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ORIGINAL PAPER

Electrocatalytic oxidation of aspirin and acetaminophen on a cobalt hydroxide nanoparticles modified glassy carbon electrode

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Abstract The electrocatalytic oxidation of aspirin and acetaminophen on nanoparticles of cobalt hydroxide electrodeposited on the surface of a glassy carbon electrode in alkaline solution was investigated. The process of oxidation and the kinetics have been investigated using cyclic voltammetry, chronoamperometry, and steady-state polarization measurements. Voltammetric studies have indicated that in the presence of drugs, the anodic peak current of low valence cobalt species increases, followed by a decrease in the corresponding cathodic current. This indicates that drugs are oxidized on the redox mediator which is immobilized on the electrode surface via an electrocatalytic mechanism. With the use of Laviron's equation, the values of anodic and cathodic electron-transfer coefficients and charge-transfer rate constant for the immobilized redox species were determined as $\alpha_{s,a}=0.72$, $\alpha_{s,c}=0.30$, and $k_s=0.22\ s^{-1}$. The rate constant, the electron transfer coefficient, and the diffusion coefficient involved in the electrocatalytic oxidation of drugs were reported. It was shown that by using the modified electrode, aspirin and acetaminophen can be determined by amperometric technique with detection limits of 1.88×10^{-6} and 1.83×10^{-6} M, respectively. By analyzing the content of acetaminophen and aspirin in bulk forms using chronoamperometric and amperometric techniques, the analytical utility of the modified electrode was achieved. The method was also proven to be valid for analyzing these drugs in urine samples.

Keywords Aspirin · Acetaminophen · Electrocatalysis · Nanoparticles · Cobalt oxide

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Introduction

Aspirin (acetylsalicylic acid, ASA) is arguably the world's oldest and best-known pharmaceutical product with accepted anti-inflammatory, antipyretic, antioxidant, and analgesic properties [1, 2]. It is used in acute conditions such as headaches, arthralgia, myalgia, and other cases requiring mild analgesia. Once ingested, ASA is rapidly hydrolyzed in the body to produce salicylic acid (SA), the compound that is primarily responsible for the pharmacological activity of ASA. Acetaminophen, or paracetamol (*N*-acetyl-*p*-aminophenol), is an antipyretic and minor analgesic drug which practically has no anti-inflammatory action. It is an effective and safe analgesic agent used worldwide for the relief of mild to moderate pain associated with headaches, backaches, arthritis, and postoperative pains. It is also used for reduction of fevers of bacterial or viral origin [3, 4]. Being similar to aspirin in terms of function, acetaminophen is considered a suitable alternative for the patients who are sensitive to aspirin and safe up to therapeutic doses [5]. Unfortunately, owing to its easy accessibility, the use of acetaminophen in suicide attempts and overdoses has been increased. It is known that overdoses will cause serious or fatal liver and kidney damage [6].

Current methods for the analysis of acetaminophen and aspirin include spectrofluorimetry [7, 8], spectrophotometry [9, 10], chromatography [11, 12], and electrochemical approaches [13–15]. However, the development of a

simple, specific, sensitive, and inexpensive method for determination of these drugs is yet highly desirable.

Intensive researches have been directed toward the development of electrocatalyst, aimed at lowering the normally large over-potential and raising the faradaic current encountered in the electrooxidation of materials. In this context, a great deal of attention has recently been centered on the materials that are immobilized onto the electrode surface and capable of mediating fast electron transfer under the effect of external electric field, namely, chemically modified electrodes [15–18].

The application of nano-structured materials has recently attracted a lot of attention in electrochemical researches. Owing to their small size, nanoparticles exhibit unique physicochemical and electronic properties which are not represented by those bulk forms [19]. Electrochemistry can cover the whole range of nanoparticle researches, from nanoparticle preparation to electrochemical sensor application and from band gap determination to photonic cell operation. Many types of nanoparticles including metal, oxide, semiconductor, and composite nanoparticles have often been used in electrochemical studies. Many nano-structured materials, especially metal nanoparticles, represent excellent electronic conductivity and electrocatalytic properties which cause acceleration of electron transfer rate between electrode surface and redox species [20].

Immobilized cobalt ions-based materials, which can, in principle, flip-flop between various valence states under the effect of external electric field on the one hand and the potential reducing agent on the other, are of particular interest in this regard. The preparation, characterization, and electrochemistry of cobalt hydroxide (oxide) containing films have been extensively studied in alkaline medium [21, 22]. Various methods of preparation, ranging from spray pyrolysis [23], sonication [24], sputtering [25] to electrodeposition from aqueous solutions containing complexing agents and at various pH values, have been considered [26–28]. Meanwhile, little attention has been paid to the electrocatalytic activities of cobalt hydroxide (oxide) modified electrodes in the electrooxidation of drugs.

The present study was an attempt at continuing our recent studies on the development and application of the modified electrodes which were aimed at inspecting the kinetics and mechanisms of electrochemical processes [15–18, 27, 29]. The findings of this study show the results of the anodic oxidation of aspirin and acetaminophen on a glassy carbon surface where nanoparticles of catalytically active cobalt hydroxide are deposited. The studies were

