Talanta 85 (2011) 2128–2134

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Fabrication of a nanostructure-based electrochemical sensor for simultaneous determination of *N*-acetylcysteine and acetaminophen

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ARTICLE INFO

Article history:
Received 20 May 2011
Received in revised form 10 July 2011
Accepted 13 July 2011
Available online 22 July 2011

Keywords:
N-acetylcysteine
Acetaminophen
Carbon nanotubes
Modified carbon paste electrode
Voltammetry

ABSTRACT

A carbon-paste electrode modified with 2,7-bis(ferrocenyl ethyl)fluoren-9-one (2,7-BF) and carbon nanotubes (CNTs) was used for the sensitive and selective voltammetric determination of *N*-acetylcysteine (NAC). The mediated oxidation of NAC at the modified electrode was investigated by cyclic voltammetry (CV). Also, the values of catalytic rate constant (k), and diffusion coefficient (D) for NAC were calculated. Differential pulse voltammetry (DPV) of NAC at the modified electrode exhibited two linear dynamic ranges with a detection limit (3σ) of 52.0 nmol L^{-1}. DPV was used for simultaneous determination of NAC and acetaminophen (AC) at the modified electrode, and quantitation of NAC and AC in some real samples by the standard addition method.

1. Introduction

N-acetylcysteine (NAC), is a pharmaceutical drug and nutritional supplement with numerous uses. Its primary use is as a samucolytic agent. It has also found applications in the management of paracetamol (acetaminophen) overdose and sulfate repletion as may occur in a utism, which is associated with the depletion of cysteine and related sulfur amino acids [1]. The drug rapidly metabolizes to intracellular glutathione which acts as a powerful antioxidant in the body. NAC has been reported to detoxify heavy metals (lead, mercury and arsenic) and remove them from the body. When taken for long periods, however, it increases the excretion of zinc and other essential minerals. To overcome this, NAC is usually supplemented with zinc, copper, and other trace minerals. Studies have indicated that it reduces the proliferation of certain cells lining the colon and may thus reduce the risk of colon cancer in people with recurrent polyps in the colon. Finally, it has been claimed to have a protective effect against cancer for its action as an antioxidant and a glutathione precursor [2]. Several methods for the determination of NAC have been described in literature including chromatography [3], spectrophotometry [4], fluorimetry [5], flow injection [6] and electrochemical methods [7–11].

Acetaminophen (*N*-acetyl-*p*-aminophenol or Paracetamol, AC) 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 leads 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 of AC; for quality control analysis (in pharmaceutical formulations) and for medical control (in biological fluids such as urine, blood and plasma) [12,13].

Several methods have been used for the determination of AC in pharmaceutical formulations and biological fluids including titrimetry [14], UV–vis spectrophotometry [15], flow-injection [16,17] and chromatographic methods [18,19]. Among these methods, electrochemical methods maybe the most widely applied because of high sensitivity, simplicity and reproducibility of this approach [20–23].

Intravenous NAC is typically administered for the treatment of AC overdose. Large quantities of paracetamol cause a minor metabolite called *N*-acetyl-*p*-benzoquinone imine (NAPQI) that accumulates in the body and is normally conjugated by glutathione. When taken in excess, the body's limited glutathione reserves fail to inactivate the toxic NAPQI. The metabolite thus produced is then free to react with key hepatic enzymes, damaging hepatocytes. This may lead to severe liver damage and even to death by fulminant

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doi:10.1016/j.talanta.2011.07.054

liver failure [24]. Due to this fatal effect, simultaneous determination of these compounds (NAC and AC) is very important. However, a major problem is that at bare electrodes, the anodic peak potentials for NAC and AC are almost the same, which results in their overlapped current responses and makes their discrimination very difficult.

Carbon nanotube (CNT) is a new material [25] and has been widely recognized as an important nano-material for the design of electrochemical sensors and biosensors [26–31] since its discovery in 1991. CNT possesses a strong electrocatalytic effect, fast electron transfer rate, high conductance, tensile strength, good chemical stability, and excellent biocompatibility. The poor solubility of CNTs, however, partially impairs the fabrication of CNT-based electronic devices. With an aim to immobilize CNTs on electrode surfaces without dissolving the CNTs in solvents, several types of modified electrodes have been reported recently. They include CNT paste electrode [32–34], CNT film-coated electrode [35], CNT powder microelectrode [36], CNT paper electrode [37], and polymer/CNT modified electrodes [38].

To the best of our knowledge, most previously published electrochemical studies have dealt with individual determination of NAC or AC utilizing carbon paste electrodes or other kinds of modified electrode. Only one study has been reported on the simultaneous determination of NAC and AC using modified carbon nanotube paste electrodes [9], which is the focus of the present study. Therefore, in continuation of our recently studies concerning the preparation of modified electrodes [39–43], in the present work, we describe the preparation of a new electrode composed of CNPE modified with 2,7-bis(ferrocenyl ethyl) fluoren-9-one (2,7-BFCNPE) and investigate its performance for the electrocatalytic determination of NAC in aqueous solutions. We also evaluate the analytical performance of the modified electrode for quantification of NAC in the presence of AC.

