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Electrocatalytic Determination of Carbidopa and Acetaminophen Using a Modified Carbon Nanotube Paste Electrode

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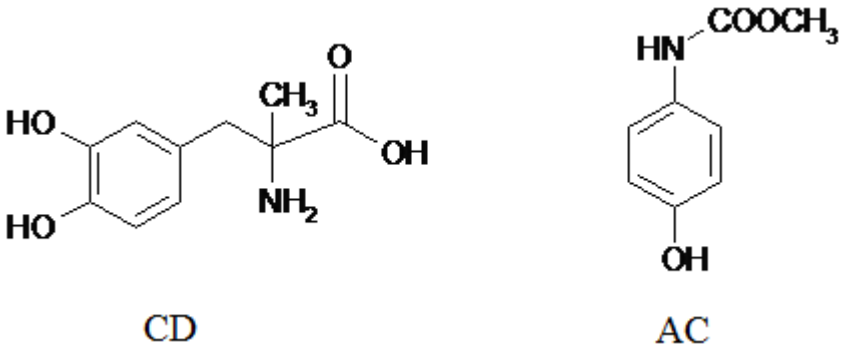
A carbon nanotube (CNT) paste electrode was constructed for the determination of carbidopa (CD). Owing to the unique structure and extraordinary properties of CNTs, the modified electrode has shown an obvious electrocatalytic activity towards oxidation of CD, which leads to lowering its overpotential by more than 400 mV. Also, the values of electron transfer (α=0.34), and diffusion coefficient (D_0=5.9 $\times 10^{-6}$ cm^2/s) for CD were calculated. Under the optimum conditions, the oxidation peak currents were linearly proportional to the concentration of CD in the range from 0.07-600.0 μM. The detection limit was 29.0 nM. Then the modified electrode was used to determine CD in an excess of acetaminophen (AC). Finally, the proposed sensitive and simple electrochemical method was successfully applied to CD and AC determination in urine samples.

Keywords: Carbidopa, Acetaminophen; Modified Carbon Paste Electrode; Carbon Nanotubes; Electrocatalysis

1. INTRODUCTION

Drug analysis is one of the important tools for drug quality control. Therefore, the development of simple, sensitive, rapid and reliable method for the determination of drug is of great importance [1-3]. Parkinson's disease victims show a significant depletion of dopamine in the brain. Since this neurotransmitter can not cross the blood–brain barrier into the central nervous system and it can not be employed to restore its normal level, levodopa (LD) (a precursor of dopamine) has been successfully used and is the most widely prescribed drug for the treatment of such patients [4, 5]. After its

administration, LD is converted into dopamine via an enzymatic reaction catalyzed by dopa-decarboxylase. However, since the metabolism of LD is also extra cerebral, several side effects of systemic dopamine can arise if LD is administered in high dosages.



Scheme 1. Structures of carbidopa and acetaminophen.

In order to achieve better a therapeutic effect and lower toxicity, carbidopa (CD) (Scheme 1) is administered in association with LD in pharmaceutical preparations, which contain 10–25 % CD [6]. This catecholamine acts as an inhibitor for the decarboxylase activity. Hence, a combination of LD with CD leads to a control of the dopamine concentration at suitable levels, reducing the side effects and improving the efficiency of the therapy. Accordingly, the development of an analytical method is very important to control the content of these catecholamines in pharmaceuticals. Different techniques have been employed for the determination of CD in pharmaceutical formulations [7-11]. Long analysis times, the use of organic solvents and high costs are some of the drawbacks associated with these techniques. Voltammetry is considered as an important electrochemical technique utilized in electroanalytical chemistry because it provides low cost, sensitivity, precision, accuracy, simplicity and rapidity [12-14].

Acetaminophen (AC) (Scheme 1) is a long-established substance being one of the most extensively employed drugs in the world. It is an antipyretic and analgesic drug commonly used against mild to moderate pain or for reduction of fevers. It is also non-carcinogenic and an effective substitute for aspirin for the patients who are sensitive to aspirin and safe up to therapeutic doses. AC is metabolized predominantly in the liver where it generates toxic metabolites. Overdose ingestions of AC lead to accumulation of toxic metabolites, which may cause severe and sometimes fatal hepatotoxicity and nephrotoxicity, in some cases associate with renal failure. The large scale therapeutic use of this drug generated the need for the development of fast, simple and accurate methodologies for the detection AC; for quality control analysis (in pharmaceutical formulations) and for medical control (in biological fluids as urine, blood and plasma) [15, 1 6].

