===== ARTICLES =====

Voltammetric Determination of Flavonoids in Medicinal Plant Materials Using Electrodes Modified by Cerium Dioxide Nanoparticles and Surfactants

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Abstracts—Methods for the voltammetric determination of flavonoids (rutin and quercetin) using electrodes modified with CeO2 nanoparticles and various surfactants have been developed. The voltammetric characteristics of analytes are most properly recorded on a glassy carbon electrode modified with CeO_2 nanoparticles dispersed in anionic sodium dodecyl sulfate. The electro-oxidation of quercetin and rutin is adsorption-controlled and proceeds with the participation of two electrons and two protons. Under conditions of differential pulse voltammetry in a Britton−Robinson buffer solution with pH 2.0, the analytical ranges are 0.01−1.0 and 1.0−250 µM for quercetin and 0.10−100 µM for rutin with the limits of detection (S/N = 3) of 2.9 and 28 nM, respectively. The proposed approaches were tested in analyzing water and alcohol extracts from medicinal plant materials (St. John's wort herb, marigold flowers, and bearberry leaves). The conditions for the extraction of flavonoids from raw materials with ethanol are found. The results of the voltammetric determination of quercetin and rutin in plant raw materials correlate with the total flavonoids according to spectrophotometry: $r = 0.929$ with $r_{crit} = 0.521$ for $n = 11$ in the case of quercetin and $r = 0.951$ at $r_{crit} = 0.729$ for $n = 6$ for rutin.

Flavonoids are the most representative group of natural phenolic antioxidants preventing the development of oxidative stress and minimizing its effects in biological systems [1]. Quercetin (3,3',4',5,7-pentahydroxyflavone) and its glycosides, in particular, rutin (quercetin-3-*O*-rutinozide), are among the most common flavonoids. They are secondary metabolites synthesized by higher plants and were found in fruits, vegetables, seeds, and medicinal plant materials [1, 2]. Like other flavonoids, quercetin and its glycosides have pharmacological activity: antioxidant, antitumor, antibacterial, and anti-inflammatory [1, 3, 4]. Quercetin and rutin are widely used in pharmacy as an active ingredient of medicines for the prevention and treatment of various diseases, as well as in dietary supplements and in phytotherapy as active components of medicinal plant materials. The concentration of quercetin and rutin in medicinal samples must be controlled, which requires the development of sensitive and selective methods for their determination.

Based on the electrochemical activity of quercetin and rutin [1], voltammetry with chemically modified electrodes is often used to solve this problem, ensuring high analytical and operational characteristics of the determination of analytes. Modifiers include a wide range of carbon nanomaterials [5, 6]; nanoparticles of metals, their oxides, and other compounds [7, 8], polymer coatings of various types [9−12], ionic liquids [13], as well as their combinations, enabling creating composite and hybrid electrodes [14−20] (Table 1). Further development in this field consists in using cerium dioxide nanoparticles dispersed in surfactants as modifiers of electrode surface. Surfactants as modifiers of electrode surface perform a dual function: they ensure the stability of a suspension of CeO_2 nanoparticles in an aqueous medium (up to 1 month) and affect the voltammetric characteristics of analytes. Varying the nature of surfactants gives a possibility of controlling the electrochemical characteristics of the electrodes and the selectivity of their response to target analytes by changing the electrostatic and hydrophilic−lipophilic properties of the electrode surface [21]. This approach to electrode modification has been successfully applied to the determination of eugenol [22], capsaicin [23], and thymol [24].

This paper is focused on the development of sensitive and selective methods for the determination of quercetin and rutin using glassy carbon electrodes

Table 1. Analytical characteristics of the voltammetric determination of quercetin and rutin using chemically modified electrodes

Electrode	Method	LOD, μM	Analytical range, μM	Reference
Quercetin				
MWCNT in 1% SDS/GCE	CV	1.0	2.0−220	[5]
Graphene/GCE	AdADPV	0.0039	0.006−10, 10−100	[6]
Au NP/cystamine/Au	CV	0.001	10−100	[7]
Co_3O_4 NP/GCE	VA	0.10	0.5−330	[8]
Poly(5-amino-2-mercapto-1,3,4-thiadiazole)/rod GE	DPV	2.2	0.33−16.5	[9]
1-Methyl-3-butylimidazolium bromide−NiO−CNT−CPE	SWV	0.03	0.08−400	[14]
Mercapto-β-cyclodextrin/Au NP/MWCNT/GCE	DPV	0.0069	0.005−7.0	[15]
β-Cyclodextrin−CPE	DPV	0.3	6.0−20	[16]
MIP−graphene oxide/GCE	DPV	0.048	0.6−15	[17]
Pt-polydopamine@SiO_2/GCE	SWV	0.016	0.05−0.383	[18]
Poly(gallic acid)/MWCNT/GCE	DPV	0.054	0.075−25, 25−100	[19]
Rutin				
Polyglutamic acid/GCE	SWV	0.34	0.7−10	[10]
Polyvinylpyrrolidone/CPE	VA	0.15	0.39−13	[11]
Poly(p-aminobenzene sulfonic acid)/GCE	DPV	0.1	0.25−10	[12]
N-Butylpyridinium hexafluorophosphate/CPE	CV	0.35	0.5−100	[13]
Au NP/ethylenediamine/MWCNT/GCE	AdASDPV	0.032	0.048−0.96	[20]
MWCNT in 1% SDS/GCE	CV	0.71	1.4−28, 28−210	[5]

LOD, limit of detection; MWCNT, multi-walled carbon nanotubes, CV, cyclic voltammetry, AdADPV, adsorptive anodic differential pulse voltammetry; NP, nanoparticles; VA, voltammetry with linear potential sweep; GE, graphite electrode; DPV, differential pulse voltammetry; CNT, carbon nanotubes; CPE, carbon paste electrode; SWV, square-wave voltammetry; MIP, molecularly imprinted polymer; AdASDPV, adsorptive anodic stripping differential pulse voltammetry.

