

Anodic Oxidation of Phenoxyethanol in Nonaqueous Media

Magdalena Jakubczyk*, Sławomir Michalkiewicz

Institute of Chemistry, Jan Kochanowski University, Świetokrzyska St. 15G, PL-25406 Kielce, Poland

*E-mail: magdalenajakubczyk2@gmail.com

Received: 10 March 2019 / Accepted: 7 May 2019 / Published: 10 June 2019

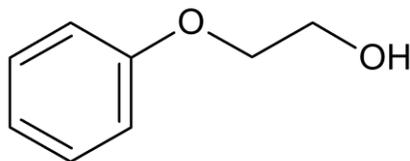
The unknown electrochemical properties of phenoxyethanol (PE) - the most commonly used preservative in cosmetics were studied. The measurements were performed on platinum micro- and macroelectrodes by linear sweep (LSV), cyclic (CV) and differential pulse voltammetry (DPV) in mixed solvent acetic acid-acetonitrile (20%, v/v) containing NaClO₄ as a supporting electrolyte. The anodic oxidation process has proved to be quasireversible, diffusion-controlled and proceeding with exchange of one electron giving the unstable cation radical as a primary product (E_qC_i mechanism). Very good reproducibility of the DPV curves and the wide linearity range up to 1 mmol L⁻¹ indicate that the proposed medium can be successfully applied to develop the first voltammetric method of this preservative determination in pharmaceutical and cosmetic products.

Keywords: Phenoxyethanol, Oxidation, Voltammetry, Acetic Acid, Acetonitrile

1. INTRODUCTION

One of the major economic problems of recent years is the degradation of different products such as food, cosmetics, and pharmaceuticals, due to the influence of microorganisms - bacteria and fungi. Biochemical processes occurring with the participation of these organisms cause deterioration of organoleptic characteristics, i.e. taste, color, odor, and limit their shelf life. Extending the durability of products requires the use of various preservatives. Their function is to maintain the appropriate quality and microbiological purity of the material protected. Phenoxyethanol (PE) is a commonly used preservative. Scheme 1 presents its molecular structure. This preservative is mainly applied to protect pharmaceutical and cosmetic preparations against the growth of microorganisms. Recently, the number of cosmetics containing PE has increased significantly, achieving 13 thousand in the year 2014 alone [1]. Nivea Visage brands, for example, are in 82% protected with phenoxyethanol [2]. The influence of PE on human health is not fully clear. It is officially recognized as safe for people [3,4]. Its presence in cosmetics is permitted under EU Directive No 1223/2009 [5]. However, a great deal of the information available indicates that the use of PE is not completely safe. Phenoxyethanol is suspected of causing

allergic skin reactions, e.g. contact urticaria [6-8], transient erythema on the skin [9], as well as having a toxic effect on the central nervous system [10].



Scheme 1. Molecular structure of phenoxyethanol (PE).

The acceptable content of PE in cosmetics and pharmaceuticals should not exceed 1% [11,12] and must be carefully controlled. For this purpose, various chromatographic techniques are used: high performance liquid chromatography in reverse phase (RP-HPLC) with photodiode array detector in the UV range [13-18], gas chromatography (GC) with tandem mass spectrometry [19,20] and micellar electrokinetic capillary chromatography (MECC) [21]. These techniques are characterized by high sensitivity and selectivity, as well as low limits of detection and quantification. However, they need expensive instrumentation and usually a complicated procedure of sample preparation, including extraction and/or derivatization.

To the best of our knowledge, there is no information available about electroanalytical methods of PE determination. So far, the electrochemical properties of this preservative have not been investigated either in aqueous and or in organic solvents. Therefore, the objective of this work was to investigate the anodic oxidation process of phenoxyethanol in acetic acid solutions as a starting point to develop a voltammetric method of its determination in pharmaceutical and cosmetic preparations.

2. EXPERIMENTAL

2.1. Reagents

The chemicals used were as follows: phenoxyethanol (PE), $\geq 99\%$ (Fluka, Germany), sodium perchlorate, NaClO_4 , anhydrous, p.a. (Sigma-Aldrich, USA), and sodium acetate, CH_3COONa (AcNa), anhydrous, $\geq 99.5\%$ (Fluka, Netherlands). The electrochemical experiments were carried out in solutions of acetic acid (HAc), p.a. ACS, acetonitrile (AN), p.a. anhydride (each Merck, Germany), or in their mixture. All chemicals and solvents used in this study were of high purity and used as received.

2.2. Apparatus and voltammetric procedures

Voltammetric experiments were performed with the use of a Model M161E electrochemical analyzer coupled with a Model M162 preamplifier used to measure of small currents (both mtm-anko, Poland) or with a Model RDE-2 rotating disk electrode (BASi, USA) cooperating with the software mEALab 2.1. and EALab 2.1., respectively (mtm-anko, Poland). Different voltammetric techniques such

as linear sweep (LSV), cyclic (CV) and differential pulse voltammetry (DPV) were applied in these measurements.

A conventional three-electrode cell was used, with a platinum disk microelectrode of 50 μm diameter (Mineral, Poland) and a stationary or rotating (RDE) platinum disk macroelectrode of 3 mm diameter, $A = 0.071 \text{ cm}^2$ (BASi, USA), as working electrodes. Some voltammetric experiments were carried out with the use of the disk microelectrodes made of platinum (10, 20, 25 μm diameter), gold (25 μm diameter), palladium (25 μm diameter) (each Mineral, Poland) and carbon fiber (33 μm diameter, BASi, USA). In order to ensure the reproducibility of the measurements, the surface of the working electrodes was polished with 0.05 μm alumina powder on a polishing cloth (BASi, USA), rinsed with deionized water and dried before use. A platinum wire (BASi, USA) and Ag/AgCl with 1 mol L⁻¹ NaCl (Mineral, Poland) were used as an auxiliary and a reference electrode, respectively. To avoid electrical noise, especially when the microelectrodes were used, the electrochemical cell was placed in the grounded Faraday cage. The Model CX-732 multifunction computer meter, equipped with a glass indicator electrode and Ag/AgCl reference electrode (Elmetron, Poland), was applied to pH measurements.

All experiments were performed at room temperature ($25 \pm 1^\circ \text{C}$).

In order to achieve steady-state conditions, LSV experiments with the use of microelectrodes were carried out at the potential scan rate of 6.25 mV s⁻¹.

Differential pulse voltammograms (DPVs) were recorded using the following optimized parameters: pulse amplitude 20 mV, pulse width 80 ms and the scan rate 20 mV s⁻¹.

