STU
FCHPT

Differential pulse voltammetric assay of H_1-antihistamine fexofenadine in pharmaceutical formulations using a bare glassy carbon electrode

Monika Čerňanská[1], Romana Králiková[1], Jana Blaškovičová[1, 2], Ľubomír Švorc[1]

[1]*Institute of Analytical Chemistry, Faculty of Chemical and Food Technology, Slovak University of Technology in Bratislava, Radlinského 9, Bratislava, SK-812 37, Slovakia*
[2]*Department of Microbiology and Virology, Faculty of Natural Sciences, Comenius University Bratislava, Mlynská dolina, Ilkovičova ulica č. 6, Bratislava, SK-842 15, Slovakia*
lubomir.svorc@stuba.sk

Abstract: A simple differential pulse voltammetric procedure was developed for the determination of the H_1-antihistamine fexofenadine in commercial pharmaceutical formulations using a bare glassy carbon electrode. The electrochemical behavior of fexofenadine was investigated by cyclic voltammetry in phosphate buffer solutions. The analyte provided an irreversible anodic signal at approximately +0.75 V versus an Ag/AgCl/3 mol·L^{-1} KCl reference electrode in phosphate buffer at pH 10, where the highest current response was obtained. The influence of scan rate indicated that the oxidation process was predominantly diffusion-controlled. Differential pulse voltammetry was optimized and then used for quantitative analysis. Under the optimized conditions, the method provided a linear concentration range from 9.5 to 67.9 µmol·L^{-1}, a detection limit of 2.7 µmol·L^{-1}, and repeatability expressed as a relative standard deviation of 4.8 % for twelve replicate measurements. The influence of selected tablet excipients, including glucose, sucrose, starch, and cellulose, was evaluated, with changes in the integrated fexofenadine response remaining below 5 % at all tested mass ratios. The proposed procedure was applied to the assay of two commercial fexofenadine tablet products, *Allegra*® 120 mg and *Ewofex*® 120 mg, using the standard addition method, providing recoveries of 99.4 % and 98.7 %, respectively. The method offers a simple option for the differential pulse voltammetric assay of fexofenadine in tablet formulations.

Keywords: differential pulse voltammetry, fexofenadine, glassy carbon electrode, pharmaceutical analysis

Abbreviations: CV — cyclic voltammetry, DPV — differential pulse voltammetry, FEX — fexofenadine, GCE — glassy carbon electrode, LOD — limit of detection, PB — phosphate buffer, RSD — relative standard deviation

Introduction

Determination of active pharmaceutical ingredients in commercial dosage forms remains an important part of pharmaceutical quality control. Chromatographic and mass-spectrometric methods provide high selectivity and low detection limits, particularly in complex biological matrices, but they usually require expensive instrumentation, skilled operators, longer analysis time, and higher consumption of organic solvents (Hofmann et al., 2002; Radhakrishna and Reddy, 2002; Oliveira et al., 2007). For routine screening, basic laboratory use or tablet-assay applications, simpler analytical procedures may be useful if they provide accuracy sufficient for the intended purpose and do not require chromatographic instrumentation.

Fexofenadine (FEX) is a non-sedating H_1-antihistamine used for the treatment of seasonal allergic rhinitis and chronic idiopathic urticaria. It is a pharmacologically active carboxylate metabolite of terfenadine with high selectivity towards peripheral H_1 receptors (Simpson and Jarvis, 2000). Because of its limited penetration through the blood-brain barrier, FEX has a lower tendency to cause central nervous system-related sedative effects than first-generation antihistamines. Recent systematic evaluation also supports its antihistamine efficacy and favorable safety profile compared to other antihistamines (Huang et al., 2019). Owing to its therapeutic relevance and broad clinical use, FEX represents a suitable target for practical analytical methods applicable to pharmaceutical formulations.

Several analytical approaches for FEX determination have been reported, including spectrophotometric, chromatographic, electrophoretic, and electroanalytical methods. Spectrophotometric assays have been proposed for pharmaceutical dosage forms because of their simplicity and low instrumental requirements (Suresh Kumar et al., 2011). Liquid chromatographic methods have been applied to FEX and related compounds, tablets, dis-

solution studies, and biological matrices, generally providing higher selectivity and lower detection limits (Hofmann et al., 2002; Radhakrishna and Reddy, 2002; Oliveira et al., 2007). Capillary electrophoresis has also been described as an alternative separation technique for FEX in capsules (Breier et al., 2005). These methods are powerful, but their use may be less convenient when rapid and low-cost assay of a simple tablet formulation is the main analytical task.

