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Study on Electrochemical Behaviours and Diffusion Mechanism of Acetaminophen and Dopamine at Pre-Anodized Carbon Paste Electrode

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A pre-anodized carbon paste electrode (PACPE) was fabricated and used to investigate the electrochemical behaviours of acetaminophen and dopamine. The results indicated that the voltammetric responses of acetaminophen and dopamine were considerably enhanced at PACPE in pH = 7.0 phosphate buffer solution. Furthermore, the diffusion mechanism of the influence on oxidation peak currents of acetaminophen and dopamine has been put forward. The driving force for the diffusion of acetaminophen and dopamine toward anode not only related to concentration diffusion but also involved with transport of H^+ in the feed phase along a concentration gradient toward cathode. Under the optimized conditions in linear scan voltammetry technique, acetaminophen and dopamine gave linear response over the range of 2.0×10^{-6}-5.0×10^{-4} mol/L, 2.0×10^{-6}-4.0×10^{-4} mol/L, respectively. The detection limits (S/N =11) were found to be 0.42 μmol/L for acetaminophen and 0.21 μmol/L for dopamine. The proposed method was successfully applied to the determination of acetaminophen and dopamine in commercial pharmaceutical samples.

Keywords: Acetaminophen, Dopamine, Diffusion mechanism, Pre-anodized carbon paste electrode.

INTRODUCTION

Acetaminophen (N-acetyl-*p*-aminophenol or paracetamol, APA), a widely used analgesic and antipyretic drug, plays an important role in the relief of headaches, arthritis, fever, *etc*. However, overdoses ingestions of acetaminophen produce the accumulation of toxic metabolites, which may result in severe side effects[1]. Dopamine (3,4-dihydroxyphenylethylamine, DA) is an important neurotransmitter in central nervous systems. The previous researches indicated that lack of dopamine in the brain will cause some serious diseases such as Schizophrenia and Parkinson's disease[2,3]. Therefore, the determination of acetaminophen and dopamine has a great signicance in clinical diagnosis and bioscience field. Several analytical techniques have been developed for the determination of acetaminophen or dopamine. These include spectrophotometry[4,5], high-performance liquid chromatography[6] flow injection analysis[7,8], fluorescence[9,10] and electrochemical method[11-15].

The electrophysiological effects support that acetaminophen relieves pain in the central nervous system and the concentration of it is high[16]. In contrary, the physiological levels of dopamine are below 200 μmol/L[15]. Moreover, acetaminophen will interfere with dopamine measurements in biological samples[17]. Thus, it is necessary to measure the concentration of dopamine in the presence of acetaminophen. Various types of chemically modified electrodes have been used for simultaneous determination of acetaminophen and dopamine, for example, carbon nanotube modied electrode[18-20], nano-TiO_2/polymer coated electrode[21], polypyrrole/aszophloxine film modified electrode[22] and carbon-coated nickel magnetic nanoparticles modified electrode[23].

In our work, pre-anodized carbon paste electrode (PACPE) was fabricated and characterized by the simple cyclic voltammetry. Some activity sites and surface oxides such as lactones, carboxyl, phenolic hydroxyl and ethers were produced on the electrode surface during the pre-anodization[24]. The functional PACPE exhibited a high electrocatalytic activity toward for the electrochemical behavours of acetaminophen and dopamine. The PACPE not only greatly improved the determining sensitivity of acetaminophen and dopamine, but also achieved the simultaneous determination of acetaminophen and dopamine.

EXPERIMENTAL

The experiments were carried out using a CHI660C electrochemical workstation (ChenHua Instrument, Shanghai, China). The scanning electron microscope (SEM) image was

obtained with a JEOL-JSM-6390LV field emission scanning electron microscope. A conventional three-electrode system was employed for the electrochemical studies, which consisted of a carbon paste electrode (CPE) or PACPE as working electrode, a platinum wire as counter electrode and a saturated calomel electrode as reference electrode.

The acetaminophen and dopamine were purchased from Alfa Aesar and Sigma-Alorich, respectively. The supporting electrolyte phosphate buffer solutions (PBS) were prepared from stock solutions of 0.1 mol/L NaH_2PO_4 and Na_2HPO_4. All other chemicals were of analytical reagent grade. Aqueous solutions were prepared with double distilled water.