Cyclic voltammetric measurements were performed on a stationary Pt macroelectrode in the potential range from 0 to 2.4 V and at the scan rate of 6.25 to 200 mV s⁻¹ if not stated otherwise. The same potential range was explored with the use of platinum RDE (scan rate of 6.25 mV s⁻¹, rotation speed 500 – 3000 rpm).

3. RESULTS AND DISCUSSION

3.1. Selection of the best voltammetric conditions

The preliminary experiments aimed at selecting a suitable material of the working electrode. Different materials were tested in this purpose: platinum, gold, palladium and carbon fiber. Due to restricted solubility of PE in water (1/43, v/v [12]), there was chosen a mixed solvent containing acetic acid and acetonitrile (20%, v/v), with NaClO₄ as a supporting electrolyte. The presence of AN in the solutions tested increased their electrical permittivity ($\epsilon_{\text{HAc}} = 6.19$, $\epsilon_{\text{AN}} = 35.9$ at 25°C [22]) and diminished the viscosity (0.341 and 1.130 mPa s, for AN and HAc, respectively [22]). This ensured an increase in the voltammetric signals (data not shown). Such composition of the solution guarantees a wide potential window, especially in the anodic region and thus is suitable for the investigation of the oxidation processes. Our earlier results indicate that the medium chosen was appropriate to study the electrochemical properties of hydrophobic antioxidants such as BHA, BHT [23], coenzyme Q10 [24,25] and preservatives (parabens) [26] and to their determination in real samples without the need to separate

them. The ability to soluble of hydrophobic organic compounds can be important in the potential future voltammetric determination of PE in the presence of their matrix with the same properties. Differential pulse voltammetry (DPV) on the microelectrodes was used to select the optimal working electrode material. The advantages of this technique are good sensibility, selectivity and resolution of the signals, limited influence of adsorption phenomena on recorded curves and thus satisfactory reproducibility [27,28]. In addition, the use of microelectrodes permits to diminish the influence of the ohmic potential drop, IR which is the result of a slight dissociation of supporting electrolyte in organic solvents of low dielectric constant. As the currents recorded on these electrodes are relatively small (nA or pA), the influence of IR drop on curves recorded in this medium can be neglected, even at the lowered concentration of the supporting electrolyte to 0.1 mol L^{-1} [29].

As can be seen from Fig. 1, a single peak in the potential range from 1.5 to 1.7 V vs Ag/AgCl attributed to PE oxidation was recorded on microelectrodes made of platinum, gold and carbon fiber with comparable diameters. Due to restricted anodic stability of the solution on palladium, the curve is not shaped as peak (curve c in Fig. 1). This indicates that this metal is not a suitable as a working electrode material for the anodic oxidation of PE. The best shaped, symmetrical and narrow peak was recorded on platinum (curve a in Fig. 1). In addition, very good reproducibility of the successively recorded curves was observed (inset on Fig. 1). This phenomenon is characteristic of the platinum microelectrodes both with 25 and 50 μm diameter. Considering these results, future experiments will be carried out on microelectrode made of platinum with 50 μm diameter, which ensures the increase of the peak currents and thus relatively high sensitivity of the measurements. The same electrode material will be applied in the experiments with the use of cyclic voltammetry and with the rotating disk electrode.

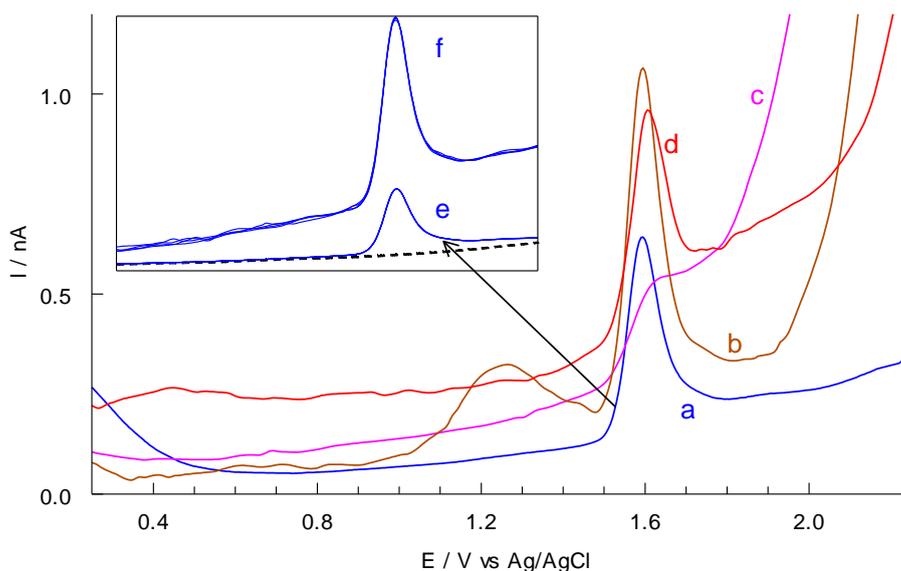


Figure 1. DPV curves of 0.1 mmol L^{-1} PE recorded in HAc containing 20% AN (v/v) and 0.1 mol L^{-1} NaClO_4 on (a) platinum, (b) gold, (c) palladium (each 25 μm diameter) and (d) carbon fiber (33 μm diameter) disk microelectrodes. Inset: Five consecutively recorded DPVs on platinum microelectrodes with (e) 25 μm and (f) 50 μm diameter.

3.2. Voltammetry on platinum microelectrode

The anodic oxidation process of phenoxyethanol in the selected medium was investigated using the LSV and DPV techniques on the platinum disk microelectrode (50 μm diameter). The results are presented in Fig. 2. Well-shaped single signals attributed to the oxidation of PE are observed with half-wave potentials, $E_{1/2} = 1.585$ V and peak potentials, $E_p = 1.595$ V vs Ag/AgCl for LSV and DPV, respectively (Table 1). Additionally, poorly formed and difficult to analyze signals can be observed in the range of higher potentials of the working electrode. They are particularly seen on the DPV curves at potentials of about 1.8 V and 2.2 V (Fig. 2B). The existence of these signals can probably be attributed to the successive oxidation reactions of the products formed during the first stage of the electrode process.

In order to check the reversibility of PE anodic oxidation, the Tomes criterion was applied [30]. The obtained difference between the potentials corresponding to $3/4$ ($E_{3/4}$) and $1/4$ ($E_{1/4}$) of the limiting current recorded with the use of LSV was 0.0569 V (Table 1). This value is close to theoretical one predicted for the one-electron and reversible electrode process ($0.0564/n$ V).