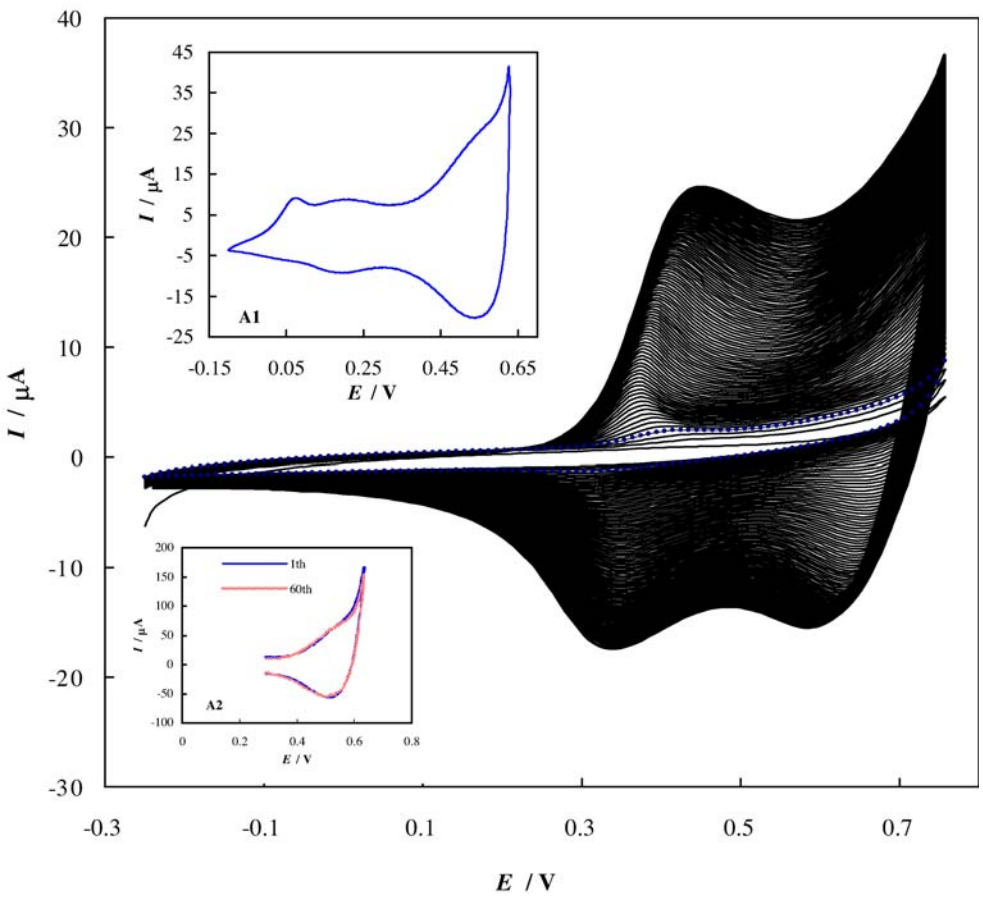


Fig. 1 Cyclic voltammograms for 4 mM $CoCl_2$ + 40 mM KNa tartrate+0.1 M Na_2CO_3 using a glassy carbon electrode. The potential was scanned continuously at 100 mV/s between −250 and 750 mV. *Inset A1*: Cyclic voltammogram of the CHNM-GC electrode in 0.1 M NaOH solution in the range of −100 to 630 mV with a sweep rate of 100 mV/s. *Inset A2*: The first and 60th cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH solution. The data selected from 60 consecutive cyclic voltammograms obtained using the CHNM-GC electrode in 0.1 M NaOH solution

carried out in 0.1 M sodium hydroxide solution. The response of the cobalt hydroxide nanoparticles modified glassy carbon (CHNM-GC) electrode towards acetaminophen and aspirin in bulk forms in 0.1 M sodium hydroxide solution as well as human urine medium was also tested.

Materials and methods

All chemicals used in this work were of analytical reagent grade from Merck. Acetylsalicylic acid was synthesized and further purified by recrystallization in water/ethanol mixture. Acetaminophen was obtained as a gift from Center of Quality Control of Drugs, Tehran, Iran. The standard solutions of acetylsalicylic acid and acetaminophen were prepared by dissolving an accurate mass of the bulk drugs in an appropriate volume of 0.1 M sodium hydroxide solution (which was also used as a supporting electrolyte) and then stored in the dark at 4 °C.

Electrochemical measurements were carried out in a conventional three-electrode cell (from Goldis, Iran) powered by an electrochemical system comprising of AUTOLAB system with PGSTAT30 (Eco Chemic, Utrecht, The Netherlands). The system was run by a PC via the GPES 4.9 software. CV data were recorded in the analogue mode with a fast analogue scan generator (SCANGEN) in combination with a fast AD converter (ADC750). In all voltammetric measurements, the IR drop compensation was performed by positive feedback. An Ag/AgCl, 3 M KCl (from Metrohm) and a platinum disk (from Azar Electrode, Iran) and a glassy carbon (GC) disk electrode (from Azar Electrode) with surface area of 0.0314 cm^2 which was modified were used as reference, counter, and working electrodes, respectively. All studies were carried out at room temperature.

The GC electrode was further polished on a polishing leathern pad with 0.05 μM α-alumina powder and rinsed thoroughly with distilled water followed by placing in HNO_3 1:1 and then ultrasonicated in water/acetone mixture for 3 min before the modification. Films of cobalt hydroxide were formed on the GC surface by the methods previously reported [27, 28]. Briefly, the electrode was placed in the synthesis solution containing 0.1 M Na_2CO_3+ 40 mM NaK tartrate+4 mM $CoCl_2$ at pH=11.6, and the modification was performed under the regime of cyclic voltammetry where 100 consecutive cycles in the range of −250 to −750 mV Ag/AgCl with a potential sweep rate of 100 mV/s were applied. The surface concentration of cobalt hydroxide nanoparticles which is controlled by the number of cycles applied in the deposition process was chemically evaluated in 0.1 M NaOH solution. Working potentials of 620/550 mV for aspirin/acetaminophen were applied for amperometric measurements in which the transient currents were allowed to decay to steady-state values.

Urine samples taken from a healthy person were, at first, filtered with filter papers. Then, these samples were diluted (1:10) with 0.1 M NaOH solution followed by adding an appropriate amount of standard drug solutions. The resulting solution was then directly analyzed based on our

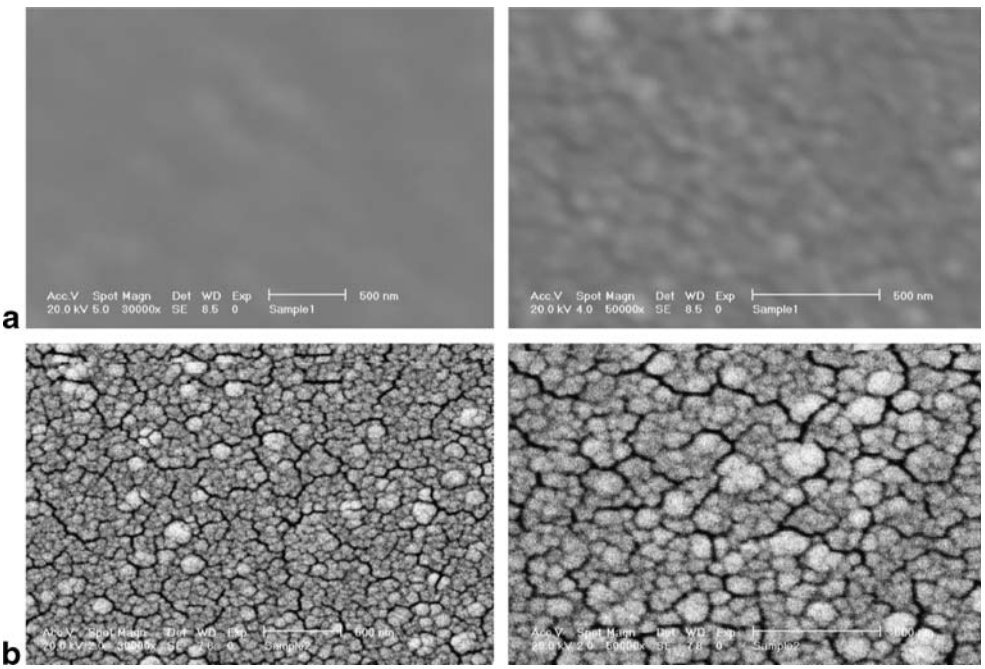
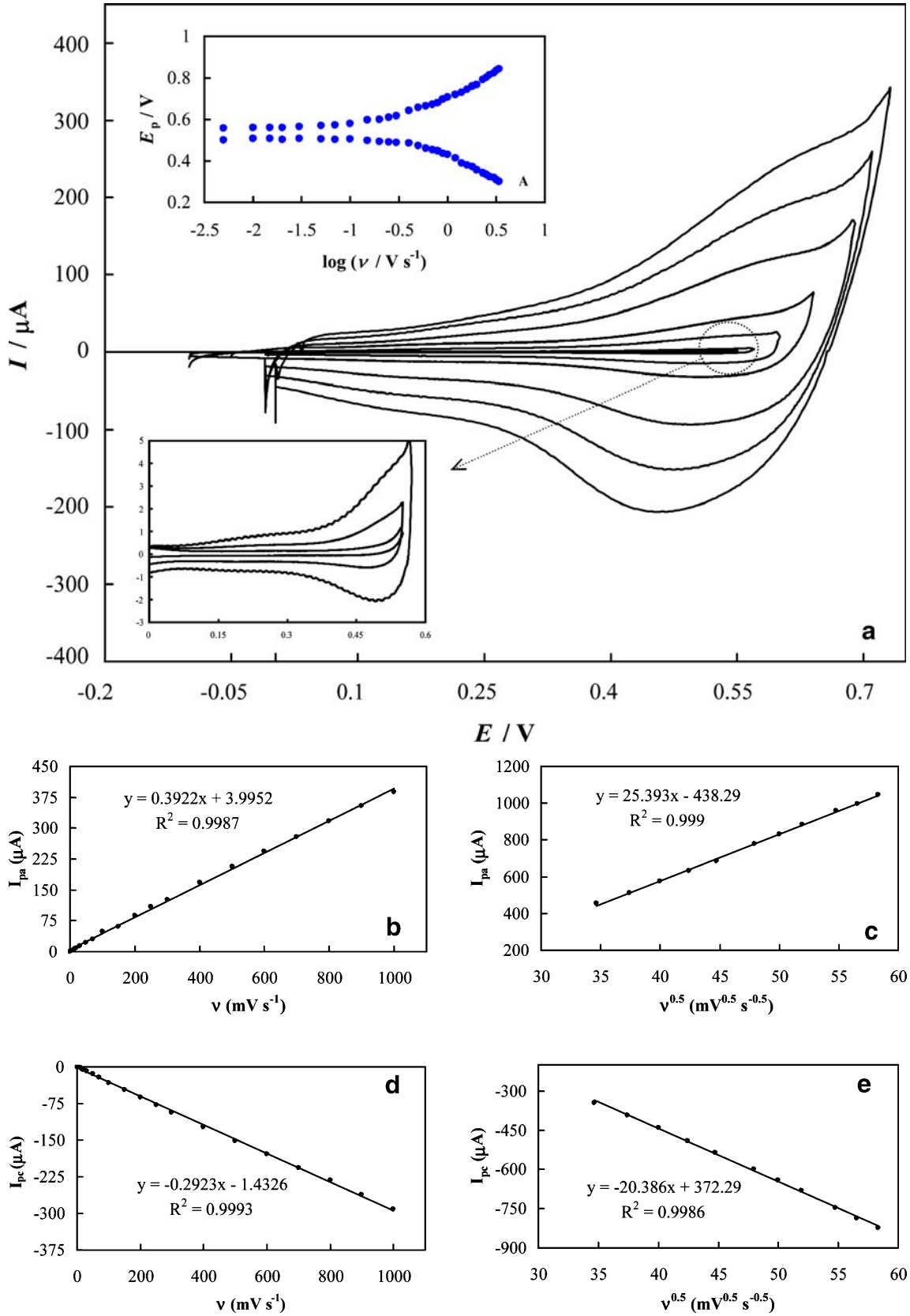


