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**Research Article** 

# Voltammetric determination of famotidine on a disposable pencil graphite electrode

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Abstract: The present paper describes the use of a disposable pencil graphite electrode (PGE) for the voltammetric determination of famotidine. Cyclic voltammetric studies using different supporting electrolytes emphasized an irreversible oxidation of famotidine on the PGE. The electrode process is diffusion-controlled and pH-dependent. Differential pulse voltammetry (DPV) in phosphate buffer solution of pH 6.81 was employed for famotidine's quantitative determination. The anodic peak current of famotidine varies linearly with the analyte concentration in the range  $4.72 \times 10^{-7}$ – $4.95 \times 10^{-4}$  M. Detection and quantification limits were  $1.51 \times 10^{-7}$  M and  $5.04 \times 10^{-7}$  M famotidine, respectively. The developed DPV method using the inexpensive, disposable PGE was successfully applied to the simple and rapid determination of famotidine from pharmaceuticals.

Key words: Famotidine, pencil graphite electrode, voltammetry, pharmaceuticals

# 1. Introduction

Famotidine (Figure 1) is a  $H_2$ -histamine receptor antagonist reducing gastric secretion. It is widely used as an antiulcer drug that can be administrated either orally or intravenously. The methods most commonly employed for famotidine analysis from both pharmaceutical preparations and biological fluids are based on chromatography with different detection modes,<sup>1,2</sup> capillary electrophoresis,<sup>1,3</sup> spectrophotometry,<sup>4</sup> spectrofluorimetry,<sup>5,6</sup> and flow injection analysis.<sup>7</sup>

Electrochemical methods using bare<sup>8-14</sup> or modified electrodes<sup>15-19</sup> are often preferred for the analysis of drugs and other biologically important compounds, due to the fact that they are simpler and faster, necessitate fewer reagents, and the instrumentation is less expensive than in the case of chromatographic or spectrometric ones. One inconvenience of the voltammetric methods on solid electrodes is related to electrode surface fouling during the measurements, which involves a time consuming cleaning step before each new recording. This drawback can be eliminated by using disposable working electrodes like the pencil graphite electrode (PGE).<sup>11-13,19</sup>

The literature reports some studies of the electrochemical behavior of famotidine at different working electrodes like spectral-grade paraffin-impregnated graphite rod, <sup>20</sup> controlled growth mercury electrode, <sup>21</sup> and composite polymer membrane electrode, <sup>22</sup> whereas others are related to the potentiometric <sup>23,24</sup> or voltammetric determination of famotidine from different matrices.  $^{25-30}$ 

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Figure 1. Famotidine structure.

As mentioned above, the studies already existing in the literature related to famotidine voltammetry were performed mainly on mercury or glassy carbon electrodes. Therefore, the aim of the present study was to investigate the voltammetric behavior of famotidine on a disposable, commonly available PGE and to develop a sensitive and simple voltammetric method for the rapid and inexpensive determination of famotidine in both pure and pharmaceutical dosage forms.

## 2. Results and discussion

## 2.1. Cyclic voltammetric investigation; selection of the optimum working conditions

## 2.1.1. The influence of the working electrode

It is well known that the electrode material influences the electrochemical behavior of an analyte and the shape of the corresponding voltammograms. Therefore, the cyclic voltammograms were recorded on 2 carbonbased working electrodes, namely the glassy carbon electrode (GCE) and the PGE for a 9.9 × 10<sup>-4</sup> M famotidine solution in different supporting electrolytes (0.1 M H<sub>2</sub>SO<sub>4</sub>, acetate buffer solution (ABS) pH 4.06, and phosphate buffer solution (PBS) pH 6.81). Better shaped voltammograms and higher peaks were obtained on PGE when compared with GCE. The sensitivities (S,  $\mu$ A/mm<sup>2</sup> M) of the famotidine response on the 2 electrodes in the investigated media are given in Table 1. The results obtained indicate that the famotidine peak potentials are somewhat less positive and the voltammetric determinations of famotidine are more sensitive on PGE in comparison to GCE. Thus, PGE was further used as working electrode for voltammetric studies of famotidine.

Table 1. Anodic peak potentials  $(E_p)$  and sensitivities (S) of famotidine determination by CV on GCE and PGE in different media.