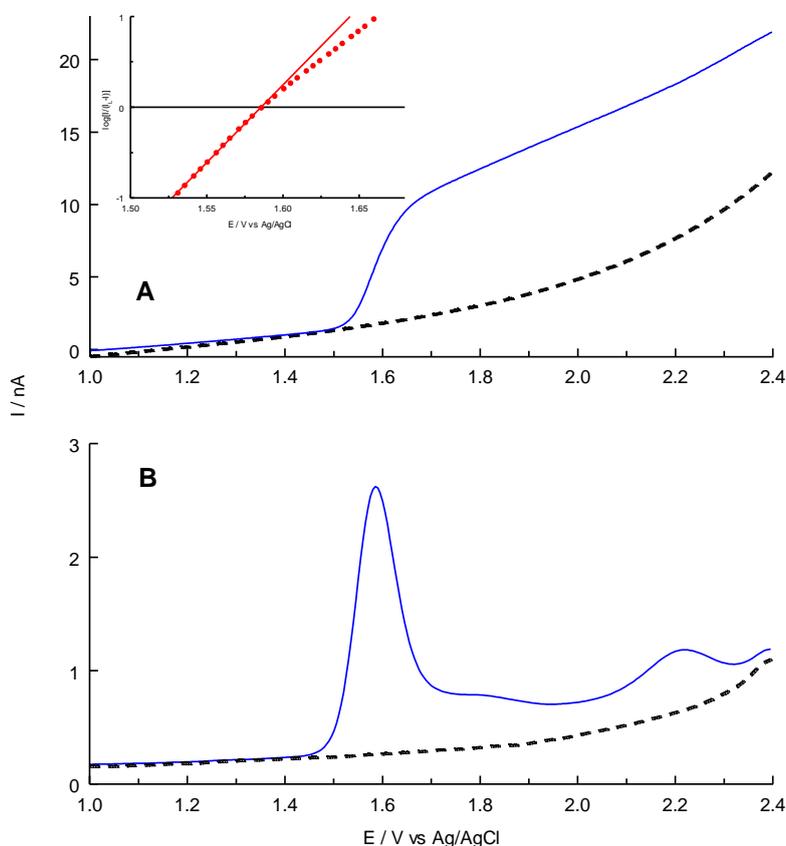


Figure 2. Anodic oxidation curves of 0.25 mmol L^{-1} PE recorded on Pt disk microelectrode (50 μm diameter) by (A) LSV and (B) DPV in HAc containing 20% AN (v/v) and 0.1 mol L^{-1} NaClO_4 . Dashed line is residual current. Inset: Semi-logarithmic analysis of the LSV curve from panel (A).

Table 1. Voltammetric parameters of the anodic oxidation of PE obtained by LSV and DPV on platinum microelectrode (50 μm diameter) and by CV on platinum macroelectrode (3 mm diameter, $A = 0.071 \text{ cm}^2$).

Parameter	Technique			$D \times 10^9 / \text{m}^2 \text{ s}^{-1}$	
	LSV ($\nu = 6.25 \text{ mV s}^{-1}$)	DPV ($dE = 20 \text{ mV}$)	CV ($\nu = 50 \text{ mV s}^{-1}$)		
¹ $E_{1/2} / \text{V}$ vs Ag/AgCl	1.585	–	–	3.06 ± 0.02	
² $E_{3/4} - E_{1/4} / \text{V}$	0.0569				
³ $S_{\text{LSV}} / \text{V}$	0.0582				
⁴ E_p (DPV) / V vs Ag/AgCl	–	1.595	–	–	
⁵ $W_{1/2} / \text{V}$		0.0930			
E_p (CV) / V vs Ag/AgCl		–			1.600 ^a 1.628 ^b
⁶ $E_p - E_{p/2} / \text{V}$					0.0550 ^a 0.0635 ^b
⁷ $S_{\text{CV}} / \mu\text{A s V}^{-1}$					0.47

¹half-wave potential, ²Tomes criterion, ³slope of the semi-logarithmic analysis expressed as $dE/d(\log[I/(I_L-I)])$, ⁴peak potential, ⁵peak width at a half-height (DPV), ⁶criterion of reversibility in CV registered at ν : ^a12.5, ^b100 mV s^{-1} , ⁷slope of the relationship $\log(I_p, \mu\text{A}) = f(\log \nu, \text{V s}^{-1})$

The reversibility of PE anodic reaction confirms the result of a semi-logarithmic analysis of the LSV curve (inset in Fig. 2(A)). According to the equation [28]:

$$E = E_{1/2} + (2.303RT / nF) \log [I / (I_L - I)] \quad (1)$$

where E (V) is the electrode potential, $E_{1/2}$ (V) is the half-wave potential, n is the number of electrons involved in the electrode reaction, I (A) is the current at a given potential E , I_L (A) is the steady-state limiting current for a reversible electrode process, the slope, S of the linear plot of E vs. $\log[I/(I_L - I)]$ should have a value of $0.0591/n \text{ V}$ at 25°C . The linear relationship with a slope of 0.0582 V (Table 1) and with deviation from linearity at higher potentials was obtained. This means that the oxidation process of PE is not in fully reversible and can be described as quasireversible, one-electron process.

The reversible character of the electrode reaction can also be checked with the use of the peak width at a half height ($W_{1/2}$) of the curves recorded by DPV. This parameter can be expressed by the equation [28,31]:

$$W_{1/2} = 3.52 RT/nF \quad (2)$$

The obtained value of $W_{1/2} = 0.0930 \text{ V}$ (Table 1) is close to 0.0904 V at 25°C predicted by equation (2) and confirms the quasireversible exchange of one electron in the anodic oxidation of this preservative. In order to check whether the process investigated is diffusion or adsorption controlled, the LSV curves on microelectrodes with different radius were recorded. The results were presented in

Fig. 3. As can be seen, the limiting current increases with the increase in the size of the microelectrode. According to the equation describing I_L (A) on the microelectrodes [28]:

$$I_L = 4nFrDc \quad (3)$$

where r (m) is the radius of the microelectrode, c (mol m^{-3}) is the concentration of the analyte, and D ($\text{m}^2 \text{s}^{-1}$) denotes the diffusion coefficient of the analyte, the linear relationship $I_L = f(r)$ was obtained (inset in Fig. 3). This clearly indicates that the oxidation process of PE in solution tested is diffusion controlled.

Taking into account that the anodic oxidation process of PE is diffusion controlled and proceeds with the exchange of one electron, the diffusion coefficient of this analyte was calculated from the equation (3). The obtained value of $(3.06 \pm 0.02) \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ (Table 1) is typical for the organic compounds.

It was found that the limiting currents of the LSV curves and the peak currents of the DPV ones increased with an increase in the phenoxyethanol concentration (Fig. 4A and 4B). Well-shaped LSV curves were registered when the amount of PE did not exceed 0.8 mM. The linear relationship $I_L = f(c)$ was obtained in this concentration range (Fig. 4A1), which is described by the equation: I_L (nA) = 30.0c (mM) + 0.05 ($r = 0.9999$, $n = 9$).