Fig. 2 Scanning electron micrographs of the surface of bare GC electrode (**a**) and the surface of CHNM-GC electrode (**b**)


a
I / μA
E / V
E_p / V
log (ν / V s^-1)
A
b
I_pa (μA)
y = 0.3922x + 3.9952
R^2 = 0.9987
ν (mV s^-1)
c
I_pa (μA)
y = 25.393x - 438.29
R^2 = 0.999
ν^0.5 (mV^0.5 s^-0.5)
d
I_pc (μA)
y = -0.2923x - 1.4326
R^2 = 0.9993
ν (mV s^-1)
e
I_pc (μA)
y = -20.386x + 372.29
R^2 = 0.9986
ν^0.5 (mV^0.5 s^-0.5)

◀ **Fig. 3** **a** Typical cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH solution recorded at various potential sweep rates from inner to the outer of 10, 20, 50, 100, 200, 300, 500 mV/s. *Inset A*: ($E_p - E^{0\prime}$) vs logarithm ν from cyclic voltammograms recorded for CHNM-GC electrode in 0.1 M NaOH at potential sweep rates of 2 to 3,400 mV/s. **b** Dependency of anodic peak current on the potential sweep rate at lower values of 2, 5, 10, 20, 30, 50, 70, 100, 200, 300, 400, 500, 700, 800, 1,000 mV/s. **c** Dependency of anodic peak current on the square root of potential sweep rate at higher values of 1,200, 1,400, 1,600, 1,800, 2,000, 2,300, 2,500, 2,700, 3,000, 3,200, 3,400 mV/s. **d** Dependency of cathodic peak current on the potential sweep rate at lower values of 2, 5, 10, 20, 30, 50, 70, 100, 200, 300, 400, 500, 700, 800, 1,000 mV/s. **e** Dependency of cathodic peak current on the square root of potential sweep rate at higher values of 1,200, 1,400, 1,600, 1,800, 2,000, 2,300, 2,500, 2,700, 3,000, 3,200, 3,400 mV/s

proposed procedure and without any pretreatment or extraction steps.

Results and discussion

The electrodeposition of cobalt oxide nanoparticles from Co(II)–tartrate complex in carbonate solution as consecutive cyclic voltammograms is shown in Fig. 1. As can be seen, the current grew during cycling, which indicates a continuous deposition of the conducting oxide layer. After 80–100 potential scans, a uniform bluish deposit appeared on the glassy carbon electrode. Inset A1 in Fig. 1 shows a cyclic voltammogram of CHNM-GC electrode in 0.1 M NaOH solution in the range of −100 to 630 mV recorded at a potential sweep rate of 100 mV/s. The voltammogram is similar to those reported in the literature [27, 28]. It consists of anodic peaks located at 200 and 565 mV which are attributed to Co(II)/Co(III) and Co(III)/Co(IV) redox transition associated with different cobalt oxide species on the electrode surface [22]. The anodic peak at around 70 mV is properly due to the adsorption of oxygen-containing species, H_2O, OH^- [30]. The cathodic peaks at 190 and 540 mV correspond to the reduction of the various cobalt oxide species formed during the positive sweep. To evaluate the stability of CHNM-GC electrode in the solution, consecutive cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH solution were recorded, and inset A2 in Fig. 1 shows the first and 60th cyclic voltammograms of CHNM-GC electrode. The peak current related to Co(III)/Co(IV) transition in 60th voltammogram changes only slightly upon potential cycling (≤5%). This indicates that the modified electrode is stable in the solution.

To investigate the surface morphology of the cobalt hydroxide film formed on the GC surface, it was examined by scanning electron microscopy. Figure 2 shows the scanning electron micrographs of the surface of the bare GC electrode (a) and the surface of CHNM-GC electrode (b) with different magnifications. The GC electrode surface has a smooth morphology, while relatively uniform spherical nanoparticles of cobalt hydroxide which have an average size of 100 nm are deposited on the GC surface.

Figure 3a represents typical cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH solution recorded at different potential sweep rates in a wide range of 2 to 3,400 mV/s. The peak to peak potential separation in the potential sweep rate of 10 mV/s is 40 mV, which is deviated from the theoretical value of zero and increases at higher potential sweep rates. This indicates a limitation in the charge transfer kinetics arising from the chemical interaction between the electrolyte ions and the modifier film, the lateral interaction of the immobilized redox couples present on the surface, dominated electrostatics factors, coupled diffusion–migration processes in the bulk of film, and/or the presence of non-equivalent sites in the film.

