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# Simultaneous Voltammetric Determination of Epinephrine and Acetaminophene at the Surface of Modified Carbon Nanotube Paste Electrode

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A carbon paste electrode (CPE) modified with ferrocenedicarboxylic acid (FCD) and carbon nanotubes (CNTs), was prepared for determination of epinephrine (EP) in the presence of acetaminophen (AC). The electrochemical response characteristics of the modified electrode toward EP and AC were investigated by differential pulse voltammetry (DPV). The results showed an efficient catalytic role for the electro-oxidation of EP and AC, leading to a remarkable peak resolution (~250 mV) for two compounds. Under the optimum conditions, the calibration curve for EP was obtained in the range of $5.0\times10^{-8}$ to $4.5\times10^{-4}$ M. The proposed method was applied to determination of EP and AC in real samples and the obtained results were satisfactory.

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**Keywords:** Epinephrine, Acetaminophen, Carbon Paste Electrode, Carbon Nanotubes,

## 1. INTRODUCTION

Epinephrine (EP) is an important neurotransmitters in mammalian central nervous systems [1], and it exits in the nervous tissue and body fluid in the form of large organic cations. The changes of its concentration may result in many diseases [2]. Thus, a quantitative determination of EP concentration is significant for developing nerve physiology, pharmacological research and life science. There are some methods applied for the determination of EP. As an electroactive device, it can also be studied via electrochemical techniques. Some reports showed the electrochemical response of EP on different kinds of electrodes [3-7].

Carbon paste electrode (CPE) is a special kind of heterogeneous carbon electrode consisting of mixture prepared from carbon powder and a suitable water-immiscible or non-conducting binder [19–21]. The use of carbon paste as an electrode was initially reported in 1958 by Adams [22]. In afterward researches a wide variety of modifiers [23–36] have been used with these versatile electrodes. CPEs are widely applicable in both electrochemical studies and electroanalysis thank to their advantages such as very low background current (compared to solid graphite or noble metal electrodes), facility to prepare, low cost, large potential window, simple surface renewal process and easiness of miniaturization [37–39]. Besides the advantageous properties and characteristics listed before, the feasibility of incorporation different substances during the paste preparation (which resulting in the so-called modified carbon paste electrode), allow the fabrication of electrodes with desired composition, and hence, with pre-determined properties [40, 41].

Since the discovery of carbon nanotubes (CNTs) in 1991 [42], numerous investigations were focused on the studies of their properties and applications [43–45]. Because of the special tube structure, CNTs possess several unique properties such as good electrical conductivity, high chemical stability and extremely high mechanical strength [46, 47]. In addition, the subtle electronic behavior of CNTs reveals that they have the ability to promote electron-transfer reaction and have a high electrocatalytic effect when used as electrode materials [48, 49]. All these fascinating properties make CNTs as a suitable candidate for the modification of electrodes [50-52].

Acetaminophen (AC) is a widely used analgesic and antipyretic medicine [8]. However, overdose of AC may be toxic and results in severe side effects [9]. Therefore, the detection of AC is quite important. AC contains phenolic hydroxyl group, which is electrochemical active and can be oxidized. Thus, various modified electrodes [10-18] were used to prepare electrochemical sensors for the detection of AC.

To our knowledge, no study has reported the electrocatalytic and simultaneous determination of EP and AC by using ferrocenedicarboxylic acid modified carbon nanotube paste electrode (FCDMCNPE). Thus, in the present work, we described initially the preparation and suitability of a FCDMCNPE as a new electrode in the electrocatalysis and determination of EP in an aqueous buffer solution and then we evaluated the analytical performance of the modified electrode in quantification of EP in the presence of AC. Finally, in order to demonstrate the catalytic ability of the modified electrode in the electrooxidation of EP and AC in real samples, we examined this method for the voltammetric determination of EP and AC in injection samples.