Several methods have been used for the determination of AC in pharmaceutical formulations and biological fluids [17-21]. Among different methods, electrochemical methods maybe the most widely applied because of high sensitivity, simplicity and reproducibility of this approach [22- 28].

Electrochemical detection of analyte is a very elegant method in analytical chemistry [29]. The interest in developing electrochemical-sensing devices for use in environmental monitoring, clinical assays or process control is growing rapidly. Electrochemical sensors satisfy many of the requirements for such tasks particularly owing to their inherent specificity, rapid response, sensitivity and simplicity of preparation for the determination of organic molecules, including drugs and related molecules in pharmaceutical dosage forms and biological fluids [30, 31]. Carbon electrodes, especially glassy and paste electrodes are widely used in electrochemical investigations [32-36].

Electrochemical sensors based on carbon nanotubes (CNTs) represent a new and interesting alternative for quantification of different analytes. There are reports on the synthesis of multi-walled carbon nanotubes (MWCNTs) [37] and single-walled carbon nanotubes (SWCNTs) [38]. These materials have attracted enormous interest because of their unique structural, mechanical, electronic and chemical properties. Some of these properties include high chemical and thermal stability, high elasticity, high tensile strength and in some instances, metallic conductivity. The subtle electronic properties suggest that CNTs have capability to promote electron transfer reactions and improve sensitivity in electrochemistry and thus they are widely used as electrodes [39-41]. CNT modified electrodes have been proved to have excellent electroanalytical properties, such as wide potential window, low background current, low detection limits, high sensitivities, reduction of over potentials and resistance to surface fouling. There are reports which reveal that CNT modified electrodes have shown electrocatalytic behavior with excellent performance in the study of a number of biological species [42-46].

In the present work, we describe the preparation of a new electrode composed of CNPE modified with ferrocene monocarboxylic acid (FMCNPE) and investigate its performance for the electrocatalytic determination of CD in aqueous solutions. We also evaluate the analytical performance of the modified electrode for quantification of CD in the presence of AC.

2. EXPERIMENTAL

2.1. Apparatus and chemicals

The electrochemical measurements were performed using Metrohm 797 VA Computrace Model. A conventional three electrode cell was used. An Ag/AgCl/KCl (3.0 M) electrode, a platinum wire, and the FMCNPE were used as the reference, auxiliary and working electrodes, respectively. A Metrohm 827 pH/Ion Meter was used for pH measurements.

All solutions were freshly prepared with double distilled water. CD, AC, FM and all other reagents were of analytical grade from Merck (Darmstadt, Germany). Graphite powder and paraffin oil (DC 350, density = 0.88 g cm^{-3}) as the binding agent (both from Merck) were used for preparing the pastes. Multiwalled 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 10 to 30 μm were prepared from Nanostructured & Amorphous Materials, Inc. The buffer solutions were prepared from orthophosphoric acid and its salts in the pH range of 2.0-11.0.

2.2. Preparation of the electrode

The FMCNPEs were prepared by hand mixing 0.01 g of FM with 0.89 g graphite powder and 0.1 g CNTs with a mortar and pestle. Then, ~ 0.7 mL of paraffin was added to the above mixture and mixed for 20 min until a uniformly-wetted paste was obtained. The paste was then packed into the end of a glass tube (ca. 4.0 mm i.d. and 10 cm long). A copper wire inserted into the carbon paste provided the electrical contact. When necessary, a new surface was obtained by pushing an excess of the paste out of the tube and polishing with a weighing paper.

3. RESULTS AND DISCUSSION

3.1. Electrocatalytic oxidation of CD at a FMCNPE

The utility of the modified electrode for oxidation of CD was evaluated by cyclic voltammetry. The cyclic voltammetric responses of a bare carbon-paste electrode in 0.1M phosphate buffer (pH 7.0), without and with CD, are shown in Fig. 1 (curves c and d, respectively).

