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Amperometric Detection of Caffeine and Paracetamol on A Dual Screen Printed Electrode Modified with Mixed-Valence Ruthenium and Cobalt Oxides in Flow-Injection Analysis.

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ABSTRACT

It is found that the mixed-valence ruthenium and cobalt oxides (CoO_x-RuO_x) composite electrodeposited on screen printed electrode exhibits catalytic activity during caffeine and paracetamol electrooxidation. These compounds are oxidized at different potentials which provides selective voltammetric determination at simultaneous presence. A method of amperometric determination of caffeine and paracetamol on a dual electrode modified with CoO_x-RuO_x composite in a flow injection analysis is developed. The linear relationship between an analytical signal and analyte concentration is found in the range from 5×10^{-7} mol/l to 5×10^{-3} mol/l. Using a modified dual screen printed electrode as an amperometric detector in flow injection analysis allows to determine up to 360 samples/hour. The developed method has been tested in the analysis of some pharmaceuticals.

Keywords: chemically modified electrodes, modified dual screen printed electrode, mixed-valence ruthenium and cobalt oxides, caffeine and paracetamol electrooxidation, flow injection analysis of pharmaceuticals.

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INTRODUCTION

The combined caffeine (CF) and paracetamol (PC) based analgesics are non-narcotic drugs and widely distributed in the pharmacy network. This growth of marketed drugs, observed in recent years supposed a need to introduce more advanced analysis and to develop the methods for appropriate drugs quality assessment techniques provided simplicity, accuracy, sensitivity, selectivity and rapidity of analysis.

The most common methods for the determination of CF and PC presented in literature are chromatographic [1], spectral [2-5] and electrochemical [6-13]. However, the chromatographic methods have a number of limitations related to need for sample preparation, the duration of analysis as well as the high cost of equipment. The disadvantages of spectral methods consist of a lack of sensitivity and complexity of multicomponent analysis. Among the electrochemical method, the voltammetry has several advantages which provide a high sensitivity, rapidity, low cost of the used equipment as well as its operational simplicity.

On the carbon electrodes, CF and PC can not be determined at their simultaneous presence because the compounds are oxidized with overvoltage at the more positive potentials. In order to eliminate this drawback, chemically modified electrodes (CMEs) are usually used. They can increase the sensitivity and selectivity of detecting biologically active compounds [14, 15]. Thus, various materials are applied as modifiers to determine CF and PC; they include polymer films [6-8], metal oxides [9], graphene [10], carbon nanotubes [11-13, 16-17] and other carbon materials. The catalytic properties of modifiers help to reduce the overvoltage of CF and PC oxidation and to increase the sensitivity, and in some cases, the selectivity of their determination. For example, application of a carbon-paste electrode modified with multilayer carbon nanotubes [17] or poly-1.5-diaminonaphthalene [8] allows increasing the selectivity of CF and PC voltammetric determination.

This work is devoted to the study of electrocatalytic properties of the mixed-valence ruthenium and cobalt oxides (CoO_x-RuO_x) composite electrodeposited on screen printed electrode (SPE) or a dual screen printed electrode (DSPE) during electrooxidation of CF and PC for the development of sensitive, selective and express method of amperometric detection of these compounds in flow injection analysis (FIA).

EXPERIMENTAL PART

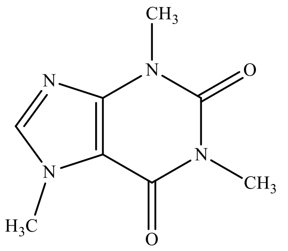
The cyclic voltammograms were recorded using a μSTAT400 bipotentiostat by DropSens (Spain) with a 10 mL electrochemical cell containing PE or DPE produced by DropSens (Spain). The working and auxiliary electrodes were made from a carbon paste and the reference electrode - from a silver paste. The planar electrode sizes were 33×10×0.5 mm. The composite based on the cobalt and ruthenium oxides was used as a modifier. The cyclic voltammogram curves were recorded at a potential sweep rate (v) 20-100 mV/s.