## 2. EXPERIMENTAL

### 2.1. Apparatus and chemicals

All the cyclic voltammetric measurements were performed using a BHP $2063^+$ Electrochemical Analysis System, Behpajooh, Iran potentiostat/galvanostat coupled with a Pentium IV personal computer connected to a HP laser jet 6L printer.

An Ag / AgCl / KCl 3 M, a platinum wire, and a FCDMCNPE were used as reference, auxiliary and working electrodes, respectively. A digital pH/mV meter (Metrohm model 710) was applied for pH measurements. Graphite powder, paraffin oil and reagents were analytical grade from Merck. EP and AC were purchased from Merck. Multi-walled carbon nanotubes (purity more than 95%) with o.d. between 10 and 20 nm, i.d. between 5 and 10 nm and tube length from 0.5 to 200 nm were prepared from Nanostruc-tured & Amorphous Materials (USA). The buffer solutions were prepared from ortho phosphoric acid and its salts in the pH range 2.0-12.0.

### *2.2. Preparation of the electrode*

Modified carbon nanotube paste electrodes were prepared by dissolve 0.01 g of FCD in diethyl ether and hand mixing with 89-times its weight of graphite powder and 10-times its weight of carbon nanotube with a mortar and pestle. The solvent was evaporated by stirring. A 70:30 (w/w) mixture of FCD spiked carbon nanotube powder and paraffin oil was blended by hand mixing for 20 min until a uniformly-wetted paste was obtained. The paste was then packed into the end of a glass tube (*ca.* 3.4 mm *i.d.* and 10 cm long). Electrical contact was made by inserting a copper wire into the glass tube at the back of the mixture. When necessary, a new surface was obtained by pushing an excess of paste out of the tube and polishing it on a weighing paper. Unmodified carbon paste, prepared in the same way without adding FCD and carbon nanotube to the mixture and was used for comparison purposes.

## **3. RESULTS AND DISCUSSION**

### *3.1. Electrochemical Behavior of FCDMCNPE*

Cyclic voltammetry was employed for investigation the electrochemical properties of FCDMCNPE in a pure buffered aqueous solution (pH 5.0). The cyclic voltammogram exhibits an anodic and corresponding cathodic peaks with $E_{pa}$= 0.50 V and $E_{pc}$= 0.38 V vs. Ag / AgCl / KCl 3 M. The experimental results show well-defined and reproducible anodic and cathodic peaks related to $Fc/Fc^+$ redox couple with quasireversible behavior, because of the peak separation potential, $\Delta E_p = (E_{pa} – E_{pc})$, is greater than that 59/n mV expected for a reversible system. Also, the obtained results from cyclic voltammetry of this modified electrode in various buffered solutions do not show any shift in the anodic and cathodic peak potentials. Therefore, the electrochemical behavior of the redox process of $Fc/Fc^+$ in FCDMCNPE is independent on the pH of aqueous solution.

### *3.2. Electrochemistry of EP at FCDMCNPE*

The utility of the modified electrode for oxidation of EP was evaluated by cyclic voltammetry. The cyclic voltammetric responses of a bare carbon-paste electrode in 0.1 M phosphate buffer (pH 5.0), without and with EP, are shown in Fig. 1 (curves c and d, respectively).