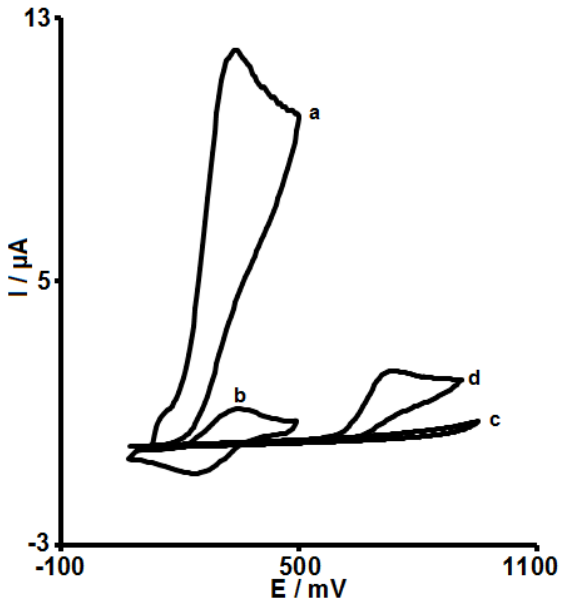


Figure 1. Cyclic voltammograms of FMCNPE at 10 mV s^{-1} in 0.1M phosphate buffer (pH 7.0): (a) In the presence and (b) in the absence of 200.0 µM CD; (c) and (d) for an unmodified carbon paste electrode in the absence and presence of 200.0 µM CD, respectively.

Figures 1a and b show cyclic voltammograms of modified electrode in the buffer solution with 200.0 µM of CD and without CD, respectively. The results show that the sensor produces a large anodic peak current in the presence of CD without a cathodic counterpart (Fig. 1, curve a). That the current observed is associated with CD oxidation and not the oxidation of modifier is demonstrated by

comparing the current in Fig. 1 (curve b, without CD) with the one in the presence of CD 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 CD. At the surface of a bare electrode, CD was oxidized around 740 mV. As can be seen, the electroactivity of CD on the modified electrode was significant (Figs. 1 curve a), with strongly defined peak potential, around 340 mV *vs.* Ag/AgCl/KCl (3.0 M) electrode. Thus, a decrease in overpotential and enhancement of peak current for CD oxidation are achieved with the modified electrode. Such a behavior is indicative of an EC´ mechanism [47].

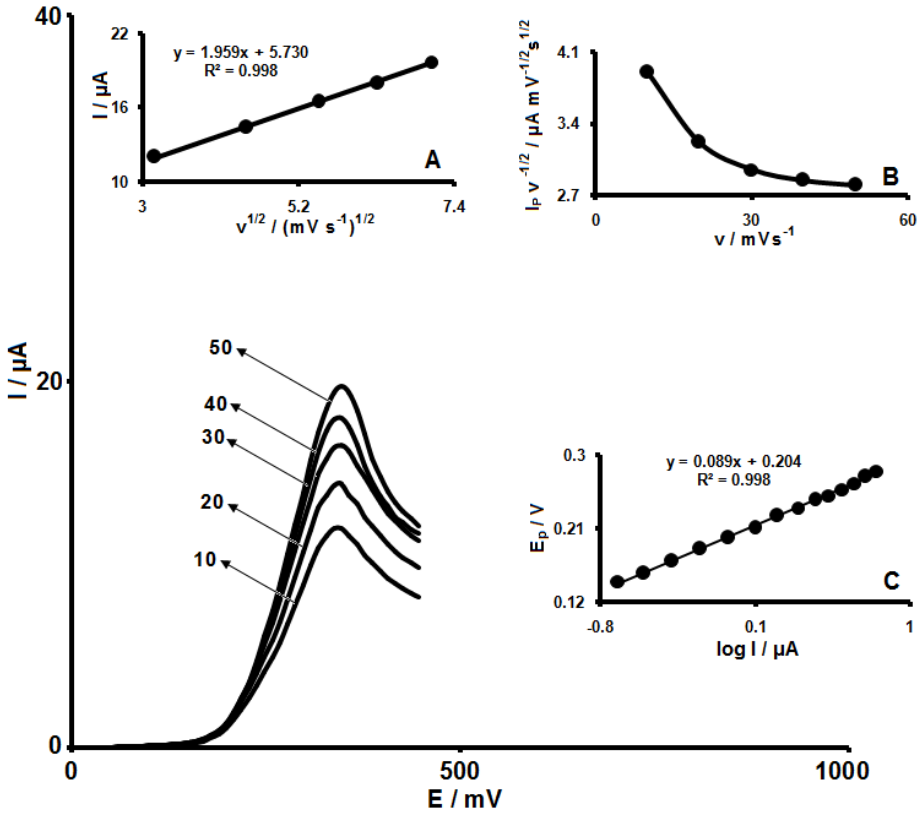


Figure 2. Linear sweep voltammograms of FMCNPE in 0.1 M phosphate buffer solution (pH 7.0) containing 200.0 µM CD at various scan rates; From inner to outer scan rates of 10, 20, 30, 40 and 50 mV s^{-1}, respectively. Insets: Variation of (A) anodic peak current vs. $\nu^{1/2}$; (B) normalized current ($I_p/\nu^{1/2}$) vs. ν; (C) Tafel plot derived from the linear sweep voltammogram in scan rate of 10 mV s^{-1}.

