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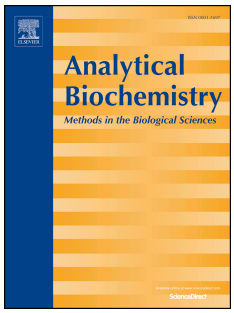

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Preparation of Quantum Dots CdTe Decorated Graphene Composite for Sensitive Detection of Uric Acid and Dopamine

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Abstract: The assembly of quantum dots (QDs) in a simply method opens up opportunities to obtain access to the full potential of assembled QDs by virtue of the collective properties of the ensembles. In this study, quantum dots CdTe and graphene (Gr) nanocomposite was constructed for the simultaneous determination of uric acid (UA) and dopamine (DA). The CdTe QDs-Gr nanocomposite was prepared by ultrasonication and was characterized with microscopic techniques. The nanocomposite modified electrode was characterized by cyclicvoltammetry (CV), differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS). Due to the synergistic effects between CdTe QDs and Gr, the fabricated electrode exhibited excellent electrochemical catalytic activities, good biological compatibility and high sensitivity toward the oxidation of UA and DA. Under optimum conditions, in the co-existence system the linear calibration plots for UA and DA were obtained over the range of 3-600 μM and 1-500 μM with detection limits of 1.0 μM and 0.33 μM. The fabricated biosensor also exhibits the excellent repeatability, reproducibility, storage stability along with acceptable selectivity.

Key words: Quantum dot; Graphene; Simultaneous detection；Dopamine；Uric acid.

Introduction

Dopamine is produced by decarboxylation of 3,4-dihydroxyphenyl ethylamine, known to be a significant catecholamine neurotransmitter for the nervous system of human and other mammals. It acts as a neuromodulator in brain circuitry and responsible for several physiological conditions such as mood, behavior, memory, attention and movement endocrine function, reward, emotion and cognition[1,2,3,4]. Dysregulation of dopaminergic neurotransmission is associated with attention deficit hyperactivity disorder, mood disorders, schizophrenia and neurodegenerative diseases

such as Parkinson's disease and Alzheimer[5,6,7]. The currently available analytical methods for dopamine determination are spectrophotometry, chromatography[8], UV spectrometry[9], chemiluminescence, capillary electrophoresis[10] and electrochemical methods[11]. Uric acid (UA) is the primary end product of proteins and nucleic acids in human. It is mainly excreted by kidney and to a less extent by liver. Elevated uric acid levels in the urine may indicate gout, Lesch-Nyhan syndrome[12,13], arthritis, leukemia, lymphoma[14], Consequently, serum/urine uric acid measurement is routinely required for diagnosis. Among the various methods available for determination of UA, such as electrochemical[15], HPLC[16], chemiluminescence method, fluorescence method[17]. However, these methods generally involve a time-consuming sample pretreatment step and long analysis times and are relatively expensive and only focus on individual determination. Therefore, a sensitive and selective method for simultaneous determination of DA and UA is highly desirable for investigating their physiological functions and diagnosing diseases.

Recently, electrochemical techniques have received considerable interest for the detection of small biomolecules owing to their high sensitivity, rapid response, and low expense. Some multimaterials were reported. UA and DA were simultaneously determined with poly (eriochrome black T)/GCE[18], silver hexacyanoferrate/MWNT/GCE[19], Fe_3O_4 NPs/reduced graphene oxide (rGO)/GCE[20], palladium NP-loaded carbon nanofibers/ CPE[21]. Although various materials have been utilized to modify electrodes in order to resolve the above problem, developing a facile method to simultaneously determine UA, DA is still a challenge.

Quantum dots (QDs) are nanoparticles made of semiconductor materials that usually consist of IIB~VIB or IIIB~VB elements and the diameter stable at 2-20 nm, QDs have gained increasing interest during the past decade due to their unique properties and biomedical applications.[22,23]. Recently, QDs have been used for the study of direct electrochemistry of biomolecules[24], however, numerous studies only focus on the optical research of QDs and ignored strong physical adsorption capacity.

Graphene (Gr), a new two-dimensional (2D) carbon material, is highly anticipated to be an excellent electrode material due to its notable characteristics, such as excellent electrical conductivity, rapid electron mobility, high surface area, good thermal and electrochemical properties[25]. Considering the outstanding performance of CdTe QDs[26] and Gr[27], in this paper, we present the well-organized assembly of zero-dimensional (0D) functional QDs into 2D graphene (Gr) which was used for the construction a modified electrode by simple drop casting method for simultaneous determination of UA and DA. The attractive response performances of the proposed method and potential merits are presented in details by cyclic voltammetry (CV) and differential pulse voltammetry (DPV). With its good sensitivity, selectivity and stability, CdTe QDs-Gr/GCE has been used for the determination of UA and DA in serum with satisfactory results.