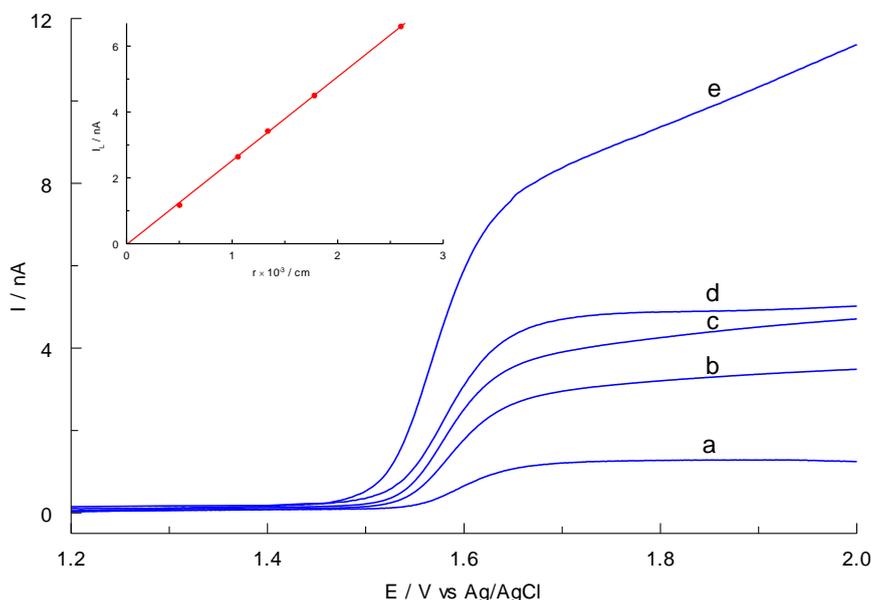


Figure 3. LSV curves of 0.25 mmol L^{-1} PE obtained on Pt disk microelectrodes with (a) 10, (b) 20, (c) 25 (e) $50 \mu\text{m}$ diameter and (d) on carbon fiber ($33 \mu\text{m}$ diameter) after subtracting the residual current. Inset: relationship between steady-state limiting current (I_L) and radius (r) of the electrode.

When the amount of PE exceeded 0.8 mM (Fig. 4A, curve e), the deepening distortions of LSV curves and deviation from linearity were observed. This indicates the participation of adsorption phenomena accompanying the oxidation of phenoxyethanol on the surface of the working electrode. This conclusion confirms hysteresis existence on the LSV curves recorded on the platinum

microelectrode (Fig. 5A) and on the rotating disk electrode (RDE) made from the same material (Fig. 5B). The observed hysteresis increased when direction of polarization was changed from anodic to cathodic at higher potentials. Since the anodic process was found to be diffusion controlled, the final products of PE oxidation are likely to be adsorbed. These products block the surface of the working electrode and make the successively recorded LSV curves irreproducible. To obtain the reproducibility of the results, polishing its surface after each recorded curve was needed.

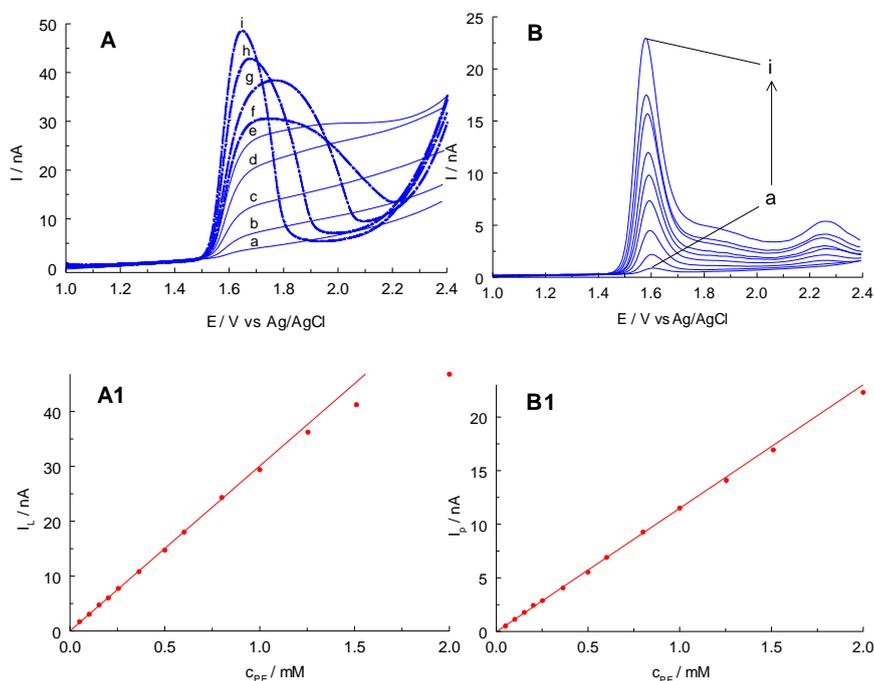


Figure 4. LSV (A) and DPV (B) curves recorded in solutions containing PE in the concentration range from (a) 0.05 to (i) 2.00 mmol L⁻¹. Other components of the solutions as in Figure 2. (A1), (A2) Calibration curves obtained using LSV and DPV, respectively.

The same results were obtained with the use of RDE with diameter of 3 mm. As a result of rotation, all soluble products were removed from its surface, unlike the stationary electrode surface. Thus, only strongly adsorbed products of the anodic oxidation of PE can be a reason for the existence of the hysteresis recorded on RDE (Fig. 5B). Partial removal of these adsorbed products combined with their reduction was seen as a small signal at the potential of about 0.4 V vs Ag / AgCl (inset in Fig. 5B). The magnitude of this signal grew together with an increase in the potential at which the direction of the electrode polarization changed from anodic to cathodic. This is undoubtedly related to the increased amount of the final products formed during the oxidation of PE.