The surface of the working SPE or DSPE was modified by electrolysis. The composite RuO_x-CoO_x was formed on the electrode surface step by step using firstly potentiodynamic electrodeposition of the RuO_x oxide layer and then potentiostatic electrodeposition of CoO_x oxide layer. The electrodeposition was carried out in solutions containing a chemically pure $RuCl_3$ by Aldrich and a chemically pure $CoCl_2$ by Acros Organics with a background of 0.1 M solution of KNO_3. Solutions of these compounds were prepared by dissolving accurately weighed substances.

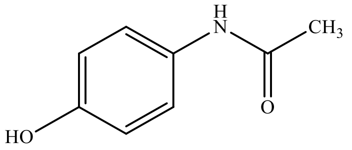
FIA was conducted with PERIMAX 12 peristaltic pump (Germany), injector, mixer, electrochemical flow cell and a recording device - μSTAT400 bipotentiostat by DropSens combined with a personal computer. An analyte was detected in a wall-jet electrochemical flow cell with SPE or DSPE. The cell volume was 8 μl.

When using a thin layer flow cell, the nominal values of the flow rate varied from 0.65 till 4.74 ml/min. The supporting electrolyte supply, transportation of a liquid mixture were carried out through the tubes of a constant internal diameter of 1.4 mm.

The chemically pure CF and PC by Aldrich with the following structures were used as analytes:



Caffeine
(1,3,7-trimethyl-1H-purine-2,6(3H, 7H) -dione)

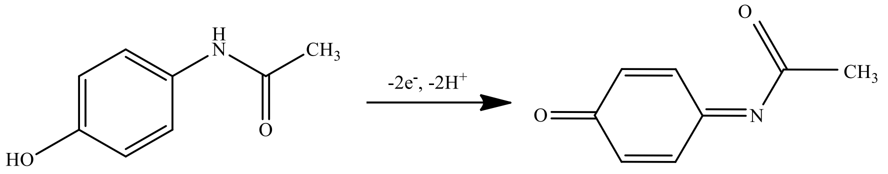


Paracetamol
(N-(4-hydroxyphenyl)acetamide)

The CF and PC solutions were prepared by accurately weighed portions of reagents. Solutions of lower concentrations were obtained by diluting the initial solution directly before measurements. A phosphate buffer solution with pH 6.9 was used as a supporting electrolyte in stationary mode conditions and as a carrier flow in flow systems.

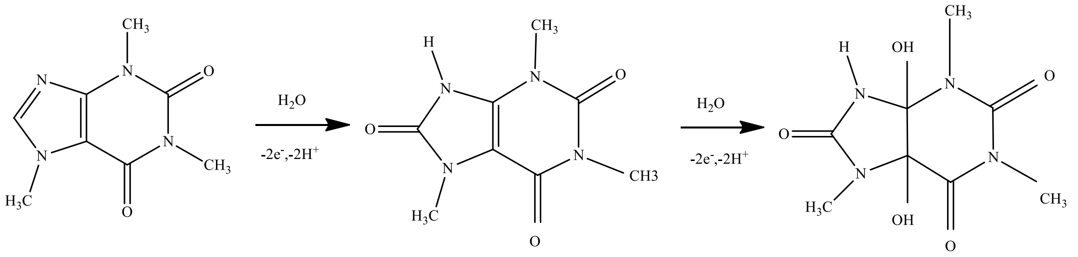
RESULTS AND DISCUSSION

The PC and CF co-determination on an unmodified electrode is impossible in a neutral aqueous medium, since PC is oxidized with overvoltage at high potentials (at E 0.80 V), and CF is not oxidized in the working area of potentials. The following equations usually represent the electrooxidation schemes of PC and CF [17]:



(1)

Scheme 1. Paracetamol electrooxidation



(2)

Scheme 2. Caffeine electrooxidation.