(GCEs) modified with CeO_2 nanoparticles and surfactants and their use in the analysis of medicinal plant materials.

EXPERIMENTAL

Reagents and solutions. We used 95% quercetin (Sigma, Germany) and 97% rutin trihydrate (Alfa Aesar, United Kingdom), stock 1.0 mM solutions of which were prepared by dissolving accurately weighed portions in 5.0 mL of rectified ethanol. Stock 0.10 M solutions of sodium dodecyl sulfate (SDS) (Panreac, Spain) and Brij® 35 (Sigma, Germany) and 0.50 mM solution of cetylpyridinium bromide (CPB) (Aldrich, Germany) were prepared by dissolving accurately weighed portions in distilled water in 10.0-mL volumetric flasks. Working solutions were prepared by diluting stock solutions. Other reagents were of cp grade.

To modify the working electrode, dispersions of CeO_2 nanoparticles (Aldrich, Germany) in water and various surfactant solutions with a concentration of 1.0 mg/mL were used; the solutions were prepared by ultrasonic treatment for 10 min.

Voltammetric measurements were carried out using a μAutolab Type III potentiostat/galvanostat (Eco Chemie B.V., the Netherlands) in a three-electrode cell consisting of a working (GCE, CeO_2−H_2O/GCE, or CeO_2−surfactant/GCE), auxiliary (platinum), and saturated silver−silver chloride electrodes. Modified electrodes were obtained by the droplet evaporation of 5 μL of dispersions of CeO_2 nanoparticles. Prior to modification, the GCE working surface was renewed mechanically, by polishing it with alumina with a particle size of 0.05 μm. Then, the electrode was rinsed with acetone and distilled water. The platinum electrode was purified in HNO_3 (1 : 1) for 3 min and washed with distilled water.

Electrochemical measurements were carried out in a 25.0-mL cell. Ten milliliters of a supporting electrolyte (Britton−Robinson buffer solution with pH 2.0−8.0) or a supporting electrolyte with an aliquot portion of a quercetin or a rutin solution were placed in the cell (the solution volume in the cell was 10.0 mL), and cyclic voltammograms were recorded in the range of 0 to 1.0 V with a potential sweep rate of 100 mV/s or differential pulse voltammograms were obtained in the range of 0 to 0.9 V. The pulse parameters were varied. We used the baseline correction tool in the GPES 4.9

software (Eco Chemie B.V., the Netherlands) for a more accurate calculation of the peaks.

To determine the pH of the supporting electrolyte, an Ekspert-001 pH meter (Econix-Expert, Russia) was used.

Sample preparation of medicinal plant materials consisted in obtaining infusions and decoctions according to the standard method [25], as well as alcohol extracts and acid hydrolysates. For the preparation of infusions and decoctions, an accurately weighed portion of a medicinal plant material (10.000 ± 0.005 g) was placed in an enameled bowl. To prepare the decoctions, 200 mL of distilled water at room temperature was added and boiled in a water bath for 30 min. In the case of infusions, medicinal plant materials were poured with 200 mL of boiling distilled water and infused for 15 min. Then the extracts were cooled at room temperature (for decoctions for 10 min), filtered, and made up to volume with water. Alcoholic extracts were obtained by placing an accurately weighed portion of a raw material (1.0000 ± 0.0005 g) in a 50-mL separatory funnel and setting the working conditions for extracting analytes by varying the volume of the extractant (ethanol) and the extraction time. The extracts were filtered and used for further research. To obtain hydrolysates, an accurately weighed portion (1.0000 ± 0.0005 g) of raw material was placed in a round-bottomed flask, poured with 20.0 mL (for bearberry leaves and marigold flowers) or 30.0 mL (for St. John's wort herb) of 1.1 M HCl in ethanol, and boiled in a water bath for 10 (for bearberry leaves), 15 (for St. John's wort herb), or 20 min (for marigold flowers) with a reflux condenser. The resulting hydrolysates were filtered and made up to the appropriate volume with alcohol [26].

Spectrophotometric determination of total flavonoids was carried out according to the procedure [27]. For this, 0.50 mL extracts of medicinal plant materials, 2.0 mL of distilled water, and 0.15 mL of a 5% $NaNO_2$ solution were placed in a test tube and incubated for 6 min. Then, 0.15 mL of a 10% $AlCl_3$ solution was added; after 6 min, 2.0 mL of a 4% NaOH solution was added, and the volume was adjusted with distilled water to 5.0 mL. After 15 min, the absorbance of the solutions was measured at 510 nm, using distilled water as a reference solution. The total concentration of flavonoids in plant raw materials was expressed in terms of quercetin (for hydrolyzates of bearberry leaves, marigold flowers, and St. John's wort herb) or rutin (for extracts, tinctures, and decoctions of St. John's wort herb).

