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The development of spectrophotometric and electroanalytical methods for ascorbic acid and acetaminophen and their applications in the analysis of effervescent dosage forms

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Abstract

The electroanalytical study of ascorbic acid, acetaminophen and of several mixtures of these compounds in different ratios has been made by using a carbon paste electrode (CPE-graphite:solid paraffin 2:1) as working electrode and an Ag/AgCl reference electrode. The potential curves were recorded using different concentrations of ascorbic acid and acetaminophen by measuring samples between 10 and 50 μl. The oxidation reactions were studied in a potential range from -0.1 to $+1.3$ V with different sweep rates, at different current sensitivities, in stationary working conditions and stirring before each replicate. The oxidation of ascorbic acid occurs at $+0.31 \pm 0.02$ V and the oxidation of acetaminophen at $+0.60 \pm 0.05$ V; meanwhile, the current has a linear variation for the following concentration ranges: 10^{-3}–10^{-2} M for the ascorbic acid and 3×10^{-6}–7.5×10^{-3} M for acetaminophen ($r^2 = 0.999$ for both ascorbic acid and acetaminophen). The mixtures of ascorbic acid and acetaminophen were made as follows: 1:1, 1:2, 1:3, 2:1, and 3:1. The studies revealed the alteration of the voltammograms processed according to the validation methodology. The best potential variation range for different current sensitivities, the influence of the sweep rate, of the solvent volume and of the pH were studied. The mutual interferences of the compounds in the mixtures and the electroactive compounds in the pharmaceutical dosage forms, especially effervescent ones, also made the object of the research. The same mixtures were studied using the direct spectrophotometric method that revealed a lot of spectral interferences. In order to solve this problem, an appropriate separation or an indirect spectrophotometric method (the apparent content curves method) were used. The spectrophotometric and voltammetric methods developed were used to determine ascorbic acid and acetaminophen in different dosage forms (vials, tablets, suppositories and effervescent dosage forms). The results were compared with those obtained by other techniques.

Keywords: Effervescent dosage forms; Ascorbic acid; Acetaminophen

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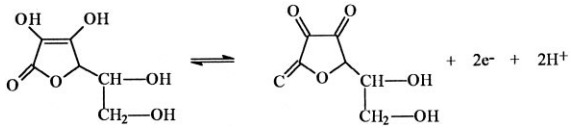
1. Introduction

The outstanding development of analytical instrumentation during the last decades determined the reconsideration of electroanalysis, especially in the field of new chemosensors with improved selectivity and sensitivity. This trend increased tremendously the development of new electroanalytical techniques [1–3], and detectors. The electrochemical sensors based on carbon paste are applied more and more in the pharmaceutical and biomedical analysis. The electroanalytical features and performances of carbon paste electrodes (CPE), several techniques for the design of chemo and biosensors through the modification of carbon paste, the trends and strategies for developing CPEs and their analytical applications were presented in some recent reviews [4–9].

The determination of two or more components associated is often a difficult task for the analyst and the problem is even more complicate if these compounds are included in a dosage form where excipients are interfering. The effervescent solid dosage forms are largely used nowadays due to their pharmacotherapeutic advantages but they are a real challenge to the analyst. In order to develop a quantitative analytical method for Efferalgan-effervescent tablets, different mixtures of ascorbic acid and acetaminophen were studied by UV-Visible spectrophotometry and linear sweep voltammetry. Ascorbic acid is one of the most important vitamins due to its antioxidant and pH regulator properties, being often added to various food products and pharmaceuticals. Its determination from different and complex matrices (natural products, food, beverage, dosage forms) is frequently asked for, especially by spectrophotometric and electrochemical methods. The voltammetric, potentiometric or amperometric determination of ascorbic acid is based on its electrochemical behavior. The oxidation of ascorbic with CPE versus an Ag/AgCl reference electrode occurs at +0.31 V (buffer pH 4.7), mainly due to the formation of dehydroascorbic acid.

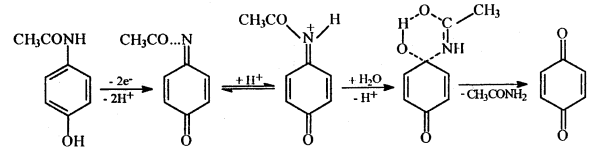


The voltammetric method for the determination of ascorbic acid with CPEs that have been conceived, was applied with good results to several dosage forms (tablets, vials) [10] and even to an effervescent dosage form containing a mixture of ascorbic and acetylsalicylic acid [11].

A voltammetric determination of ascorbic acid in foodstuffs using modified carbon paste electrodes was reported by the group of Kalcher and Vytraš et al. [12], their paper giving a good review of the electroanalytical methods.

Acetaminophen (paracetamol), the active ingredient of several pharmaceutical products, in different dosage forms and doses, alone or in association, is widely used as an analgesic, its primary metabolic pathways involving the liver oxidation. Electrochemical methods, especially the voltammetric and amperometric ones give the opportunity to study the oxidation mechanisms, the redox metabolites and their detection from pharmaceuticals and body fluids.