Preparation of pre-anodized carbon paste electrode (PACPE): The carbon paste was prepared by mixing graphite powder and paraffin oil at a mass ratio of 7:3 uniformly. A portion of the paste was tightly packed into the tip of a glass tube (4 mm inner diameter). A copper rod was inserted into one end for electrode connection and the other end was polished on a piece of weighing paper. Then the assembled carbon paste electrode was soaked into 0.2 mol/L NaOH solution and anodized by running cyclic voltammetry from -0.3 to +2.1 V for 30 cycles at a scan rate of 100mV/s. Finally, the PACPE was rinsed with deionized water and dried at room temperature.

RESULTS AND DISCUSSION

Surface morphology characteristic of PACPE: Typical SEM images of different electrodes are shown in Fig. 1. The SEM of PACPE (Fig. 1b) reveals that the size of preanodized graphite flake was smaller than that of non-preanodized one (Fig. 1a) and some fragments of graphite formed three-dimensional gaps with multi-hole, which would effectively increase the apparent electroactive surface area of the electrode.

Electrochemical properties of PACPE: The $Fe(CN)_6^{3-/4-}$ was taken as probe ions to clearly observe the changes of the electrode introduced by pre-anodization. Fig. 2 presents the cyclic voltammograms (CV) of the CPE and PACPE in 1.0×10^{-3} mol/L $K_4[Fe(CN)_6]$ and 0.1 M H_2SO_4. The electrochemical response of $Fe(CN)_6^{3-/4-}$ on CPE was poor with a large peak separation (ΔE_p) between the oxidation and reduction peak, showing a slow electron transfer rate and a irreversible electrochemical process. At PACPE, the redox peak currents were increased and the anodic to cathodic peak current ratio was 0.969 and thus, ΔE_p was reduced to 50 mV, indicating a rapid electron transfer rate and a quasi-reversible electrochemical response. The CPE surface film dissolved easily to refresh the surface in alkaline solution, the fresh exposed carbon atoms acted as an active center in catalyzing the electrode reactions[25,26]. In addition, various oxygen-containing functional groups (-OH, -COOH and-O-) were generated on the surface of the electrode in the process of pre-anodization. Hence, the PACPE can accelerate electron transfer and improve the reversibility of electrode reactions.

Voltammetric studies of acetaminophen and dopamine: The CPE and PACPE had been applied to the simultaneous determination of 2.0×10^{-5} mol/L acetaminophen and dopamine in pH 7 PBS buffer solution. As Fig. 3 depicts, acetaminophen and dopamine overlapped to form a weak and wide oxidation peak at CPE (curve 2), which meaned the CPE could not be

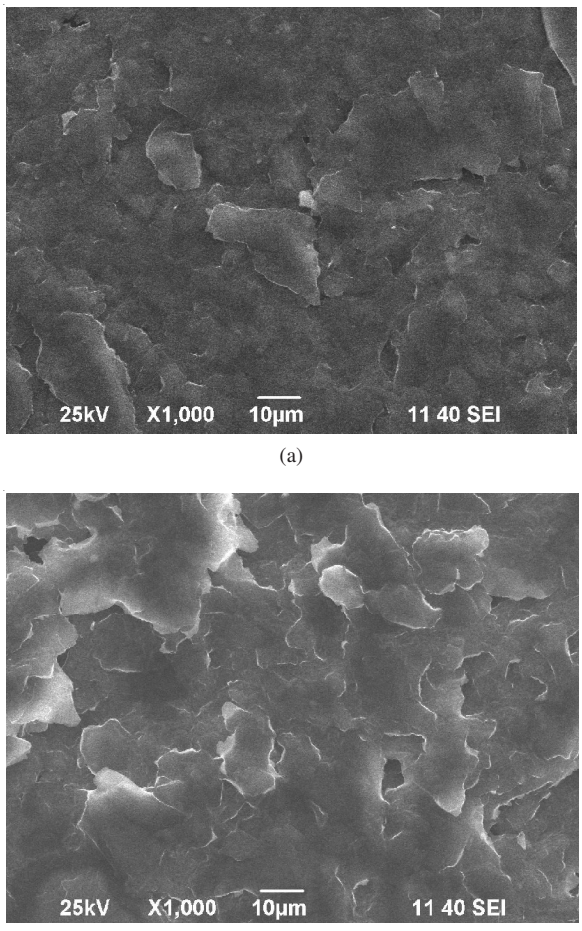

Fig. 1. SEM images of carbon paste electrode (a) pre-anodized carbon paste electrode (b)