1.Experimental

1.1. Reagents

Uric acid ($C_5H_4N_4O_3$, UA), Dopamine ($C_8H_{11}NO_2$) and 3-Mercaptopropionic acid (3-MPA) were purchased from Sigma (St. Loius, MO, USA). UA stock solution (4.0×10^{-3} mol·L^{-1}) was prepared with phosphate buffer solution. A phosphate buffer was used to control the pH. Cadmium chloride ($CdCl_2\cdot2.5H_2O$), Graphene was purchased from JCNANO Co. (Nanjing, China). sodium borohydride ($NaBH_4$) and tellurium powder (Te) were purchased from Sinopharm Chemical Reagent Co. Ltd (Shanghai, China). Other reagents were of analytical-reagent grade and Deionized water purified with Millipore system (Millipore Ltd. China) was used throughout this study. All experiments were conducted at the room temperature of 25 ºC. Human urine samples were generously supplied by The First Affiliated Hospital of the Harbin Medical University. No. 23 Youzheng Street, Harbin, Heilongjiang Province, P. R. China

1.2. Apparatus

The cyclic voltammetry (CV), differential pulse voltammetry (DPV) and

electrochemical impedance spectroscopy (EIS) were performed with a model CHI660C electrochemical workstation (Shanghai Chenhua Instruments Co. Shanghai, China). Electrochemical measurements were performed using a three-electrode system consist of an Ag/AgCl reference electrode, a platinum wire auxiliary electrode and CdTe QDs-Gr modified electrode as working electrode (3 mm in diameter), (All from Incole Union Technology Co. Ltd, Tianjin, China). Solution pH was measured on pH meter (from Precision Scientific Instruments Co. Shanghai, China). Images of the CdTe QDs were observed using JEM-2100 transmission electron microscope was purchased from Japan Electron Optics Laboratory Co. (JEOL, Japan). Scanning Electron Microscope (SEM) images were obtained using FEI Sirion 2000 SEM. Ultrasonic cleaning machine (from Kunshang. Co. Ltd. China).

1.3. Preparation of CdTe QDs

According to the literature[26,28] the molar ratio of Cd^{2+}/MPA/Te^{-} was optimized for 1:2.5:0.5. Tellurium powder was selected as a source of tellurium to synthetic the tellurium sodium hydride (NaHTe). After 435.7 μL MPA solution were piped into 100 mL of 2.0×10^{-2} mol·L^{-1} $CdCl_2$ solution, then were sufficiently stirred with a magnetic stirrer, the solution was adjusted with 1 M NaOH to pH 10.5, degassed with N_2 for 30 min. The following, the fresh 1 mM NaHTe solution which synthetized by reaction of $NaBH_4$ solution with Te powder was slowly poured into it with stirring drastically under N_2 and then heated to reflux at 100 ºC for 6 h. Then, the QDs solution was purified by ethanol and separated by centrifugation for three times. Finally, 0.1 g of the precipitate was re-dissolved 50 ml in ultrapure water and preserved at 4 ºC in dark.

1.4. Preparation of CdTe QDs-Gr nanocomposite modified electrode

CdTe QDs-Gr nanocomposite was prepared by ultrasonically dispersing 100 μL CdTe QDs with 2 mL N,N-Dimethylformamide containing 1 mg of Gr for 2 h. The bare electrode was polished into a mirror with 0.3 and 0.05 μm alumina powder, rinsed with water, washed ultrasonically for 5 min in anhydrous ethanol and double

distilled water in turn, and then dried in N_2. Then By dropping 5 μL of the CdTe QDs dispersion onto the pretreated surface of GCE and dried for 8 h to obtained the CdTe QDs-Gr modified electrode. For comparison 5 μL of Gr and 5 μL CdTe QDs was dropcasted on GCE respectively to get Gr/GCE and CdTe/GCE.

2. Results and discussion

2.1. Nanoparticle characterization

In order to investigate the surface morphology of CdTe QDs, TEM was employed to characterize the morphology of the MPA-capped QDs. Figure 1A shows the TEM micrograph of CdTe QDs dispersed uniformly with spherical shape and the size of the particles ranges between 3-5 nm. The evidence why high quality CdTe QDs could be obtained, the X-ray diffraction (XRD) pattern was employed to explain this. Three obvious peaks were observed at 23.7°, 40.2° and 46.9° in degrees and intensity of 111, 220, 311, the results were showed in Figure 1D. The morphology of Gr was examined by SEM. Figure 1B shows the typical crumpled and flake structure, this helps to load more amount of CdTe QDs on the surface of Gr. Figure 1C shows the TEM image of CdTe QDs-Gr nanocomposite. This confirms that the QDs are dispersed onto the Gr surface.

Fig. 1. TEM image of (A) QDs/GCE, (B) Gr/GCE and (C) CdTe QDs-Gr/GCE.(D) XRD pattern of CdTe QDs.