The cyclic voltammetric study concerning the electrochemical oxidation of acetaminophen was described in the works of Kissinger et al. [13,14].



The first reaction is an electrochemical oxidation by a two-electron, two-proton process; the result is *N*-acetyl-*p*-quinoneimine, which suffers some nonelectrochemical, but pH dependent reactions, and the final product is a benzoquinone.

Most of the scientific literature reports about the major interferences between ascorbic acid and/or acetaminophen with a great number of chemical species, in a variety of matrices.

The interferences between paracetamol and ascorbic acid in the UV spectrophotometry are well known because of the high overlapping degree of their spectra (Fig. 1). In addition, the UV spectrophotometry has a low selectivity. Precisely this low selectivity allows one to develop analytical methods in order to analyze multicomponent

samples, by multiwavelength measurements. The apparent content curves method [15] has been chosen in order to solve the interferences between the two compounds.

2. Experimental

2.1. Apparatus

A Bruker E 100 potentiostat and XY Hewlett-Packard 7035 B recorder were used for linear sweep voltammetric studies. The measurements have been performed in a polarographic cell with magnetic stirrer containing the carbon paste working electrode (CPE), Ag/AgCl as a reference electrode and a platinum wire as auxiliary electrode.

Samples were measured with 10, 100 and 500 μl Hamilton syringes and with adjustable volume digital pipette (Biohit-OY, Finland).

The pH of solutions was determined with a Chemcadet 5986-62 pH-meter (Cole Parmer) using a combined glass electrode. All experiments were carried out at room temperature (22 ± 1°C).

Spectrophotometric measurements were performed with an Ultrospec III UV-VIS spectrophotometer (Pharmacia LKB, UK), in the 10 mm quartz cell.

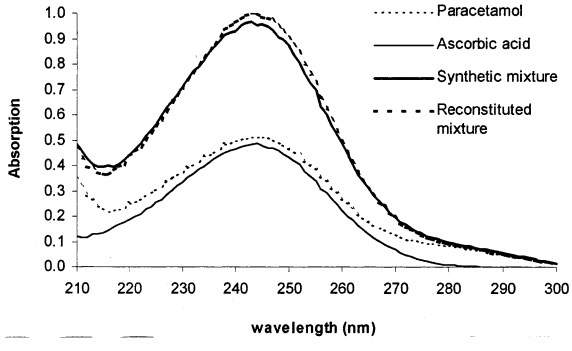


Fig. 1. UV spectra for paracetamol, ascorbic acid and their synthetic and reconstituted mixtures.

2.2. Reagents

All chemicals were of analytical grade (Merck or Reactivul Bucureşti) and were used as received. Ascorbic acid, acetaminophen and glycocole were of pharmaceutical grade (FR X-Romanian Pharmacopoeia Xth edition). Bidistilled and deionized water was used. The H_2SO_4 0.1 N solution was prepared by dissolving 200 ml of H_2SO_4 1 N in a 2000 ml calibrated flask.

Electrochemical and spectrophotometric measurements were carried out on the following pharmaceuticals: Paracetamol-tablets (Sicomed), Paracetamol-tablets (Europharm S.A.), Tylenol-tablets (Family Pharmacy), Efferalgan 500 mg-effervescent tablets (UPSA), Efferalgan-Vitamin C-effervescent tablets (UPSA), Vitamina C 200-tablets (Sicomed), Vitamina C 5 ml-vials (Sicomed).

2.2.1. Solutions used for the electrochemical method

Around 0.080 g ascorbic acid, respectively, 0.075 g acetaminophen were precisely weighted and dissolved in water in a 50 ml calibrated flask (standard solutions). A total of 10^{-1} M glycocole solution was prepared by weighing 7.505 g glycocole and 5.850 g NaCl. The substances were transferred into a 1 l calibrated volumetric flask, dissolved in deionized water and diluted to 1000 ml by using deionized water.

The buffer solutions were prepared by mixing in 100 ml calibrated flasks different volumes of glycocole solution, the pH being adjusted to the desired value with HCl (pH 1.0–3.0) and NaOH (pH 9.0). For the pH 7.0 we used a Radelkis (Hungary) buffer solution, and for pH 4.7–6.0 we used the acetate buffer.

Ascorbic acid–acetaminophen mixtures in different ratios: 1:1; 1:2; 2:1; 1:3 and 3:1 were prepared 'ex tempore' by mixing the initial standard solutions. The sample solutions (containing approximately 10^{-2} M active compound) were prepared by weighing the correspondent amounts of ascorbic acid, acetaminophen or tablet powder, dissolving them in deionized water and filtering them into 50 ml calibrated flasks.