The statistical treatment of results was carried out for five measurements at a confidence level of 0.95. The results were presented as $X \pm \Delta X$, where X is the mean value and ΔX is the confidence interval. The random error of determination was estimated by the magnitude of the relative standard deviation (RSD).

Correlation analysis was performed using an Origin-Pro 8.0 software (OriginLab, United States).

RESULTS AND DISCUSSION

Oxidation of quercetin and rutin on surfactant-modified electrodes. Quercetin and rutin are oxidized at 0.25 and 0.32 V, respectively, on both GCE and GCE modified with cerium dioxide nanoparticles (CeO_2–H_2O/GCE) (Fig. 1, curves *2* and *3*). There are weakly expressed steps in the cathodic branches of cyclic voltammograms, the heights of which are much smaller than the height of the steps in the anodic branches, which evidences the irreversibility of the electro-oxidation. In the case of the modified electrode, the shape of voltammograms was improved, and the oxidation currents of quercetin and rutin increased by 2.1 and 2.3 times, respectively, compared to the GCE. The deposition of CeO_2 nanoparticles led to an increase in the effective surface area of the electrode and, consequently, of the oxidation currents of quercetin and rutin.

Further, we studied dispersions of CeO_2 nanoparticles in surfactants of different nature (CPB, SDS, and Brij® 35) to improve the voltammetric characteristics of the oxidation of flavonoids. In this case, surfactants act as comodifiers of the electrode surface. CeO_2 nanoparticles at pH 6.0 carry a partial positive surface charge [28], which determines their electrostatic interaction with negatively charged "heads" of SDS. Under these conditions, cationic CPB undergoes electrostatic repulsion, and for nonionic Brij® 35, hydrophobic interactions play a key role. The voltammetric characteristics of quercetin and rutin for the electrodes modified with CeO_2 nanoparticles and surfactants are presented in Table 2. It was found that, on CeO_2–CPB/GCE, there is a noticeable decrease in the oxidation currents of quercetin and rutin as compared with CeO_2–H_2O/GCE, which is probably due to the partial leaching of the modifier from the electrode surface due to the above reasons. In cases of anionic SDS and nonionic Brij® 35, oxidation currents of the analytes increase while maintaining the oxidation potentials. This can be explained by the hydrophobic interactions of the aromatic rings of flavonoids with the hydrophobic tails of surfactant molecules, which leads to the preconcentration of analytes on the electrode surface. The best shape of voltammograms and the maximum oxidation currents of flavonoids were obtained using CeO_2–SDS/GCE. Varying the concentration of SDS in the range of 1.0 µM to 1.00 mM shows that the best peak parameters of the oxidation of quercetin were obtained for 10 µM SDS (the peak current is 4.3 ± 0.1 µA at a potential of 0.25 V). A further increase in the SDS concentration led to a decrease in currents and anodic displacement of the oxidation potential of quercetin, which is probably due to an increase in the thickness of
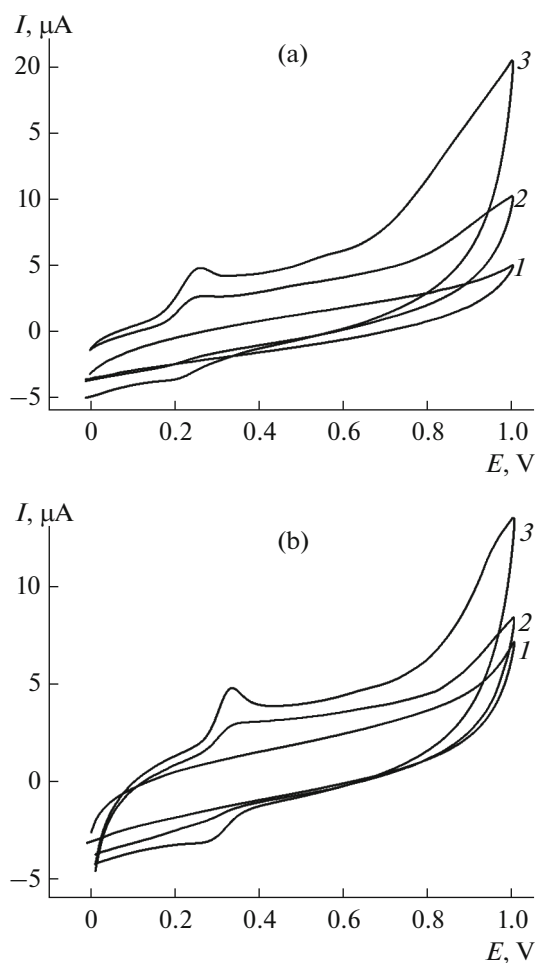
Fig. 1. Cyclic voltammograms of 100 µM of (a) quercetin and (b) rutin at (*2*) a GCE and (*3*) a CeO_2-H_2O/GCE in (*1*) Britton−Robinson buffer solution at pH 6.0; potential scan rate, 100 mV/s.

the surfactant coating and its partial leaching from the electrode surface when placed in a supporting electrolyte solution.