2. Experimental

2.1. Apparatus and chemicals

The electrochemical measurements were performed with an Autolab potentiostat/galvanostat (PGSTAT-302 N, Eco Chemie, The Netherlands). The experimental conditions were controlled with General Purpose Electrochemical System (GPES) software. A conventional three electrode cell was used at $25 \pm 1\ ^{\circ}C$. An Ag/AgCl/KCl (3.0 M) electrode, a platinum wire, and the 2,7-BFCNPE were used as the reference, auxiliary and working electrodes, respectively. A Metrohm 691 pH/Ion Meter was used for pH measurements.

All solutions were freshly prepared with double distilled water. NAC, AC 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. 2,7-BF was synthesized in our laboratory as reported previously [41].

2.2. Preparation of the electrode

The 2,7-BFCNPEs were prepared by hand mixing 0.01 g of 2,7-BF 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. 3.4 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.

For comparison, 2,7-BF modified CPE electrode (2,7-BFCPE) without CNTs, CNT paste electrode (CNPE) without 2,7-BF, and unmodified CPE in the absence of both 2,7-BF and CNTs were also prepared in the same way.

2.3. Procedure of real samples preparation

Five NAC tablets (labeled 600 mg) were grinding. Then, the tablet solution was prepared by dissolving 600 mg of the powder in 100 mL water by ultrasonication. Then, different volume of the diluted solution was transferred into a 10 mL volumetric flask and diluted to the mark with phosphate buffer (pH 7.0). The NAC content was analyzed by the proposed method using the standard addition method.

The AC oral solution was diluted 1000 times with water; then, different volume of the diluted solution was transferred into a 10 mL volumetric flask and diluted to the mark with phosphate buffer (pH 7.0).

Urine samples were stored in a refrigerator immediately after collection. Ten milliliters of the sample was centrifuged for 15 min at 2000 rpm. The supernatant was filtered out using a 0.45 μm filter. Then, different volume of the solution was transferred into a 10 mL volumetric flask and diluted to the mark with phosphate buffer (pH 7.0). The diluted urine sample was spiked with different amounts of NAC and AC.

The serum sample was centrifuged and then after filtering, diluted with phosphate buffer (pH 7.0) without any further treatment. The diluted serum sample was spiked with different amounts of NAC and AC.

3. Results and discussion

3.1. Electrochemical behavior of 2,7-BFCNPE

We have previously shown that a carbon paste electrode spiked with 2,7-BF can be constructed by the incorporation of 2,7-BF in a graphite powder-paraffin oil matrix [41]. The experimental results show well-defined and reproducible anodic and cathodic peaks related to 2,7-bis(ferrocenyl ethyl)fluoren-9-one/2,7-bis(ferricenium ethyl)fluoren-9-one (Fc/Fc^{+}) redox system, which show a quasireversible behavior in an aqueous medium [44]. The electrode capability for the generation of a reproducible surface was examined by cyclic voltammetric data obtained in optimum solution pH 7.0 from five separately prepared 2,7-BFCNPEs (Table 1). The calculated RSD for various parameters accepted as the criteria for a satisfactory surface reproducibility (about 1–4%), which is virtually the same as that expected for the renewal or ordinary carbon paste surface [40,41]. However we regenerated the surface of 2,7-BFCNPE before each experiment according to our previous results [41].

In addition, the longterm stability of the 2,7-BFCNPE was tested over a 3-week period. When CVs were recorded after the modified electrode was stored in atmosphere at room temperature, the peak potential for NAC oxidation was unchanged and the current signals showed less than 2.1% decrease relative to the initial response. The antifouling properties of the modified electrode toward NAC oxidation and its oxidation products were investigated by recording the cyclic voltammograms of the modified electrode before and after use in the presence of NAC. Cyclic voltammograms were recorded in the presence of NAC after having cycled the potential 20 times at a scan rate of $10\ mV\ s^{-1}$. The peak potentials were unchanged and

Table 1
Cyclic voltammetric data obtained for constructed 2,7-BFCNPE in 0.1 M phosphate buffer solution (pH 7.0) at 10 mV s^{-1}.

E_{pa} (V)[a]	E_{pc} (V)	$E_{1/2}$ (V)	ΔE_p (V)	I_{pa} (μA)	I_{pc} (μA)
0.320 ± 1.1[b]	0.255 ± 1.2	0.287 ± 1.0	0.065 ± 1.1	0.79 ± 1.8	0.77 ± 1.9

[a] Versus Ag/AgCl/KCl (3.0 M) as reference electrode.
[b] All the '±' values are RSD% (n = 5).

the currents decreased by less than 2.4%. Therefore, at the surface of 2,7-BFCNPE, not only the sensitivity increase, but the fouling effect of the analyte and its oxidation product also decreases.