2.2. Electrochemical behavior of CdTe QDs-Gr nanocomposite modified electrode

Electrochemical properties of the electrodes were studied by cyclic voltammetry (Fig. 2A). Cyclic voltammograms for bare GCE (a), CdTe QDs/GCE (b) and Gr/GCE (c) CdTe QDs-Gr/GCE (d) in the mixture solution of 300 μM UA and 300 μM DA. It is noticed that the anodic peak potentials on the CdTe QDs/GCE, Gr/GCE CdTe QDs-Gr/GCE are close. However, the anodic peak currents of UA and DA on CdTe QDs-Gr/GCE are much higher than others, indicating CdTe QDs-Gr/GCE has the

greatest electrochemical activity, which ought to be attributed to the synergistic effects between CdTe QDs and Gr. This result indicates that the simultaneous determination of UA and DA could be achieved without separation. Combining the good electrical conductivity, electrocatalytic activity, high surface area and strong physical adsorption capacity, CdTe QDs-Gr/GCE is appropriate to be employed to investigate the electrochemical behavior of UA and DA.

Fig. 2B depicts the electrochemical impedance spectra of bare GCE (a), CdTe QDs/GCE (b) and Gr/GCE (c), CdTe QDs-Gr/GCE (d). The order of the diameter of the semicircle, which reflects the electron transfer resistance (R_{ct}) for different electrodes is as follows: CdTe QDs/GCE > bare GCE > CdTe QDs-Gr/GCE > Gr/GCE. For Gr/GCE, an almost straight line of EIS was obtained (curve c), that was characteristic of a diffusional limiting step of the electrochemical process. The charge transfer resistance (R_{CT}) values were determined directly from the diameters of the high frequency semicircle. In addition, the diameters of the high frequency semicircle of Gr/GCE is lower than CdTe QDs-Gr/GCE shows that the CdTe QDs were successful dispersed onto the Gr surface.

Fig. 2. (A) Cyclic voltammograms for bare GCE (a), CdTe QDs/GCE (b) and Gr/GCE (c) CdTe QDs-Gr/GCE (d) nanocomposite in the mixture solution of 400 μM UA and 400 μM DA. (B) EIS of bare GCE (a), CdTe QDs/GCE (b) and Gr/GCE (c), CdTe QDs-Gr/GCE (d).

2.3. Optimization of detection conditions

In most cases, the electrolyte pH is an important condition to the electrochemical reaction. The effect of pH value on the simultaneous determination of UA and DA at CdTe QDs-Gr/GCE was investigated by DPV method. Fig.3A presents the effect of pH value on the peak current and peak potential for 400 μM UA and 400 μM DA in various pH values of PBS. As seen from Fig. 3A, the peak currents of UA and DA reached the maximum at pH 3.0. Furthermore, the peak currents of UA and DA in pH 7.0 were higher than other pH except pH 3.0. The CdTe QDs-Gr film can be regarded

as negative charge film due to MPA-capped QDs, which would effectively collect the cations and reject the diffusion of anions to the films due to the electrostatic interaction, pH 3.0 may be more beneficial to the adsorption and electrochemical oxidation of UA and DA on the CdTe QDs-Gr composite modified electrode. Fig. 3B shows the effect of pH on the oxidation potentials of UA and DA at CdTe QDs-Gr/GCE. As we can seen, the oxidation potentials shifted negatively with increasing pH, indicating that protons participated in the electrode reaction process, and the maximum separation of peak potentials for UA and DA was observed at pH 3.0. Considering the effect of pH on both peak currents and the separations of peak potentials, pH 3.0 PBS was chosen as the supporting buffer solution for further experiments.

Fig. 3. Effect of pH on (A) DPV peak current and (B) DPV peak potential for the oxidation of 400 μM UA and 400 μM DA.

2.4. Cyclic voltammetry and differential pulse voltammetry

Initially, cyclic voltammograms of UA and DA were recorded to get information about the oxidation behavior. Fig. 4 shows the CV of CdTe QDs-Gr/GCE for different concentrations of UA and DA, Fig. 5 shows the DPV of CdTe QDs-Gr/GCE for different concentrations of UA and DA. table 1 lists their linear ranges, detection limits, and so forth. The results in Table 1 demonstrated that the proposed method had wide linear range and high sensitivity.

Fig. 4. CV curves at CdTe QDs-Gr/GCE in 0.01 μM PBS (pH 3.0) for (A) individual response to UA (from outer to inner): 700 μM, 600, 500, 400, 300, 200, 150, 100, 80, 50, 20, 10 μM and (B) Calibration curves for UA detection. (C) CV curves at CdTe QDs-Gr/GCE in 0.01 M PBS (pH 3.0) for individual response to DA (from outer to inner): 400 μM, 300, 200, 150, 80, 50, 25, 10 μM and (D) Calibration curves for DA detection.