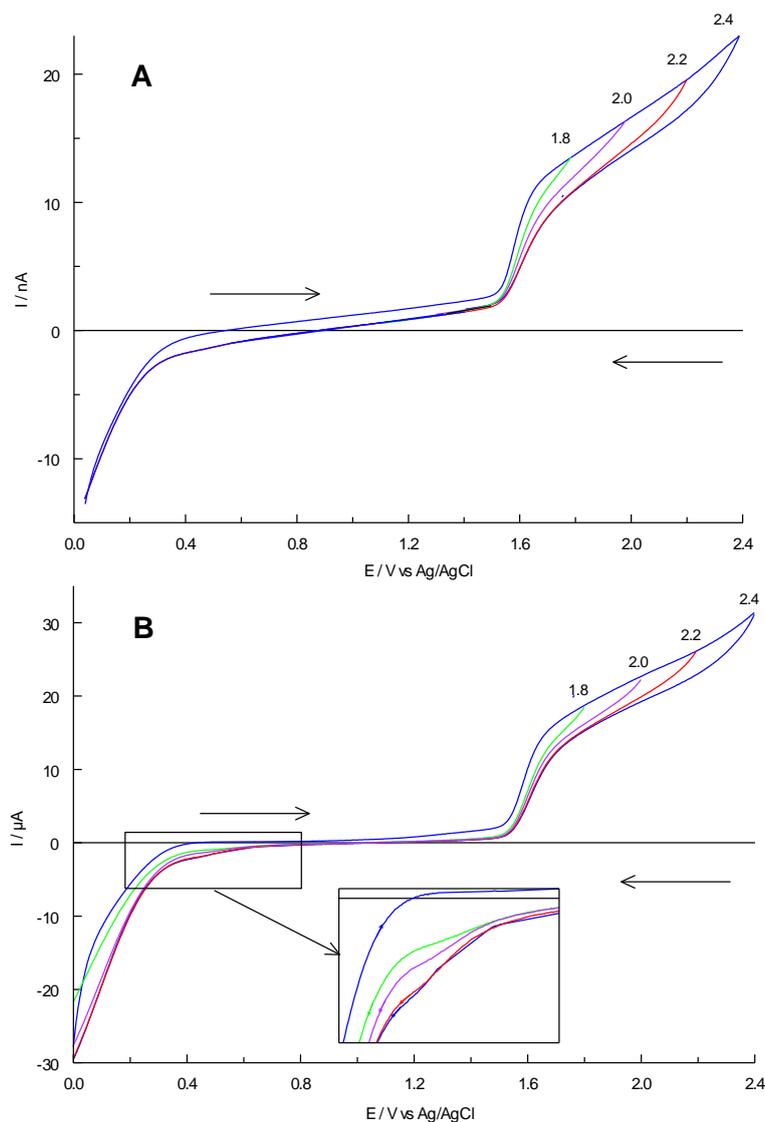


Figure 5. Cyclic LSV curves of 0.25 mmol L^{-1} PE recorded on (A) Pt disk microelectrode ($\phi = 50 \mu\text{m}$) and (B) RDE (Pt, $\phi = 3 \text{ mm}$, 500 rpm) in HAc containing 20% AN (v/v) and (A) 0.1 or (B) 0.5 mol L^{-1} NaClO_4 . Direction of electrode polarization was reversed from anodic to cathodic at potentials, E_λ given at the curves.

Very good reproducibility of the successively recorded curves without the need for electrode polishing was achieved when DPV was used. This was possible due to the reduction of adsorption phenomena, which is characteristic of this voltammetric technique. It was found that the peak currents (I_p) of the DPV curves grew alongside an increase in PE concentration (Fig. 4B), and the linear dependence of $I_p = f(c)$ presented in Fig. 4B1 covers a wider concentration range (up to 1 mmol L^{-1}) than the one obtained with the use of the LSV technique. This relationship is described by the equation: I_p (nA) = $-0.03 + 11.5c$ (mM) ($r = 0.9997$, $n = 10$).

The participation of protons in the electrode process was checked for pH effect on the peak potentials of the DPV curves recorded on Pt microelectrode. The increasing concentration of acetate anions as the strongest base in acetic acid solutions caused relative changes in their pH. DPV curves were thus recorded in solutions containing different amounts of CH_3COONa and NaClO_4 , but with their total concentration of 0.1 mol L^{-1} . Since the pH scales in water and in acetic acid differ one from the

other, their values in this organic solvent can be used to determine only relative acidities [32]. Thus, the abbreviation pH(HAc) for acidities in acetic acid solutions will be used. The obtained results indicate that the increased concentration of acetate ions, and thus increased pH of the solutions, caused only a slight shift in the oxidation peak potentials toward less positive values (data not shown). The obtained dependence between the peak potentials, E_p and pH(HAc), is linear and is expressed by the equation: E_p (V) = 0.67 - 0.011 pH(HAc) ($r = 0.997$). A slight slope of this relationship (0.011 V/pH) differs significantly from the theoretical one expected for equal numbers of protons and electrons involved in an electrode reaction (0.0591 V/pH) and can result from increased irreversibility of the process in the presence of the increased concentration of acetate ions. These results indicate that the anodic oxidation of phenoxyethanol proceeds with no exchange of protons.

3.3. Cyclic voltammetry on platinum electrode

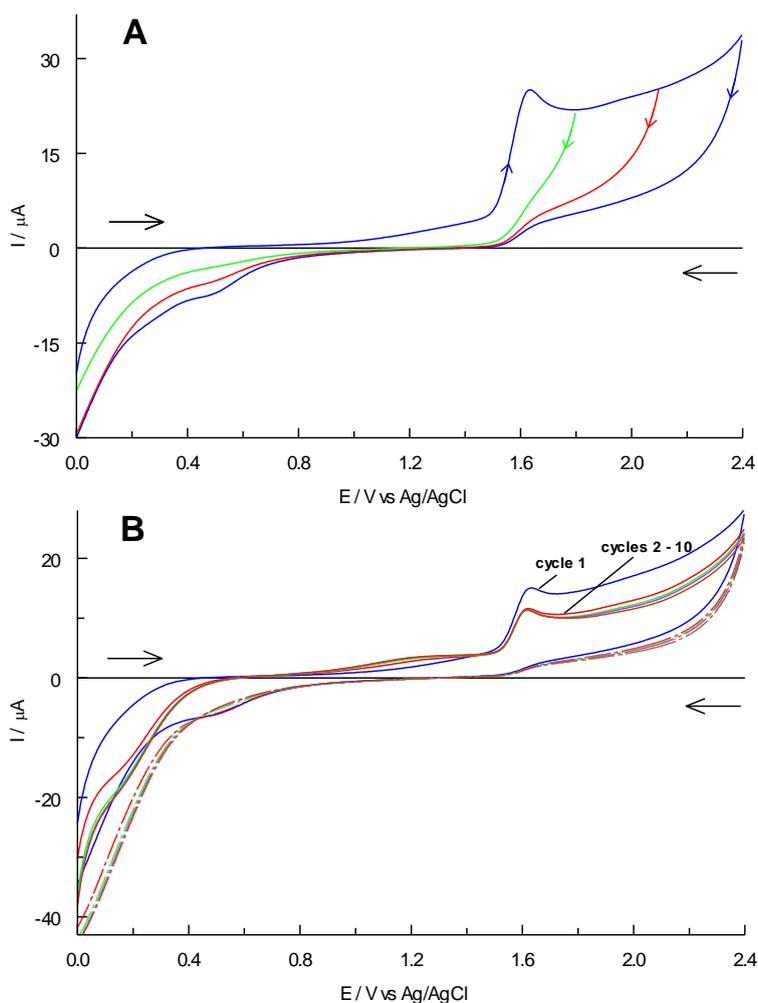


Figure 6. (A) CV curves ($v = 50 \text{ mV s}^{-1}$) of 0.5 mmol L^{-1} PE recorded on Pt disk electrode (3 mm diameter) in HAc containing 20% AN (v/v) and 0.5 mol L^{-1} NaClO₄. Direction of electrode polarization was reversed from anodic to cathodic at potentials E_λ : 1.8, 2.1 and 2.4 V. (B) 10 consecutively recorded CV curves in the same conditions.