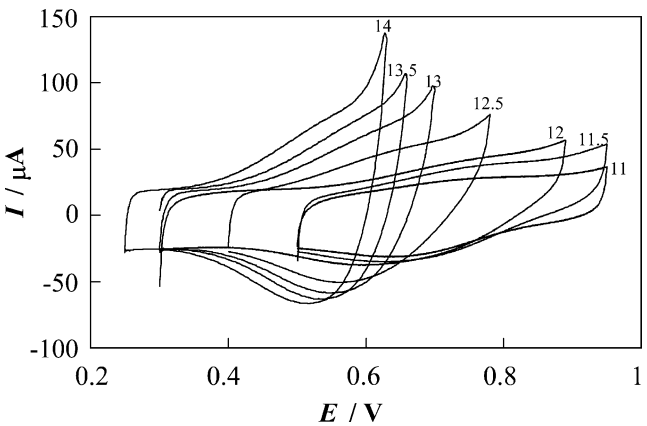


Fig. 4 Cyclic voltammograms of CHNM-GC electrode in the potential range of Co(III)/Co(IV) transition recorded at different pH of 11, 11.5, 12, 12.5, 13, 13.5, and 14

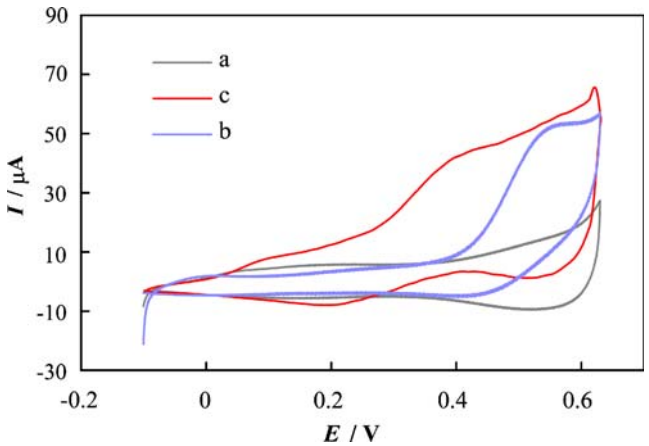
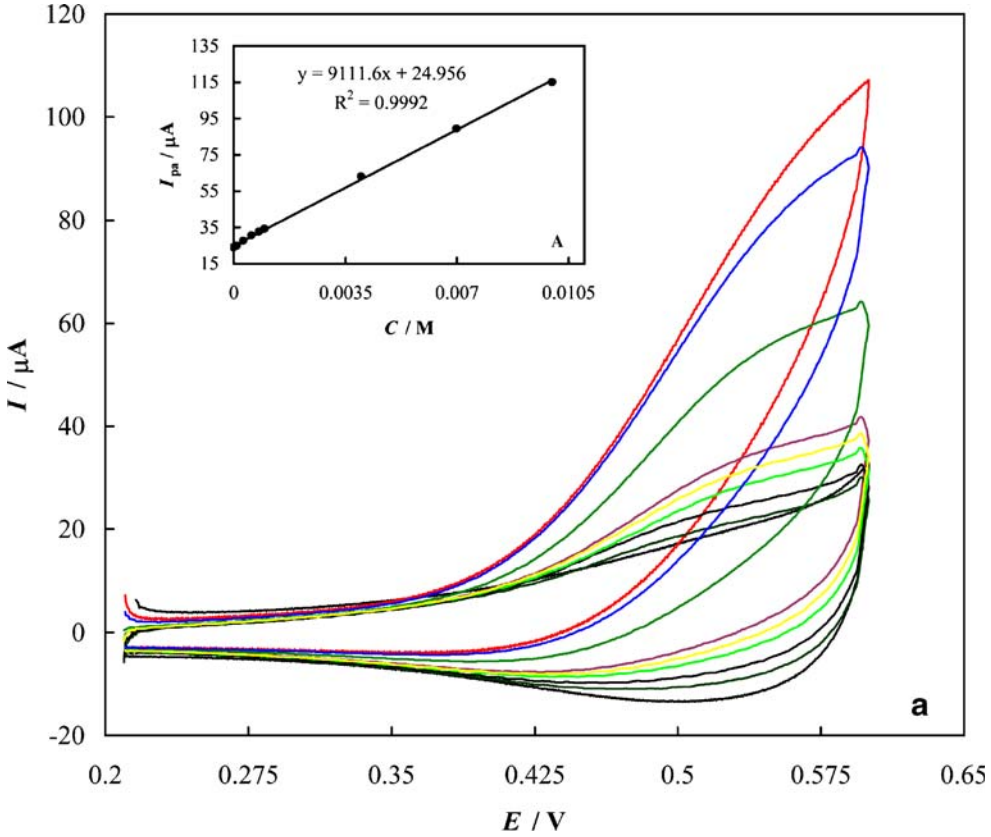
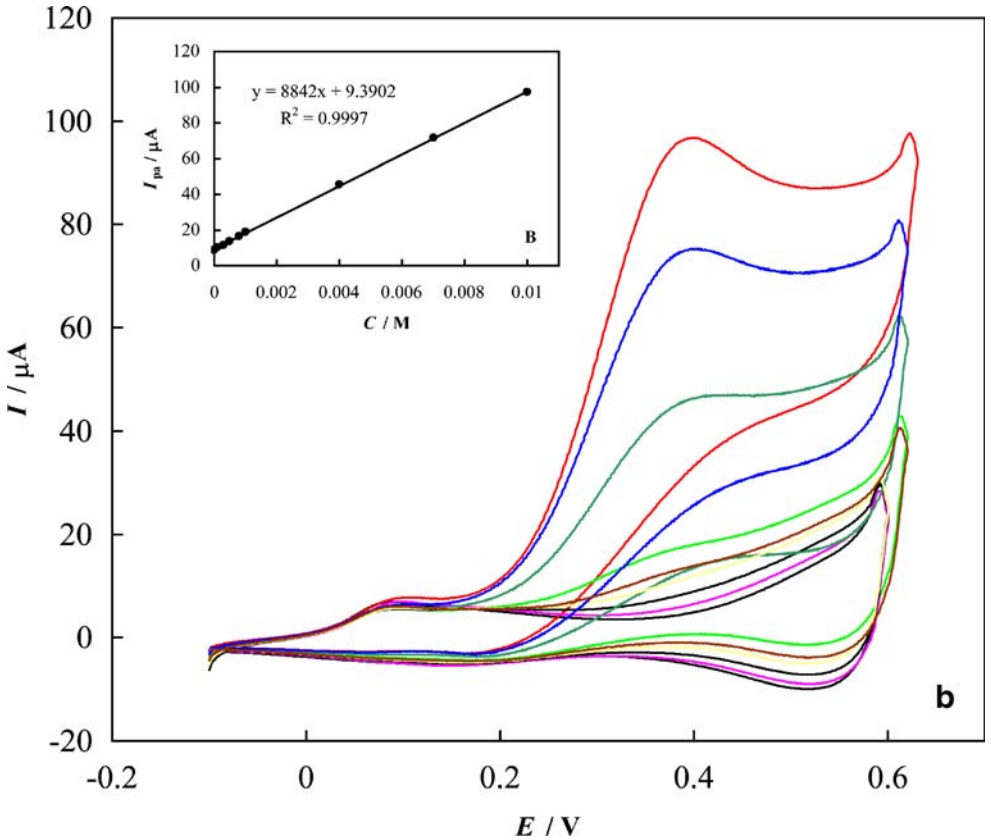