3.2. Electrocatalytic oxidation of NAC at a 2,7-BFCNPE

The electrochemical behavior of NAC is dependent on the pH value of the aqueous solution, whereas the electrochemical properties of Fc/Fc^+ redox couple are independent on pH. Therefore, pH optimization of the solution seems to be necessary in order to obtain the electrocatalytic oxidation of NAC. Thus the electrochemical behavior of NAC was studied in 0.1 M phosphate buffer solutions in different pH values (2.0 < pH < 11.0) at the surface of 2,7-BFCNPE by cyclic voltammetry. It was found that the electrocatalytic oxidation of NAC at the surface of 2,7-BFCNPE was more favored under neutral conditions than in acidic or basic medium. This appears as a gradual growth in the anodic peak current and a simultaneous decrease in the cathodic peak current in the cyclic voltammograms of 2,7-BFCNPE. Thus, the pH 7.0 was chosen as the optimum pH for electrocatalysis of NAC oxidation at the surface of 2,7-BFCNPE.

Fig. 1 depicts the CV responses for the electrochemical oxidation of 50.0 μmol L^{-1} NAC at unmodified CPE (curve b), CNPE (curve d), 2,7-BFCPE (curve e) and 2,7-BFCNPE (curve f). As it is seen, while the anodic peak potential for NAC oxidation at the CNPE, and unmodified CPE are 740 and 790 mV, respectively, the corresponding potential at 2,7-BFCNPE and 2,7-BFCPE is ~320 mV. These results indicate that the peak potential for NAC oxidation at the 2,7-BFCNPE and 2,7-BFCPE electrodes shift by ~420 and 470 mV toward negative values compared to CNPE and unmodified CPE, respectively. However, 2,7-BFCNPE shows higher anodic peak current for the oxidation of NAC compared to 2,7-BFCPE, indicating that the combination of CNTs and the mediator (2,7-BF) has significantly improved the performance of the electrode toward NAC oxidation. In fact, 2,7-BFCNPE in the absence of NAC exhibited a well-behaved redox reaction (Fig. 1, curve c) in 0.1 M phosphate buffer (pH 7.0). However, there was a drastic increase in the anodic peak current in the presence of 50.0 μmol L^{-1} NAC (curve f), which can be related to the strong electrocatalytic effect of the 2,7-BFCNPE toward this compound [44].

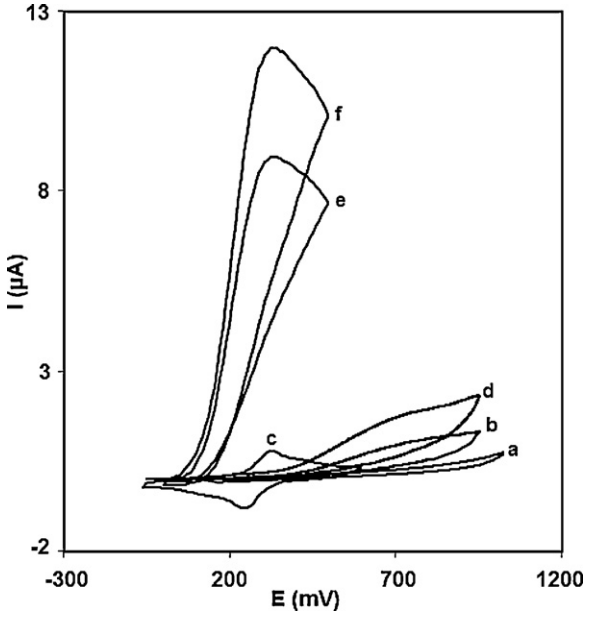

Fig. 1. CVs of (a) unmodified CPE in 0.1 M phosphate buffer solution (pH 7.0) at scan rate of 10 mV s^{-1}; (b) as (a) + 50.0 μmol L^{-1} NAC; (c) as (a) at the surface of 2,7-BFCNPE; (d) as (b) at the surface of CNPE; (e) as (b) at the surface of 2,7-BFCPE; (f) as (b) at the surface of 2,7-BFCNPE.

The effect of scan rate on the electrocatalytic oxidation of NAC at the 2,7-BFCNPE 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 10–70 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 [44].

The Tafel slope (b) can be obtained from the slope of E_p vs. log ν using Eq. (1) [45]:

$$E_p = \frac{b}{2}\log\nu + \text{constant} \quad (1)$$

The Tafel slope was found to be 103.0 mV (Fig. 2, inset C), which indicates that a one-electron transfer process is the rate limiting step assuming a transfer coefficient (α) is about 0.43.

3.3. Chronoamperometric measurements

Chronoamperometric measurements of NAC at 2,7-BFCNPE 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 NAC in buffered aqueous solutions (pH 7.0) (Fig. 3). For an electroactive material (NAC in this case) with a diffusion coefficient of D, the current observed for the electrochemical reaction at the mass transport limited condition is described by the Cottrell equation [44]. Experimental plots of I vs. $t^{-1/2}$ were employed, with the best fits for different concentrations of NAC (Fig. 3A). The slopes of the resulting straight lines were then plotted vs. NAC concentration (Fig. 4B). From the resulting slope and Cottrell equation the mean value of the D was found to be 2.87×10^{-5} cm^2/s.