To determine the nature of the electrochemical process, we estimated the effect of potential scan rate on the oxidation currents of quercetin and rutin in the range of 0.01 to 1 V/s (Fig. 2). It was found that the electro-oxidation of quercetin and rutin is controlled by the analyte adsorption. This is confirmed by the linear dependences of the oxidation currents on the potential scan rate and the slopes of the linear dependences of $\ln I_p$ on $\ln v$ [29] equaled to 0.90 [Eqs. (1) and (3) for quercetin and Eqs. (2) and (4) for rutin]:

$$I_p\,(\mu A)$$
$$= (0.51 \pm 0.04) + (37.5 \pm 0.7) \times 10^{-3} v\,(\text{mV/s}), \quad (1)$$
$$R^2 = 0.9974,$$

$$I_p\,(\mu A)$$
$$= (0.25 \pm 0.02) + (22.4 \pm 0.4) \times 10^{-3} v\,(\text{mV/s}), \quad (2)$$
$$R^2 = 0.9973,$$

$$\ln I_p\,(\mu A)$$
$$= (3.59 \pm 0.06) + (0.90 \pm 0.03)\ln v\,(\text{V/s}), \quad (3)$$
$$R^2 = 0.9942,$$

$$\ln I_p\,(\mu A)$$
$$= (3.10 \pm 0.03) + (0.90 \pm 0.01)\ln v\,(\text{V/s}), \quad (4)$$
$$R^2 = 0.9988.$$

The oxidation of quercetin and rutin is irreversible, as evidenced by the ratio of currents of the cathodic and anodic peaks, as well as by the shift of the oxidation potentials with an increase in scanning rate. In this case, the number of electrons participating in the

Table 2. Voltammetric characteristics of quercetin and rutin on electrodes modified with CeO_2 nanoparticles and surfactants ($n = 5$, $P = 0.95$)

Analyte	Electrode	$c_{\text{surfactant}}$, mM	E, V	I, µA
Quercetin	CeO_2-H_2O/GCE	0	0.25	2.31 ± 0.07
	CeO_2-CPB/GCE	0.50	0.23	1.54 ± 0.04
	CeO_2-SDS/GCE	1.0	0.25	3.2 ± 0.1
	CeO_2-Brij® 35/GCE	1.0	0.27	2.88 ± 0.09
Rutin	CeO_2-H_2O/GCE	0	0.33	2.23 ± 0.08
	CeO_2-CPB/GCE	0.50	0.33	2.10 ± 0.04
	CeO_2-SDS/GCE	1.0	0.32	3.08 ± 0.05
	CeO_2-Brij® 35/GCE	1.0	0.33	3.06 ± 0.04

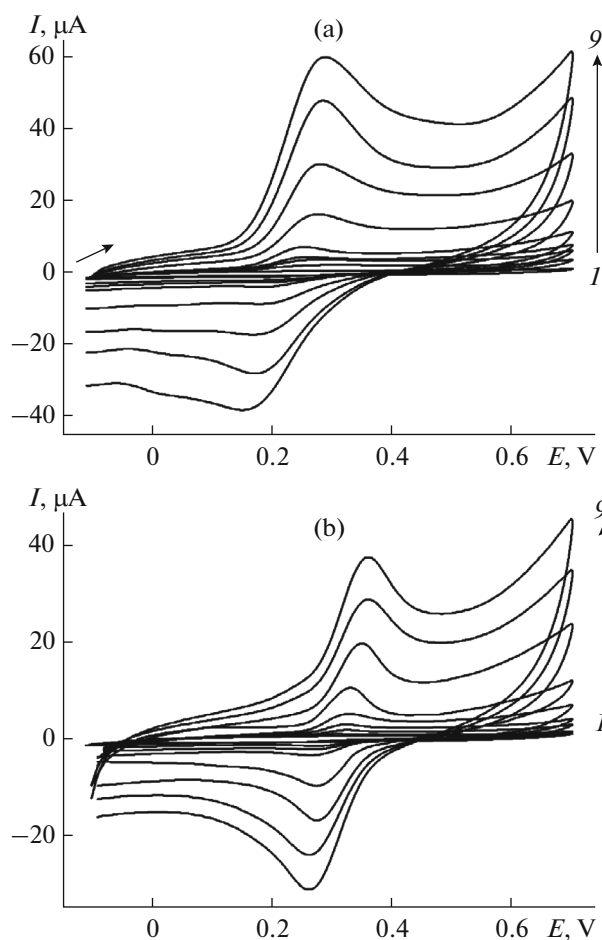**Fig. 2.** Cyclic voltammograms of 100 μM of (a) quercetin and (b) rutin at CeO$_2$−SDS/GCE in (*1*) Britton−Robinson buffer solution with pH 6.0 at the potential scan rate of (*2*) 10, (*3*) 25, (*4*) 50, (*5*) 100, (*6*) 250, (*7*) 500, (*8*) 750, and (*9*) 1000 mV/s.

Fig. 3. Effect of the pH of the supporting electrolyte on the voltammetric characteristics of 100 μM of (a) quercetin and (b) rutin on CeO$_2$−SDS/GCE.

reaction can be calculated using the equation $\Delta E_{1/2}$ (mV) $= 62.5/[(1 - \alpha)n]$ at 298 K. For an irreversible process, $\alpha = 0.5$ [29]. The width of the oxidation peak at half height is 61 ± 3 mV for quercetin and 56 ± 1 mV for rutin; therefore, the number of electrons participating in the reaction is 2.0 ± 0.1 and 2.23 ± 0.04, which agrees well with the data of [5, 8, 30].