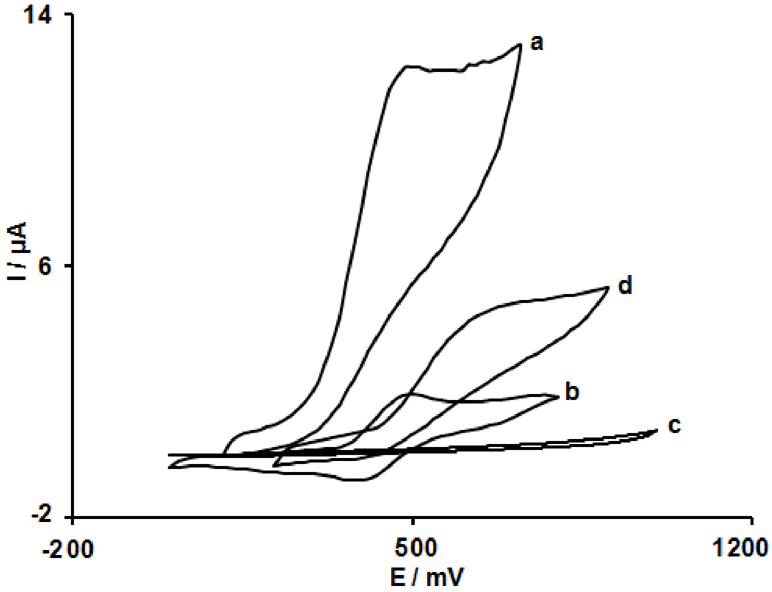

**Figure 1.** Cyclic voltammograms of FCDMCNPE at 10 mV $s^{-1}$ in 0.1M phosphate buffer (pH 5.0): (a) In the presence and (b) in the absence of 0.15 mM EP; (c) and (d) for an unmodified carbon-paste electrode in the absence and presence of 0.15 mM EP, respectively.

Figures 1a and b show cyclic voltammograms of modified electrode in the buffer solution with 150 µM of EP and without EP, respectively. The results show that the sensor produces a large anodic peak current in the presence of EP without a cathodic counterpart (Fig. 1, curve a). That the current observed is associated with EP oxidation and not the oxidation of modifier is demonstrated by comparing the current in Fig. 1 (curve b, without EP) with the one in the presence of EP in Fig. 1 (curve a). It is apparent that the anodic current associated with the surface-attached materials is significantly less than that obtained in the solution containing EP. At the surface of a bare electrode, EP was oxidized around 690 mV. As can be seen, the electroactivity of EP on the modified electrode was significant (Figs. 1 curve a), with strongly defined peak potential, around 500 mV vs. Ag/AgCl electrode. Thus, a decrease in overpotential and enhancement of peak current for EP oxidation are achieved with the modified electrode. Such a behavior is indicative of an EC′ mechanism [53].

The effect of scan rate on the electrocatalytic oxidation of 150 µM EP at the FCDMCNPE was investigated by cyclic voltammetry. The oxidation peak potential shifts with increasing scan rates towards a more positive potential, confirming the kinetic limitation of the electrochemical reaction. Also, a plot of peak height ($I_p$) against square root of scan rate ($v^{1/2}$), in range of 10-10 $mVs^{-1}$, was constructed (Fig. 2A), which was found to be linear, suggesting that at sufficient overpotential the process is diffusion rather than surface controlled. A plot of the sweep rate normalized current ($I_p/v^{1/2}$) versus sweep rate (Fig. 2B) exhibits the characteristic shape typical of an $EC_{cat}$ process [53].

In order to obtain information on the rate-determining step, Tafel slope b, was determined using the following equation for a totally irreversible diffusion controlled process [54]:

$$Ep = b/2\log v + \text{constant} \qquad (1)$$

On the basis of Eq. (1), the slope of Ep vs. log v plot is b/2, where b indicates the Tafel slope. The slope of Ep vs. log v plot is ∂ Ep/∂ (log v) and was found to be 51.3 mV in this work (Fig. 2C), so, b=2×51.3 = 100.6 mV. The value of Tafel slope indicates that a one-electron transfer process is the rate-limiting step assuming a transfer coefficient of ¸ about 0.41.