Electrolyte	0.1 M H <sub>2</sub> SO <sub>4</sub>		ABS pH 4.06		PBS pH 6.81		
Electrode	$E_p (mV)$	S ( $\mu A \text{ mm}^{-2} \text{ M}^{-1}$ )	$E_p (mV)$	S ( $\mu A \text{ mm}^{-2} \text{ M}^{-1}$ )	$E_p (mV)$	S ( $\mu$ A mm <sup>-2</sup> M <sup>-1</sup> )	
GCE	1196	870.17	1075	917.62	874	1096.15	
PGE	1136	1247.02	1015	1345.74	856	1471.84	

Electrochemical pretreatment is usually employed to activate carbon electrodes in order to enhance their reactivity and selectivity towards positively charged redox systems.<sup>31</sup> As famotidine is protonated at pH values below  $7^{32,33}$  cyclic voltammograms of famotidine were recorded in Britton–Robinson buffer (BRB) with pH values in the range 2.21 to 6.81 using a PGE electroactivated as described in section 3.3.1. Unfortunately, famotidine did not present any oxidation peak on the electroactivated PGE regardless of the solution pH.

The possibility of employing a pencil lead for several voltammetric measurements of famotidine was investigated in all the previously mentioned supporting electrolytes. In this respect, 5 successive cyclic voltammograms were recorded on the same electrode using the same solution of famotidine. It was observed that in all cases the famotidine oxidation peak decreased so that in the further investigations each voltammetric measurement was performed on a new pencil lead acting as working electrode.

## 2.1.2. The influence of the nature and the pH of the supporting electrolyte

The voltammetric behavior of an analyte is influenced by the type, the concentration, and the pH of the supporting electrolyte used. Thus, in the first step the voltammetric response of famotidine on PGE was investigated by selecting various media of different pH values, i.e.  $H_2SO_4$  (0.05 M, 0.1 M, and 0.2 M) (voltammograms not shown), ABS pH 4.06, PBS pH 6.81, PBS pH 7.30, and 0.1 M NaOH. Cyclic voltammetric recordings emphasized that famotidine presents an irreversible oxidation peak in all investigated media. The peak appears at potentials more positive than 700 mV. The peak potential is affected by the pH and its value shifts towards more positive values when the solution pH decreases (Figure 2). When  $H_2SO_4$  of different concentrations was used as supporting electrolyte, the smallest famotidine oxidation peak was obtained in 0.05 M  $H_2SO_4$ , whereas almost identical peaks were recorded in 0.1 M and 0.2 M  $H_2SO_4$ . In NaOH medium the famotidine peak is ill-defined, whereas the highest peak currents were recorded in ABS pH 4.06 and PBS pH 6.81.

The pH-dependence of the anodic peak potential indicates that the famotidine electrooxidation also involves proton transfer. The number of the protons involved in the electrode process can be estimated from the  $E_p = f$  (pH) dependence. For a more precise investigation of this influence, cyclic voltammograms of famotidine were recorded in the pH range 2.21 to 11.58 using the universal BRB. As shown in Figure 3, the famotidine anodic peak potential varies linearly with the solution pH, presenting a slope change at pH < 7.00. This pH value can be correlated with famotidine's pK<sub>a</sub>, which was reported to be 6.8 and corresponds to the equilibrium involving the protonation of the guanidine group of famotidine.<sup>32,33</sup>



Figure 2. Cyclic voltammograms recorded on PGE for a  $9.9 \times 10^{-4}$  M famotidine solution in different supporting electrolytes: (a) 0.1 M H<sub>2</sub>SO<sub>4</sub>; (b) ABS pH 4.06; (c) PBS pH 6.81; (d) PBS pH 7.30, and (e) 0.1 M NaOH. v = 100 mV/s.



Figure 3. The pH dependence of the famotidine oxidation peak obtained in BRB by cyclic voltammetry on PGE. v = 100 mV/s.

According to the Nernst equation, the slope of the  $E_p = f(pH)$  dependence for a pH-dependent electrode process is  $-\frac{59x}{n}$  mV/pH at 25 °C, where x represents the number of protons and n the number of electrons involved in the electrochemical reaction. For pH < 7.00 the slope of the linear dependence of the famotidine peak potential on the solution pH obtained on PGE is close to the theoretical value of -59 mV/pH at 25 °C, indicating thus that the number of protons involved in the electrode process is equal to that of the electrons donated in the oxidation reaction of famotidine.<sup>34</sup> The slope of the  $E_p = f(pH)$  dependence obtained for famotidine for pH values higher than 7.00 is close to -29.5 mV/pH at 25 °C, suggesting that in these conditions the ratio of electrons:protons (n:x) involved in the famotidine electrode process is 2 (x = 1 and n = 2).