Varying the pH of the supporting electrolyte in the range from 2.0 to 8.0 showed that one oxidation peak was observed for quercetin at pH 2.0−6.0, which at pH ≥ 7.0 split into two peaks, and the second peak was poorly pronounced. For rutin, there was one oxidation peak over the entire range of pH values studied. The oxidation potentials of quercetin and rutin shifted proportionally to lower values as the pH of the supporting electrolyte increases (Fig. 3), confirming the participation of protons in the electrode reaction. The obtained values of the slopes for quercetin and rutin, 64 and 60.3 mV, respectively [Eqs. (5) and (6)], indi-
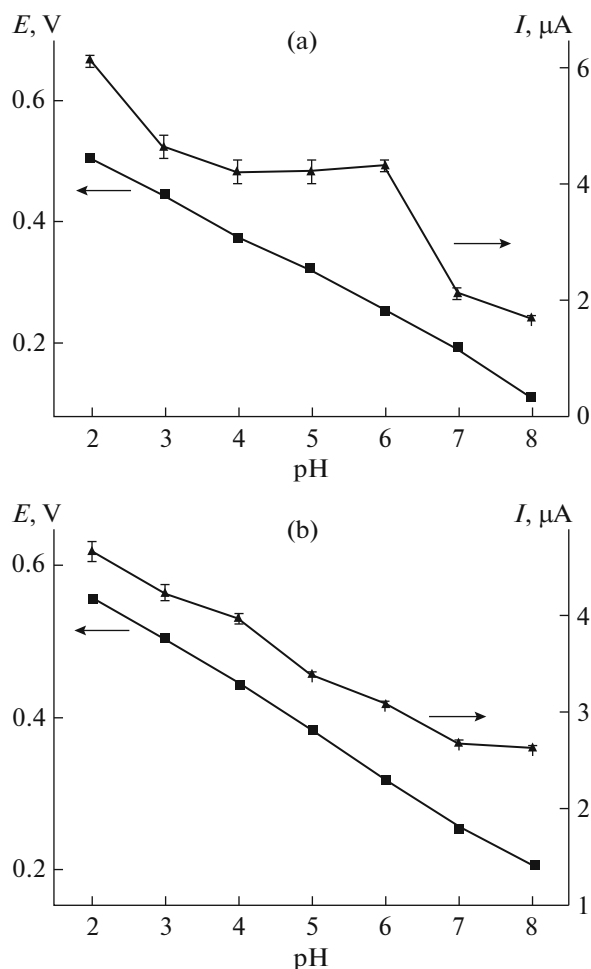
cated an equal number of protons and electrons participating in the reaction, that is,

$$E\,(\text{V}) = (0.636 \pm 0.007) - (0.064 \pm 0.001)\,\text{pH},$$
$$R^2 = 0.9974, \tag{5}$$

$$E\,(\text{V}) = (0.681 \pm 0.005) - (0.0603 \pm 0.0009)\,\text{pH},$$
$$R^2 = 0.9986. \tag{6}$$

The oxidation currents of quercetin and rutin decreased with increasing pH; therefore, pH 2.0 was selected for further studies.

Based on these results and data [5, 8, 31], it can be concluded that the hydroxyl groups of ring B are involved in the oxidation reaction of quercetin and rutin with the formation of the corresponding *o*-quinones according to the scheme
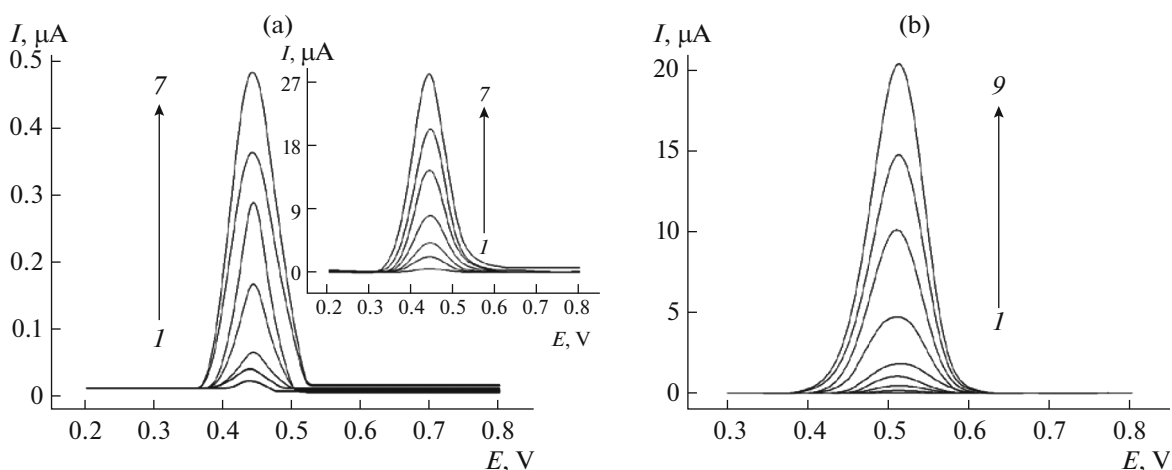
Fig. 4. Differential pulse voltammograms of (a) quercetin and (b) rutin at various concentrations on CeO_2–SDS/GCE in Britton–Robinson buffer solution with pH 2.0 with baseline correction: (a) (*1*) 0.010, (*2*) 0.050, (*3*) 0.10, (*4*) 0.25, (*5*) 0.50, (*6*) 0.75, and (*7*) 1.00 µM; insert: (*1*) 1.00, (*2*) 5.00, (*3*) 10.0, (*4*) 25.0, (*5*) 50.0, (*6*) 75.0, and (*7*) 100 µM; (b) (*1*) 0.10, (*2*) 0.50, (*3*) 1.00, (*4*) 5.00, (*5*) 10.0, (*6*) 25.0, (*7*) 50.0, (*8*) 75.0, (*9*) 100 µM. Pulse amplitude, 75 mV; pulse time, 25 ms; the potential scan rate, 10 mV/s.