Table 1
Validation parameters for samples containing pure analytes

Analyt	Parameters	Voltammetry	Spectrophotometry
Acetaminophen	Linearity	$y = 2.97x + 1.9$ $r^2 = 0.998$	$Y = 0.074x + 0.0003$ $r^2 = 0.999$
	Accuracy	99.6 ± 2	100.3 ± 2.1
	Fidelity	$C_{computed} = 0.662$ $C(0.05,\ 3,\ 6) = 0.677$ $CV_r = 3.1$ $CV_R = 4.2$	$C_{computed} = 0.510$ $C(0.05,\ 3,\ 5) = 0.707$ $CV_r = 8.1$ $CV_R = 12.4$
Ascorbic acid	Linearity	$y = 5.95x + 0.75$ $r^2 = 0.999$	$y = 0.0525x - 0.013$ $r^2 = 0.9985$
	Accuracy	98.1 ± 1.1	100.6 ± 1.4
	Fidelity	$C_{computed} = 0.564$ $C(0.05,\ 4,\ 5) = 0.590$ $CV_r = 2.3$ $CV_R = 2.5$	$C_{computed} = 0.516$ $C(0.05,\ 4,\ 5) = 0.590$ $CV_r = 1.1$ $CV_R = 1.5$

Table 2
Acetaminophen determination from pharmaceuticals

Pharmaceuticals	Recovery (% of the nominal values)	
	Voltammetry	Spectrophotometry
Tylenol	101.46 ± 2.48	99.9 ± 2.3
Paracetamol (Sicomed)	98.71 ± 2.43	92.9 ± 1.2
Paracetamol (Europharm)	108.47 ± 2.44	101.0 ± 1.8
Efferalgan	109.59 ± 2.36	110.0 ± 1.8

2.2.2. Solutions used in the spectrophotometric method

The standard solutions were prepared by dissolving 81.44 mg of paracetamol and respectively 113.69 mg of ascorbic acid in 200 ml of H_2SO_4 0.1 N. 0.5 ml of the obtained solutions were mixed and diluted with H_2SO_4 0.1 N in calibrated flasks. This solution (solution A) contains 8.144 μg ml^{-1} paracetamol and respectively 11.369 μg ml^{-1} ascorbic acid.

The sample solutions were prepared in the same way as mentioned in Section 2.2.1. Using H_2SO_4 instead of water. From the Efferalgan (UPSA) effervescent tablets, 239 mg were accurately weighted, transferred into a 200 ml calibrated flask and dissolved in H_2SO_4 0.1 N. Aliquots of 0.6, 0.8 and 1.0 ml were diluted to 25 ml.

2.3. Electrode preparation

The CPE was prepared by using two types of carbon paste: the 'solid carbon paste' as reported by Petit and Kauffmann [16,17] and a modified one with stearic acid. The solid paraffin was melted in a porcelain capsule at a temperature close to its melting point (46–48°C), and the graphite particles were added and mixed with a glassy spatula for the homogenization. The final 'solid carbon paste' was obtained by thoroughly mixing and crushing the mixture in a mortar with a pestle. The graphite–paraffin ratio for 'solid carbon paste' was 2:1 (w/w). For the modified carbon paste, the stearic acid (5%) was melted together with the solid paraffin, the rest of the proceedings being the same as mentioned above. The two pastes were packed into the Teflon body of the electrode (3 mm i.d.). Before each new measurement, the electrode was smoothed to a mirror finish using a clean paper card.

2.4. Linear sweep voltammetry

The study of electrochemical behavior of ascorbic acid and acetaminophen has been performed by LSV using both the solid CPE and the modified electrode, versus an Ag/AgCl reference electrode. The determinations were made by successively adding different volumes of 10^{-2} M solutions in acetate buffer (pH 4.7), from -0.1 to

+1.1 V, with a sweep rate of 50 mV s^{-1} at 1 μA sensitivity. The samples have been statistically interpreted through the least squares method and the calibration curves obtained (illustrated in Table 1) were used for the determination of ascorbic acid and acetaminophen from several dosage forms (see Table 2).

The different ratio mixtures of ascorbic acid and acetaminophen were studied in a similar manner. The intensity/potential curves obtained with the solid CPE and the modified CPE with stearic acid were also compared.

Finally the voltammetric method was applied to Efferalgan-Vitamin C (UPSA), samples prepared as mentioned in Section 2.2.1.

2.5. Spectrophotometric study

2.5.1. Apparent content curves of paracetamol–ascorbic acid mixtures

The apparent content curves were obtained by plotting the function $F_i = (A)_i/(\varepsilon_A)_i$ against λ_i where $(A)_i$ means the absorbance of the standard mixture solution (solution A) and $(\varepsilon_A)_i$ the molar absorption coefficient of the compound to be determined. Fig. 2 shows the apparent content curves for solution A considering paracetamol (a) and ascorbic acid (b) as interferent compounds. Paracetamol has been chosen as interferent because of its higher degree of interference in the 250–290 nm range as Fig. 2b shows.