Several typical peaks (Figure 1a) for Ru and Co oxides are recorded on the voltammogram obtained on the SPE modified with a composite based on mixed-valence ruthenium and cobalt oxides (RuO_x-CoO_x-SPE) in a background phosphate buffer solution pH 6.9. In accordance with the published data [18, 19], it can be assumed that the electron transfers Ru(II) $\rightarrow$ Ru(III), Ru(III) $\rightarrow$ Ru(IV), Ru(IV) $\rightarrow$ Ru(VI) и Co(II) $\rightarrow$ Co(III) take place at the relevant potentials of the peak current.

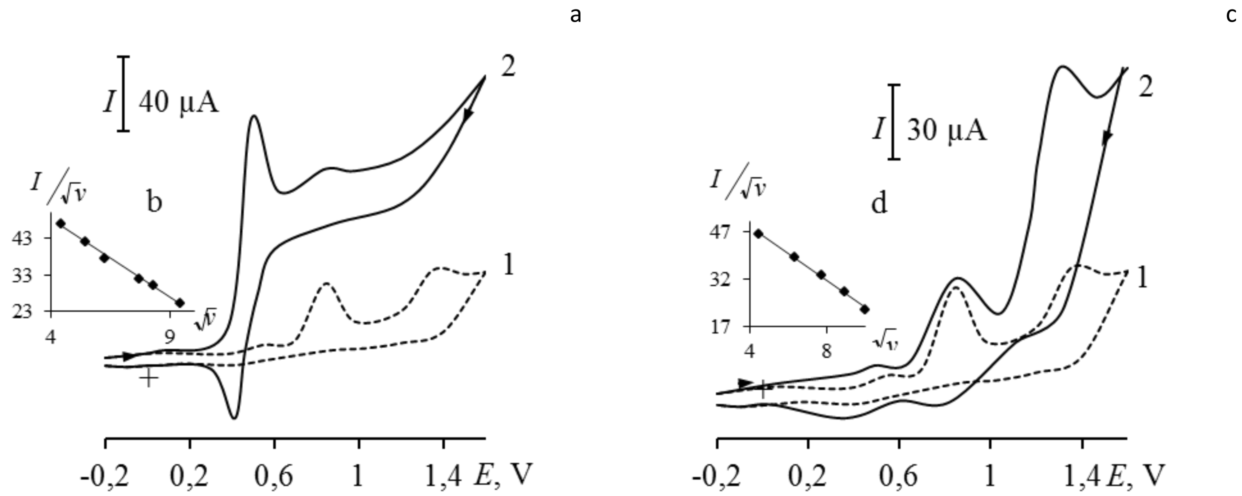


Figure 1. Cyclic voltammograms on the RuO_x-CoO_x-SPE in phosphate buffer pH 6.9 in the absence (Curve 1a and 1c) and in the presence of paracetamol (Curve 2a) and caffeine (Curve 2c) (C = 5×10^{-3} mol/l); the dependence of $I/\sqrt{v}$ from $\sqrt{v}$ dependency diagrams for the electrooxidation of paracetamol (b) and caffeine (d) at this CME.

A single peak of CF and PC electrooxidation is observed in the modifier's oxidation area on the anodic curve of the cyclic voltammogram on RuO_x-CoO_x-SPE in background phosphate buffer pH 6.9. Height of the peak depends on the analyte concentration. The PC is oxidized at E_p 0.50 V (Figure 1a). The negative slope of the relationship between peak current (I) and scan rate for $I/\sqrt{v}$ and $\sqrt{v}$ shows kinetic nature of the analytes oxidation (Figure 1b) that is evidence for the electrode process complicated with a chemical reaction. Electrooxidation of CF on the RuO_x-CoO_x-SPE occurs at E_p 1.30 V (Figure 1c); relationship between peak current (I) and scan rate also has a negative slope (Figure 1d). Electrooxidation of the studied compounds under consideration occurs at the modifiers' oxidation potentials and a multiple current gain compared with the modifier's oxidation current is being while there is a decreased overvoltage of analyte oxidation as compared with its oxidation potential on an unmodified electrode. All these facts point to the demonstration of immobilized modifier catalytic activity during to PC and CF electrooxidation. The catalytic effect calculated against the relationship between the catalytic current of substrate oxidation on a CME and the modifier oxidation current is equal to 16.0 and 4.0 for PC and CF, respectively.