The effect of scan rate on the electrocatalytic oxidation of CD at the FMCNPE was investigated by linear sweep voltammetry (Fig. 2). As can be observed in Fig. 2, the oxidation peak potential shifted to more positive potentials with increasing scan rate, confirming the kinetic limitation in the electrochemical reaction. Also, a plot of peak height (I_p) vs. the square root of scan rate ($\nu^{1/2}$) was found to be linear in the range of 10–50 mV s^{-1}, suggesting that, at sufficient overpotential, the process is diffusion rather than surface controlled. A plot of the scan rate-normalized current ($I_p/\nu^{1/2}$) vs. scan rate (Fig. 2B) exhibits the characteristic shape typical of an EC´process [47].

The inset C of Fig. 2 shows a Tafel plot that was drawn from points of the Tafel region of the linear sweep voltammogram. The Tafel slope of 89.8 mV obtained in this case agrees well with the involvement of one electron in the rate determining step of the electrode process, assuming a charge transfer coefficient of α=0.34.

3.2. Chronoamperometric measurements

Chronoamperometric measurements of CD at FMCNPE were carried out by setting the working electrode potential at 0.4 V *vs.* Ag/AgCl/KCl (3.0 M) for the various concentration of CD in buffered aqueous solutions (pH 7.0) (Fig.3).

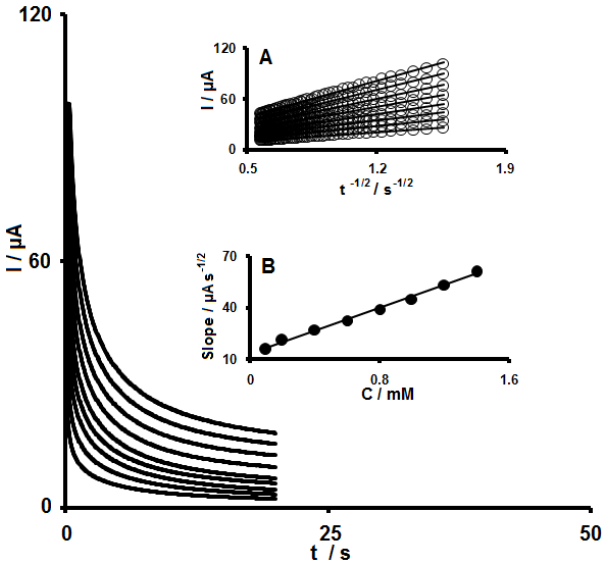


Figure 3. (A) Chronoamperograms obtained at FMCNPE in 0.1 M phosphate buffer solution (pH 7.0) for different concentration of CD, 0.0, 0.1, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2 and 1.4 mM of CD. Insets: (A) Plots of I vs. $t^{-1/2}$. (B) Plot of the slope of the straight lines against CD concentration.

For an electroactive material (CD in this case) with a diffusion coefficient of D_0, the current observed for the electrochemical reaction at the mass transport limited condition is described by the Cottrell equation [47]. Experimental plots of I vs. $t^{-1/2}$ were employed, with the best fits for different concentrations of CD (Fig. 3A). The slopes of the resulting straight lines were then plotted vs. CD concentration (Fig. 3B). From the resulting slope and Cottrell equation the mean value of the D_0 was found to be 5.9×10^{-6} cm^2/s.

3.3. Calibration plot and limit of detection

The electrocatalytic peak current of CD oxidation at the surface of the modified electrode can be used for determination of CD in solution. Therefore, DPV experiments were performed using

modified electrode in phosphate buffer solution containing various concentration of CD. The results show the electrocatalytic peak current of CD oxidation at the surface of modified electrode was linearly dependent on the CD concentrations. The mediated oxidation peak currents of CD at the surface of a modified electrode were proportional to the concentration of the CD within the ranges 0.07-600.0 μM in the DPV (Fig. 4). The detection limits (3σ) wad 29.0 nM.