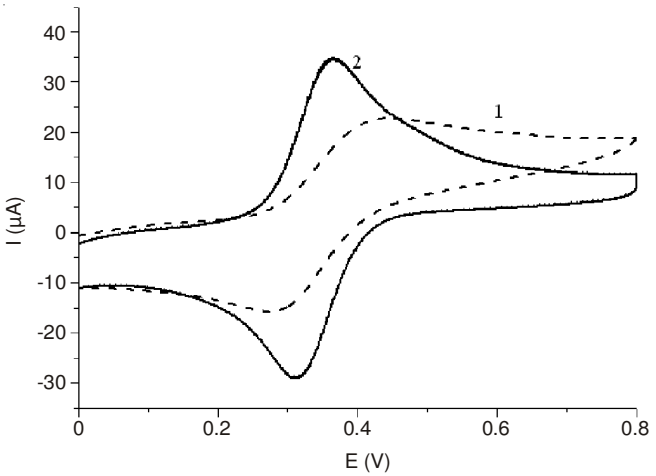

Fig. 2. Cyclic voltammograms of $K_4[Fe(CN)_6]$ on different electrodes (1) CPE; (2) PACPE. $C_{(K_4[Fe(CN)_6])} = 1.0 \times 10^{-3}$ mol/L; supporting electrolyte: 0.1 mol/L H_2SO_4; scan rate: 100 mV/s

used for any real application for the detection of acetaminophen and dopamine. Under the same condition, the acetaminophen and dopamine can be identified simultaneously at PACPE (curve 3) with two well-resolved voltammetric peaks and the remarkable peak currents. Two anodic peaks appeared at 345 and 149 mV, corresponding to the oxidation of acetaminophen and dopamine, respectively. The peak difference of 196 mV

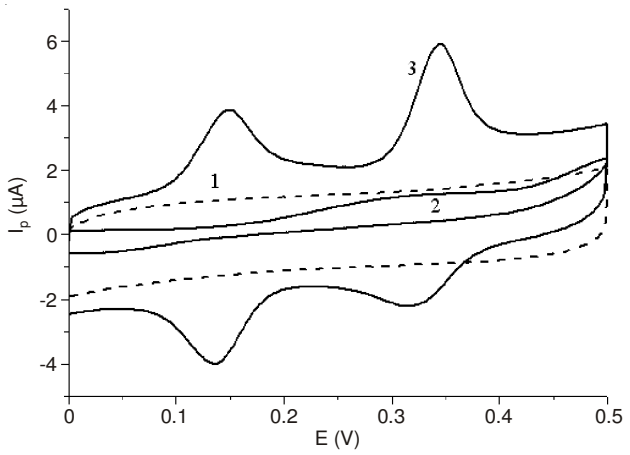

Fig. 3. Cyclic voltammograms of acetaminophen and dopamine on different electrodes. (1) PACPE in supporting solution; (2) CPE in solution containing acetaminophen and dopamine; (3) PACPE in solution containing acetaminophen and dopamine. Supporting electrolyte: pH 7.0 PBS; scan rate: 100 mV/s

allowed simultaneous detecting of acetaminophen and dopamine in their mixture solution. Moreover, two reduction peaks were observed for acetaminophen and dopamine with cathodic peak potentials at 315 and 135 mV, respectively. Results showed that the PACPE gave a more reversible electron transfer process to acetaminophen and dopamine. In conclusion, the PACPE had strong catalytic activity toward the voltammetric behaviours of acetaminophen and dopamine.

Effect of scan rate: The influences of scan rate on the peak currents of acetaminophen and dopamine (Fig. 4) were studied using cyclic voltammetry. The anodic and cathodic peaks current of acetaminophen varied linearly with the square rote of scan rate from 10 to 200 mV/s. The linear regression equations were I_{pa} = -1.01+ 14.92 $v^{1/2}$ (R = 0.9966) and I_{pc} = -0.02- 4.52$v^{1/2}$ (R = 0.9981). The ratio of slopes of two equations was 3.30, the anodic and cathodic peak current values of acetaminophen had a big difference. Well-defined CVs of dopamine at a large range of scan rates in the range 10-350 mV/s can be observed in Fig. 4a, both anodic and cathodic peak currents were linearly dependent on $v^{1/2}$(Fig. 4b), the linear equations were I_{pa} =-0.97+ 13.41$v^{1/2}$ (R = 0.9978) and I_{pc} = 1.25 -13.66$v^{1/2}$ (R = 0.9986). The ratio of slopes of two equations was 0.98, the anodic peak current and cathodic peak current of dopamine was almost equal, which showed that reversibility of dopamine at PACPE was better than acetaminophen. Though reversibility of acetaminophen was differ from that of dopamine, both the electrooxidation of acetaminophen and dopamine were diffusion-controlled process.