Electroanalytical approaches to FEX determination have also been reported, although the number of truly voltammetric studies remains limited. Abbas et al. (2004) applied a potentiometric membrane sensor for FEX based on ion-pair formation to tablet analysis. Ashour and Khateeb (2013) proposed a conductometric titration method for FEX hydrochloride in pharmaceutical formulations using sodium tetraphenylborate. More recent electrochemical strategies have mainly relied on membrane-based or modified-electrode sensors. Nashed et al. (2020) developed coated pencil graphite electrodes for potentiometric determination of FEX hydrochloride and montelukast sodium in combined dosage forms. Oghli and Soleymanpour (2021) reported a nitrogen-doped graphene/molecularly imprinted polymer-modified pencil graphite electrode for sensitive FEX determination in biological media. Liquid membrane and PVC-based sensors for FEX determination have also been described by Abass et al. (2021) and Rajendraprasad and Siddaraju (2022), respectively. Among the available electrochemical studies, the most directly comparable voltammetric work remains that of Golcu et al. (2005), who investigated the anodic behavior of FEX at a glassy carbon electrode (GCE) using several voltammetric techniques. Their work established the basic voltammetric response of FEX at an unmodified GCE and reported sensitive determination in Britton-Robinson buffer containing 20 % methanol, with applications in pharmaceutical dosage forms and biological fluids. The present study does not challenge their work as a more sensitive alternative. Its purpose is narrower and practical: to evaluate whether a phosphate buffer-based differential pulse voltammetric protocol with a mechanically renewed bare GCE can provide sufficient performance for the assay of simple single-active-ingredient tablet formulations. In addition, the present work employs integrated evaluation of the partially resolved anodic response observed in the calibration range and verifies the procedure on two commercial 120 mg FEX tablet products using the standard addition method.

Accordingly, the present work evaluates the analytical performance of a simplified differential pulse voltammetric protocol for FEX assay in commercial tablet formulations using a bare, mechanically renewed GCE and PB at pH 10. Cyclic voltammetry was used to study the electrochemical behavior of FEX and the influence of pH and scan rate. Differential pulse voltammetry was then optimized and applied for quantitative purposes. The analytical performance of the method was evaluated in terms of linear concentration range, sensitivity, detection limit, repeatability, and interference effects from common tablet excipients. Finally, the procedure was applied to FEX determination in two commercial 120 mg tablet products, *Allegra*® and *Ewofex*®. The method is therefore positioned as a simple laboratory assay for tablet formulations, not as a trace-level, bioanalytical, or stability-indicating method.

Material and Methods

Chemicals

Fexofenadine hydrochloride was used as the reference substance (Sigma-Aldrich, Slovakia). Methanol, disodium hydrogen phosphate, sodium dihydrogen phosphate, potassium chloride, sodium hydroxide, and alumina slurry used for mechanical polishing of the glassy carbon electrode were of analytical grade. Deionized water was used throughout the experiments. Because of the limited aqueous solubility of FEX, stock solutions with concentrations of 1.0 $mmol \cdot L^{-1}$ and 10.0 $mmol \cdot L^{-1}$ were prepared in methanol. Working solutions of lower concentrations were prepared by dilution with the supporting electrolyte in the electrochemical cell immediately before use. Phosphate buffer (PB) at pH 10 was used as the supporting electrolyte for further voltammetric measurements. The buffer was prepared from disodium hydrogen phosphate and sodium dihydrogen phosphate solutions, followed by an addition of potassium chloride. The final pH was adjusted to 10 with 0.2 $mol \cdot L^{-1}$ sodium hydroxide solution. The potential influence of selected tablet excipients was evaluated using glucose, sucrose, starch, and cellulose. Commercial *Allegra*® 120 mg and *Ewofex*® 120 mg tablets were purchased from a local pharmacy and used for the pharmaceutical sample analysis.

Apparatus

Voltammetric measurements were carried out using an AUTOLAB M204 potentiostat/galvanostat controlled by NOVA electrochemical software, version 1.11 (Metrohm Autolab). A conventional three-electrode system, consisting of a bare disk GCE (disk diameter of 4 mm) as the working electrode, an Ag/AgCl/3 $mol \cdot L^{-1}$ KCl reference electrode,

and a platinum auxiliary electrode, was used. All potentials reported in this work refer to the Ag/AgCl/3 mol·L^{-1} KCl reference electrode. Before measurements, the GCE surface was mechanically polished with a 0.3 μm of alumina slurry, rinsed thoroughly with methanol and deionized water, and gently dried. The same surface-renewal step was applied between measurements when required to maintain reproducible voltammetric responses and to remove possible oxidation products adsorbed on the electrode surface. The pH value of buffer solutions was measured using a Model 215 pH meter (Denver Instrument, USA).