2.5.2. Concentration calculus

The solution A was subjected to successive dilutions. The difference $R_p = \lambda_j - \lambda_k$ (j, k being the selected wavelength, respectively 260 and 280 nm) of the obtained solutions were plotted against $1/i$ were i is the degree of dilution. A straight line was obtained. The regression equation was used to compute the necessary dilution for an unknown sample, in order to obtain a standard mixture with the same concentration of interferent as the sample.

The UV spectra of the samples were recorded. The absorbance values were used in order to compute the R_x values for the sample.

The paracetamol concentration considered as interferent is calculated using the following expression:

$$(C_I)_x = \frac{R_x}{R_p}(C_I)_p \quad (1)$$

where R_p and R_x are the above mentioned parameters for the standard solution A and respectively for the sample.

For the determination of the analyte concentration, the following equation is applied:

$$(C_A)_x = F_x \frac{(C_I)_x}{(R_I)_p}[(C_A)_p - F_p] \quad (2)$$

F_p and F_x being computed as the F values for the standard solution and respectively for the sample, at the chosen wavelength, considering ascorbic acid as the analyt and paracetamol as the interferent.

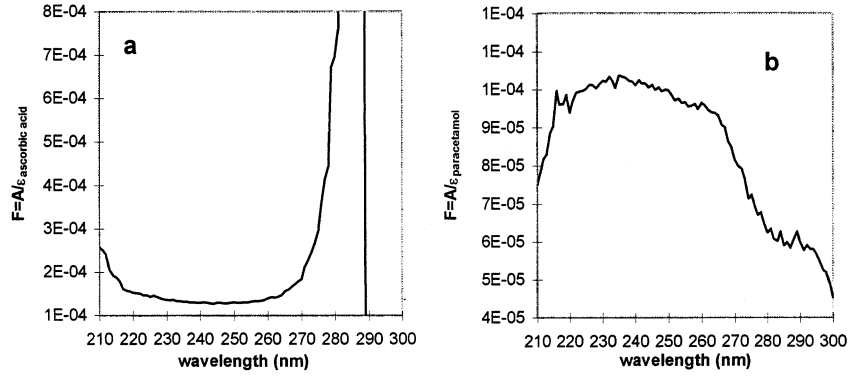


Fig. 2. Apparent content curves for ascorbic acid (6.46×10^{-5} M)–paracetamol (5.39×10^{-5} M) mixture. (a) Influence of paracetamol interference, (b) influence of ascorbic acid interference.

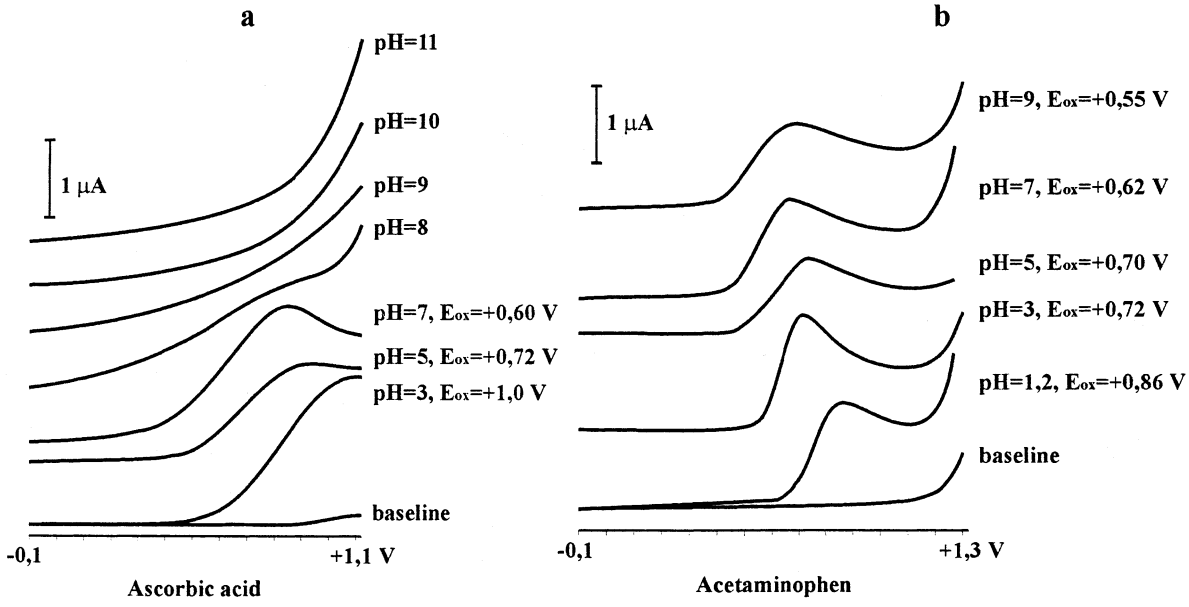


Fig. 3. Intensity/potential curves and relative peak oxidation potential (E_{ox}) versus pH (potential range $-0.1-+1.3$ V; 20 mV s^{-1}; 1 μA V^{-1}); (a) 1.25×10^{-4} ascorbic acid; (b) 1.25×10^{-4} acetaminophen.