Effect of solution pH: The influence of pH on acetaminophen and dopamine oxidation was studied in solutions of different pH values in the range between 5.52 and 8.44. The peak potentials of acetaminophen and dopamine shifted toward negative linearly with increasing pH and fitted the two following equations: E_p = 0.68254 - 0.04675 pH (R = -0.9962) and E_p = 0.49426 - 0.04838 pH (R = -0.9975). The slopes of the above equations revealed that same number of electrons and protons involved in the redox reaction of acetaminophen and dopamine[27]. It showed that acetaminophen and dopamine were prone to lose electron and to be oxidized with pH value

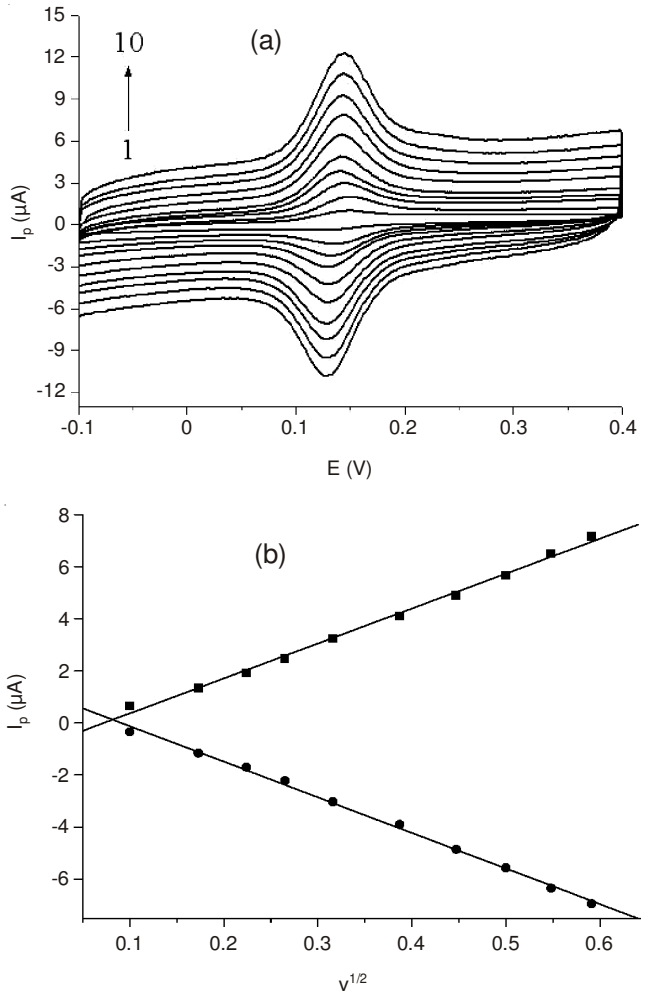

Fig. 4. Cyclic voltammograms of 2.0×10^{-5} mol/L dopamine with different scan rates and (a) Curves 1-10 are 10, 30, 50, 70, 100, 150, 200, 250, 300 and 350 mV s^{-1}, respectively; $C_{dopamine} = 2.0 \times 10^{-5}$ mol/L; Supporting electrolyte: pH 7.0 PBS; (b) The variation of the anodic and cathodic peak currents with the square root of scan rate

increasing. Correspondingly, the oxidation peak currents should also be enhanced. However, the fact was that the peak currents of the acetaminophen and dopamine declined as the pH increased gradually (Fig. 5).