Voltammetric procedures

Cyclic voltammetry (CV) was used for preliminary investigation of the electrochemical behavior of fexofenadine (FEX) at the bare glassy carbon electrode (GCE). The effect of pH was examined in phosphate buffer (PB) solutions over the selected pH range. The influence of scan rate was studied by recording cyclic voltammograms at different scan rates. Differential pulse voltammetry (DPV) was used for quantitative measurements. The effects of modulation amplitude and modulation time on the FEX response were examined separately while the remaining instrumental parameters were kept constant. The final DPV parameters used for calibration and sample analysis were: modulation amplitude of 100 mV, modulation time of 25 ms, and step potential of 5 mV. All quantitative measurements were carried out in PB at pH 10. Calibration measurements were performed by successive additions of FEX standard solution into the electrochemical cell containing the supporting electrolyte. During DPV optimization performed at higher FEX concentration, the voltammetric response was dominated mainly by one anodic peak. However, in the lower concentration range used for calibration, two partially resolved anodic responses were visible in the investigated potential region. For quantitative evaluation, these responses were not treated separately. The combined anodic signal was integrated between the local minimum preceding the first peak and the local minimum following the second peak. The calibration dependence was constructed by plotting this integrated response against the FEX concentration. The limit of detection (LOD) was calculated according to Eq. 1:

$$\mathrm{LOD} = 3s_a / b \qquad (1)$$

where s_a is the standard deviation of the intercept and b is the slope of the calibration curve. Repeatability was evaluated from twelve replicate measurements under the selected experimental conditions and expressed as a relative standard deviation (RSD).

Preparation and analysis of pharmaceutical samples

Allegra® 120 mg and *Ewofex*® 120 mg tablets were used for the pharmaceutical application of the presented method. For each product, the tablets were weighed, finely powdered, and a portion of the homogenized powder corresponding to 0.1300 g was transferred into a 50 mL volumetric flask. The sample was extracted with methanol and diluted to the mark with the same solvent. An aliquot of 300 μL of the prepared sample solution was transferred into an electrochemical cell containing 2.700 mL of PB at pH 10. FEX concentration in each pharmaceutical sample was determined by the standard addition method using DPV. Three consecutive 300 μL additions of 1.0 mmol·L^{-1} FEX standard solution were made into the electrochemical cell. After each addition, the solution was mixed and the voltammetric response was recorded. The amount of FEX in one tablet was calculated from the standard addition plot considering the dilution factor and the average tablet mass. The analysis was performed in triplicate for each pharmaceutical product.

Results and Discussion

Electrochemical behavior study of FEX at the bare GCE

The electrochemical behavior of FEX at the bare GCE was first examined by CV. The supporting electrolyte (PB) itself did not show any relevant anodic signal in the potential region used for FEX oxidation. After the addition of 1 mmol·L^{-1} FEX, a well-defined anodic response was observed, while no corresponding cathodic peak appeared during the reverse scan. This behavior shows that FEX undergoes irreversible electrochemical oxidation at the bare GCE under the applied experimental conditions.

The pH of the supporting electrolyte had a significant effect on both the peak current (I_p) and the peak potential (E_p) of FEX (Fig. 1). During the preliminary screening, no well-defined oxidation signal of FEX was observed in acidic media under the applied experimental conditions. Therefore, the pH effect was evaluated mainly in the neutral-to-alkaline region where a measurable anodic response was obtained. Cyclic voltammograms were recorded in the pH range from 7 to 12; however, only the pH interval from 7 to 11 was used for the quantitative evaluation of E_p and I_p because the voltammogram recorded at pH 12 showed a markedly increased background current and a less reliable peak definition. In the evaluated pH range from 7 to 11, the peak potential shifted systematically toward less positive values with increasing pH. This dependence shows that the composition and pH of the

supporting electrolyte affect the oxidation response of FEX at the bare GCE.

The E_p–pH dependence was linear in the evaluated pH interval and can be described by Eq. 2:

$$E_p\ (V) = 1.237 - 0.025 \times pH,\ R^2 = 0.952 \qquad (2)$$

Since FEX oxidation at the bare GCE is irreversible, a mechanistic assignment of the electron/proton stoichiometry requires an independent estimation of the kinetic parameter αn, for example from peak-width analysis or from the rising part of the cyclic voltammogram. Such analysis was not performed in the present work. Therefore, the E_p–pH dependence is not used here to assign the number of electrons or protons involved in the electrode reaction. It is considered only as an empirical description of the pH effect and as a basis for selecting suitable analytical conditions. Golcu et al. (2005) reported a lower E_p–pH slope of approximately −12.2 mV · pH^{-1} for FEX at a GCE in Britton-Robinson buffer containing 20 % of methanol and concluded that the electron transfer was practically pH-independent. The difference between their value and the slope obtained in the present work may be related to the different supporting electrolyte, the presence of methanol as an organic cosolvent, the evaluated pH interval, and the previously reported occurrence of one- or two-step FEX oxidation under different experimental conditions. However, both studies indicate only a relatively small shift of the FEX oxidation potential with pH. No electron/proton stoichiometry is inferred from the present dependence.