Chronoamperometry can also be employed to evaluate the catalytic rate constant, k, for the reaction between NAC and the 2,7-BFCNPE according to the method of Galus [46]:

$$\frac{I_C}{I_L} = \gamma^{1/2}\left[\pi^{1/2}\,\mathrm{erf}(\gamma^{1/2}) + \exp\left(\frac{(-\gamma)}{\gamma^{1/2}}\right)\right] \quad (2)$$

where I_C is the catalytic current of NAC at the 2,7-BFCNPE, I_L is the limited current in the absence of NAC and $\gamma = kC_bt$ is the argument of the error function (C_b is the bulk concentration of NAC). In cases where γ exceeds the value of 2, the error func-

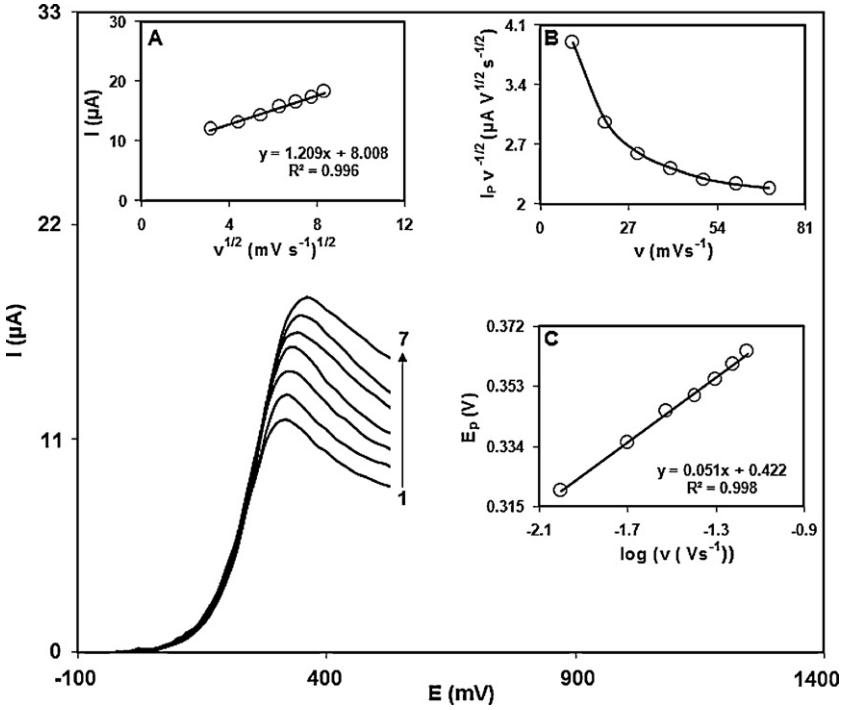

Fig. 2. Linear sweep voltammograms of 2,7-BFCNPE in 0.1 M phosphate buffer solution (pH 7.0) containing 50.0 μmol L^{-1} NAC at various scan rates; From inner to outer scan rates of 10, 20, 30, 40, 50, 60 and 70 mV s^{-1}, respectively. Insets: Variation of (A) anodic peak current vs. $\nu^{1/2}$; (B) normalized current ($I_p/\nu^{1/2}$) vs. ν; (C) anodic peak potential vs. log ν.

tion is almost equal to 1 and therefore, the above equation can be reduced to:

$$\frac{I_C}{I_L} = \pi^{1/2}\gamma^{1/2} = \pi^{1/2}(kC_b t)^{1/2} \quad (3)$$

where t is the time elapsed. The above equation can be used to calculate the rate constant, k, of the catalytic process from the slope of I_C/I_L vs. $t^{1/2}$ at a given NAC concentration. From the values of the slopes, the average value of k was found to be 2.6×10^3 mol^{-1} L s^{-1}.

3.4. Calibration plot and limit of detection

DPV method was used to determine the concentration of NAC (Fig. 4). The plot of peak current vs. NAC con-