3. Results and discussion

3.1. LSV study of ascorbic acid and acetaminophen

The intensity/potential curves show for ascorbic acid an oxidation peak strongly dependent on the pH, the shape of the curves being useless at pH smaller than 3.0 and greater than 7.0 (Fig. 3a).

The pH influences the oxidation potential as well as the current and the shape of the intensity–potential curve also in the case of acetaminophen (Fig. 3b). It is to be noted that the oxidation potential (E_{ox}) decreases from $+0.86 \pm 0.02$ (at pH 1.2) to $+0.55 \pm 0.05$ V (at pH 9.0), probably due to the hydrolysis in alkaline medium, which brings more reducing compounds, as *p*-hidroxyaniline. Acid pHs are keeping the stability of acetaminophen, by inhibition of the hydrolysis. The best results, concerning both the current intensity and the reproducibility were obtained in the pH 5.0–7.0 range (Table 1).

In order to calculate the regression equation, oxidation curves were recorded, using linear sweep voltammetry at pH 4.7 (acetate buffer) (Fig. 4). Samples of 10–50 μl of 10^{-2} M ascorbic acid and acetaminophen solutions were added successively and recorded between -0.1 and $+1.1$ V, with a sweep rate of 50 mV s^{-1}, on the 1 μA scale. Each determination was repeated three times, after stirring the solution 60 s between replicates. The equations of the calibration curves, the concentration ranges and the validation parameters calculated for the studied compounds are illustrated in Table 1.

The electrochemical and spectrophotometric method was applied for the quantitative determination of ascorbic acid and acetaminophen from several dosage forms, with good results illustrated in Tables 2 and 3.

3.2. Electrochemical study of different mixtures of ascorbic acid and acetaminophen

The studies made on 1:1, 1:2, 2:1, 1:3 and 3:1 ratio mixtures of ascorbic acid and acetaminophen revealed the alteration of the voltammograms that were processed according to the validation method.

In all the studied mixtures the pH influences not only the oxidation curves, but the E_{ox} and current intensity too as it can be seen in Table 4.

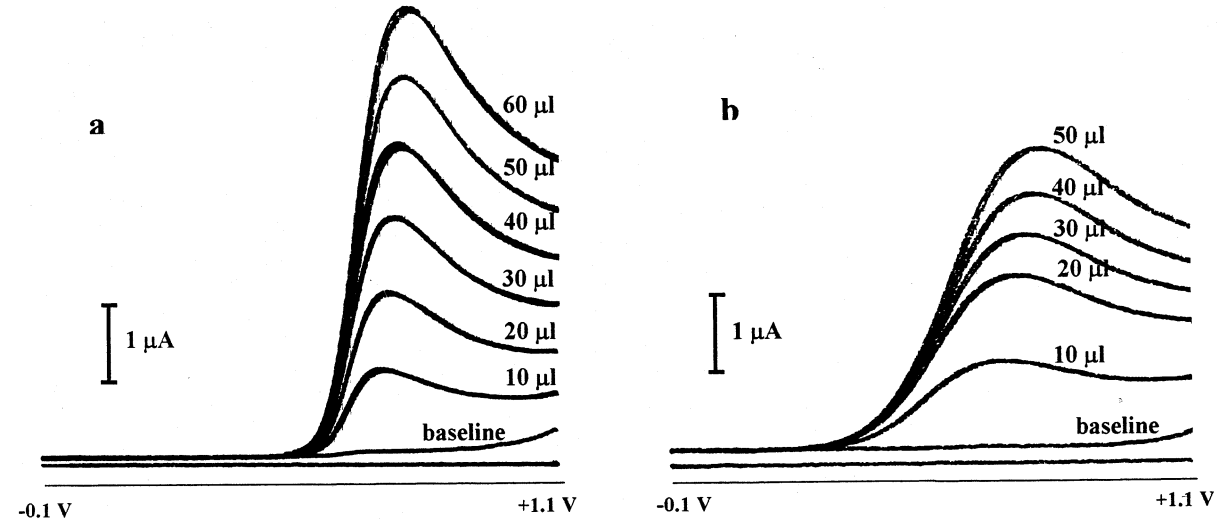


Fig. 4. Linear sweep voltammograms at different concentrations (50 mV s^{-1}; 1 µA; 4 ml acetate buffer pH 4.7). (a) 10^{-2} M acetaminophen solution; (b) 10^{-2} M ascorbic acid solution.

Intensity/potential curves for ascorbic acid–acetaminophen in equimolar mixture show a linear relationship between the current and the concentration, except for ascorbic acid at pH 9.0 where the current decreases dramatically, the shape of the curve is useless, in spite of the fact that the ascorbic acid oxidation seems to be happening at the same potential value. The oxidation of acetaminophen, at pH 9.0 occurs at smaller potentials ($+0.67 \pm 0.03$ V) and the current decreases, comparing with the acetate buffer (pH 4.7; $E_{ox} = +0.88 \pm 0.02$ V).