The effect of scan rate on the electrochemical response of FEX was investigated by CV in PB at pH 10, as illustrated in Fig. 2. The measurements were carried out for 1 mmol · L^{-1} FEX at scan rates ranging from 5 to 200 mV · s^{-1}. With the increasing scan rate, the anodic peak current increased progressively, while the oxidation peak potential shifted toward more positive values. This behavior is typical for irreversible electrode processes, where the observed peak potential depends on the kinetics of heterogeneous electron transfer and on the time scale of the voltammetric experiment. To obtain information on the mass-transfer character of the electrode process, the dependence of the anodic peak current (I_p) on the square root of scan rate ($v^{1/2}$) was evaluated. A linear relationship was obtained over the investigated scan rate range (Eq. 3):

$$I_p\ (\mu A) = -0.57 + 1.02 \times v^{1/2},\ R^2 = 0.988 \qquad (3)$$

where v is expressed in mV · s^{-1}. The proportionality between I_p and $v^{1/2}$ is consistent with a diffusion-controlled contribution to the voltammetric response, as expected for electroactive species transported from the bulk solution to the electrode surface (Bard and Faulkner, 2001). The negative intercept has no mechanistic meaning and results only from the linear regression within the experimentally studied range.

This conclusion was further supported by the logarithmic dependence between peak current and scan rate (Eq. 4):

$$\log I_p = -6.17 + 0.58 \times \log v,\ R^2 = 0.995 \qquad (4)$$

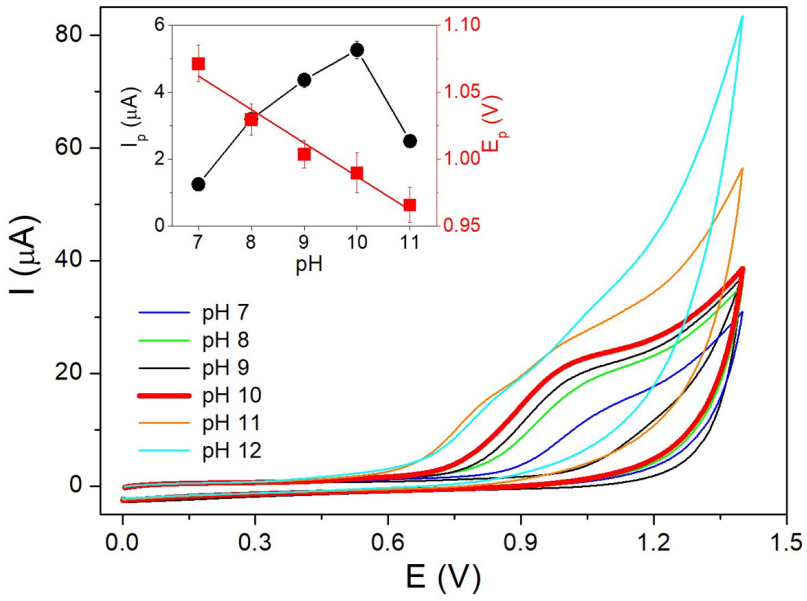


Fig. 1. Cyclic voltammograms of 1 mmol · L^{-1} FEX recorded at the bare GCE in PB solutions with pH values from 7 to 12 at a scan rate of 100 mV · s^{-1}. The inset shows the dependence of peak potential (E_p) and peak current (I_p) on pH in the evaluated pH range from 7 to 11.