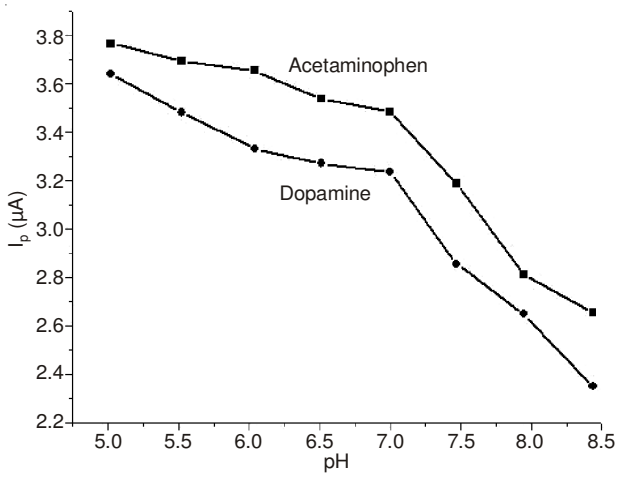

Fig. 5. Influence of pH on the oxidation current of acetaminophen and dopamine. $C_{acetaminophen} = 2.0 \times 10^{-5}$mol/L; $C_{dopamine} = 2.0 \times 10^{-5}$ mol/L; supporting electrolyte: pH 7.0PBS; scan rate: 100mV/s

For acetaminophen, in the electrochemical process, acetaminophen lost two electrons to be oxidized at PACPE and oxygen dissolved in the solution conducted reduction reaction at platinum electrode. The proposed electrode reaction mechanism of acetaminophen was given in Fig. 6. The concentration diffusion rate of H^+ in feed toward platinum electrode surface had a direct effect on the reaction rate and amount of oxygen at the cathode. To be specific, with content of H^+ in feed increasing(at lower pH), H^+ diffused toward platinum electrode surface along a concentration gradient at an increasing velocity, which resulted in the improved reaction rate and amount of oxygen on cathode. And the cathode reaction required consuming a certain amount of H^+, which can promote the reaction of acetaminophen on anode. Therefore, the oxidative peak current became stronger at lower pH because of the fast diffusion rate and the large transport amount of acetaminophen toward PACPE. The result indicated that the driving force for the diffusion of acetaminophen was not only involved with concentration diffusion but also related to the transport of H^+ in the feed phase toward cathode along a concentration gradient. On the contrary, the concentration of H^+ in feed reduced at higher pH and the diffusion rate of H^+ toward platinum electrode surface along a concentration gradient was slower, the reaction rate and amount of oxygen decreased. Based on the principle of equal numbers of electron gain and loss, the amount of oxidized acetaminophen decreased as well. So with the increase of pH value, the oxidization ability of acetaminophen was improved but the peak current declined. The diffusion mechanism of dopamine was identical with the description of acetaminophen. In order to obtain high sensitivity and selectivity, PBS of pH 7 (pH of biological medium) was selected as supporting electrolyte for the subsequent analytical experiments.

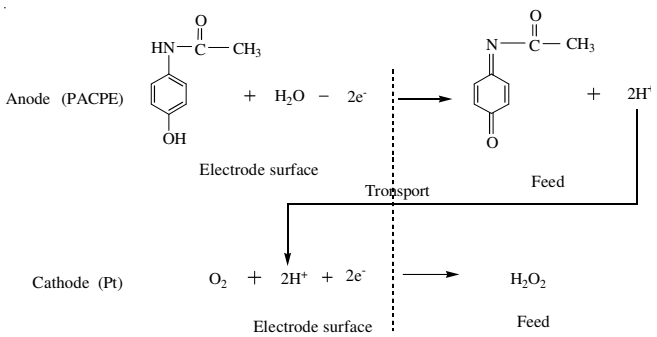

Fig. 6. Diffusion mechanism of acetaminophen

Reproducibility and stability of PACPE: The repeatability and stability of PACPE were investigated using linear scan voltammetric measurements of 2.0×10^{-5} mol/L acetaminophen and dopamine. The relative standard deviation (RSD) for seven successive assays of acetaminophen and dopamine was 2.57 and 2.66 %, respectively. After storing the PACPE in the refrigerator at 4 ºC for 10 days, the current response decreased by less than 1.5 %, which revealed a long-term stability.

Interferences: The interferences of some inorganic ions and organic species on the determination of 2.0×10^{-5} mol/L acetaminophen and dopamine were studied. The tolerable limit of the foreign substance was defined as the deviations produced by them below 5 %. 500-fold concentration of Ca^{2+},Na^+, K^+, NH_4^+, NO_3^-, Cl^-, SO_4^{2-}, CO_3^{2-}, F^-, HCO_3^-, 400-fold of Fe^{3+}, Al^{3+}, 20-fold of glucose, L-glutamic acid, L-cysteine, benzoic acid, ethanol and methanol did not interfere with the determination of acetaminophen and dopamine.