Fig.5 DPV curves at CdTe QDs-Gr/GCE in 0.01 M PBS (pH 3.0) for (A) individual response to UA (from outer to inner): 600 μM, 500, 400, 300, 200, 150, 80, 20, 10 μM and (B) Calibration curves for UA detection. (C) DPV curves at CdTe QDs-Gr/GCE in 0.01 M PBS (pH 3.0) for (A) individual response to DA (from outer to inner) 600 μM, 500, 400，300, 200, 150, 100, 20, 10 μM and (D) Calibration curves for UA detection.

Table 1: CV and DPV methods for individual determination of UA and DA.

2.5. Simultaneous detection of UA and DA

The primary intention of the present investigation is to simultaneously detect UA and DA. The oxidation peak currents of these four molecules linearly increased with their concentrations (Fig. 6A), For DA (Fig. 6B), the linear regression equations is obtained which is expressed as Ip = 0.1241x + 14.092, R^2=0.9901. For UA (Fig. 6C), the linear regression equations is obtained which is expressed as Ip = 0.1228x - 0.0338, R^2=0.9907. This experiment result indicated that the simultaneous discrimination of above two species was feasible in mixture solution using DPV. The comparison between this method and other electrochemical methods for simultaneous determination of UA and DA was listed in Table 2.

Fig. 6. (A) DPVs of CdTe QDs-Gr/GCE in PBS solution (0.01 M, pH 3.0) containing mixed concentrations of the UA and DA mixture. [UA] 400 μM, 350, 333,3, 300, 250, 170, 80, 40, 20 μM. [DA] 300 μM,270, 250, 225, 150, 100, 60, 30, 5 μM. (B) Plot of oxidation peak currents *vs*. the concentration of DA. (C) Plot of oxidation peak currents *vs*. the concentration of UA.

Table 2. Comparison of performances of proposal sensor for the detection of DA, UA with those of sensors based on different matrices.

2.6. Reproducibility and Stability

The mixed solution of 400 μM UA and 300 μM DA were DPV measured for 10 parallel experiments, The relative standard deviations (RSD) of the peak currents for UA and DA were 4.31% and 3.92%, respectively, implying remarkable reproducibility. After the modified electrode was stored in 4 ºC N_2 environment for 30 days, it retained 95% of its original response and held the similar shape of the original curves, suggesting an acceptable stability of CdTe QDs-Gr/GCE.

2.7. Interference.

The influences of various foreign species were investigated in a mixture solution containing 400 μM UA and 300 μM DA. The tolerance limit was set as the maximum concentration of the foreign substances that caused an approximately ±5% relative error in the determination. the tolerated concentrations of coexisted species were 200 μM acetaminophen; 60 μM cysteine and 80 μM ascorbic acid had no interference with the determination of UA and DA. Therefore, it is possible to simultaneously determine UA and DA in a sample on CdTe QDs-Gr/GCE.

2.8. Determination of DA in human serum samples.

In order to evaluate the feasibility of the modified electrode in real samples analyses, human urine samples were selected for analysis using the standard addition method. The human urine samples were diluted 10-fold with 0.01 M PBS without any other treatment. The recovery tests were carried out by adding known amounts of pure DA and UA to the real sample solutions and the calibration plots were used for their determination. The results for the detection of UA and DA in three samples are shown in the table 3. According to these results, the proposed sensor could be effectively used for the determination of UA and DA in real samples. The recoveries of DA and UA fall in 91-108%, validating that the proposed system is suitable for determination of DA and UA in human urine samples.

Table 3. Determination results of UA and DA in real samples (n=5)

3. Conclusion

In this work, a novel CdTe QDs-Gr nanocomposite modified glass carbon electrode was fabricated by drop casting method. The electrochemical behavior of nanocomposite was characterized by TEM, CV and DPV. The results clearly shows that the presence of CdTe QDs-Gr nanocomposite has enhanced the electron transfer property than Gr and CdTe QDs alone modified electrode in pH 3.0 solution. With the good selectivity and practicability, the proposed method has been applied to the determination of UA and DA in real samples with satisfactory results and the fabricated sensor may provided a new electrochemical method for clinical diagnosis in the future.

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Table 1: CV and DPV methods for individual determination of UA and DA.

Analye	Method	Linear range (μM)	Detection limit (μM)	Linear regression equation	Correlation coefficient
UA	CV	2-700	0.67	Ip=0.010C+0.477	0.992
	DPV	1-600	0.33	Ip=0.110C+2.851	0.994
DA	CV	1-700	0.33	Ip=0.097C+32.14	0.991
	DPV	1-600	0.33	Ip=0.108C+3.078	0.994

Ip is μA and C is μM.

Table 2. Comparison of performances of proposal sensor for the detection of DA, UA with those of sensors based on different matrices.