Fig. 5 Cyclic voltammograms of the CHNM-GC electrode in 0.1 M NaOH solution in the absence of drugs (**a**) and the presence of 10^{-3} M aspirin (**b**) and the presence of 5×10^{-4} M acetaminophen (**c**) in the solution. Potential sweep rate was 50 mV/s


y = 9111.6x + 24.956
R² = 0.9992
I_pa / μA
C / M
A
I / μA
E / V
a


y = 8842x + 9.3902
R² = 0.9997
I_pa / μA
C / M
B
I / μA
E / V
b

◀ **Fig. 6** **a** Cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH in the absence and presence of different concentrations of aspirin: 0, 10^{-4}, 3×10^{-4}, 5×10^{-4}, 8×10^{-4}, 1×10^{-3}, 4×10^{-3}, 7×10^{-3}, and 10^{-2} M. *Inset A*: Dependency of the anodic peak current on aspirin concentration. **b** Cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH in the absence and presence of different concentrations of acetaminophen: 0, 10^{-4}, 3×10^{-4}, 5×10^{-4}, 8×10^{-4}, 1×10^{-3}, 4×10^{-3}, 7×10^{-3}, and 10^{-2} M. *Inset B*: Dependency of the anodic peak current on acetaminophen concentration

Laviron [31] derived a general expression for the linear potential sweep voltammetric response in the case of surface-confined electroreactive species at small concentration. The expression for peak-to-peak separation (ΔE_p)> 200/n mV where n is the number of exchanged electrons is as follows:

$$E_{pa} = E^{0\prime} + \mathrm{T}\ \ln\left[(1-\alpha_s)/u\right] \quad (1)$$

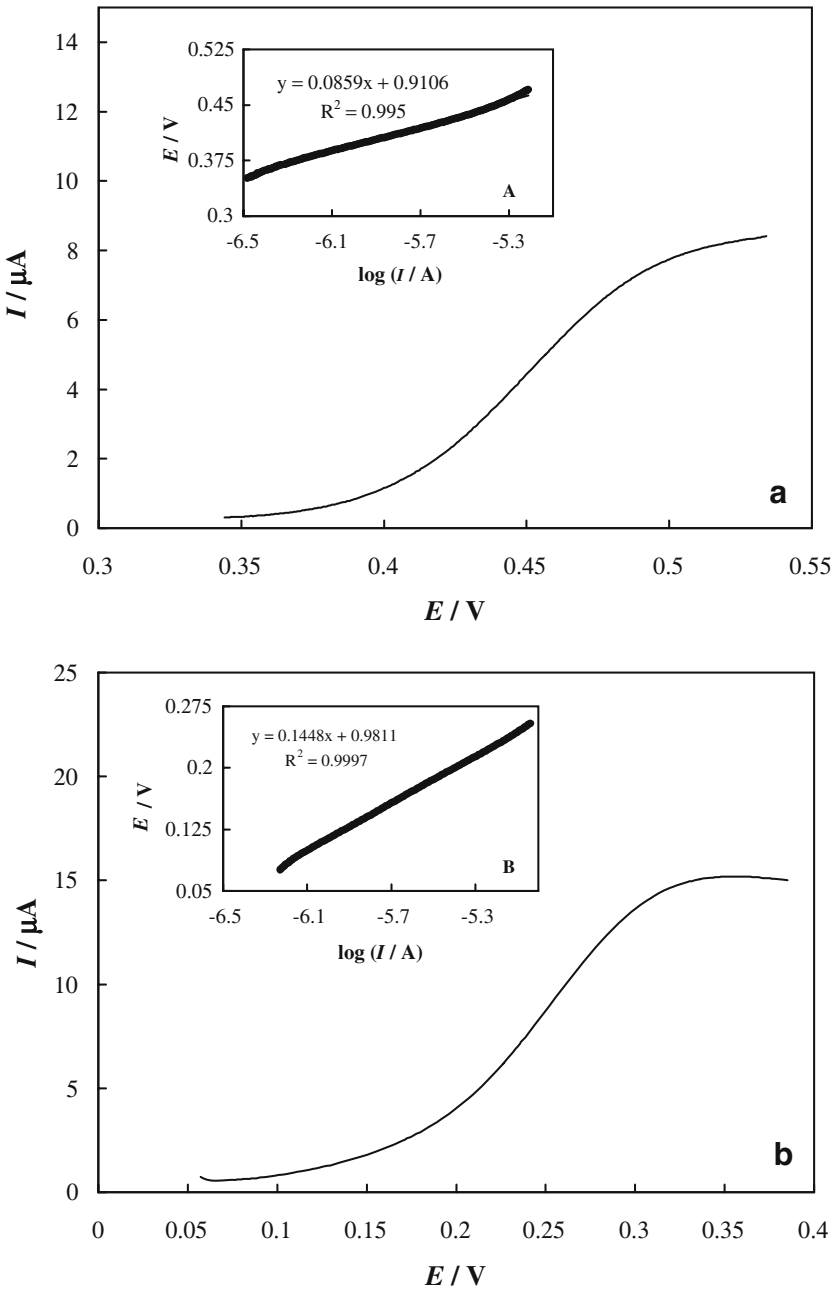
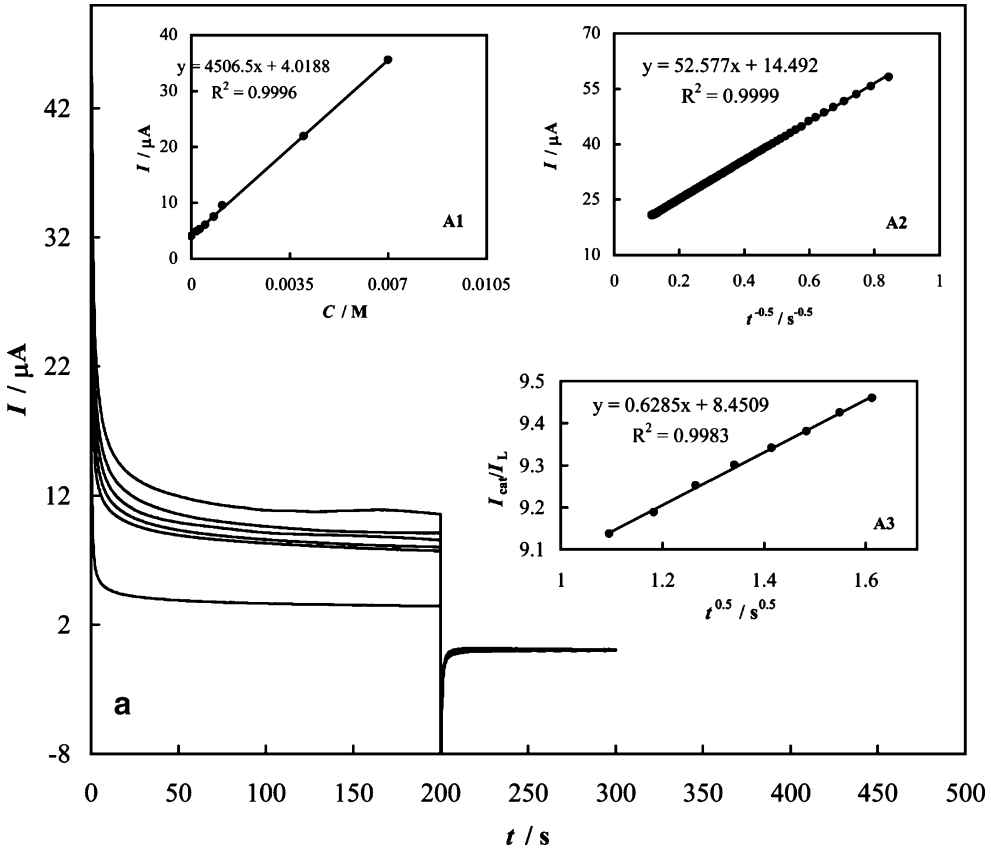