Calibration curve: Fig. 7a exhibits linear scan voltammograms (LSV) that were obtained in different concentrations (2.0×10^{-6}-5.0×10^{-4} mol/L) of acetaminophen in the presence of 20 µmol/L dopamine. The peak current increased linearly with acetaminophen concentration and the linear regression equation was I (µA) = 0.13372C + 2.59987 with a correlation coefficient of 0.9956.And that of dopamine was I (µA) = 0.08564C + 0.72996 in the range of $2.0 \times 10^{-6} - 4.0 \times 10^{-4}$ mol/L with a correlation coefficient of 0.9975, which was obtained in the presence of 15 µmol/L acetaminophen (Fig. 7b). The detection limit (S/N = 11) of acetaminophen and dopamine were calculated to be 0.42 and 0.21 µmol/L, respectively.

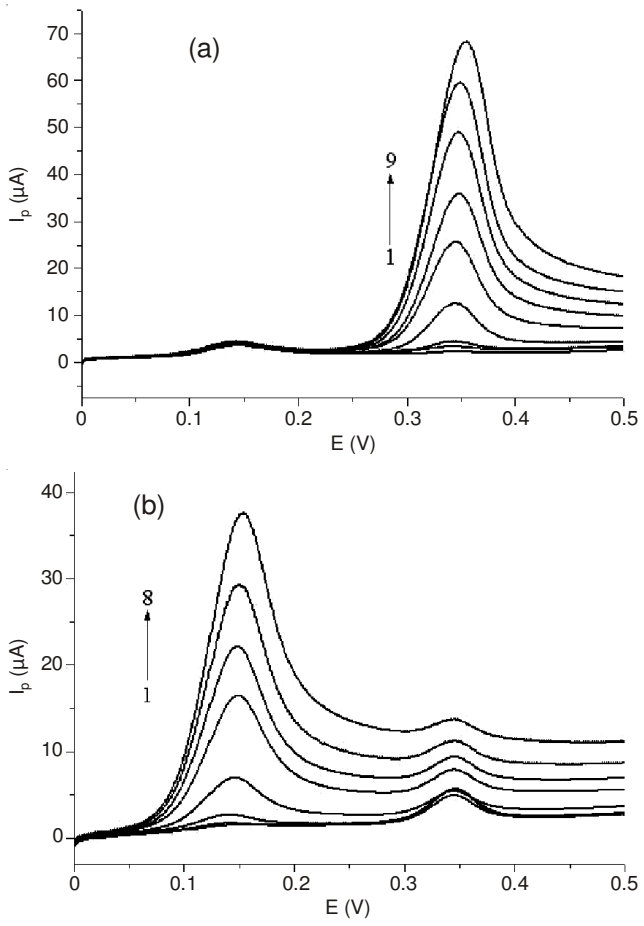

Fig. 7. (a) Linear sweep voltammograms of acetaminophen at PACPE in the presence of 20 µmol/L dopamine in PBS (pH 7.0). acetaminophen concentrations (from 1-9): 2, 5, 10, 50, 130, 210, 300, 400, 500 µmol L^{-1}. (b) Linear sweep voltammograms of dopamine at PACPE in the presence of 15 µmol/L acetaminophen in PBS (pH 7.0). dopamine concentrations (from 1 to 8): 2, 5, 10, 50, 130,210, 300, 400 µmol L^{-1}

The utilization of the PACPE for the simultaneous determination of acetaminophen and dopamine was demonstrated by synchronously changing the concentrations of acetaminophen and dopamine. Linear sweep voltammogram results in Fig. 8 showed that the oxidation peak currents of acetaminophen and

TABLE-1
DETERMINATION OF ACETAMINOPHEN AND DOPAMINE IN SAMPLES (n = 5)

Samples	No.	Contents (μmol/L)	Added (μmol/L)	Found (μmol/L)	Recovery (%)	RSD (%)
Acetaminophen table	1	25.10	5.00	29.41	97.7	1.91
	2	25.10	10.00	34.54	98.4	1.53
	3	25.10	20.00	43.39	96.2	1.78
Dopamine injection solution	1	21.20	6.00	27.28	100.3	2.37
	2	21.20	12.00	33.60	101.2	2.42
	3	21.20	24.00	44.61	98.7	2.68