Cyclic voltammetry (CV) on a stationary electrode is a good tool for an electrode reaction investigation. This technique is particularly useful for exploring products formed during this process. As the currents recorded on platinum with a diameter of 3 mm ($A = 0.071 \text{ cm}^2$) are relatively high, in comparison to those observed on the microelectrode, the CV experiments were performed in the presence of the increased up to 0.5 mol L^{-1} concentration of the supporting electrolyte. This amount of the electrolyte caused an increase in the conductivity of the solutions and a decrease in the ohmic potential drop, IR . Fig. 6A presents a typical CV curve recorded in the solutions containing phenoxyethanol. When polarizing the working electrode in the anodic direction, one oxidation peak at the potential of about 1.6 V vs Ag/AgCl was observed. Its location is related to the oxidation of PE and corresponds to the signals observed on the curves recorded using the platinum microelectrode and RDE (Figs 2-4).

After switching the polarization potential from anodic to cathodic, the reduction peak was not observed, even when such a change occurred at the potentials only slightly higher than the peak potential of phenoxyethanol. The absence of this peak indicates that primary products of the anodic oxidation of PE are unstable and undergo successive irreversible homogenous reaction giving the final products which probably undergo reduction at the potentials 0.4 – 0.6 V vs Ag/AgCl (Fig. 6A). As can be seen, the signal magnitude grows together with an increase of the potential switching, E_{λ} to the cathodic one, and thus of the time when the chemical reaction occurs. The active surface of the electrode is reduced by the layer of the absorbed products. As a result, the peak current drops after the first cycle. This is confirmed by the "pre-wave" formed during the second and subsequent cycles (Fig. 6B). The results reproducibility needed electrode polishing after each registered curve.

To confirm the reversibility of the anodic oxidation of PE, there was applied the diagnostic criterion based on the difference between the peak potential and the potential at half height of the peak (E_p and $E_{p/2}$, respectively) at 298 K [31]: (Eq. 4)

$$E_p - E_{p/2} = 2.218 (RT/nF) = 0.0565/n \text{ V} \quad (4)$$

The obtained values of this parameter (Table 1) grew slightly together with an increase in the potential scan rate, ν (0.0550 V and 0.0635 V for 12.5 mV s^{-1} and 100 mV s^{-1} , respectively, Table 1), and they are close to those expected for a heterogeneous reaction which proceeds with a reversible exchange of one electron (0.056 V). These results indicate that the electrode process is not fully reversible and can be described as quasireversible. This conclusion is confirmed by the results obtained during the studies on the influence of the scan rate on the anodic peak currents. As can be seen from Fig. 7A, an increase in the scan rate causes slow changes in the peak potentials (Table 1). According to the Randles-Sevcik equation, the linear dependence of the peak currents, I_p on the square root of the scan rate, $\nu^{1/2}$, was obtained (Fig. 7B). This indicates that the anodic oxidation of PE is diffusion controlled. The linear relationship between I_p and ν in a logarithmic scale with the value of a slope near to 0.5: $\log(I_p / \mu\text{A}) = 1.92 + 0.47\log(\nu / \text{Vs}^{-1})$ confirms this conclusion (Table 1, Fig. 7C).

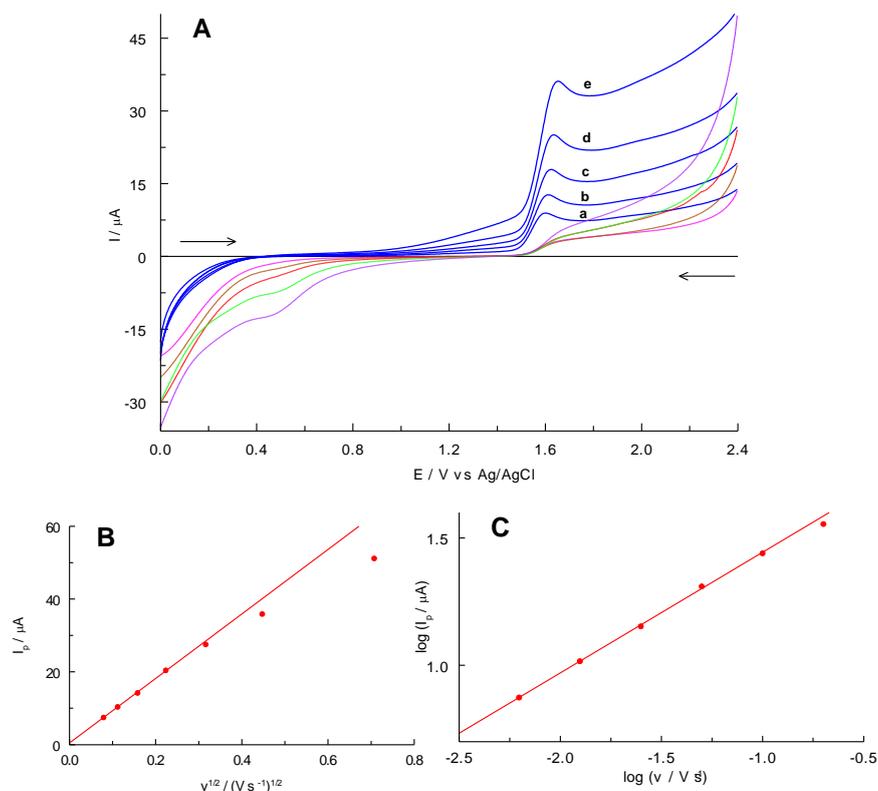


Figure 7. (A) CV curves recorded on Pt electrode (3 mm diameter) in solutions containing 0.5 mmol L⁻¹ PE at different scan rates: (a) 6.25, (b) 12.5, (c) 25, (d) 50 and (e) 100 mV s⁻¹. Other components of the solutions as in Fig. 6. Relationships: (B) $I_p = f(v^{1/2})$ and (C) $\log(I_p) = f(\log v)$.