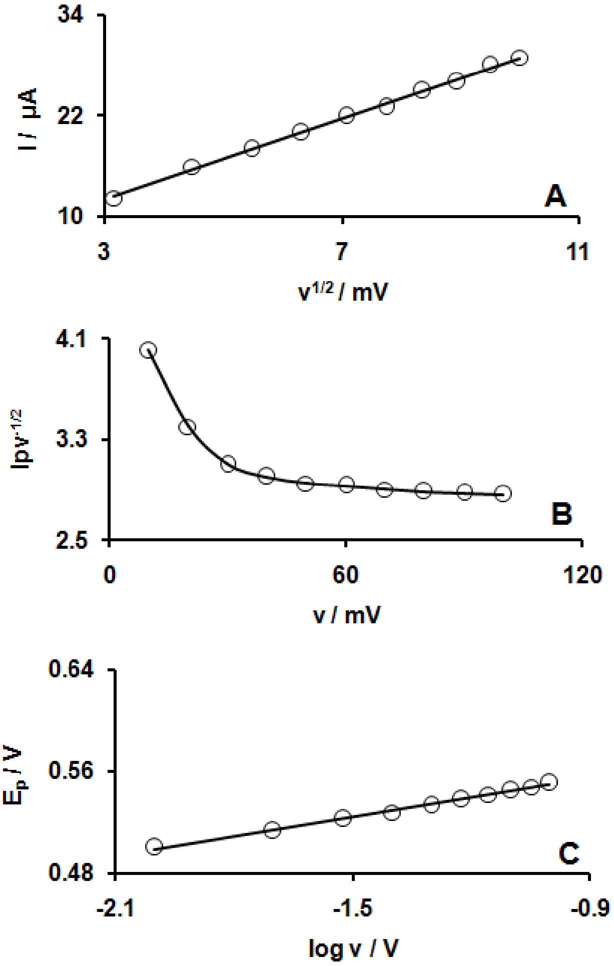

**Figure 2.** (A) The variation of the anodic peak currents vs. $v^{1/2}$. (B) variation of the scan rate-normalized current ($Ip/v^{1/2}$) with scan rate. (C) Variation of the anodic peak potential vs. log *v*.

### *3.3. Chronocoloumetric measurements*

The chronocoloumetric as well as the other electrochemical methods was employed for the investigation of electrode processes at chemically modified electrodes. Chronoamperometric measurements of EP at FCDMCNPE were done by setting the working electrode potential at 550 mV (at the first potential step) and at 100 mV (at second potential step) for various concentrations of EP (Fig.3A). For an electroactive material (EP in this case) with a diffusion coefficient of D, the current for the electrochemical reaction (at a mass transport limited rate) is described by the Cottrell equation [53]. Under diffusion control, a plot of I versus $t^{1/2}$ will be linear, and from the slope the value of D can be obtained (Fig.3B). The mean value of the D was found to be $9.39\times10^{-6}$cm$^2$/s (Fig.3C).