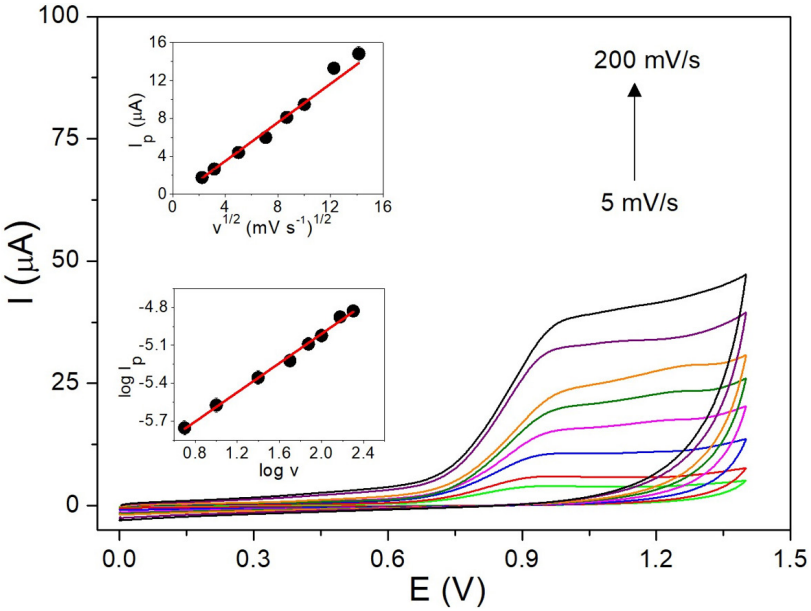
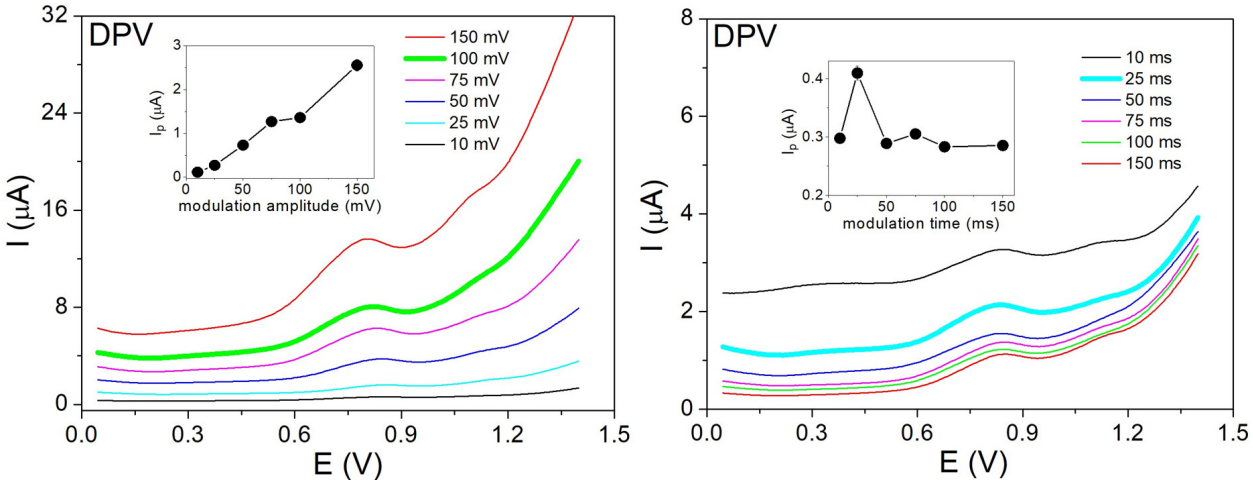


Fig. 2. Cyclic voltammograms of 1 mmol · L^{-1} FEX recorded at the bare GCE in PB at pH 10 at different scan rates. Insets show the dependence of the anodic peak current on the square root of the scan rate and the logarithmic dependence of the peak current on the scan rate.



a) b)

Fig. 3. Optimization of DPV parameters for 1 mmol · L^{-1} FEX at the bare GCE in PB at pH 10: a) effect of modulation amplitude at constant modulation time of 50 ms and step potential of 5 mV; b) effect of modulation time at constant modulation amplitude of 25 mV and step potential of 5 mV.

where I_p is expressed in A and v in mV · s^{-1}. The slope of the log I_p vs. log v plot was 0.58. In voltammetric analysis, a slope close to 0.5 is usually evidence of a diffusion-controlled process, whereas a slope approaching 1.0 indicates a process dominated by adsorption of the electroactive species on the electrode surface (Bard and Faulkner, 2001). The obtained value therefore supports a predominantly diffusion-controlled oxidation of FEX at the bare GCE. The slightly higher value than the theoretical diffusion-controlled limit may be related to the irreversible character of the oxidation process and to minor surface effects during repeated scans. Overall, the scan rate study confirms that the electrochemical oxidation of FEX at the bare GCE in PB at pH 10 proceeds as an irreversible process with dominant diffusion control.

Optimization of DPV parameters

After the initial CV study, DPV was optimized for quantitative FEX determination. This technique was selected because it provides better discrimination of faradaic current from the background current than CV and is therefore more suitable for

analytical measurements. In this study, modulation amplitude and modulation time were optimized. The effect of modulation amplitude is shown in Fig. 3a. The modulation amplitude was examined in the range from 10 to 150 mV at constant modulation time of 50 ms and step potential of 5 mV. The anodic response increased up to 100 mV, which provided a suitable compromise between peak height and peak definition. At 150 mV, the background current increased and the analytical signal became less favorable. Therefore, a modulation amplitude of 100 mV was selected for further measurements. The effect of modulation time is depicted in Fig. 3b. The modulation time was evaluated in the range from 10 to 150 ms, and modulation time of 25 ms was selected for further DPV measurements because it provided a well-defined FEX peak with acceptable background contribution. The selected DPV parameters were then used for calibration, where the lower FEX concentration range led to a partially split anodic response which was evaluated as an integrated combined signal.