Electrode	Method	Linear response range (μM)		Limit of detection (μM)		Ref.
		DA	UA	DA	UA	
CTAB-GO/MWNT/GCE	DPV	5.0-500	3.0-60	1.5	1.0	[29]
Poly-CDDA/GCE	DPV	5.0-280	0.1-18	0.29	0.016	[30]
PImox-GO/GCE	DPV	12-278	3.6-249	0.63	0.59	[31]
AgNP/Zeo-Y/GCE	DPV	0.02-0.18	0.05-0.7	0.016	0.025	[32]
CNDs-rGO/GCE	Amperometric	0.08–227	0.08-328	0.03	0.05	[33]
ERGO-PLL	DPV	2.0-60	20-200	0.10	0.15	[34]
MWCNTs	DPV	0.5-100	0.55-90	0.31	0.42	[35]
PANI-AuNP	DPV	7-148	29-720	3.0	20	[36]
CdTe QDs-Gr/GCE	DPV	1-500	3-600	0.33	1.0	This work

Table 3. Determination results of UA and DA in real samples (n=5)

Sample		Analyte concentration in the unspiked sample (μM)	Known spike added concentration (μM)	Analyte concentration in the spiked sample (μM)	Recovery (%)	RSD (%)
serum 1	DA	-	20	21.72	108.6	4.0
	UA	15	20	33.20	94.9	3.9
serum 2	DA	-	30	27.48	91.6	3.8
	UA	20	30	50.36	100.7	2.4
Serum 3	DA	-	55	57	103.6	2.3
	UA	50	35	82.8	97.4	3.3