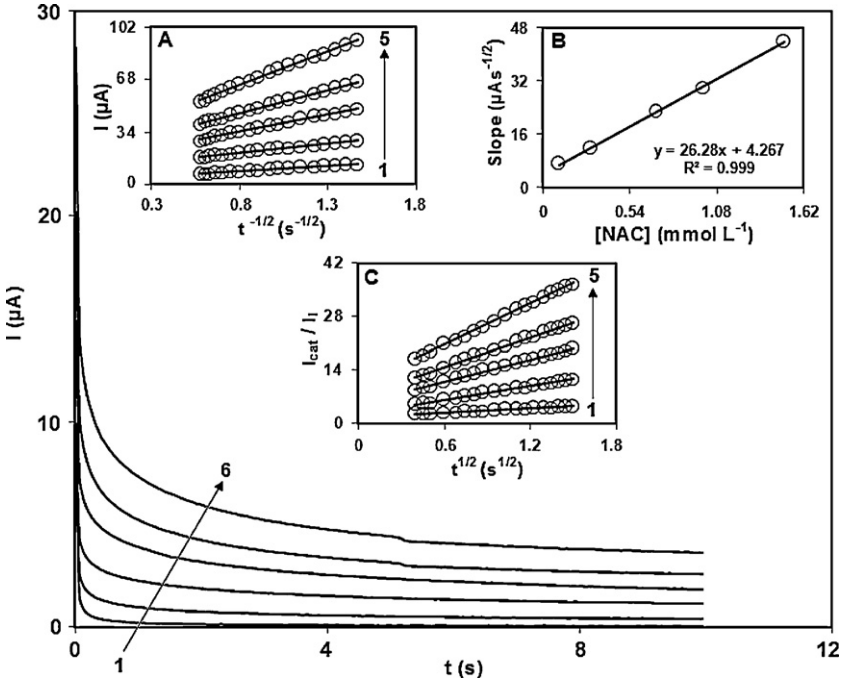

Fig. 3. (A) Chronoamperograms obtained at 2,7-BFCNPE in 0.1 M phosphate buffer solution (pH 7.0) for different concentration of NAC. The numbers 1–6 correspond to 0.0, 0.1, 0.3, 0.7, 1.0 and 1.5 mmol L^{-1} of NAC. Insets: (A) Plots of I vs. $t^{-1/2}$ obtained from chronoamperograms 2–6. (B) Plot of the slope of the straight lines against NAC concentration; (C) dependence of I_{cat}/I_l on $t^{1/2}$ derived from the data of chronoamperograms 1–6.

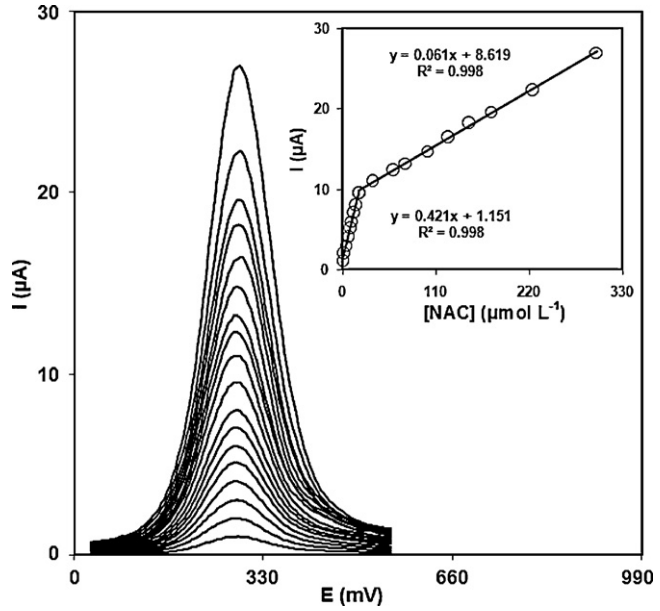

Fig. 4. Differential pulse voltammograms of 2,7-BFCNPE in 0.1 M phosphate buffer solution (pH 7.0) containing different concentrations of NAC. From inner to outer correspond to 0.07, 2.0, 4.0, 6.5, 9.5, 11.5, 14.0, 16.0, 20.0, 35.0, 60.0, 75.0, 100.0, 125.0, 150.0, 175.0, 225.0 and 300.0 μmol L^{-1} of NAC. Inset show the plots of the electrocatalytic peak current as a function of NAC concentration in the range of 0.07–300.0 μmol L^{-1}.

centration consisted of two linear segments with slopes of 0.4216 and 0.0617 μA/μmol L^{-1} in the concentration ranges of 0.07–20.0 μmol L^{-1} and 20.0–300.0 μmol L^{-1}, respectively. The decrease in sensitivity (slope) of the second linear segment is likely due to kinetic limitation. The detection limit (3σ) of NAC was found to be 52.0 nmol L^{-1}. These values are compared with values reported by other research groups for electrocatalytic oxidation of NAC at the surface of chemically modified electrodes by other mediators (Table 2).

3.5. Simultaneous determination of NAC and AC

To our knowledge, there is no report on the simultaneous determination of NAC and AC using 2,7-BFCNPE. Therefore, the main object of this study was to detect NAC and AC simultaneously using 2,7-BFCNPE. This was performed by simultaneously changing the concentrations of NAC and AC, and recording the DPVs. The voltammetric results showed well-defined anodic peaks at potentials of 290 and 470 mV, corresponding to the oxidation of NAC and AC, respectively, indicating that simultaneous determination of these compounds is feasible at the 2,7-BFCNPE as shown in Fig. 5.

The sensitivity of the modified electrode toward the oxidation of NAC was found to be 0.4275 μA/μmol L^{-1}. This is very close to the value obtained in the absence of AC (0.4216 μA/μmol L^{-1}, see Section 3.4), indicating that the oxidation processes of these compounds at the 2,7-BFCNPE are independent and therefore, simultaneous determination of their mixtures is possible without significant interferences.