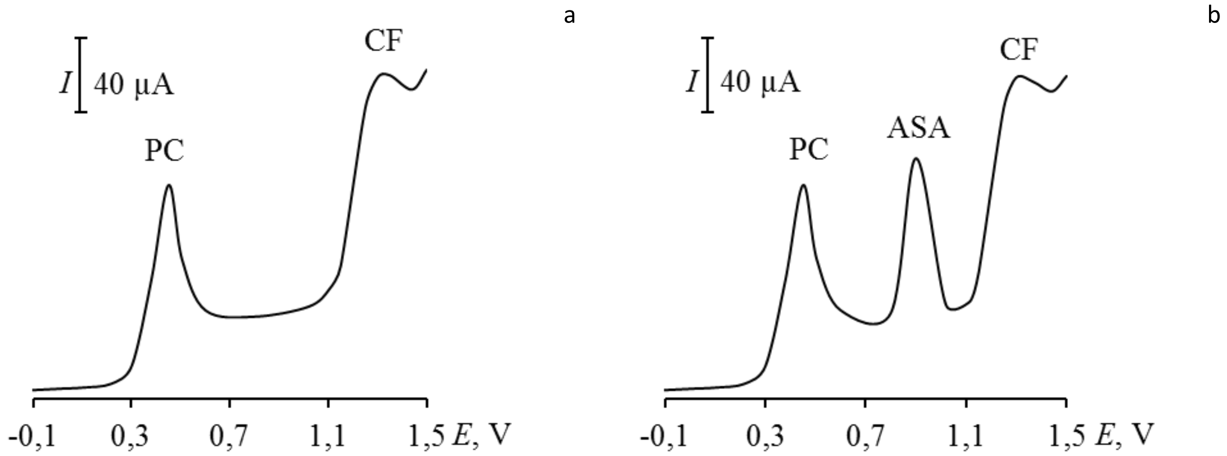


Figure 2. Voltammograms of caffeine and paracetamol electrooxidation (a) or of caffeine, paracetamol and acetylsalicylic acid electrooxidation (b) (C = 5×10^{-3} mol/l) at simultaneous presence on the RuO_x-CoO_x-SPE in phosphate buffer solution pH 6.9

It should be noted that the catalytic response of the RuO_x-CoO_x-SPE is highly stabile and reproducible. Electrooxidation of PC and CF occurs on the modified electrode at different potentials 0.45 V and 1.30 V, respectively, the potential difference of the analyte oxidation peaks is 850 mV (Figure 2a) which allows their selective voltammetric determination at simultaneous presence.

The RuO_x-CoO_x-SPE with electrocatalytic properties was used for the voltammetric determination of PC and CF in phosphate buffer solution pH 6.9. The concentration of analytes was found using the calibration curves. The intervals of linear relationships between the catalytic current and analyte concentration and the corresponding regression equation are presented in Table 1. As can be seen from Table 1, relationships between the current detected on the CME and the analyte concentration are linear for a wide range.

Table 1. Analytical characteristics of the voltammetric determination of paracetamol and caffeine on the RuO_x-CoO_x-SPE in phosphate buffer solution pH 6.9

Analyte	Electrode	Range of concentrations, mol/l	Regression equation lg*I* = a + b lg*c*, (*I*, μA; s, mol/l)		R
			a	b	
Paracetamol	RuO_x-CoO_x-SPE	$5\times10^{-6}\div5\times10^{-3}$	2.7±0.2	4.3±0.2	0.988
Caffeine	RuO_x-CoO_x-SPE	$5\times10^{-6}\div5\times10^{-3}$	3.2±0.2	3.5±0.2	0.997

The accuracy of determination results is estimated by the added-found approach. The relative standard deviation (S_r) does not exceed 5% for the range of studied concentrations.