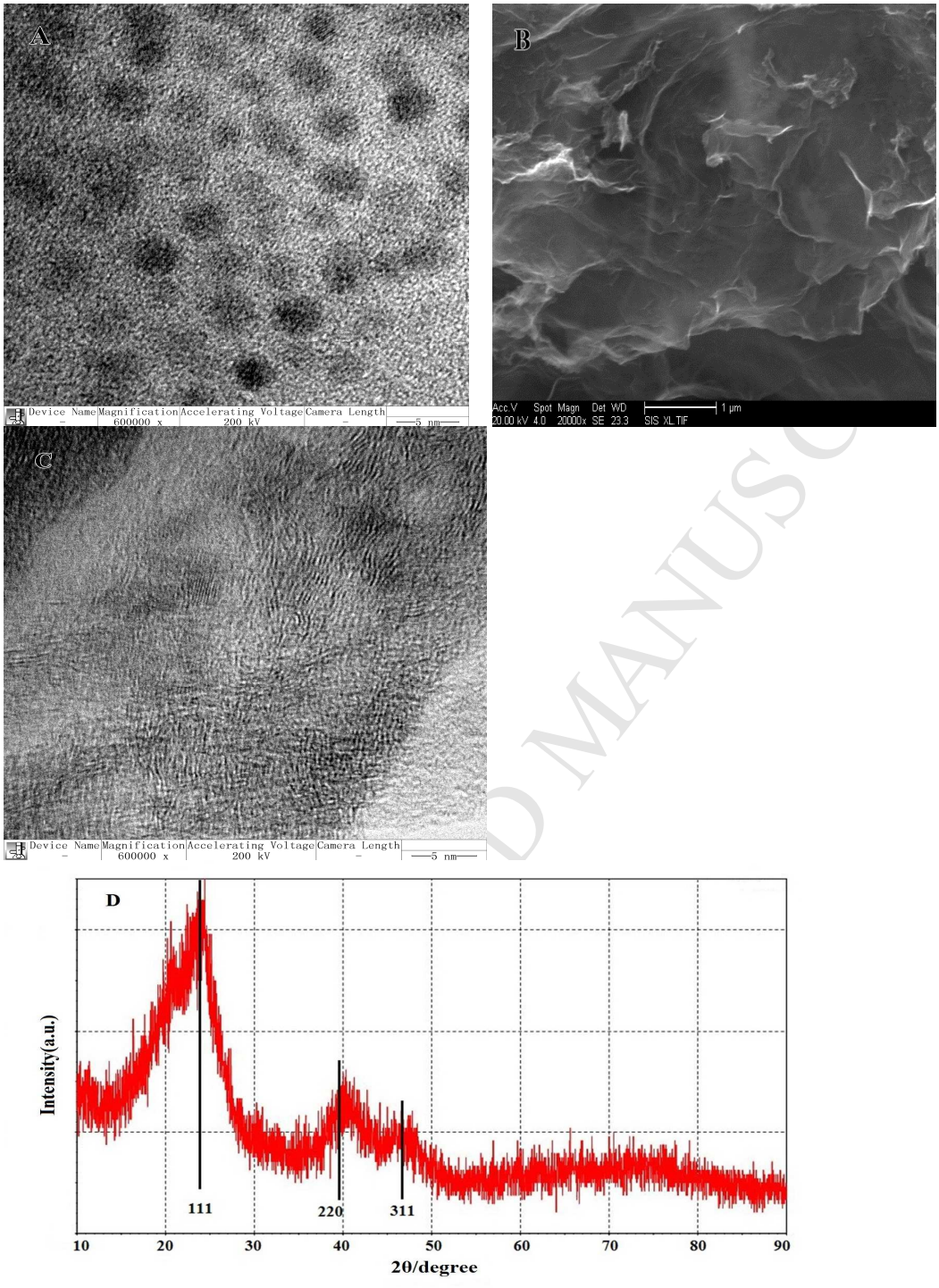


Fig. 1. TEM image of (A) QDs, (B) SEM image of Gr/GCE and (C) TEM image of CdTe QDs-Gr nanocomposite. (D) XRD pattern of CdTe QDs.

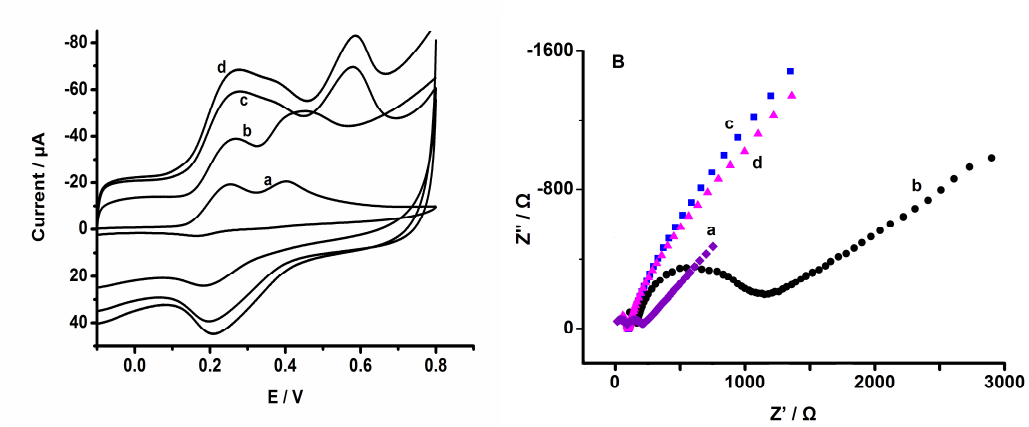


Fig. 2. (A) Cyclic voltammograms for bare GCE (a), CdTe QDs/GCE (b) and Gr/GCE (c) CdSe QDs-Gr/GCE (d) nanocomposite in the mixture solution of 400 μM UA and 400 μM DA. (B) EIS of bare GCE (a), CdTe QDs/GCE (b) and Gr/GCE (c), CdSe QDs-Gr/GCE (d).

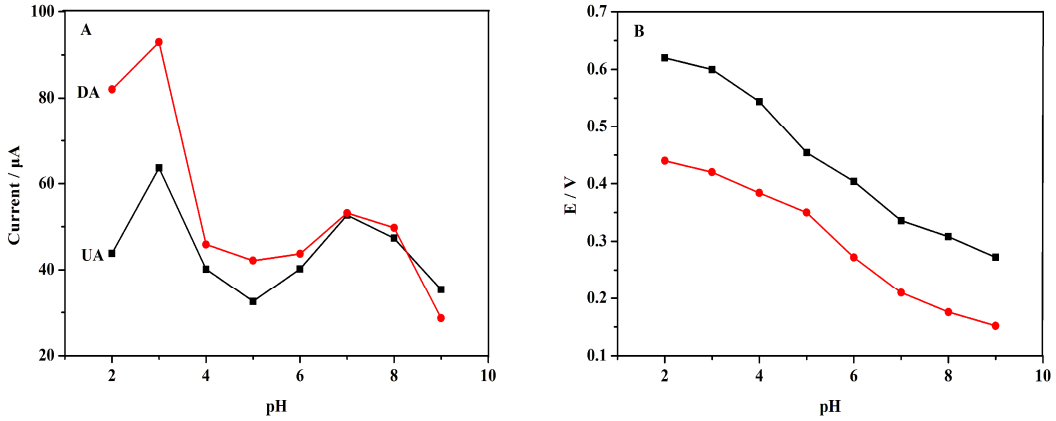


Fig. 3. Effect of pH on (A) DPV peak current and (B) DPV peak potential for the oxidation of 400 μM UA and 400 μM DA.