R = H or glucose + rhamnose
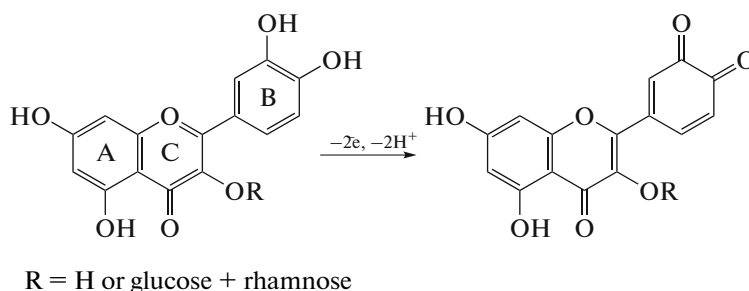
Differential pulse voltammetry of flavonoids using CeO_2–SDS/GCE. Differential pulse voltammetry was used for the quantification of quercetin and rutin. The variation of the pulse amplitude in the range from 25 to 100 mV and the pulse time from 25 to 75 ms showed that the best parameters for the electro-oxidation peaks of analytes were achieved with a pulse amplitude of 75 mV and a pulse time of 25 ms. Under these conditions, differential pulse voltammograms of quercetin and rutin showed distinct oxidation peaks at 0.44 and 0.51 V, respectively; their height increased with the analyte concentration in the cell (Fig. 4). The analytical ranges are 0.010–1.00 and 1.00–250 µM for quercetin [Eqs. (7) and (8)] and 0.10–100 µM for rutin [Eq. (9)] with the limits of detection (S/N = 3) of 2.9 and 28 nM, respectively.

$$I_p \ (\mu A) = (0.001 \pm 0.002)$$
$$+ \ (5.07 \pm 0.05) \times 10^3 c_{quercetin} \ (M), \quad R^2 = 0.9996, \quad (7)$$

$$I_p \ (\mu A) = (0.9 \pm 0.2)$$
$$+ \ (2.78 \pm 0.02) \times 10^3 c_{quercetin} \ (M), \quad R^2 = 0.9997, \quad (8)$$

$$I_p \ (\mu A) = (0.2 \pm 0.1)$$
$$+ \ (2.04 \pm 0.02) \times 10^3 c_{rutin} \ (M), \quad R^2 = 0.9994. \quad (9)$$

The analytical characteristics obtained for quercetin and rutin are superior to those previously described, including the use of other modified elec-

Table 3. Voltammetric determination of quercetin and rutin in model solutions using CeO_2–SDS/GCE in Britton–Robinson buffer solution with pH 2.0 (*n* = 5, *P* = 0.95)

Analyte	Added, µg	Found, µg	RSD, %	R, %
Quercetin	0.030	0.031 ± 0.002	5	103
	0.30	0.30 ± 0.02	4	100
	3.0	2.99 ± 0.04	1	99.7
	30	30 ± 1	4	100
	302	301 ± 5	1	99.7
Rutin	5.6	5.7 ± 0.1	1	102
	28	28 ± 1	3	100
	56	56 ± 2	3	100
	305	307 ± 2	0.5	101
	611	610 ± 4	0.5	99.8

trodes (Table 1). It should be noted that even square-wave voltammetry, characterized by higher sensitivity than differential pulse voltammetry, does not ensure lower limits of detection.

Quercetin and rutin were determined in model solutions. The accuracy of the procedure was evaluated by the added-found method (Table 3). The relative standard deviation did not exceed 5%. The values of the recovery testify to the high accuracy of the proposed method.

The selectivity of the electrode response to quercetin and rutin, the concentration of which in the cell was 10 μM, was evaluated. It was found that a 1000-fold excess of inorganic ions (K^+, Na^+, Mg^{2+}, Ca^{2+}, NO_3^-, Cl^-, and SO_4^{2-}) and a 100-fold excess of glucose, sucrose, and rhamnose, as well as ascorbic acid, do not interfere with the determination of flavonoids.

Determination of quercetin and rutin in medicinal plant materials. The developed approach was tested in analyzing samples of medicinal plant materials, which is an essential source of rutin and quercetin. St. John's wort herb (*Hyperici herba*), marigold flowers (*Calendulae officinalis flores*), and bearberry leaves (*Arctostaphyli uvae ursi folia*) from different manufacturers were studied as test samples. The main flavonoids were rutin for St. John's wort [26, 32] and quercetin and its monoglycosides for marigold [33] and bearberry [34].