Ascorbic acid–acetaminophen, in 1:2 mixture has a similar behavior, the single oxidation peak being observed at $E_{ox} = +0.77 \pm 0.03$ V (pH 4.7) and $+0.90 \pm 0.03$ V (pH 9.0), with smaller current values for the alkaline medium.

Ascorbic acid–acetaminophen in a 2:1 mixture shows a single anodic oxidation peak at $+0.90 \pm 0.03$ V, both at pH 4.7 and pH 9.0, also with smaller current values in alkaline medium.

If the intensity/potential curves at the same pH values were compared, some differences can be noticed. At pH 4.7 (acetate buffer); the oxidation of the 1:2 ascorbic acid–acetaminophen mixture occurs at $+0.77 \pm 0.03$ V, and the oxidation of the 2:1 mixture at $+0.90 \pm 0.03$ V. At pH 9.0, the oxidation potentials are the same, $+0.90 \pm 0.03$ V for both 1:2 and 2:1 ratios. A decrease of the oxidation current that is directly related to the acetaminophen concentration was emphasized, which seems to have a major contribution.

The 1:3 ascorbic acid–acetaminophen mixture shows a well-defined oxidation peak, at $+0.78 \pm 0.02$ V (pH 4.7). This peak is strongly shifted at

Table 3
Ascorbic acid determination from pharmaceuticals

Pharmaceuticals	Recovery (%)
	Voltammetry
Vitamin C-tablets	105.5 ± 1.0
Vitamin C-vials	97.2 ± 2.1

Table 4
Relative peak oxidation of the mixture ascorbic acid–acetaminophen versus pH

Mixture	pH 4.7	pH 9.0
1: 1	0.88 ± 0.02	0.67 ± 0.03
1: 2	0.77 ± 0.03	0.90 ± 0.03
2: 1	0.90 ± 0.03	0.90 ± 0.03
1: 3	0.78 ± 0.02	0.95 ± 0.05
3: 1	0.85 ± 0.05	0.78 ± 0.02

Table 5
Current intensities (μA) for 1:2 and 2:1 mixtures of ascorbic acid and acetaminophen, recorded at pH 4.7 (acetate buffer)

Sample (μl)	Asc[a]	Par[b]	1:2 Mixture			2:1 Mixture		
			Experimental	Theoretic[c]	%	Experimental	Theoretic[c]	%
10	0.44	0.56	0.80	0.78	98	0.68	0.72	106
20	0.84	1.12	1.44	1.56	108	1.36	1.40	103
30	1.24	1.72	2.24	2.34	104	2.00	2.08	104
40	1.64	2.36	3.08	3.20	104	2.68	2.76	103
50	2.04	3.00	3.92	4.02	104	3.44	3.52	102

[a] Asc, ascorbic acid.
[b] Par, acetaminophen.
[c] Theoretic, normalized sum of the currents for each component measured individually.

$+0.95 \pm 0.05$ V for a pH 9.0, accompanied by a slow decrease of the current intensity and the alteration of the intensity–potential curve.

In the case of 3:1 ascorbic acid–acetaminophen mixture, the potential shift is opposite, from $+0.85 \pm 0.05$ (pH 4.7) to $+0.78 \pm 0.02$ V (pH 9.0) The shape modification and also the current decrease are more discrete.

By comparing the intensity–potential curves at the same pH value, the shift of the oxidation potential to greater values at pH 4.7, and to smaller values at pH 9.0, accordingly with the concentration of ascorbic acid in the mixture were noticed. It is to be noticed that the current decreases proportionally with the acetaminophen concentration in the 3:1 and 1:3 mixtures.

3.3. Voltammetric determination of ascorbic acid and acetaminophen from effervescent tablets

As mentioned above, the intensity–potential curves of all ratios of the ascorbic acid–acetaminophen mixtures showed a single, well-defined oxidation peak which does not allow the determination of each compound separately.

For the separate detection of the mixture compounds measurements have been made in identical conditions using a CPE, modified with 5% stearic acid, which has repulsive properties against ascorbic acid due to carboxylic groups from the electrode surface. The results of the measurements confirmed the fact that the intensity/potential curves of ascorbic acid have nearly no significant values in the studied potential range from -0.1 to $+1.1$ V. With the modified CPE, the same concentrations of acetaminophen showed oxidation peaks shifted to greater potentials ($E_0 \approx 1.0$ V) with diminished current intensities (about $68 \pm 2\%$ in comparison with solid CPE). The electrochemical study of the mixtures also revealed the same linear relationship between the signal and the additivity of the current intensity, in spite of the fact that the ascorbic acid contribution was significantly reduced (see Table 5).