Fig. 7 **a** Potentiodynamic polarization curve for CHNM-GC electrode in 0.1 M NaOH in the presence of 10^{-3} M aspirin recorded using a potential sweep rate of 0.005 mV/s. *Inset A*: The corresponding Tafel plot. **b** Potentiodynamic polarization curve for CHNM-GC electrode in 0.1 M NaOH in the presence of 4×10^{-3} M acetaminophen recorded using a potential sweep rate of 0.005 mV/s. *Inset B*: The corresponding Tafel plot


y = 4506.5x + 4.0188
R² = 0.9996
I / μA
C / M
A1
y = 52.577x + 14.492
R² = 0.9999
I / μA
t^-0.5 / s^-0.5
A2
y = 0.6285x + 8.4509
R² = 0.9983
I_cat/I_L
t^0.5 / s^0.5
A3
I / μA
t / s
a

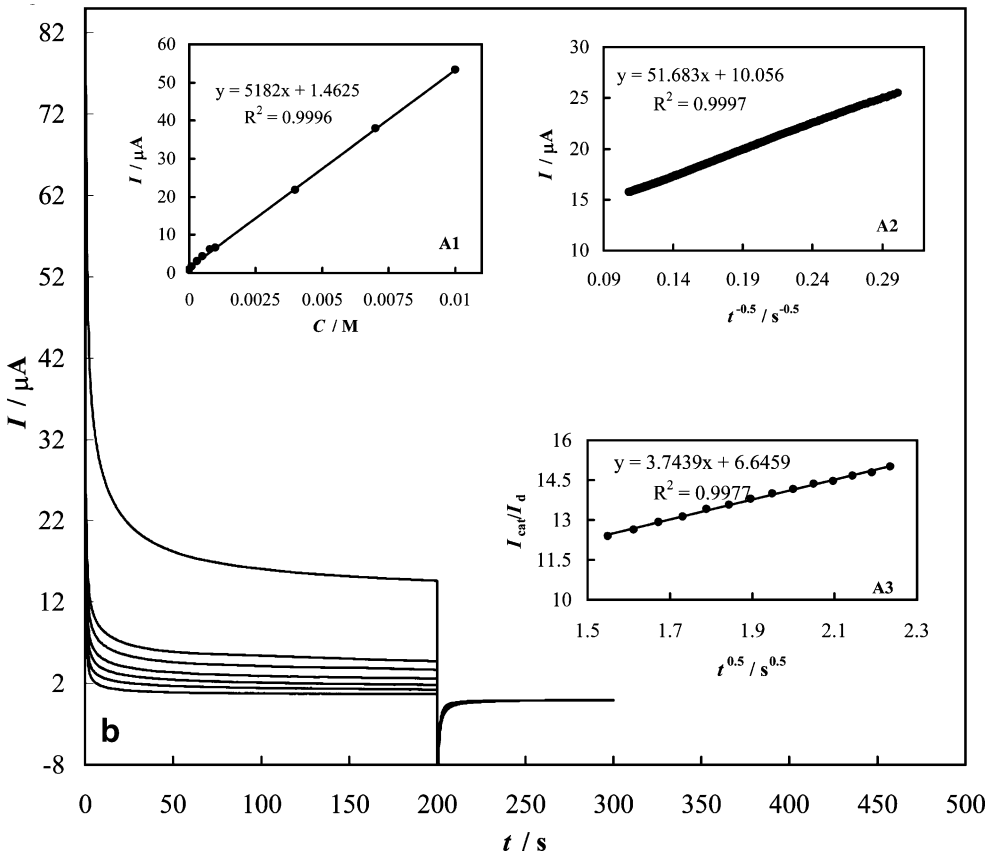

y = 5182x + 1.4625
R² = 0.9996
I / μA
C / M
A1
y = 51.683x + 10.056
R² = 0.9997
I / μA
t^-0.5 / s^-0.5
A2
y = 3.7439x + 6.6459
R² = 0.9977
I_cat/I_d
t^0.5 / s^0.5
A3
I / μA
t / s
b

Fig. 8 **a** Double-step chronoamperograms of CHNM-GC electrode in 0.1 M NaOH solution with different concentrations of aspirin: 0, 10^{-4}, 3×10^{-4}, 5×10^{-4}, 8×10^{-4}, and 10^{-3} M. *Inset A1*: Dependency of sampled current at fixed time of 15 s to the concentration of aspirin. *Inset A2*: Dependency of transient current on $t^{-0.5}$. *Inset A3*: Dependency of I_{cat}/I_d on $t^{0.5}$ derived from the data of chronoamperograms related to concentrations of 0 and 3×10^{-3} M. **b** Double-step chronoamperograms of CHNM-GC electrode in 0.1 M NaOH solution with different concentrations of acetaminophen: 0, 10^{-4}, 3×10^{-4}, 5×10^{-4}, 8×10^{-4}, 10^{-3}, and 4×10^{-3} M. *Inset A1*: Dependency of sampled current at fixed time of 15 s to the concentration of acetaminophen. *Inset A2*: Dependency of transient current on $t^{-0.5}$. *Inset A3*: Dependency of I_{cat}/I_d on $t^{0.5}$ derived from the data of chronoamperograms related to concentrations of 0 and 4×10^{-3} M

$$E_{pc} = E^{0\prime} + S\ \ln\left[\alpha_s/u\right] \tag{2}$$

$$\ln k_s = \alpha_s\ \ln(1-\alpha_s) + (1-\alpha_s)\ \ln\ \alpha_s - \ln\left(RT/nF\nu\right) - \alpha_s(1-\alpha_s)\,nF\Delta E_p/RT \tag{3}$$

where T=RT/(1−α) nF, S=RT/αnF, u=(RT/F) (k_s/nν), E_{pa} and E_{pc} are the anodic and cathodic peak potentials, respectively, and α_s, k_s, and ν are the electron-transfer coefficient, apparent charge-transfer rate, constant and potential sweep rate, respectively. From these expressions, α_s can be determined by measuring the variation of the peak potential with respect to the potential sweep rate, and k_s can be determined for electron transfer between the electrode and the surface deposited layer by measuring the ΔE_p values. The inset of Fig. 3a shows the plot of (E_p−$E^{0\prime}$) with respect to the logarithm ν from cyclic voltammograms recorded for CHNM-GC electrode in 0.1 M NaOH solution at potential sweep rates of 2–3,400 mV/s for anodic and cathodic peaks. It can be observed that for potential sweep rate of 800 to 3,400 mV/s, the values of (E_p−$E^{0\prime}$) were proportional to the logarithm of the potential sweep rate indicated by Laviron. With the use of the plot and Eqs. 1 and 3, the value of $\alpha_{s,a}$ (anodic electron-transfer coefficient) was determined as 0.72. In addition, with the use of the inset of Fig. 3a and Eqs. 2 and 3, the value of $\alpha_{s,c}$ (cathodic electron-transfer coefficient) was determined as 0.30. These discrepancies suggest that the rate-limiting steps for the reduction and oxidation processes might not be the same [32]. Moreover, the mean value of k_s was determined as 0.22 s^{-1}.