Due to necessity of the analytical control of PC and CF in the combined drugs containing acetylsalicylic acid (ASA), a possibility of selective determination of these compounds in mixture on the RuO_x-CoO_x-SPE is investigated.

The possibility of selective voltammetric determination of CF, ASA and PC in mixture using the composite electrode RuO_x-CoO_x-SPE has been established (Figure 2b). The peak potential difference of the analyte oxidation is in the range from 400 to 450 mV which allows co-determination of the CF and PC in the presence of ASA.

The possibility of amperometric detection of CF and PC on the RuO_x-CoO_x-SPE if FIA was studied. Measurements were carried out in the potentiostatic mode. As an example, Figure 3a shows a shape of analytical signal of PC electrooxidation on the RuO_x-CoO_x-SPE. Electrochemical and hydrodynamic conditions of FIA-signal were found for each compound.

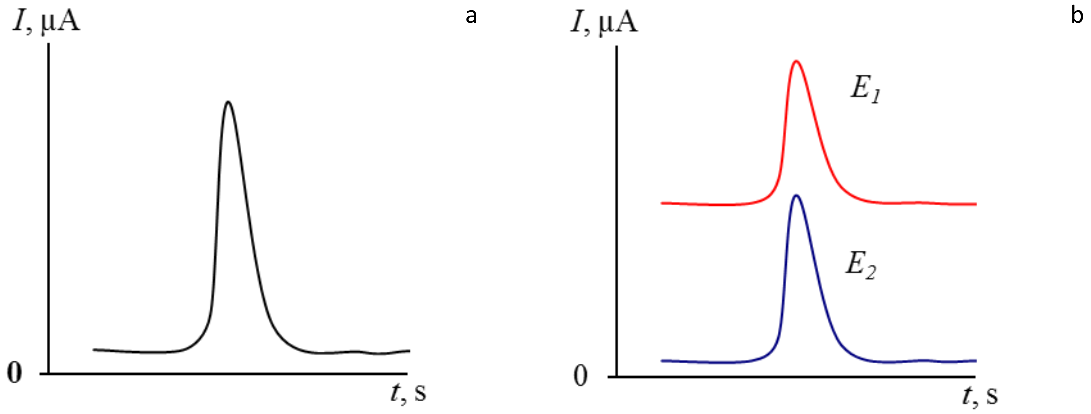


Figure 3. Analytical signals of the paracetamol electrooxidation on the RuO_x-CoO_x-SPE (a) and of the caffeine and paracetamol electrooxidation on the RuO_x-CoO_x-DSPE (b) in flow injection analysis

Based on the experimental results, the working conditions of the CF and PC determination were found for the FIA mode: PC was determined at *E* 0.50 V, CF – at *E* 1.35 V at a flow rate of 3.8 ml/min and an injected sample volume of 0.2 ml. In the selected conditions, the relationship between an analytical signal and an analyte concentration was recorded for the FIA mode (Table 2). As one can see, relationships between the current on the CME and the analyte concentration are linear for a more wide range than for batch conditions up to the lower bound of determined concentration equalled to 5×10^{-7} mol/l.