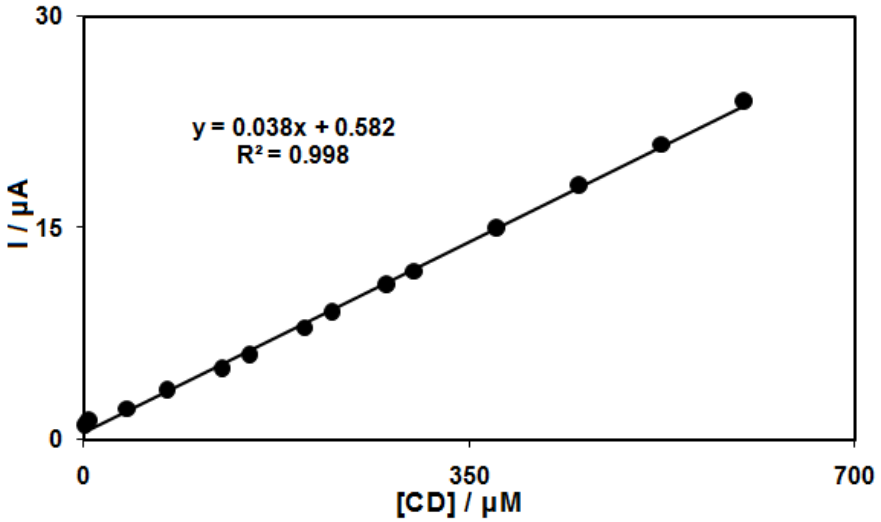
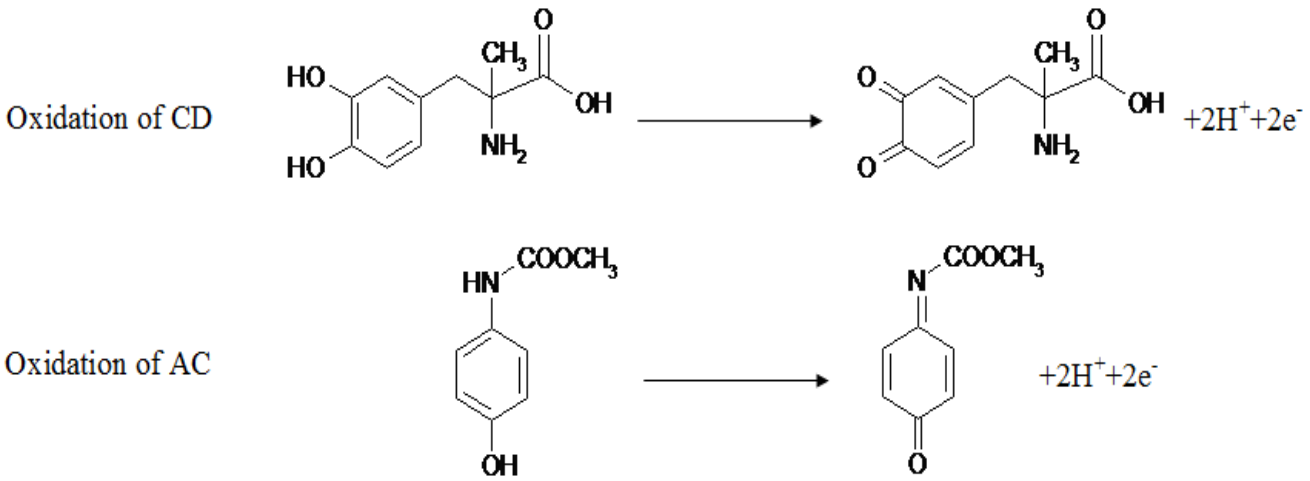


Figure 4. Plot of the electrocatalytic peak current as a function of CD concentration in the range of 0.07–600.0 μM.

3.4. Simultaneous determination of CD and AC



Scheme 2. Oxidation of carbidopa and acetaminophen

One of the main object of this study was to detect CD and AC simultaneously using FMCNPE . This was performed by simultaneously changing the concentrations of CD and AC, and recording the DPVs.

The voltammetric results showed well-defined anodic peaks at potentials of 310 and 540 mV, corresponding to the oxidation of CD and AC, respectively, indicating that simultaneous determination of these compounds is feasible at the FMCNPE as shown in Fig. 5.