Flavonoids were extracted from the raw materials with ethanol. We found the optimal conditions for extracting target analytes by varying the ratio of raw materials to extractant (1 : 20 or 1 : 30) and the duration of extraction (10−25 min). It was shown that the extraction of flavonoids was maximum at a ratio of 1 : 20 and the extraction time of 20 min for marigolds, 1 : 20 and 10 min for bearberry, and 1 : 30 and 15 min for St. John's wort. In the voltammograms of extracts, there are distinct oxidation peaks at a potential of 0.44 V for marigold and bearberry and 0.51 V for St. John's wort (Fig. 5, curve *1*) due to the oxidation of quercetin and rutin, respectively, which is confirmed by the standard addition method (Fig. 5, curves *2* and *3*). However, an increase in oxidation currents in the analysis of marigold flowers and St. John's wort herb suggests matrix effects. Therefore, we used the standard addition method for the quantitative determination of flavonoids in medicinal plant materials.

Various methods of extraction components from the medicinal plant materials was studied (ethanolic extracts, acid hydrolysates, decoctions, infusions, and calendula tincture). In the corresponding voltammograms, the oxidation peaks at 0.44 and 0.51 V (Fig. 6) are recorded as for reference solutions of quercetin and rutin (Fig. 6, curves for quercetin and rutin, respectively). The oxidation peak at 0.44 V (Fig. 6c) was observed for the hydrolysate of St. John's wort herb, indicating that rutin was converted to quercetin during
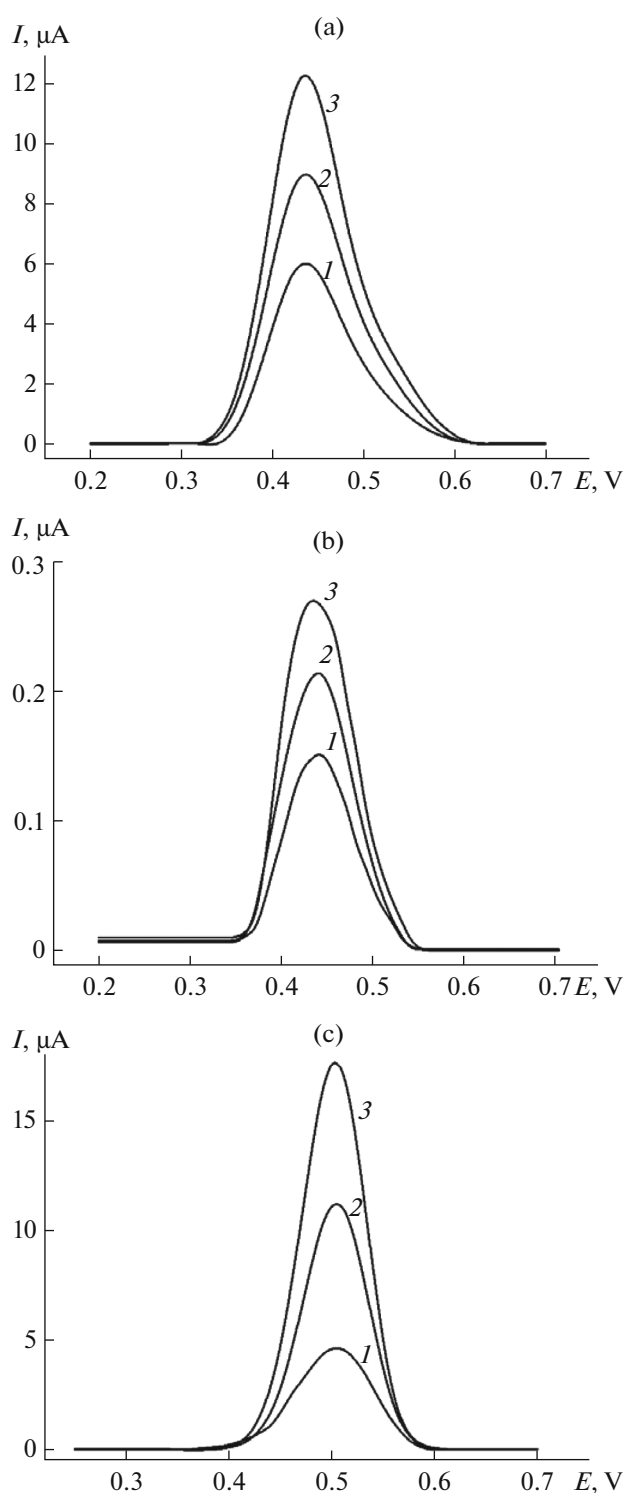