3.6. Real sample analysis

3.6.1. Determination of NAC and AC in pharmaceutical preparations

In order to evaluate the analytical applicability of the proposed method, also it was applied to the determination of NAC and AC in NAC tablets and AC oral solution respectively.

Table 2
Comparison of the efficiency of some modified electrodes used in the electrocatalysis of NAC.

Electrode	Modifier	Method	pH	Peak potential shift (mV)	Scan rate ($mV\,s^{-1}$)	Limit of detection (M)	Dynamic range (M)	Ref.
Carbon paste	Catechol	Voltammetry	6.0	400	20	1.0×10^{-5}	3.0×10^{-5}–2.0×10^{-3}	[7]
Carbon paste	*N*-(3,4-Dihydroxyphenethyl)-3,5-dinitrobenzamide	Voltammetry	7.0	576	20	2.0×10^{-7}	5.0×10^{-7}–2.0×10^{-4}	[9]
Carbon paste	Cobalt salophen	Voltammetry	7.0	–	50	5.0×10^{-8}	1.0×10^{-7}–1.0×10^{-4}	[11]
Glassy carbon	Naphthoquinone	Voltammetry	7.0	600	20	8.0×10^{-7}	4.0×10^{-6}–1.3×10^{-4}	[47]
Palladized aluminum	Prussian blue film	Amperometry	2.0	–	20	5.4×10^{-7}	2.0×10^{-6}–4.0×10^{-5}	[48]
Carbon nanotube paste	2,7-BF	Voltammetry	7.0	470	10	5.2×10^{-8}	7.0×10^{-8}–3.0×10^{-4}	This work

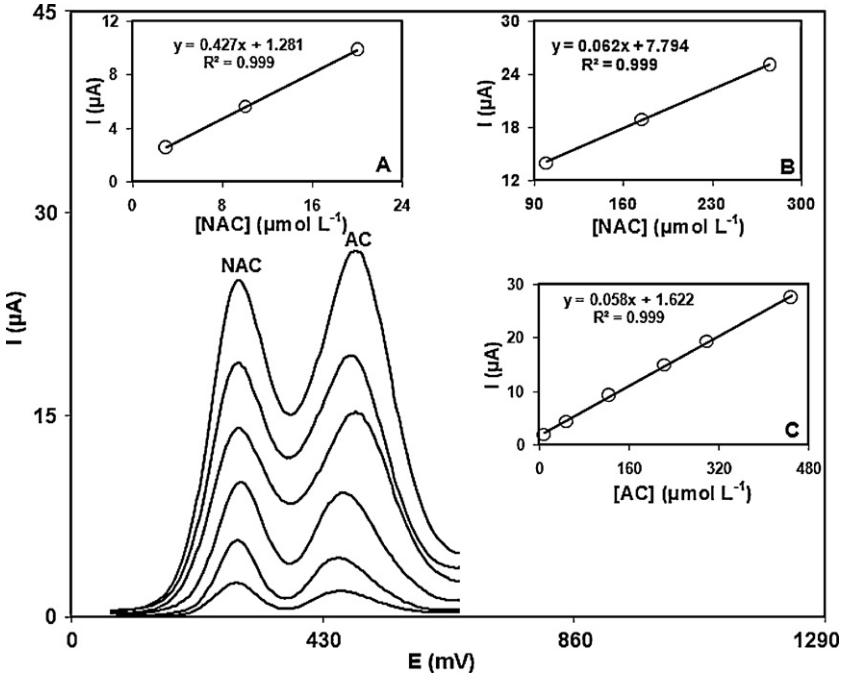

Fig. 5. DPVs of 2,7-BFCNPE in 0.1 M phosphate buffer solution (pH 7.0) containing different concentrations of NAC+AC in μmol L^{-1}, from inner to outer: 3.0 + 10.0, 10.0 + 50.0, 20.0 + 125.0, 100.0 + 225.0, 175.0 + 300.0 and 275.0 + 450, respectively. Insets (A), (B) and (C) are plots of I_p vs. NAC and AC concentrations, respectively.

Table 3
The application of 2,7-BFCNPE for simultaneous determination of NAC and AC. All concentrations are in μmol L^{-1} (n = 5).

Sample	Spiked (μmol L^{-1})		Found (μmol L^{-1})		Recovery (%)		RSD (%)	
	NAC	AC	NAC	AC	NAC	AC	NAC	AC
Acetylcysteine tablet	0	0	25.0	ND[a]	–	–	2.9	–
	5.0	15.0	30.4	14.8	101.3	98.7	3.1	1.9
	7.5	20.0	31.9	20.7	98.1	103.5	2.1	1.7
	10.0	25.0	36.1	24.9	103.1	99.6	1.6	2.9
Oral solution of AC	0	0	ND	16.0	–	–	–	3.2
	10.0	10.0	9.8	26.4	98.0	101.5	2.2	2.8
	15.0	20.0	15.4	35.4	102.7	98.3	3.1	1.7
	20.0	30.0	19.7	46.6	98.5	101.3	2.4	3.3

[a] Not detected.