Another point in the voltammograms represented in Fig. 3a is that the anodic and cathodic peak currents are proportional to the sweep rate at low values 2–1,000 mV/s (Fig. 3b and d). This points out an electrochemical activity of the surface redox transition. From the slope of this line and with the use of [33]:

$$I_p = \left(n^2F^2/4RT\right)\nu A\Gamma^* \tag{4}$$

where A is the electrode surface area, Γ* is the surface coverage of the redox species, and I_p is the peak current, and also taking the average of both cathodic and anodic currents, the total surface coverage of the electrode with the modified film of cobalt 3.36×10^{-9} mol cm^{-2} has been derived. In the high range of sweep rates (1,200–3,400 mV/s, Fig. 3c and e), this dependency is of square root form, signifying the dominance of a diffusion process as the rate limiting step in the total redox transition of the modifier film. This diffusion process, which also occurs during the redox processes of other transition metal oxides [15–17], is attributed to the charge neutralization and ion exchange between two ionic conductors of modifier film and the adjacent solution.

The effect of pH on the electrochemical behavior of CHNM-GC electrode was investigated. Figure 4 represents cyclic voltammograms of CHNM-GC electrode in the potential range of active cobalt moiety recorded at different pH of the solution. As pH decreases, the peak potential related to Co(III)/Co(IV) transition shifts positively, and the corresponding peak current decreases. This indicates that proton is involved in the immobilized redox species and also that the cobalt oxide nanoparticles are stable only in highly alkaline solutions.

Figure 5 shows cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH solution in the absence (a) and presence of 10^{-3} M aspirin (b) and 5×10^{-4} M acetaminophen (c) in the potential range of −100 to 630 mV at a potential sweep rate of 100 mV/s. At CHNM-GC electrode, oxidation of aspirin/acetaminophen gave rise to a typical electrocatalytic response. The anodic peak current related to Co(III) species greatly increases with respect to that observed for the modified surface in the absence of aspirin/acetaminophen, and it follows by a decrease in the corresponding cathodic current upon addition of drugs in the solution. In the presence of 10^{-3} M aspirin/acetaminophen with the potential sweep rate of 50 mV/s, the anodic charge associated with the anodic peak is quantitatively 81.6/95.7% of that of the corresponding cathodic peak, while in the absence of aspirin/acetaminophen, this ratio is 34.3/22.9%. This indicates that aspirin/acetaminophen is oxidized by active cobalt (IV) moiety via cyclic mediation redox processes. Cobalt species are immobilized on the electrode surface, and the one with higher valence (Co(IV) species) oxidizes aspirin/acetaminophen via a chemical

Table 1 The electrocatalytic reaction rate constants (k') and the diffusion coefficients (D) obtained from chronoamperometry and the electron transfer coefficients (α) obtained from Tafel plots for the electrocatalytic oxidation of aspirin and acetaminophen on CHM/GC electrode

Drug	k' ($cm^3\ mol^{-1}\ s^{-1}$)	D ($cm^2\ s^{-1}$)	α
Aspirin	4.21×10^4	5.91×10^{-5}	0.69
Acetaminophen	1.12×10^6	5.17×10^{-5}	0.41

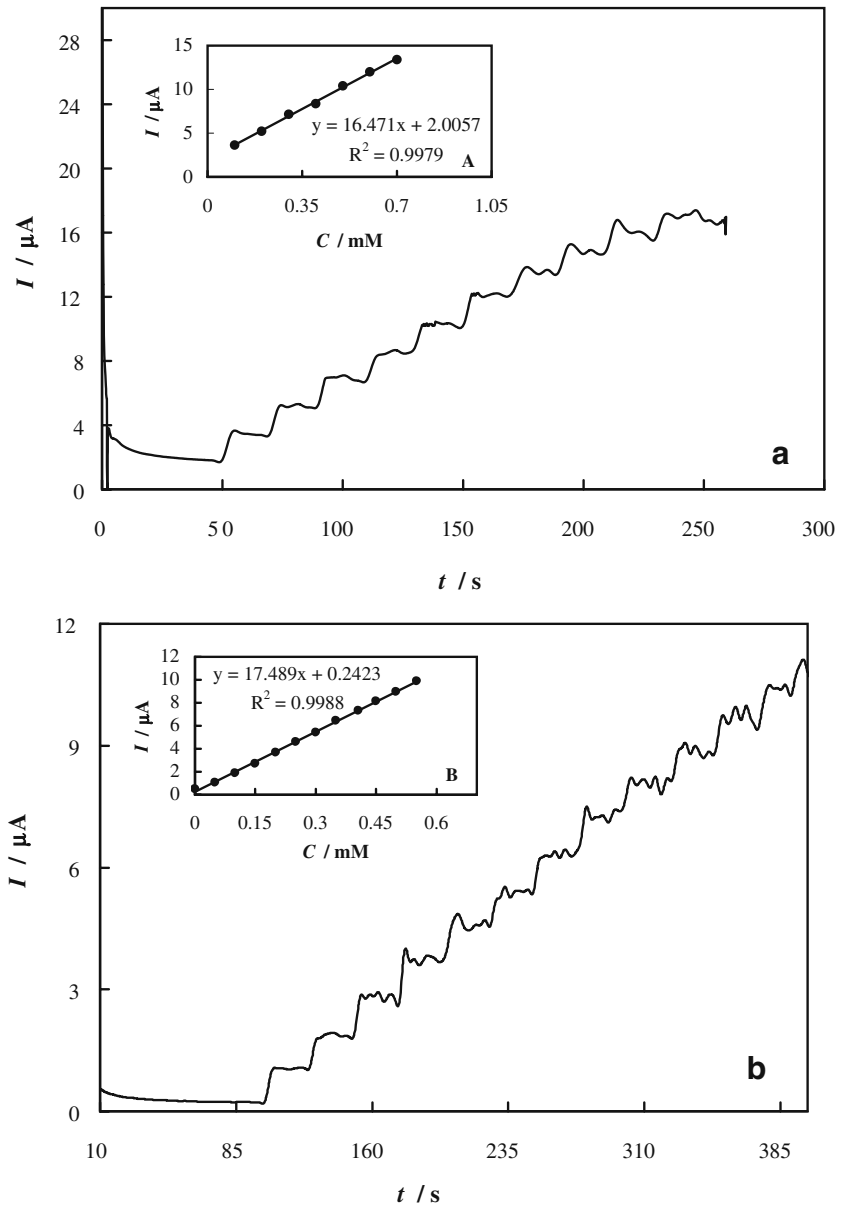


Fig. 9 **a** Amperograms obtained for CHNM-GC electrode during the successive addition of 100 μM aspirin into 0.1 M NaOH at an applied potential of 620 mV. *Inset A*: Variation of measured net current after addition of each increment of aspirin as a function of its concentration. **b** Amperograms obtained for CHNM-GC electrode during the successive addition of 50 μM acetaminophen into 0.1 M NaOH at an applied potential of 540 mV. *Inset B*: Variation of measured net current after addition of each increment of acetaminophen as a function of its concentration

reaction followed by the generation of low-valence cobalt [Co(III) species]. Along this line, the high-valence oxide is regenerated through the external electrical circuit. Accordingly, aspirin/acetaminophen is oxidized via an EC′ mechanism. Figure 5 also indicates that the onset potential of oxidation of Co(III) oxide decreases in the presence of aspirin/acetaminophen, suggesting the facilitation of oxidation of Co(III) oxide by drugs. Another point in Fig. 5 is that in the presence of acetaminophen, the anodic current related to the oxidation of Co(II) species is also increased. This indicates that acetaminophen is also oxidized via Co (III) as an active moiety via an EC′ mechanism, i.e., both Co(III) and Co(IV) species can oxidize acetaminophen electrocatalytically. We have chosen the anodic peak current generated due to chemical reaction between Co (IV) and acetaminophen for further investigation due to higher magnitude and higher sensitivity.