From the experimental data two equations were obtained which describe the current intensity of the mixtures measured with solid CPE (Eq. (3)) and with the modified CPE containing 5% stearic acid (Eq. (4)):

$$A = a_1 + a_2 \tag{3}$$

were A is the current of the mixture and a_1, a_2 are the currents for ascorbic acid, respectively acetaminophen obtained with solid CPE

$$B = b_1 + b_2 \tag{4}$$

where B is the current of the mixture and b_1, b_2 are the currents for ascorbic acid, respectively acetaminophen obtained with the stearic acid modified CPE.

If the acetaminophen contribution is the same with both electrodes, $a_2 = b_2$, and the following is obtained:

$$A - B = a_1 - b_1 \tag{5}$$

meaning that the difference between the signals obtained for the same concentration with the above-mentioned electrodes is due only to the ascorbic acid differences concerning the response for the same couple of electrodes. Plotting that difference ($A-B$) versus the ascorbic acid concentration its concentration from different mixtures could be determined (Fig. 5a). Acetaminophen concentration was determined consecutively from the plot of the current intensity of the mixture obtained with the solid CPE (A) versus acetaminophen concentration (Fig. 5b). As you can see from Eq. (3) the acetaminophen concentration can be deduced, if the contribution of ascorbic acid (a_1) determined before and the total current A is known.

The method was applied for the determination of active components from Efferalgan-Vitamin C (UPSA)-effervescent tablets, the results being illustrated in Table 6.

The intensity/potential curves recorded on fresh samples of Efferalgan-Vitamin C-effervescent tablets revealed two oxidation steps, the first corresponding to ascorbic acid, and the second to acetaminophen (Fig. 5c). Statistical processing of these data in concordance with the calibration curves from Table 1 showed acceptable results, which offers the possibility to determine ascorbic acid and acetaminophen (Table 6).

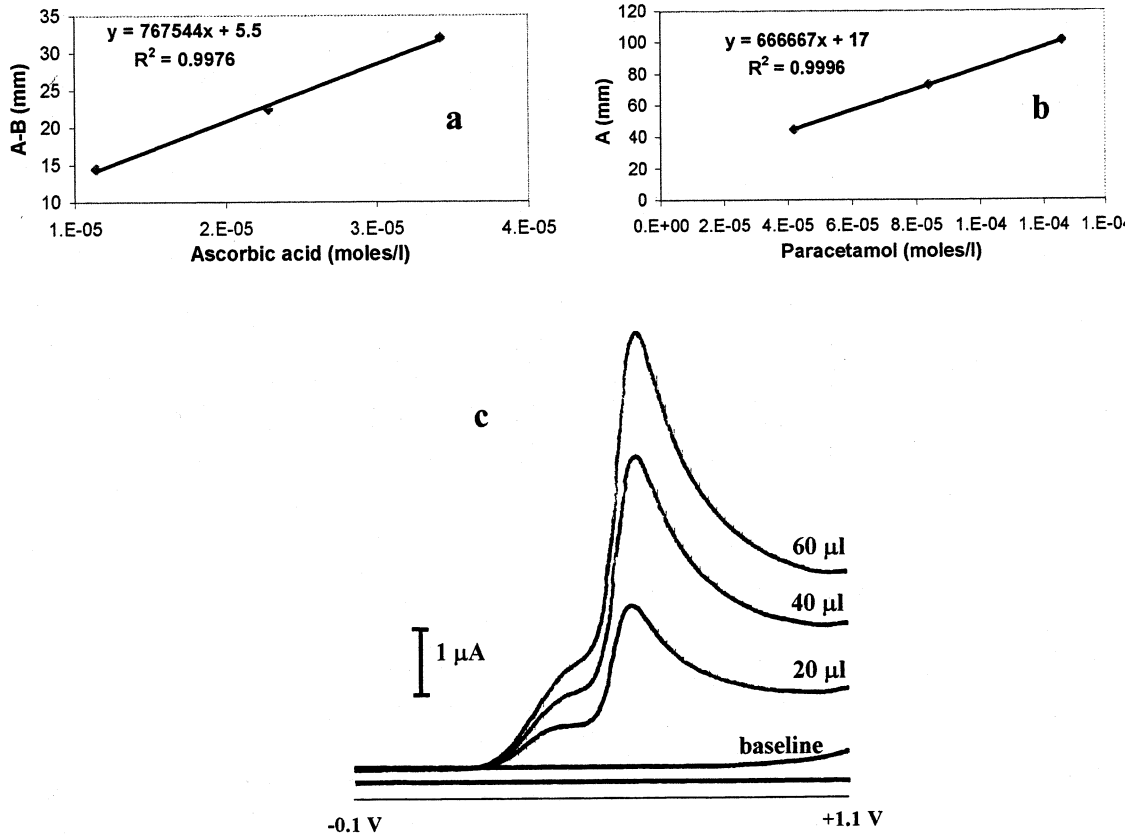


Fig. 5. Ascorbic acid and acetaminophen voltammetric determination from effervescent tablets. (a) Calibration plot of the current differences of the mixture when using solid carbon paste electrode (CPE) and modified CPE vs. ascorbic acid concentration; (b) current calibration plot of the mixture with CPE vs. acetaminophen concentration; (c) voltammograms at different concentrations of Efferalgan Vitamin C-effervescent tablets fresh samples.