Based on the repeated differential pulse voltammetric responses (n = 5) of the diluted analytes and the samples that were spiked with specified concentration of NAC and AC, measurements were made for determination of NAC and AC concentrations in the pharmaceutical preparations. The results are listed in Table 3.

The reliability of the proposed modified electrode was also evaluated by comparing the obtained results with those declared in the label of the pharmaceutical preparations (Table 4). The results in Table 3 show the relative standard derivations (RSD%) and the recovery rates of the spiked samples are acceptable. Also, the data in Table 4 indicate that the results obtained by utilizing 2,7-BFCNPE are in good agreement with those declared in the label of the preparations. Thus, the modified electrode can be efficiently used for individual or simultaneous determination of NAC and AC in pharmaceutical preparations.

Table 4
Comparison of the total values of NAC and AC of some pharmaceutical preparations obtained using 2,7-BFCNPE with declared values in the lable of the samples (n = 5).

Samples	Declared value	Found value	RSD%
NAC tablet (mg per tablet)	600.0	598.0	2.2
Oral solution of AC (mg mL^{-1})	24.0	24.1	2.6

Table 5
The application of 2,7-BFCNPE for simultaneous determination of NAC and AC in urine and human blood serum samples (n = 5).

Sample	Spiked (μmol L^{-1})		Found (μmol L^{-1})		Recovery (%)		RSD (%)	
	NAC	AC	NAC	AC	NAC	AC	NAC	AC
Urine	5.0	15.0	4.9	15.2	98.0	101.3	2.4	3.3
	10.0	20.0	10.1	19.7	101.0	98.5	1.9	2.1
	15.0	25.0	14.9	25.6	99.3	102.4	2.7	2.3
Human blood serum	7.5	15.0	7.7	14.8	102.7	98.7	3.4	1.7
	10.0	17.5	9.9	17.9	99.0	102.3	1.8	2.6
	12.5	20.0	12.9	19.9	103.2	99.5	2.9	3.1

3.6.2. Determination of NAC and AC in urine and human blood serum samples

In order to evaluate the analytical applicability of the proposed method, also it was applied to the determination of NAC and AC in urine and human blood serum samples. The results for determination of the two species in real samples are given in Table 5. Satisfactory recovery of the experimental results was found for NAC and AC. The reproducibility of the method was demonstrated by the mean relative standard deviation (RSD).

4. Conclusions

In the present study, carbon-paste electrode modified with 2,7-BF and CNTs was used for the determination of NAC in the presence of AC. The CV and DPV investigations showed effective electrocatalytic activity of the modified electrode in lowering the anodic over potential for the oxidation of NAC and complete resolution of its anodic wave from AC. The detected potential differences of 180 mV between NAC–AC, is large enough to allow simultaneous determination of NAC and AC in mixtures without significant interferences.