## 2.1.3. Electrochemical behavior of famotidine

In order to investigate the electrochemical behavior of famotidine on PGE, cyclic voltammograms were recorded at different scan rates using various supporting electrolytes. In all investigated media famotidine undergoes an irreversible oxidation process. The resulted oxidation signal increased with increasing scan rates (Figure 4). A linear dependence was observed between the famotidine oxidation peak current and the square root of the scan rate (Table 2), suggesting that the electrode process is diffusion controlled. This conclusion was also supported by the slopes of the logarithm of anodic peak current vs. logarithm of scan rate plots, which are near the theoretical value of 0.5 (Table 2), characteristic for a diffusion-controlled process.<sup>35</sup>



Figure 4. Cyclic voltammograms recorded on PGE for a  $9.9 \times 10^{-4}$  M famotidine solution in PBS pH 6.81 at different scan rates: (a) 10; (b) 25; (c) 50; (d) 100; (e) 500, and (f) 1000 mV/s.

Table 2.	Data obtained f	from the cyclic	voltammograms	of famotidine	recorded	on PGE in	different m	iedia
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Electrolyte	$\mathbf{I}_p = \mathbf{f}(\mathbf{v}^{1/2})$	$\log I_p = f(\log v)$	$E_p = f(\log v)$	$E^{0'}$ (mV)	$k^0 (s^{-1})$	n
	$I_p = 2.8172 \times$	$\log I_p = 0.594 \times \log$				
$0.1 \mathrm{M} \mathrm{H}_2 \mathrm{SO}_4$	$v^{1/2} - 5.513$	v + 0.1375				
	$R^2 = 0.997$	$R^2 = 0.996$				
	$I_p = 2.3295 \times$	$\log I_p = 0.4118 \times \log$	$E_p = 0.0447 \times \log$			
ABS pH 4.06	$v^{1/2} + 5.832$	v + 0.6553	v + 1.0596	968.3	$31.64 \times 10^{3}$	2.21
	$R^2 = 0.9922$	$R^2 = 0.9892$	$R^2 = 0.9768$			
	$I_p = 2.2697 \times$	$\log I_p = 0.493 \times \log$	$E_p = 0.0474 \times \log$			
PBS pH 6.81	$v^{1/2} - 0.251$	v + 0.3686	v + 0.9018	810.7	$36.76 \times 10^{3}$	2.22
	$R^2 = 0.9947$	$R^2 = 0.9966$	$R^2 = 0.9496$			

Excepting the case where 0.1 M H<sub>2</sub>SO<sub>4</sub> was used as supporting electrolyte, in all other tested media the potential of the famotidine anodic peak (E<sub>p</sub>) shifted towards more positive values when the scan rate was increased. This fact confirms the irreversibility of the oxidation process. For a further characterization of the famotidine electrode process some kinetic parameters such as number of electrons (n), electron transfer coefficient ( $\alpha$ ), and the standard heterogeneous rate constant of the reaction (k<sup>0</sup>) were evaluated. For an irreversible electrode process, according to Laviron, <sup>36</sup> E<sub>p</sub> is defined by the following equation:

$$E_p = E^{0'} + \left(\frac{2.303RT}{\alpha nF}\right) \log\left(\frac{RTk^0}{\alpha nF}\right) + \left(\frac{2.303RT}{\alpha nF}\right) \log v,\tag{1}$$

where v is the scan rate and  $E^{0}$ , is the formal redox potential. Other symbols have their usual meanings (T = 298 K, R = 8.314 J/K mol, and F = 96,480 C/mol). Thus, from the slope of the  $E_p$  vs. log v plot (Table 2) one can calculate the value of  $\alpha$ n (1.323 in ABS and 1.248 in PBS) and according to Bard and Faulkner,<sup>37</sup> using the equation

$$\alpha = \frac{47.7}{E_p - E_{p/2}} mV,$$
(2)

where  $E_{p/2}$  is the potential where the peak current is at half;  $\alpha$  was estimated to be 0.598 in ABS and 0.562 in PBS. Further, from these values of  $\alpha$ n and  $\alpha$ , the number of electrons (n) involved in the electrooxidation of famotidine was found to be near 2 in the investigated media (Table 2). The value of  $k^0$  was determined from the intercept of the previous plot if the value of  $E^0$ ' is known. The value of  $E^0$ ' in Eq. (1) was obtained from the intercept of the  $E_p = f(v)$  plot by extrapolating to the vertical axis at v = 0 (Table 2).

Keeping in mind that in cyclic voltammetry the highest peak currents corresponding to the famotidine oxidation on PGE were obtained in ABS pH 4.06 and PBS pH 6.81 and due to the fact that famotidine maximum stability was reported to be at pH 6.30,<sup>33</sup> for further studies PBS pH 6.81 was selected as supporting electrolyte.