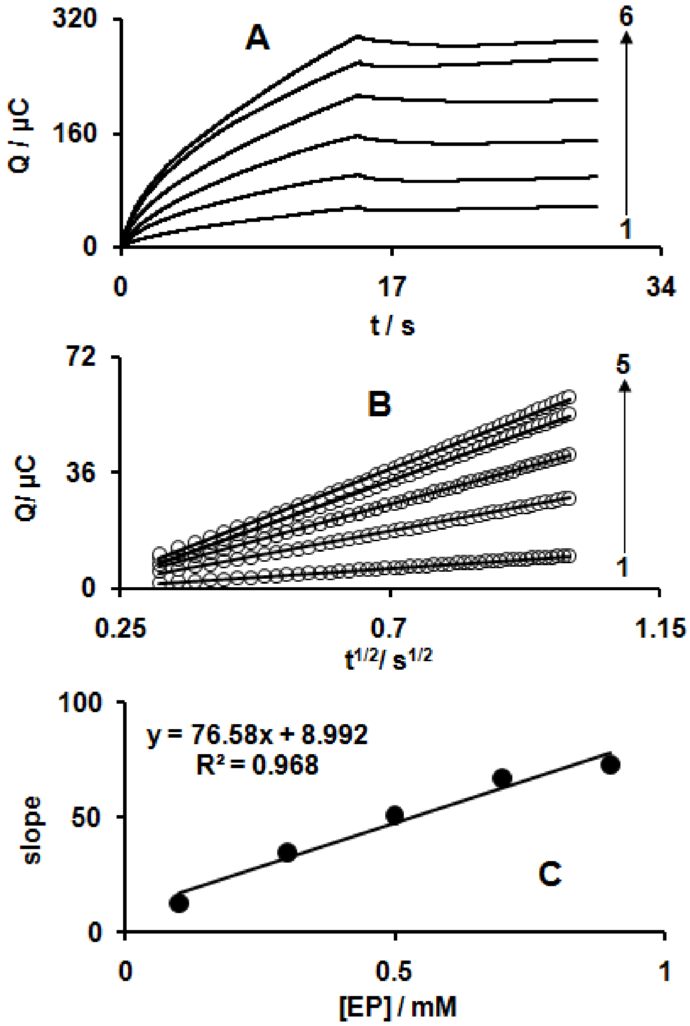

**Figure 3.** (A) Chronocolougrams of FCDMCNPE in 0.1M phosphate buffer solution (pH 5.0) containing 1) 0, 2) 0.1, 3) 0.3, 4) 0.5, 5) 0.7 and 6) 0.9 mM EP. (B) Plot of $Q$ vs. $t^{1/2}$ obtained from chronocolougrams 2-6 (C) The slopes of the resulting straight line of inset B vs. the EP concentration.

### 3.4. Calibration plot and limit of detection

Differential pulse voltammetry (DPV) was used to determine the concentration of EP. Voltammograms clearly show that the plot of peak current versus EP concentration is linear in the range of 0.05-450.0 μM EP with slope of 0.0536 μA.μM$^{-1}$. The detection limit (3σ) for EP was found to be 35 nM.

### 3.5. Simultaneous determination of EP and AC at FCDMCNPE

One of the main objectives of the present study was the development of a modified electrode capable of the electro-catalytic oxidation of EP and separation of the electrochemical responses of EP and AC.

The utilization of the FCDMCNPE for the simultaneous determination of EP and AC was demonstrated by simultaneously changing the concentrations of EP and AC. The DP voltammetric results show two-well-defined anodic peaks with a 250 mV separation of both peaks (Fig. 4), while the bare carbon paste electrode only gave an overlapped and broad oxidation peak. Fig. 4 insets A and B show the dependence of DPV peak currents on the concentration of EP and AC respectively.