References

[1] http://www.ncbi.nlm.nih.gov/pubmed/16825783, August 15, 2010.
[2] http://www.Wikipedia.com, June 7, 2010.
[3] V. Concha-Herrera, J.R. Torres-Lapasio, M.C. Garcia-Alvarez-Coque, J. Liq. Chromatogr. Relat. Technol. 27 (2004) 1593–1609.
[4] W.T. Suarez, H.J. Vieira, O. Fatibello-Filho, J. Pharm. Biomed. Anal. 37 (2005) 771–775.
[5] S.M. Al-Ghannam, A.M. El-Brashy, B.M. Al-Farhan, Farmaco 57 (2002) 625–629.
[6] W.T. Suarez, A.A. Madi, F.C. Vicentini, O. Fatibello-Filho, Anal. Lett. 40 (2007) 3417–3429.
[7] J.B. Raoof, R. Ojani, M. Amiri-Aref, F. Chekin, J. Appl. Electrochem. 40 (2010) 1357–1363.
[8] I.S. da Silva, M.F. Antão Araújo, H.A. Ferreira, J.J. Gomes Varela Jr., S.M.C.N. Tanaka, A.A. Tanaka, L. Angnes, Talanta 83 (2011) 1701–1706.
[9] A.A. Ensafi, H. Karimi-Maleh, S. Mallakpour, M. Hatami, Sens. Actuators B 155 (2011) 42–49.
[10] W.T. Suarez, L.H. Marcolino Jr., O. Fatibello-Filho, Microchem. J. 82 (2006) 163–167.
[11] S. Shahrokhian, Z. Kamalzadeh, A. Bezaatpour, D.M. Boghaei, Sens. Actuators B 133 (2008) 599–606.
[12] http://en.wikipedia.org/wiki/Paracetamol.
[13] http://www.drugs.com/acetaminophen.html.
[14] G. Burgot, F. Auffret, J.L. Burgot, Anal. Chim. Acta 343 (1997) 125–128.
[15] R.S. Andulescu, S. Mirel, R. Oprean, J. Pharm. Biomed. Anal. 23 (2000) 77–87.
[16] W. Ruengsitagoon, S. Liawruangrath, A. Townshend, Talanta 69 (2006) 976–983.
[17] H. Razmi, E. Habibi, Electrochim. Acta 55 (2010) 8731–8737.
[18] M.G. Gioia, P. Andreatta, S. Boschetti, R. Gatti, J. Pharm. Biomed. Anal. 48 (2008) 331–339.
[19] J. Sun, L.K. Schnackenberg, R.D. Holland, T.C. Schmitt, G.H. Cantor, Y.P. Dragan, R.D. Berger, J. Chromatogr. B 871 (2008) 328–340.
[20] S. Ashok Kumar, C.F. Tang, S.M. Chen, Talanta 76 (2008) 997–1005.
[21] M. Mazloum-Ardakani, H. Beitollahi, M.K. Amini, F. Mirkhalaf, B.B.F. Mirjalili, Biosens. Bioelectron. 26 (2011) 2102–2106.
[22] B. Habibi, M. Jahanbakhshi, M.H. Pournaghi-Azar, Anal. Biochem. 411 (2011) 167–175.
[23] M. Mazloum-Ardakani, H. Beitollah, M.K. Amini, F. Mirkhalaf, M. Abdollahi-Alibeik, Sens. Actuators B 151 (2010) 243–249.
[24] A.H. Dawson, D.A. Henry, J. McEwen, Med. J. Aust. 150 (1989) 329–331.
[25] S. Iijima, Nature 354 (1991) 56–58.
[26] Y. Wang, X. Cao, J. Li, N. Chen, Talanta 84 (2011) 977–982.
[27] H. Beitollahi, H. Karimi-Maleh, H. Khabazzadeh, Anal. Chem. 80 (2008) 9848–9851.
[28] S. Firdoz, F. Ma, X. Yue, Z. Dai, A. Kumar, B. Jiang, Talanta 83 (2010) 269–273.
[29] H. Beitollahi, M. Mazloum Ardakani, B. Ganjipour, H. Naeimi, Biosens. Bioelectron. 24 (2008) 362–368.
[30] A.K. Upadhyay, T.W. Ting, S.M. Chen, Talanta 79 (2009) 38–45.
[31] J.M. Tulliani, A. Cavalieri, S. Musso, E. Sardella, F. Geobaldo, Sens. Actuators B 152 (2011) 144–154.
[32] H. Beitollahi, J.B. Raoof, R. Hosseinzadeh, Electroanalysis (2011), doi:10.1002/elan.201100242.
[33] S. Suresh, A.K. Gupta, V.K. Rao, R. Om kumar, Vijayaraghavan, Talanta 81 (2010) 703–708.
[34] H. Beitollahi, I. Sheikhshoaie, Anal. Methods (2011), doi:10.1039/c1ay05211j.
[35] H. Wan, F. Zhao, W. Wu, B. Zeng, Colloids Surf. B 82 (2011) 427–431.
[36] Y.D. Zhao, W.D. Zhang, H. Chen, Q.M. Luo, Talanta 58 (2002) 529–534.
[37] S.L. Chou, J.Z. Wang, S.Y. Chew, H.K. Liu, S.X. Dou, Electrochem. Commun. 10 (2008) 1724–1727.
[38] J. Zima, I. Švancara, J. Barek, K. Vytřas, Crit. Rev. Anal. Chem. 39 (2009) 204–227.
[39] M. Mazloum-Ardakani, H. Beitollahi, M.K. Amini, B.B.F. Mirjalili, F. Mirkhalaf, J. Electroanal. Chem. 651 (2011) 243–249.
[40] J.B. Raoof, R. Ojani, H. Beitollahi, Electroanalysis 19 (2007) 1822–1830.
[41] J.B. Raoof, R. Ojani, H. Beitollahi, R. Hossienzadeh, Electroanalysis 18 (2006) 1193–1201.
[42] M. Mazloum-Ardakani, H. Beitollahi, M.K. Amini, F. Mirkhalaf, B.B.F. Mirjalili, Ali Akbari, Analyst 136 (2011) 1965–1970.
[43] R. Ojani, J.B. Raoof, S. Zamani, Talanta 81 (2010) 1522–1528.
[44] A.J. Bard, L.R. Faulkner, Electrochemical Methods: Fundamentals and Applications, second ed., Wiley, New York, 2001.
[45] J.A. Harrison, Z.A. Khan, J. Electroanal. Chem. 28 (1970) 131–138.
[46] Z. Galus, Fundamentals of Electrochemical Analysis, Ellis Horwood, New York, 1976.
[47] J.B. Raoof, R. Ojani, F. Chekin, M. Jahanshahi, S. Rashid-Nadimi, Electroanalysis 21 (2009) 2674–2679.
[48] M.H. Pournaghi-Azar, F. Ahour, J. Electroanal. Chem. 622 (2008) 22–28.