TABLE-2
DETERMINATION OF ACETAMINOPHEN (APA) AND DOPAMINE (DA) IN MIXTURES (n = 5)

No.	APA table	Contents (μmol/L) DA injection solution	Added (μmol/L)		Found (μmol/L)		Recovery (%)		RSD (%)	
			APA	DA	APA	DA	APA	DA	APA	DA
1	12.55	10.60	5.00	6.00	17.98	16.50	102.5	99.4	2.74	2.95
2	12.55	10.60	10.00	12.00	22.23	22.98	98.6	101.7	3.42	3.65

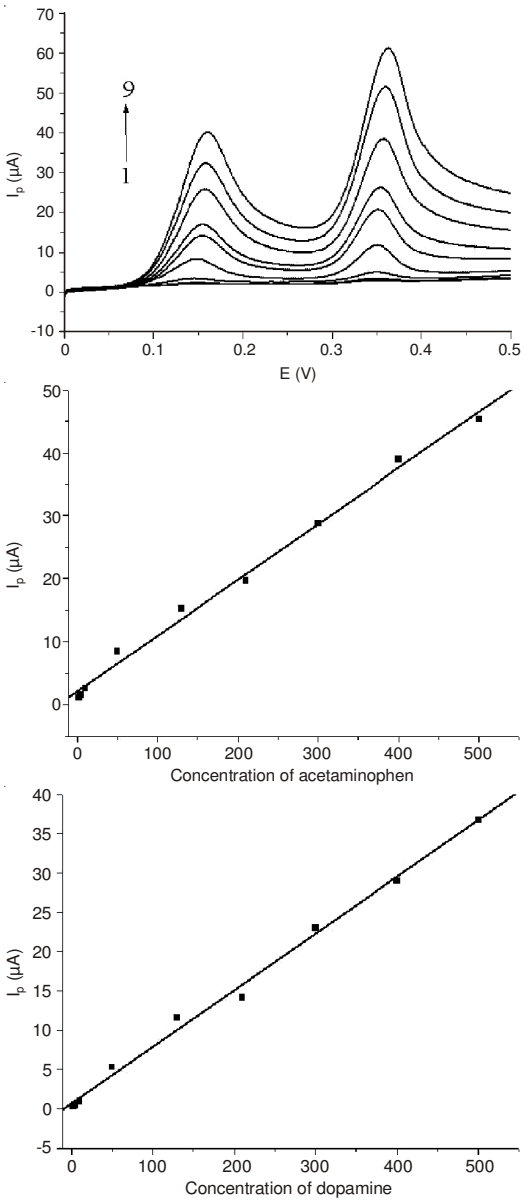

Fig. 8. Linear sweep voltammograms of the mixture containing acetaminophen and dopamine with different concentrations at PACPE in PBS (pH7.0). Concentrations of acetaminophen and dopamine (from 1 to 9): 2, 5, 10, 50, 130, 210, 300, 400, 500 μmol L^{-1}; Insets are the variation of the peak currents *vs* concentration of each compound

dopamine were proportional to their concentrations both over the range from 2×10^{-6}-5×10^{-4} mol/L, obeying the linear regression equations: I_p (μA) = 0.08886C + 2.0552 (R = 0.9971) and I_p (μA) = 0.07212C + 0.61361 (R = 0.9973), respectively.

Analytical application: The presented method was validated for the determination of acetaminophen concentration in tablets and dopamine concentration in an injection solution. The concentration of acetaminophen and dopamine was calculated by using standard-addition method. The results were listed in Table-1. The relative standard deviations (RSD) of each sample for five time's parallel detections were less than 3 %. In addition, the recovery study was carried out and the values were between 96.2 and 101.2 %. Table-2 showed the measurement results for acetaminophen and dopamine in the synthetic mixed samples, the results demonstrated that the PACPE can be efficiency used for the simultaneous determination of acetaminophen and dopamine in pharmaceutical samples.

Conclusion

A pre-anodized carbon paste electrode was prepared by electrochemical pretreatment and used for the investigation of the electrochemical behaviours of acetaminophen and dopamine. The results demonstrated that PACPE exhibited an excellent electrocatalytic activity toward the oxidation of acetaminophen and dopamine. The proposed method was sensitive, simple and economical for routine analysis. It was successfully employed to determine acetaminophen and dopamine in pharmaceutical samples.

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