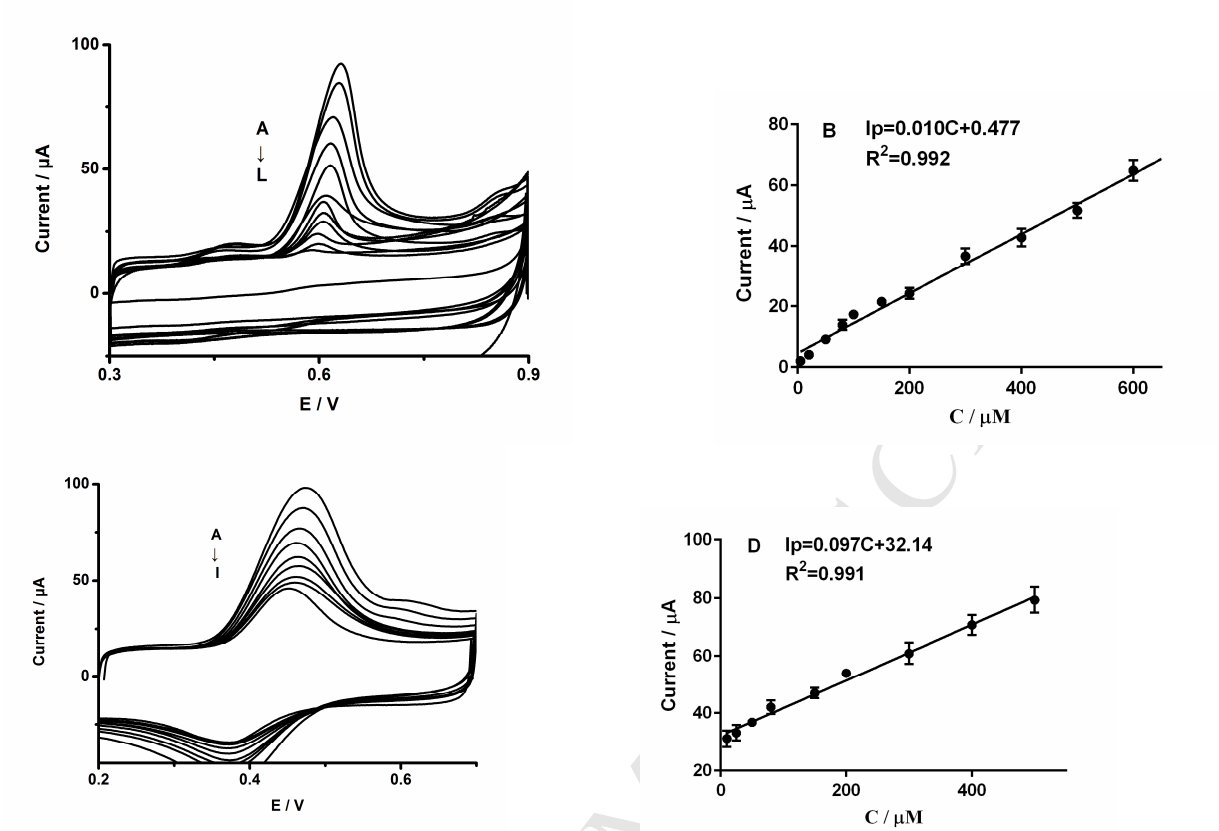


Fig. 4. CV curves at CdTe QDs-Gr/GCE in 0.01 μM PBS (pH 3.0) for (A) individual response to UA (from outer to inner): 700, 600, 500, 400, 300, 200, 150, 100, 80, 50, 20, 10 μM and (B) Calibration curves for UA detection. (C) CV curves at CdTe QDs-Gr/GCE in 0.01 M PBS (pH 3.0) for individual response to DA (from outer to inner): 400, 300, 200, 150, 80, 50, 25, 10 μM and (D) Calibration curves for DA detection.