Analytical performance evaluation

Under the optimized DPV conditions, the analytical performance of the proposed method was evaluated in PB at pH 10. Representative differential pulse voltammograms recorded for increasing FEX concentrations are shown in Fig. 4. In contrast to the optimization experiments carried out at 1 $mmol \cdot L^{-1}$ FEX, where the response was dominated mainly by one anodic peak, two partially resolved anodic responses were observed in the lower concentration range used for calibration. This concentration-dependent change in signal shape is consistent with the previously reported behavior of FEX at a GCE, where its electrochemical oxidation may proceed in one or two steps depending on experimental conditions, including pH (Golcu et al., 2005). For quantitative evaluation, the two anodic responses were not evaluated separately. Instead, the overall analytical response was obtained by integrating the combined anodic signal between the local minimum before the first peak and the local minimum after the second peak. This integrated response was used for calibration and subsequent quantitative evaluation.

The main analytical parameters are summarized in Tab. 1. The method provided a linear response in the concentration range from 9.5 to 67.9 $\mu mol \cdot L^{-1}$, with the coefficient of determination of 0.997. This concentration interval is relatively narrow, but it is adequate for the intended assay of a tablet formulation after suitable sample dilution. The slope of the calibration dependence was 8.61 $nA \cdot L \cdot \mu mol^{-1}$, showing a measurable and reproducible integrated DPV response of FEX at the bare GCE. The LOD was found to be 2.7 $\mu mol \cdot L^{-1}$, which is higher than the nanomolar LOD reported by Golcu et al. (2005) for FEX determination at GCE in aqueous–methanolic Britton-Robinson buffer. The higher LOD obtained in the present work must be interpreted in relation to the intended application. The method is not designed for trace analysis of FEX in biological fluids, where nanomolar sensitivity is required and chromatographic or more sensitive electroanalytical protocols are more appropriate. The target application is the assay of commercial 120 mg tablet formulations. For such samples, the amount of FEX is sufficiently high, and the tablet extracts can be diluted into the validated linear concentration range without approaching the LOD of the method. Therefore, the achieved LOD is analytically sufficient for the proposed tablet assay. The selection of PB at pH 10 was based on the experimentally observed peak definition, reproducibility of the integrated DPV response, and simple operation with a bare, mechanically renewed GCE. Practical usefulness of the method is thus not based on superior sensitivity, but on the combination of a straightforward electrode system, conventional supporting electrolyte, standard addition quantification, and acceptable agreement with the declared tablet content. Lower LOD values have also been reported for coated pencil graphite potentiometric sensors used for simultaneous determination of FEX and montelukast by Nashed et al. (2020), as well as for modified or recognition-based electrodes such as the nitrogen-doped graphene/molecularly imprinted polymer-modified pencil graphite electrode reported by Oghli and Soleymanpour (2021). These methods, however, are not directly equivalent to the present protocol. Several of them rely on membrane-based potentiometric detection, ion-pair formation, molecular imprinting, modified electrodes, or combined-drug analysis. The present method deliberately uses a bare, mechanically renewed GCE and a simple PB. Therefore, it should not be presented as the most sensitive electroanalytical method for FEX. Its practical value lies in the simple DPV setup which is sufficient for the assay of tablet formulations without electrode modification. Repeatability was evaluated from twelve replicate measurements of 50 $\mu mol \cdot L^{-1}$ FEX. The obtained RSD of 4.8 % indicates acceptable short-term precision for a voltammetric assay performed at an unmodified carbon electrode. This value also confirms that mechanical renewal of the GCE surface was sufficient to maintain a stable analytical response during repeated DPV measurements.

Overall, the analytical parameters confirm that the proposed DPV method is suitable for FEX determi-