Fig. 5. Differential pulse voltammograms of the extracts of (a) bearberry leaves, (b) marigold flowers, and (c) St. John's wort herb on CeO_2−SDS/GCE in Britton−Robinson buffer solution with pH 2.0 with baseline correction: (a) (*1*) extract, (*2*) extract + 9.26 μM of quercetin, and (*3*) extract + 18.5 μM of quercetin; (b) (*1*) extract, (*2*) extract + 0.220 μM of quercetin, and (*3*) extract + 0.432 μM of quercetin; and (c) (*1*) extract, (*2*) extract + 12.3 μM of rutin, and (*3*) extract + 24.6 μM of rutin. Pulse amplitude, 75 mV; pulse time, 25 ms; the potential scan rate, 10 mV/s.
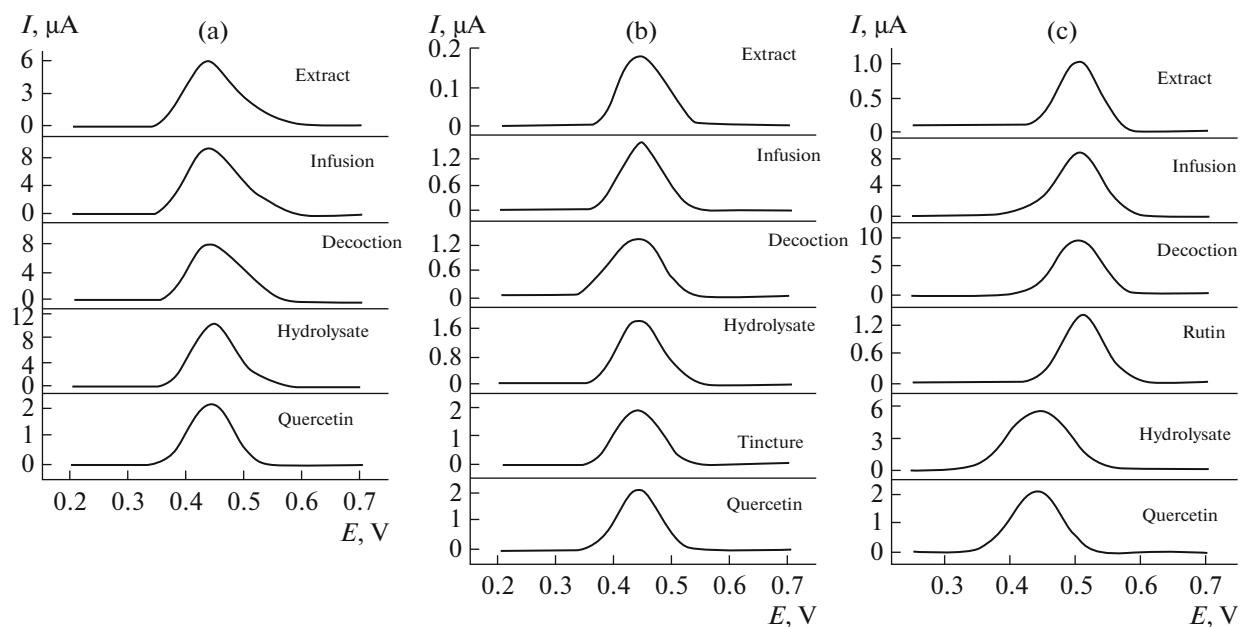
Fig. 6. Differential pulse voltammograms of the extracts from (a) bearberry leaves, (b) marigold flowers, and (c) St. John's wort herb and their main flavonoids (quercetin and rutin) on CeO_2–SDS/GCE in Britton–Robinson buffer solution with pH 2.0 with baseline correction. Pulse amplitude, 75 mV; pulse time, 25 ms; the potential scan rate, 10 mV/s.

acid hydrolysis, which agrees well with the data of [26, 35].

The results for the concentration of rutin and quercetin in extracts from medicinal plant materials are presented in Table 4. It was found that hydrolysates are

characterized with the highest content of quercetin. This proves once again that in the samples under investigation, quercetin presents mainly as glycosides, which transform into aglycones via acid hydrolysis. Decoctions and infusions are comparable in the con-

Table 4. Voltammetric determination of quercetin and rutin in medicinal plant materials ($n = 5$, $P = 0.95$)

Sample		Analyte	m, mg/g	RSD, %
Marigold flowers	extract	Quercetin	0.558 ± 0.004	0.6
	decoction		2.05 ± 0.03	2
	infusion		1.90 ± 0.05	3
	hydrolysate		15.6 ± 0.2	1
Calendula flowers	tincture	Quercetin	1.86 ± 0.03	1
Bearberry leaves	extract	Quercetin	27.8 ± 0.2	0.8
	decoction		22 ± 2	8
	infusion		31.5 ± 0.1	0.4
	hydrolysate		72.7 ± 0.3	0.5
St. John's wort herb	extract	Rutin	6.8 ± 0.2	3
	decoction		21 ± 1	5
	infusion		20.7 ± 0.5	2
	hydrolysate	Quercetin	30 ± 1	4
St. John's wort herb	extract	Rutin	5.3 ± 0.4	8
	decoction		9.7 ± 0.2	2
	infusion		10.3 ± 0.3	2
	hydrolysate	Quercetin	28 ± 1	5

centrations of the flavonoids under study (except for bearberry leaves), since extraction of the active components from loose fine raw materials (herbs, flowers, and leaves) is usually sufficient to obtain infusions; decoctions are usually prepared from more dense raw materials, for example, bark, roots and rhizomes [36]. The results of the voltammetric determination of quercetin and rutin were compared with the data of spectrophotometric determination of the total flavonoids by the reaction with aluminum chloride [27]. The total concentration of flavonoids obtained is statistically significantly higher than the concentration of rutin and quercetin, which confirms the presence of other flavonoids in medicinal plant materials. The levels of quercetin and rutin correlate with the total concentration of flavonoids: $r = 0.929$ with $r_{crit} = 0.521$ for $n = 11$ in the case of quercetin and $r = 0.951$ at $r_{crit} = 0.729$ for $n = 6$ for rutin. The data obtained allow us to recommend the developed approach for the control of medicinal plant materials and dosage forms based on it.

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