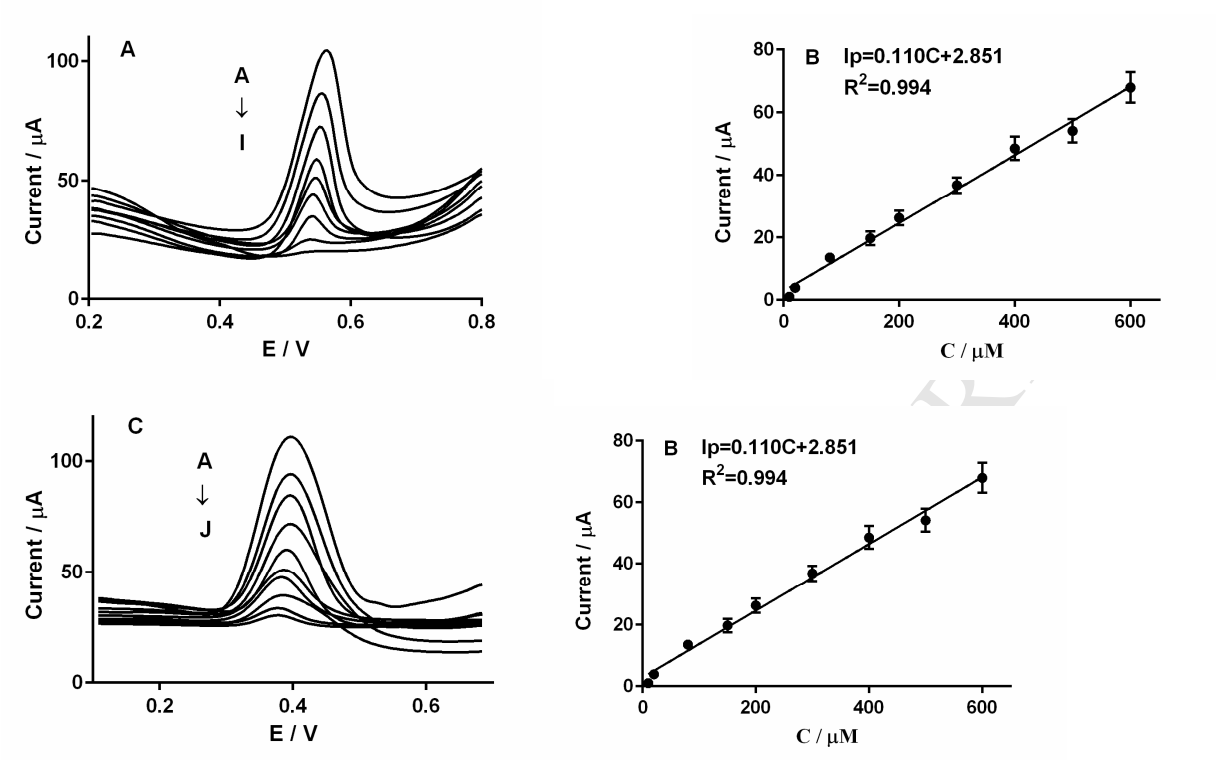
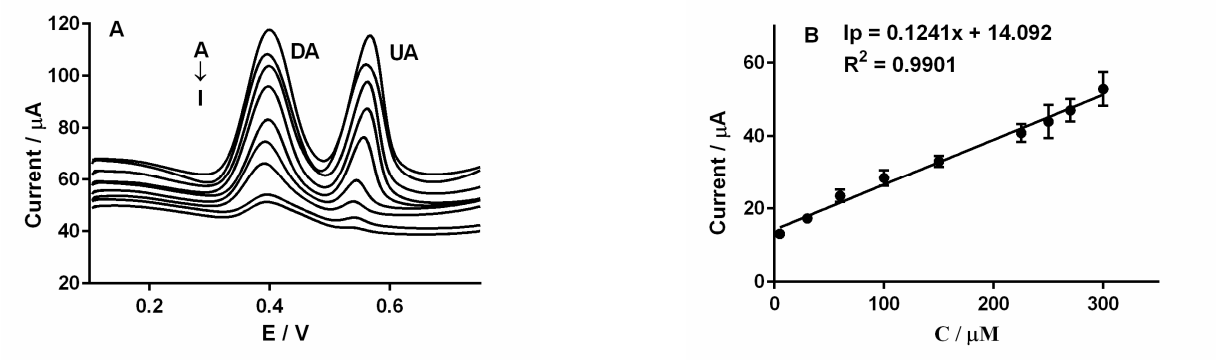


Fig.5. DPV curves at CdTe QDs-Gr/GCE in 0.01 M PBS (pH 3.0) for (A) individual response to UA (from outer to inner): 600, 500, 400, 300, 200, 150, 80, 20, 10 μM and (B) Calibration curves for UA detection. (C) DPV curves at CdTe QDs-Gr/GCE in 0.01 M PBS (pH 3.0) for (A) individual response to DA (from outer to inner) 600, 500, 400, 300, 200, 150, 100, 80, 20, 10 μM and (D) Calibration curves for UA detection.



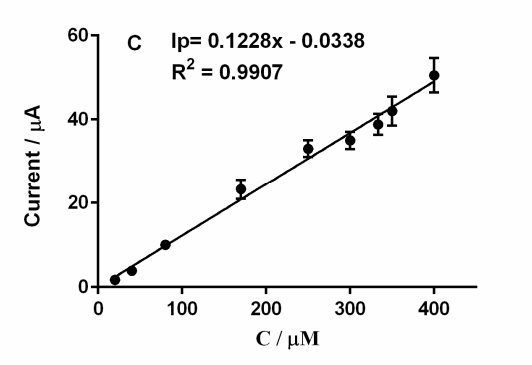


Fig. 6. DPV curves at CdTe QDs-Gr/GCE in 0.10 M PBS (pH 3.0) for (A) simultaneous response to DA (from A to I: 300 μM, 270, 250, 225, 150, 100, 60, 30, 5 μM) and UA (from A to I: 400 μM, 350, 333.3, 300, 250, 170, 80, 40, 20 μM). (B) Plot of oxidation peak currents *vs*. the concentration of DA and (C) Plot of oxidation peak currents *vs*. the concentration of UA.