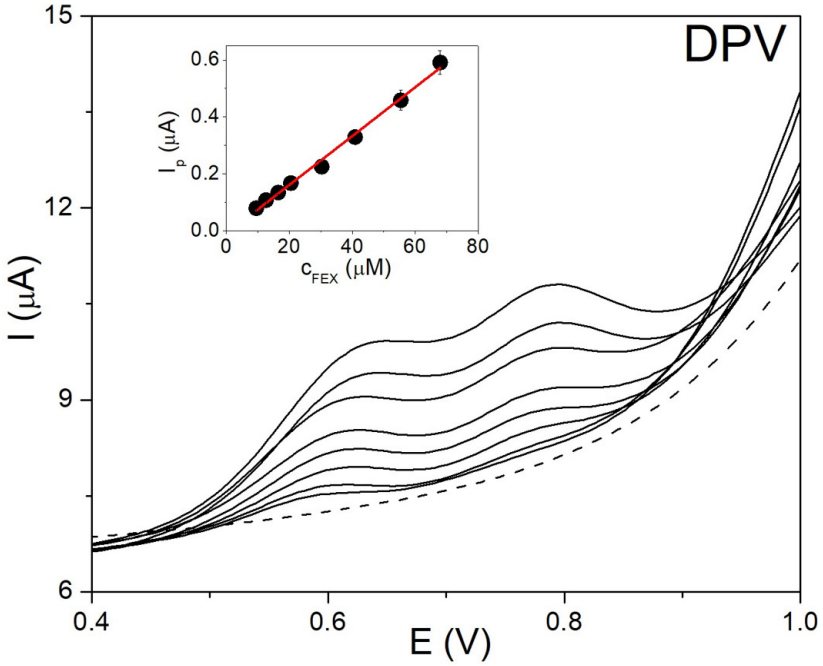


Fig. 4. Differential pulse voltammograms of FEX recorded at the bare GCE in PB at pH 10 in the concentration range from 9.5 to 67.9 μmol · L^{-1}. The dashed line represents the supporting electrolyte. The inset shows the calibration plot constructed using the integrated combined anodic response between the local minimum before the first peak and the local minimum after the second peak.

nation in the tested pharmaceutical formulations. The method is not aimed at trace analysis or bioanalytical quantification, where chromatographic methods or more sensitive voltammetric protocols are more appropriate. Its main advantage is the simple experimental arrangement and sufficient performance for tablet assay.

Tab. 1. Analytical parameters for DPV determination of FEX in PB at pH 10 using bare GCE under selected experimental conditions.

Analytical parameter	Value
Intercept ± SD (nA)	−11.14 ± 7.78
Slope ± SD (nA · L · $μmol^{-1}$)	8.61 ± 0.30
Linear concentration range (μmol · L^{-1})	9.5—67.9
Coefficient of determination R^2	0.997
LOD (μmol · L^{-1})	2.7
Repeatability (%) for 50 μmol · L^{-1} FEX, n = 12	4.8

Interference study and selectivity considerations

The influence of selected tablet excipients on the DPV response of 50 μmol · L^{-1} FEX was examined to assess the applicability of the proposed method in pharmaceutical formulation analysis. Glucose, sucrose, starch, and cellulose were selected as representative substances commonly used in solid dosage forms. These compounds may be present in tablets as fillers, binders, or auxiliary formulation components and can therefore accompany the active pharmaceutical ingredient during sample preparation. The interference study was performed under the optimized DPV conditions in PB at pH 10. The analytical response was evaluated in the same way as in the calibration measurements, i.e. by integrating the combined anodic response of FEX between the local minimum preceding the first peak and the local minimum following the second peak. The excipients were tested at FEX mass ratios of 1:1, 1:10, 1:50, and 1:100. For all tested excipients and at all evaluated ratios, the change in the integrated FEX response remained below 5 %. No additional anodic signal attributable to glucose, sucrose, starch, or cellulose was observed in the potential region used for FEX quantification. At the same time, the presence of these excipients did not cause an appreciable distortion of the combined anodic response of FEX. The observed current changes below 5 % indicate that the tested excipients did not interfere with the DPV determination of FEX under the selected experimental conditions. This observation is consistent with the absence of detectable oxidation signals from the tested excipients in the potential region used for FEX quantification. The interference study therefore supports the use of the proposed DPV method for the assay of FEX in the tested tablet formulations. Selectivity evaluation was intentionally limited to common tablet excipients because *Allegra*® and *Ewofex*® are single-active-ingredient products. Structurally related

Tab. 2. Analysis of pharmaceutical products by standard addition method using DPV at the bare GCE ($n = 3$).

Pharmaceutical product	Amount of FEX (mg)		Recovery (%)
	Label	Determined by DPV technique*	
Allegra® 120 mg	120	119.3 ± 6.2	99.4
Ewofex® 120 mg	120	118.4 ± 3.7	98.7

*Results are expressed as mean ± SD ($n = 3$).

compounds and degradation products of FEX were not experimentally investigated. Such electroactive compounds can contribute to or overlap with the FEX oxidation response because DPV at the bare GCE is not inherently structure-selective. Consequently, the proposed procedure should not be regarded as a stability-indicating method and has not been validated for biological or environmental samples, degraded formulations, or multicomponent pharmaceutical products.