3.4. Mechanism of the anodic oxidation of phenoxyethanol

The results obtained indicate that the anodic oxidation of PE on platinum in acetic acid solutions proceeds with the quasireversible exchange of one electron (E_q), is controlled by diffusion, and the protons do not participate in this heterogeneous reaction. The primary products of the process are unstable and participate in an irreversible chemical reaction (C_i) near the surface of the working electrode. The products formed during this homogeneous reaction partially adsorb on the surface of the electrode and they undergo oxidation giving additional small signals observed on the DPV curves (Fig. 2B). Thus, the anodic oxidation of PE proceeds according to the E_qC_i mechanism.

In order to check which part of PE molecule undergoes oxidation, the DPV curves were recorded in solutions containing compounds structurally similar to the analyte: methoxybenzene (anisole) and phenylethanol. The representative curves are presented in Fig. 8. As can be seen, the peaks corresponding to the oxidation of phenoxyethanol and anisole were recorded at the same potential. This clearly indicates that the oxidation process of PE proceeds on the etheric oxygen atom.

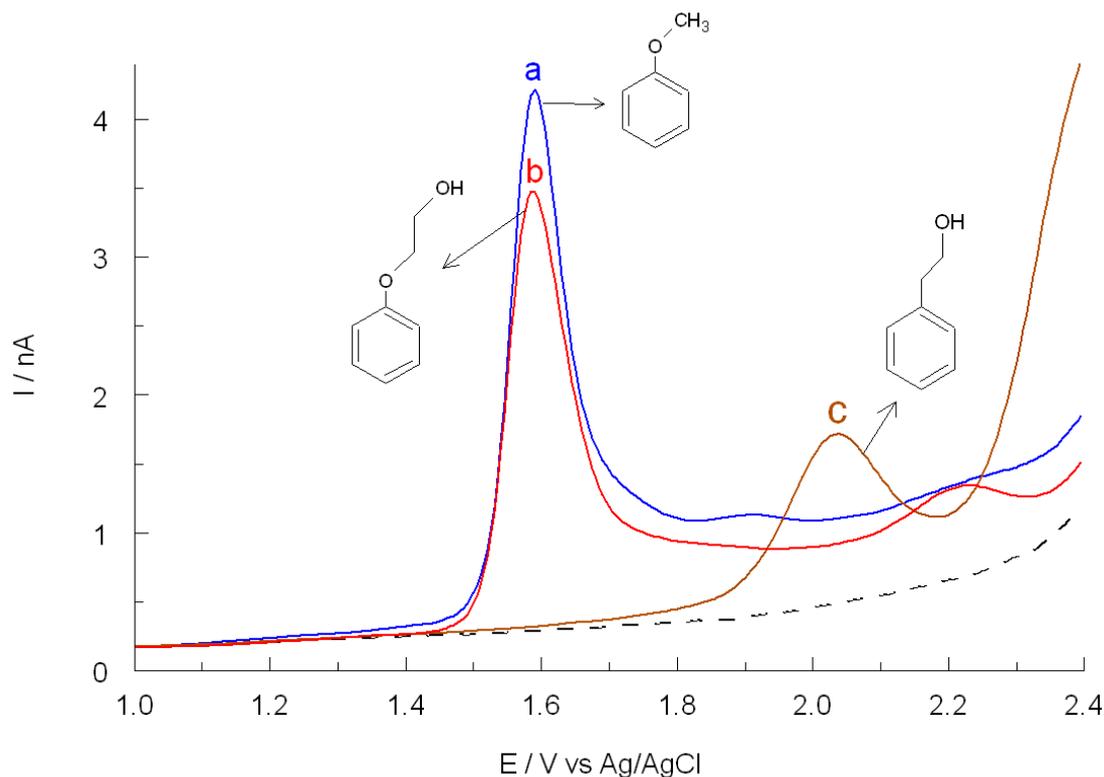
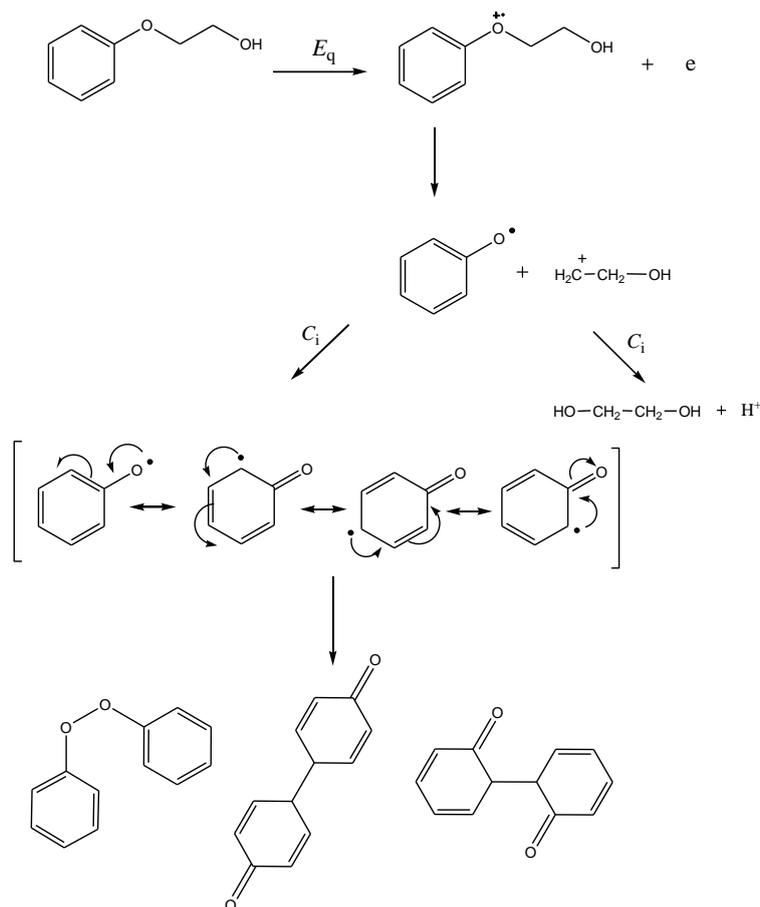


Figure 8. DPV curves recorded on Pt disk microelectrode (50 μm diameter) in solutions containing (a) anisole, (b) phenoxyethanol and (c) phenylethanol (each 0.25 mmol L^{-1}). Other components of the solutions as in Fig. 2.