Table 6
Voltammetric determination of ascorbic acid and acetaminophen from Efferalgan effervescent tablets

Sample	Ascorbic acid (g)	Acetaminophen (g)	Ascorbic acid (g tablet^{-1})	Acetaminophen (g tablet^{-1})
1[a]	0.0284	0.0458	0.245	0.396
2[a]	0.0264	0.0468	0.229	0.404
3[a]	0.0243	0.0444	0.209	0.384
4[b]	0.0234	0.0332	0.215	0.301
5[b]	0.0224	0.0389	0.207	0.336
6[b]	0.0253	0.0411	0.222	0.355

[a] Direct method.
[b] Difference method.

3.4. Spectrophotometric determination of ascorbic acid and acetaminophen from effervescent tablets

The UV spectra of the synthetic standard mixture (solution A) and its dilutions were measured and the results are presented in Table 7. According to the above-mentioned protocol, the $R_p = f(1/i)$ plot is a straight line. By linear regression, the equation $R_p = 5.47 \times 10^{-4}\ (1/i)$ with correlation coefficient $r^2 = 0.996$ was obtained (Fig. 6).

According to Eqs. (1) and (2), the concentration of the two components were computed and the results are presented in Table 8.

The results for ascorbic acid (0.216 ± 0.007 g tablet^{-1}) agree with the content given by the manufacturer (0.200 g tablet^{-1}). The paracetamol content as results from the analysis (0.415 ± 0.04 g tablet^{-1}) is about 1.2 times greater than the nominal one (0.330 g tablet^{-1}).

4. Conclusions

Ascorbic acid and acetaminophen have spectral and electrochemical properties which permits the calculation of calibration curves, in relatively large concentration range, allowing their determination from various usual dosage forms.

Ascorbic acid and acetaminophen association is accompanied by strong interferences that do not allow their determination either from the intensity–potential curves, or from the UV-visible absorption spectra.

The study of the ascorbic acid–acetaminophen mixtures in different ratios (1:1, 1:2, 2:1, 1:3 and 3:1) confirmed the strong interference, and revealed the fact that the current obtained is the sum of individual contribution and depends linearly on their concentrations. In order to determine each component from the mixture the intensity/potential curves were recorded for the same concentrations and ratios, in identical conditions with two different electrodes: a solid CPE and a modified one, with 5% stearic acid. The

Table 7
Values of R for ascorbic acid–paracetamol standard mixture

Solution	Molar concentration [$\times 10^{-5}$]		R_p	$1/i$
	Ascorbic acid	Acetaminophen		
1	6.46	5.39	5.55	1
2	5.17	4.31	4.32	0.8
3	3.88	3.23	3.13	0.6
4	2.58	2.16	2.32	0.4
5	1.29	1.08	1.07	0.2

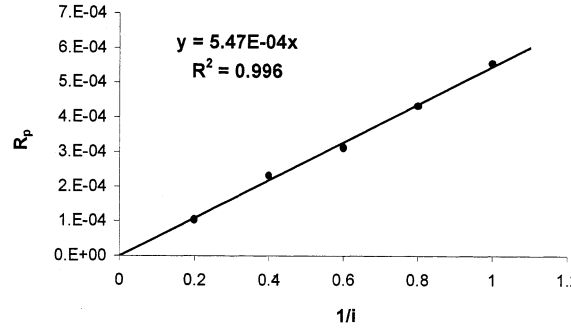


Fig. 6. Calibration curve for paracetamol (interferent) in presence of ascorbic acid (analyte).

Table 8
Results obtained for Efferalgan effervescent tablets

Sample	R_x [$\times 10^{-4}$]	$1/i$	Weight (g)		Content (g tablet^{-1})	
			Ascorbic acid	Paracetamol	Ascorbic acid	Paracetamol
1	2.61	0.48	0.0175	0.0319	0.2170	0.3943
2	3.78	0.69	0.0172	0.0346	0.2128	0.4280
3	4.68	0.86	0.0176	0.0343	0.2172	0.4248

voltammetric method was applied with good results to Efferalgan-Vitamin C effervescent tablets, using the plot of the current intensity difference obtained with the couple of electrodes for the mixture, against ascorbic acid concentration and the current of the mixture obtained with CPE versus acetaminophen concentration.

The results obtained by the spectrophotometric method using the Apparent Contents Curves method agree for the ascorbic acid determination from effervescent tablets with the nominal ones. Paracetamol determination was interfered by the ascorbic acid and the results are greater than the manufacturer declaration.

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