Analysis of pharmaceutical products

Practical applicability of the developed DPV method was tested by FEX determination in two commercial tablet products, *Allegra*® 120 mg and *Ewofex*® 120 mg. The sample solutions were prepared by extraction of powdered tablet material in methanol followed by dilution with PB at pH 10. Quantification was carried out by the standard addition method to reduce possible matrix effects caused by tablet excipients. The results are summarized in Tab. 2. For *Allegra*® 120 mg, the determined amount of FEX was 119.3 ± 6.2 mg, corresponding to a recovery of 99.4 % relative to the declared content. For *Ewofex*® 120 mg, the determined amount was 118.4 ± 3.7 mg, corresponding to a recovery of 98.7 %**.** These results confirm that the proposed DPV procedure can be used for FEX assay in the tested pharmaceutical formulations. The agreement with the declared content is sufficient for tablet analysis, although the method is not intended to replace more sensitive chromatographic procedures used for trace-level or biological analysis. The obtained recoveries are also consistent with the pharmaceutical applicability reported for other electroanalytical FEX procedures, including potentiometric membrane sensors and conductometric titration methods, where accurate assay of tablet formulations was also demonstrated (Abbas et al., 2004; Ashour and Khateeb, 2013; Rajendraprasad and Siddaraju, 2022).

Conclusions

A simple DPV procedure was developed for the assay of FEX in pharmaceutical formulations using a bare GCE. FEX underwent irreversible anodic oxidation, and its electrochemical response was markedly affected by the solution pH. PB at pH 10 provided the most suitable response for analytical measurements. The scan rate study indicated that the oxidation process was predominantly diffusion-controlled, although a minor contribution from surface processes cannot be excluded. Under the optimized DPV conditions, the method provided a linear response from 9.5 to 67.9 $\mu mol \cdot L^{-1}$, LOD of 2.7 $\mu mol \cdot L^{-1}$, and repeatability expressed as RSD of 4.8 %. Common tablet excipients, including glucose, sucrose, starch, and cellulose, caused changes in the integrated FEX response of less than 5 % at the tested FEX-to-excipient mass ratios. The method was applied to *Allegra*® 120 mg and *Ewofex*® 120 mg tablets, yielding 119.3 ±6.2 mg and 118.4 ±3.7 mg of FEX per tablet, with recoveries of 99.4 % and 98.7 %, respectively. The analytical contribution of the procedure lies not in trace-level sensitivity but in the use of a bare GCE, simple mechanical surface renewal, uncomplicated PB medium, and straightforward sample preparation. The method is therefore suitable for the assay of FEX in single-active-ingredient tablet formulations. Its application to biological samples, degraded formulations, or multicomponent pharmaceutical products requires additional selectivity testing and validation.

Acknowledgement

This work has been supported by the Scientific Grant Agency of the Ministry of Education, Research, Development and Youth of the Slovak Republic and the Slovak Academy of Sciences (VEGA No. 1/0036/24) and the Slovak Research and Development Agency under the Contract no. APVV-23-0066.

References

Abass AM, Hassan OS, Al Rikabi HTHS, Ahmed A (2021) Egypt. J. Chem. 64: 6293–6300.

Abbas MN, Abdel Fattah AAA, Zahran E (2004) Anal. Sci. 20: 1137–1142.

Ashour S, Khateeb M (2013) Can. Chem. Trans. 1: 292–304.

Bard AJ, Faulkner LR (2001) Electrochemical Methods: Fundamentals and Applications, 2nd ed. John Wiley & Sons, New York.

Breier AR, Garcia SS, Jablonski A, Steppe M, Schapoval EES (2005) J. AOAC Int. 88: 1059–1063.

Golcu A, Dogan B, Ozkan SA (2005) Anal. Lett. 38: 1913–1931.

Hofmann U, Seiler M, Drescher S, Fromm MF (2002) J. Chromatogr. B 766: 227–233.
Huang CZ, Jiang ZH, Wang J, Luo Y, Peng H (2019) BMC Pharmacol. Toxicol. 20: 72.
Nashed D, Noureldin I, Alhaj Sakur A (2020) BMC Chem. 14: 60.
Oghli AH, Soleymanpour A (2021) Biochem. Eng. J. 167: 107920.
Oliveira DC, Weigch A, Rolim CMB (2007) Pharmazie 62: 96–100.
Radhakrishna T, Reddy GO (2002) J. Pharm. Biomed. Anal. 29: 681–690.
Rajendraprasad N, Siddaraju C (2022) Anal. Bioanal. Electrochem. 14: 934–952.
Simpson K, Jarvis B (2000) Drugs 59: 301–321.
Suresh Kumar K, Ravichandran V, Mohan Maruga Raja MK, Thyagu R, Dharamsi A (2011) Indian J. Pharm. Sci. 73: 300–302.