Figure 6a and b shows cyclic voltammograms of CHNM-GC electrode in 0.1 M NaOH solution in the presence of different concentrations of aspirin/acetaminophen. The anodic peak current associated with the oxidation of low valence cobalt species is proportional to the bulk

concentration of aspirin/acetaminophen, and any increase in the concentration of aspirin/acetaminophen causes an almost proportional linear enhancement of the anodic peak currents (Fig. 6, insets).

On the basis of the reported results, the following mechanism can be proposed for the mediated oxidation processes. The redox transition of cobalt species:

$$\mathrm{Co(III)} \rightleftarrows \mathrm{Co(IV)} + \mathrm{e} \quad (5)$$

is followed by the oxidation of drugs:

$$\mathrm{Co(IV)} + \mathrm{drug} \rightarrow \mathrm{product} + \mathrm{Co(III)} \quad (6)$$

The oxidation products can be 3,6-dioxocyclohexa-1,4-dienecarboxylate or 5,6-dioxocyclohexa-1,3-dienecarboxylate for aspirin and *N*-acetyl-*p*-quinoneimine for acetaminophen [15, 34–36].

Figure 7a and b indicates pseudo-steady-state current–potential curves recorded for the electrocatalytic oxidation of aspirin and acetaminophen, respectively. Typical S-shape plots have been obtained, and the electron transfer coefficient (α) can be found by plotting E vs log I as α= 0.69 and 0.41 for electrooxidation of aspirin and acetaminophen, respectively.

Double-step chronoamperograms were recorded by setting the working electrode potentials to desired values and used to measure the catalytic rate constant on the modified surface. Figure 8a and b shows double-step chronoamperograms for the modified electrode in the absence and presence of different concentrations of aspirin/acetaminophen. The applied potential steps were 620 and 280 mV for aspirin and 540 and 30 mV for acetaminophen, respectively. The current is negligible when the potential is stepped down to 280/30 mV, indicating that the electrocatalytic oxidation processes are irreversible. Figure 8a and b, insets A1, show the plots of sampled current at a fixed time interval of 15 s with respect to the concentration of aspirin in the range of 10^{-4} to 7×10^{-3} M and acetaminophen in the range of 10^{-4} to 10^{-2} M. Good linear dependencies have been observed, and limits of detection (LOD) of 3.92×10^{-5} M/3.30×10^{-5} M for aspirin/acetaminophen and limits of quantitation (LOQ) of 1.30×10^{-4} M/1.13×10^{-4} M for aspirin/acetaminophen have been obtained. These values were calculated according to the 3 SD/m and 10 SD/m criterions for LOD and LOQ, respectively where SD is the standard deviation of the intercept, and m is the slope of the calibration curves [37]. Plotting of net currents with respect of the minus square roots of time, present linear dependencies (Fig. 8a and b, insets A2). Therefore, a diffusion-controlled process is dominated during the electrocatalytic oxidation of both drugs. By using the slope of these lines, the diffusion coefficients of aspirin/acetaminophen can be obtained according to Cottrell equation [38]:

$$I = \mathrm{nF}AD^{1/2}C\pi^{-1/2}t^{-1/2} \quad (7)$$

where D is diffusion coefficient and C^* is the bulk concentration of the electroreactive species. The mean values of the diffusion coefficients were found to be 5.91×10^{-5} cm^2 s^{-1}/5.71×10^{-5} cm^2 s^{-1} for aspirin/acetaminophen. The value of diffusion coefficient obtained for acetaminophen is comparable with that reported in the literature [39].

Chronoamperometry can also be used for the evaluation of the catalytic rate constant according to [40]:

$$I_{\mathrm{cat}}/I_L = \gamma^{1/2}\left[\pi^{1/2}\mathrm{erf}\left(\gamma^{1/2}\right) + \exp(-\gamma)/\gamma^{1/2}\right] \quad (8)$$

where I_{cat} and I_{L} are the currents in the presence and absence of drug and $\gamma = k'Ct$ is the argument of the error function. k' is the catalytic rate constant and t is the elapsed time. In the case where γ>1.5, erf($\gamma^{1/2}$) is almost equal to unity, and the above equation can be reduced to:

$$I_{\mathrm{cat}}/I_{\mathrm{L}} = \gamma^{1/2}\pi^{1/2} = \pi^{1/2}(k'Ct)^{1/2} \quad (9)$$

From the slope of the $I_{\mathrm{cat}}/I_{\mathrm{L}}$ vs $t^{1/2}$ plot, presented in Fig. 8a and b, insets A3, the mean values of k' for aspirin/acetaminophen were obtained as 4.22×10^4 cm^3 mol^{-1} s^{-1}/1.12×10^6 cm^3 mol^{-1} s^{-1}. All of the kinetic parameters obtained in this study are summarized in Table 1.

Table 2 The determined parameters for calibration curves of aspirin/acetaminophen and accuracy and precision (n=3) for electrocatalytic oxidation of drugs on CHNM-GC electrode

	Chronoamperometry		Amperometry in 0.1 M NaOH		Amperometry in urine	
	Aspirin	Acetaminophen	Aspirin	Acetaminophen	Aspirin	Acetaminophen
LOD (M)	3.92×10^{-5}	3.30×10^{-5}	1.88×10^{-6}	1.83×10^{-6}	1.92×10^{-4}	1.83×10^{-5}
LOQ (M)	1.30×10^{-4}	1.13×10^{-4}	6.28×10^{-6}	6.09×10^{-6}	6.42×10^{-4}	6.11×10^{-5}
Linear range (μM)	100–7,000	100–10,000	100–700	50–550	250–2,250	100–1,500
Slope (AM^{-1})	0.0045	0.0052	0.0165	0.0175	0.0019	0.0209
Intercept (M)	4.30×10^{-6}	1.46×10^{-6}	2.01×10^{-6}	2.41×10^{-7}	2.44×10^{-6}	1.02×10^{-5}
RSD%	2.40	1.70	1.99	3.08	2.64	5.19

Typical amperometric signals using CHNM-GC electrode obtained during successive increments of aspirin/acetaminophen into 0.1 M NaOH in Fig. 9a and b. Gentle stirring for a few seconds was needed to promote solution homogenization after each injection. The electrode response is quite rapid and proportional to the drug concentrations. In addition, the calibration graphs for 0.1 M NaOH are depicted in the insets of Fig. 9a and b. Similar amperograms were also recorded and obtained during successive increments of aspirin/acetaminophen into urinary samples (data not shown). The LOD and LOQ of this procedure were calculated for aspirin/acetaminophen analysis in both 0.1 M NaOH as well as in urinary samples according to the method mentioned above and reported in Table 2.

Conclusion

A cobalt hydroxide nanoparticle modified glassy carbon electrode was checked for electrooxidation of aspirin and acetaminophen in alkaline media. The electrode showed electrocatalytic oxidation of these drugs. Chronoamperometric works showed a large anodic current at the oxidation potential of low-valence cobalt hydroxide in further support of the mediated electrooxidation. With the use of cyclic voltammetry and chronoamperometry techniques, the kinetic parameters of these drugs, such as charge-transfer coefficient, catalytic reaction rate constant, and diffusion coefficient for oxidation, were determined. An amperometric procedure was successfully applied for quantification of these drugs in the bulk form and to the assay of aspirin and acetaminophen in human urine samples.

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