}$
	E_{pa} (V)	I_{pa} (10^{-6} A)	E_{pa} (V)	I'_{pa} (10^{-6} A)	
DA	0.199	27.48	0.180	123.7	4.5
AA	0.208	113.5	-0.017	113.7	1.0
UA	0.302	27.00	0.310	72.33	2.7
NADH	0.357	1.248	0.205	3.599	2.9
Pyrocatechol	0.296	4.641	0.184	20.10	4.3

Concentration: DA $5.0 \times 10^{-4} \text{ mol L}^{-1}$; AA $3.0 \times 10^{-3} \text{ mol L}^{-1}$; UA $3.0 \times 10^{-4} \text{ mol L}^{-1}$; NADH $2.0 \times 10^{-4} \text{ mol L}^{-1}$; pyrocatechol $2.0 \times 10^{-3} \text{ mol L}^{-1}$, 0.1 mol L^{-1} PBS (pH 7.0). Scan rate 100 mV s^{-1} .

4. Conclusions

GO and Au (III) was chemically co-reduced to prepare GR/Au nanocomposites in aqueous solution successfully. The prepared GR/Au nanocomposites modified electrode (GR/Au/GCE) exhibited enhanced electrochemical activity towards EP. A novel and simple method for the detection of EP at GR/Au/GCE was presented in this paper. Complete peak separation between EP and ascorbic acid (AA) obtained from CV demonstrated good selectivity for determination of EP in the presence of AA. Furthermore, GR/Au/GCE also exhibited excellent electron transfer promoting ability and excellent electrocatalytic behavior toward other biomolecules, such as DA, AA, NADH and pyrocatechol, prognosticating a space for the

scientific research and application development of GR/Au nano-composites for biosensor.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.jelechem.2012.01.021](https://doi.org/10.1016/j.jelechem.2012.01.021).

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