Taking into account all the results obtained, the mechanism of the anodic oxidation of phenoxyethanol was proposed (Scheme 2). It seems likely that the loss of one electron from the oxygen atom produces the cation radical. This primary product is rather unstable and transforms into the phenoxy radical and aliphatic cation. These products undergo successive irreversible homogenous reactions giving a lot of final products. Since the traces of water are present in the solutions tested, the aliphatic cation can react with this molecule (nucleophilic addition) giving ethylene glycol. The probable reactions with the participation of the phenoxy radical can lead to the formation of many dimeric and polymeric products which adsorb on the surface of the working electrode and undergo reduction at the potentials of 0.4 - 0.6 V vs Ag/AgCl (see Figs 5-7). The existence of ethylene glycol, as one of many final products of the overall process, was confirmed by GC-MS/MS spectrometry in the solutions after the total electrolysis carried out at the constant potential of 1.75 V vs Ag/AgCl, for 9 hours (data not shown). Thus, the proposed mechanism seems to be credible.



Scheme 2. Expected mechanism of the anodic oxidation of phenoxyethanol.

3.5. Possibility of application

A linear dependence between peak current and concentration of phenoxyethanol and very good reproducibility of the successively recorded DPV curves without the need for electrode polishing indicates that the proposed medium can be a basis to develop the first voltammetric method determination of this preservative in pharmaceuticals and in cosmetics. Hence, the works will be continued.

4. CONCLUSIONS

The obtained results indicate that the process of the anodic oxidation of phenoxyethanol on the platinum electrode in acetic acid containing acetonitrile (20%, *v/v*) and NaClO_4 as a supporting electrolyte proceeds with the quasi-reversible exchange of one electron and is diffusion controlled. The cation radical as a primary product is unstable and undergoes irreversible homogeneous reactions giving a lot of different final products ($E_q C_i$ mechanism). Some of them adsorb on the working electrode and partially block its surface giving irreproducible results. Very good reproducibility of the curves with no need for electrode polishing can be obtained when the DPV technique is applied. The analysis of MS spectra allowed only to identify ethylene glycol as the final product of the oxidation of PE. Based on

these results, one can state that the proposed medium is suitable for the investigation of phenoxyethanol electrochemical properties and can also be successfully applied to develop the first voltammetric method of this preservative determination in pharmaceutical and cosmetic products.

References

1. <https://www.cosmeticsandtoiletries.com/regulatory/region/northamerica/Frequency-of-Preservative-Use-Update-Through-2014-367684531.html> (10.04.2019).
2. <http://www.cosmetoscope.com/2012/09/nivea-visage-range-exhaustive-study-part-1/> (10.04.2019).
3. J. Scognamiglio, L. Jones, C.S. Letizia and A.M. Api, *Food Chem. Toxicol.*, 50 (2012) S244.
4. J. Krowka, L. Loretz, K Brzuska, J. F. Almeida, M. Diehl, S. J. Gonsior, A. Johnson, S. Sellam, S. Bade and S. Champ, *Cosmet. Toiletries*, April 22, 2014.
5. Regulation (EC) No 1223/2009 of The European Parliament and of the Council of 30 November 2009 on cosmetic products (L 342/59 of 22.12.2009).
6. A.J. Birnie and J.S. English, *Contact Dermatitis*, 54 (2006) 349.
7. S. Bohn and A.J Bircher, *Allergy*, 56 (2001) 922.
8. B. Hernandez, F.J. Ortiz-Frutos, M. Garcia, S. Palencia, M.C. Garcia and L. Iglesias, *Contact Dermatitis*, 47 (2002) 54.
9. C. BuÈhrer, S. Bahr, J. Siebert, R. Wettstein, C. Geffers and M. Obladen, *J. Hosp. Infect.*, 51 (2002) 305.
10. W.E. Morton, *J. Occup. Environ. Med.*, 32 (1990) 42.
11. Opinion of the Scientific Committee on Consumer Safety (SCCS) – Final version of the opinion on Phenoxyethanol in cosmetic products, *Regul. Toxicol. Pharm.*, 82 (2016) 156.
12. R.C. Rowe, P.J. Sheskey and M.E. Quinn, *Handbook of pharmaceutical excipients*, Pharmaceutical Press, (2009) Chicago, USA.
13. A. Vairale, P. Sivaswaroop and P.B. Modi, *Int. J. Anal. Bioanal. Chem.*, 2 (2012) 151.
14. M. Borremans, J. Van Loco, P. Roos and L. Goeyens, *Chromatographia*, 59 (2004) 47.
15. Ch. Roy and J. Chakrabarty, *Sci. Pharm.*, 81 (2013) 951.
16. G.A. Shabir, *Indian J. Pharm. Sci.*, 72 (2010) 421.
17. B. Sharma, A. Joseph and A. Sood, *Biologicals*, 36 (2008) 61.
18. D.C.P. Abreu, B.M.C. Botrel, M.J.F. Bazana, P.V. e Rosa, P.F. Sales and M. da Silva Marques, *Food Chem.*, 270 (2019) 487.
19. R.A. Trenholm, B.J. Vanderford, J.E. Drewes and S.A. Snyder, *J. Chromatogr. A*, 1190 (2008) 253.
20. G. Alvarez-Rivera, M. Vila, M. Lores, C. Garcia-Jares, and M. Llompарт, *J. Chromatogr. A*, 1339 (2014) 13.
21. J.-Q. Huang, C.-C. Hu and T.-C. Chiu, *Int. J. Cosmet. Sci.*, 35 (2013) 346.
22. K. Izutsu, *Electrochemistry in Nonaqueous Solutions*, Wiley-VCH, (2002) Weinheim, Germany.
23. M. Jakubczyk and S. Michalkiewicz, *Int. J. Electrochem. Sci.*, 13 (2018) 4251.
24. S. Michalkiewicz, *Bioelectrochemistry*, 70 (2007) 495.
25. S. Michalkiewicz, *Bioelectrochemistry*, 73 (2008) 30.
26. S. Michalkiewicz, *J. Appl. Electrochem.*, 43 (2013) 85.
27. R. Blanc, A. Gonzalez-Casado, A. Navalon and J.L. Vilchez, *Anal. Chim. Acta*, 403 (2000) 117.
28. F. Sholz (ed), *Electroanalytical methods. Guide to Experiments and Applications*, Springer-Verlag, (2002) Berlin, Germany.
29. C.M.A. Brett and A.M.O. Brett, *Electroanalysis*, Oxford University Press, (1998) New York, USA.
30. C.G. Zoski, *Electroanalysis*, 14 (2002) 1041.
31. A.J. Bard and L.R. Faulkner, *Electrochemical methods. Fundamentals and Applications*. Wiley, (2001) New York, USA.

32. S.P. Porras and E. Kenndler, *J. Chromatogr. A*, 1037 (2004) 455.

© 2019 The Authors. Published by ESG (www.electrochemsci.org). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/4.0/>).