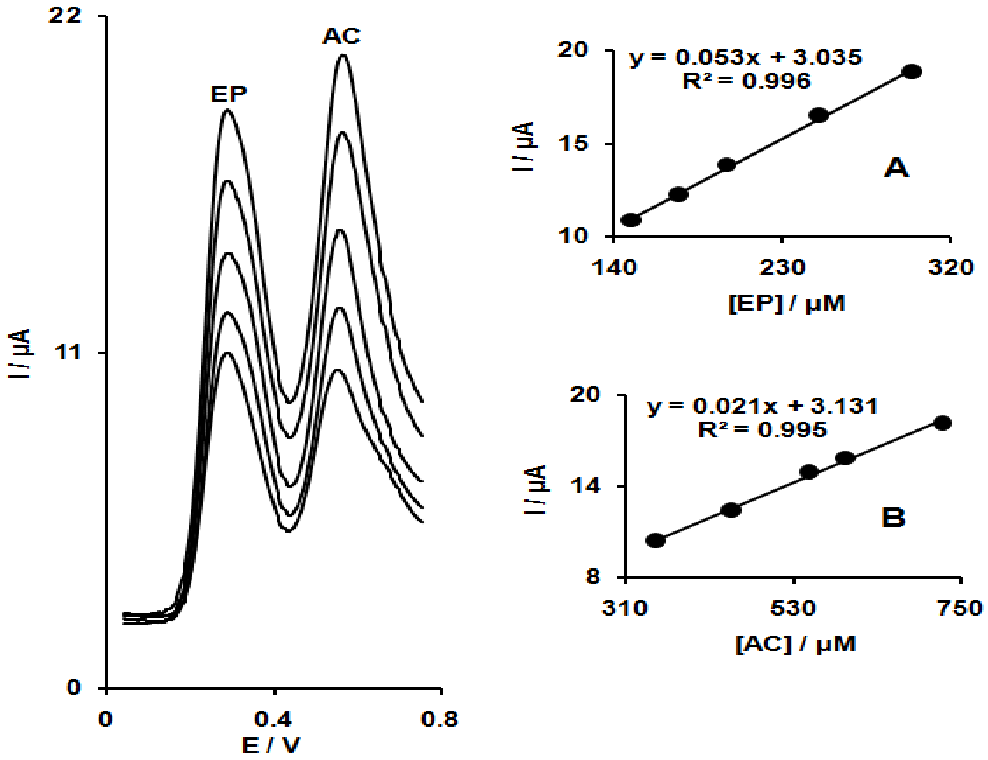

**Figure 4.** Differential pulse voltammograms of FCDMCNPE in 0.1M phosphate buffer solution (pH 5.0) containing different concentrations of EP and AC (from inner to outer) mixed solutions of 150+350, 175+450, 200+550, 250+600 and 300+725 respectively, in which the first value is concentration of EP in µM and the second value is concentration of AC in µM. Insets: (A) Plot of the peak currents as a function of EP and (B) AC concentrations respectively.

The sensitivity towards EP in the absence and presence of AC was found to be 0.0536 (absence of AC) and 0.0531 (presence of AC) $\mu A.\mu M^{-1}$. It is very interesting to note that the sensitivities of the modified electrode towards EP in the absence and presence of AC, are virtually the same, which indicate the fact that the oxidation processes of EP and AC, at the FCDMCNPE are independent and therefore simultaneous or independent measurements of the two analytes are possible without any interference. If the EP signal was affected by the AC, the above-mentioned slopes would be different.

### *3.6. Determination of EP in EP injection*

In order to assess the applicability of the proposed electrode, an attempt was made to determine EP in EP injection using the standard addition method. The potentials were controlled between 0.10

and 0.50 V for scan rate of 10 mVs$^{-1}$. The average determination results of NE in the injection were 0.97 mg mL$^{-1}$, which were quite corresponding to the value that was given by injection specification (1.0 mg mL$^{-1)}$. (Table 1).

**Table 1**. The application of FCDMCNPE for simultaneous determination of EP and AC in EP injection.

| Sample No. | EP Added (µM) | EP Found (µM) | Rec. (%) | RSD (%) | AC Added (µM) | AC Found (M) | Rec. (%) | RSD (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | 0 | 1.4 | - | - | 0 | 0 | - | - |
| 2 | 1 | 2.35 | 97.91 | 3.1 | 30 | 30.89 | 103.0 | 2.5 |
| 3 | 5 | 6.49 | 101.4 | 1.5 | 50 | 49.22 | 98.44 | 3.5 |
| 4 | 10 | 11.69 | 102.5 | 2.4 | 70 | 68.4 | 97.7 | 1.9 |

## 4. CONCLUSIONS

The results obtained in this work demonstrated the potentiality of the FCDMCNPE for simultaneous determination of EP and AC. The modified electrode exhibits highly electrocatalytic activity for the oxidation of EP and AC associated with negative shifts in anodic peak potentials. Thus, large peak separations obtained with this electrode allow it to simultaneously detect these compounds. Moreover, good sensitivity, high selectivity, low detection limits with the low cost of the sensor, makes this method very suitable for accurate determinations in real samples. The proposed method could be applied to the determination of EP and AC in EP injection.

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