Table 2. Analytical characteristics of paracetamol and caffeine determination on the RuO_x-CoO_x-SPE in phosphate buffer solution pH 6.9 in flow injection analysis

Analyte	Electrode	Range of concentrations, mol/l	Regression equation lg*I* = a + b lg*c*, (*I*, μA; c, mol/l)		R
			a	b	
Paracetamol	RuO_x-CoO_x-SPE	$5\times10^{-7}\div5\times10^{-3}$	3.1±0.3	3.8±0.3	0.996
Caffeine	RuO_x-CoO_x-SPE	$5\times10^{-7}\div5\times10^{-3}$	2.7±0.2	3.2±0.2	0.998

It has been found that after using RuO_x-CoO_x-SPE in a flow cell without refreshing the electrode surface the signal reproducibility has been enough stable. The calculated values S_r for the PC and CF oxidation current do not exceed 2.0% (when n = 20, C = 5×10^{-3}M). The proposed method has high sensitivity, rapidity and efficiency of analysis (up to 180 samples/h when the response time of modified SPE is 20 s).

The possibility of simultaneous amperometric detection of CF and PC in FIA was studied. For this purpose, modified DSPE was used – an electrode with two working electrodes which surface was modified with the RuO_x-CoO_x composite (RuO_x-CoO_x-DSPE). Using this CME provides the simultaneous determination of two compounds at two different potentials (Figure 3b) applied to the working electrodes. In this case, the measurements were also carried out in potentiostatic conditions at *E* 0.50 V and 1.35 V for PC and CF, respectively, at a flow rate of 3.8 ml/min and the injected sample volume of 0.2 ml. Such measurement of an analytical signal for FIA leads to improving selectivity and rapidity of analysis.

The developed method was used for simultaneous determination of PC and CF in drugs. Table 3 shows the results of PC and CF determination in drugs by amperometry on modified DSPE with RuO_x-CoO_x composite in FIA.

Table 3. Results of paracetamol and caffeine determination in drugs by amperometry on a modified DSPE with RuO_x-CoO_x composite in a flow injection analysis; n = 6, P = 0.95, t_{table} = 2.57

Medicinal drugs	Analyte	Content in a drug/g	Detected, g	S_r	t_{calc}
Panadol	Paracetamol	0.50	0.47 ± 0.01	0.03	1.73
	Caffeine	0.065	0.064 ± 0.002	0.04	2.00
Solpadein	Paracetamol	0.50	0.51±0.01	0.03	2.4
	Caffeine	0.065	0.067 ± 0.002	0.04	1.83
Pentalgin	Paracetamol	0.300	0.300±0.005	0.03	1.35
	Caffeine	0.050	0.054 ± 0.001	0.03	1.51

It has been established that the electrochemically inactive matrix components (sorbitol, sodium bicarbonate, povidone, sodium lauryl sulfate, dimethicone, citric acid, sodium carbonate) and ASA which is oxidized at *E* 0.90 V does not interfere with the determination. Statistical evaluation of the results using the *t*-criterion value indicates the absence of any significant systematic error: $t_{calc} < t_{table}$ (Table 3)

CONCLUSIONS

It has been established that the use of SPE modified with RuO_x-CoO_x composite reduces overvoltage of PC and CF oxidation; increases the selectivity, sensitivity and decreases the lower bound of determined concentration up to 5×10^{-6} mol/l. Using the amperometric response of the modified electrode in FIA provides decreasing the lower bound of determined concentration up to 5×10^{-7} mol/l, improving the reproducibility and rapidity of measurements, and increasing the efficiency of analysis up to 180 samples/h at a modified SPE with the electrode response time of 20 s.A highly sensitive two-component analysis was carried out using a DSPE with two working electrodes modified with the RuO_x-CoO_x composite. This increases the selectivity of the determination since detection is carried out at different potentials, rapidity since detection of two compounds occurs at the same time, and the efficiency up to 360 samples/h since response time of a modified DSPE; with for two compounds reaches 20 s.

SUMMARY

A method of amperometric detection of caffeine and paracetamol on a dual screen printed electrode modified with a composite based on mixed-valence ruthenium and cobalt oxides in a flow injection analysis has been developed that can be applied for the caffeine and paracetamol co-determination, including in the presence of acetylsalicylic acid in drugs with high sensitivity, selectivity, and rapidity. The method is simple and highly effective.

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