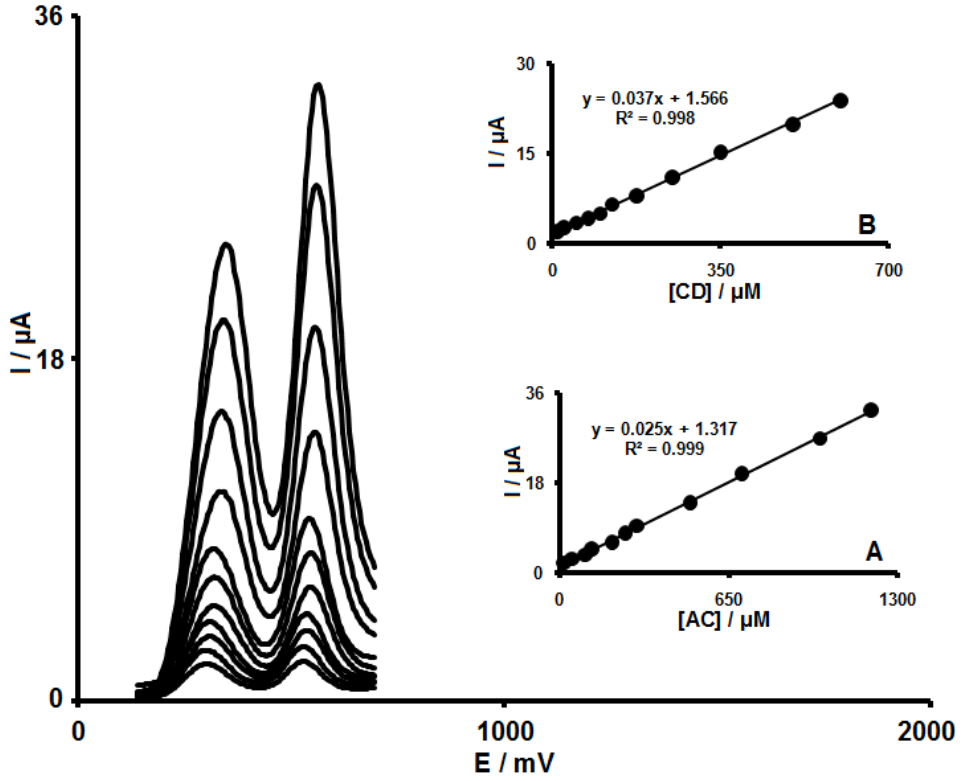


Figure 5. DPVs of FMCNPE in 0.1 M phosphate buffer solution (pH 7.0) containing different concentrations of CD+AC in µM, from inner to outer: 10.0+20.0, 25.0+50.0, 50.0+100.0, 75.0+125.0, 100.0+200.0, 125.0+250.0, 175.0+300.0, 250.0+500.0, 350.0+700.0, 500.0+1000 and 600.0+1200.0 respectively. Insets (A) and (B) are plots of I_p vs. CD and AC concentrations, respectively.

The products of oxidation of CD and AC are shown in scheme 2. From the analysis of data, the lower limit of detection of AC was estimated approximately 15.0 µM.

3.5. Determination of CD in a real sample

To evaluate the applicability of the proposed method to real samples, it was applied to the determination of CD and AC in urine samples. The CD and AC contents were measured after sample preparation using the standard addition method. The results are given in Table 1.

Table 1. The application of FMCNPE for simultaneous determination of CD and AC in urine samples. All concentrations are in μM (n=5).

Sample	Spiked (μM)		Found (μM)		Recovery (%)	
	CD	AC	CD	AC	CD	AC
1						
	10.0	30.0	9.9	31.1	99.0	103.7
	20.0	40.0	20.7	39.8	103.5	99.5
	30.0	50.0	29.5	51.0	98.3	102.0
2						
	15.0	35.0	15.5	34.8	103.3	99.4
	25.0	45.0	24.6	45.5	98.4	101.1
	35.0	55.0	35.4	54.1	101.1	98.4

4. CONCLUSIONS

The study has proved that using the ferrocene monocarboxylic acid and carbon nanotube species for surface modification of carbon paste electrode is advantageous for biosensors of CD and AC. Modified electrode showed good electrocatalytic activity for the oxidation. The proposed method can be applied for their determination in a mixture sample with satisfactory results.

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