## 2.2. Quantitative voltammetric analysis of famotidine

It is well known that cyclic voltammetry is less adequate for quantitative determinations due to its limited sensitivity. Therefore, for quantification purposes more sensitive voltammetric techniques are preferred. One of these techniques is differential pulse voltammetry (DPV), which enables a better discrimination between the faradaic current and the charging current, leading thus to the detection of lower concentrations of the analyte of interest.

#### 2.2.1. Linear range and detection limit

The influence of the famotidine concentration on the anodic peak current recorded on PGE by DPV in PBS pH 6.81 was investigated in the concentration range  $4.72 \times 10^{-7}$ – $9.9 \times 10^{-4}$  M (Figures 5A and 5B). The obtained linear range of  $4.72 \times 10^{-7}$ – $4.95 \times 10^{-4}$  M famotidine is described by the equation:  $I_p = 0.0351 \times C_{famotidine} + 1 \times 10^{-7}$  (R<sup>2</sup> = 0.9990) (if  $I_p$  is expressed in A) (Figure 5C). It is worth mentioning that the linear range of over 3 orders of magnitude obtained by DPV on PGE is larger than any other reported in the literature for the voltammetric determination of famotidine (Table 3).



Figure 5. Differential pulse voltammograms recorded in PBS pH 6.81 on PGE for different concentrations of famotidine: (A) (a)  $4.72 \times 10^{-7}$  M; (b)  $9.44 \times 10^{-7}$  M; (c)  $2.36 \times 10^{-6}$  M; (d)  $4.72 \times 10^{-6}$  M; (e)  $9.44 \times 10^{-6}$  M; (B) (f)  $2.36 \times 10^{-5}$  M; (g)  $4.72 \times 10^{-5}$  M; (h)  $9.44 \times 10^{-5}$  M; (i)  $2.36 \times 10^{-4}$  M; (j)  $4.95 \times 10^{-4}$  M; (k)  $9.9 \times 10^{-4}$  M, and (C) the corresponding linear calibration plot  $I_p = f$  (C).

Table 3. Performance characteristics of voltammetric methods previously reported for famotidine as	ssay.
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Technique	Electrode	Linear range (M)	Detection limit (M)	Sample	Ref
DPV	GCE	$8 \times 10^{-6} - 10^{-3}$	not given	tablets	26
SWV	Mercury electrode	$5 \times 10^{-7} - 5 \times 10^{-6}$	not given		27
Complexation with Ni(II): DCP DPP	DME	$\begin{array}{c} 16{-}48 \ \mu {\rm g/mL} \\ 4{-}48 \ \mu {\rm g/mL} \end{array}$	$0.38~\mu{ m g/mL}$	tablets	29
LSAdSW SWAdSV	CG-MDE	$ \begin{array}{c} 1 \times 10^{-9} - 4 \times 10^{-8} \\ 5 \times 10^{-10} - 6 \times 10^{-8} \end{array} $	$ \begin{array}{r} 1.8 \times 10^{-10} \\ 4.9 \times 10^{-11} \end{array} $	urine	28
DPV	UTGE	$2 \times 10^{-6} - 9 \times 10^{-5}$	$3.73 \times 10^{-7}$	urine, tablets	30
DPV	PGE	$\begin{array}{c} 4.72 \times 10^{-7} - \\ 4.95 \times 10^{-4} \end{array}$	$1.51 \times 10^{-7}$	tablets	this study

SWV: square wave voltammetry; DCP: direct current polarography; DPP: differential pulse polarography; LSAdSW: linear sweep adsorptive stripping voltammetry; SWAdSV: square wave adsorptive stripping voltammetry; CG-MDE: controlled growth mercury drop electrode; UTGE: ultratrace graphite electrode.

Employing the data obtained from the linearity study, the detection (LOD) and the quantification (LOQ) limits, respectively, were calculated according to  $\text{LOD} = 3s_{c_{\min}}/b$  and  $\text{LOQ} = 10s_{c_{\min}}/b$ , where  $s_{c_{\min}}$  is the

standard deviation of the smallest concentration from the calibration curve and b is the calibration curve slope.<sup>38</sup> The values obtained for the LOD and LOQ limits are  $1.51 \times 10^{-7}$  M and  $5.04 \times 10^{-7}$  M famotidine, respectively.

## 2.2.2. Repeatability

The repeatability of the famotidine electrode response, expressed as percentage relative standard deviation (RSD%), was evaluated by performing series of 10 measurements at 3 famotidine concentrations, i.e. at the lowest  $(4.72 \times 10^{-7} \text{ M})$  and highest  $(4.95 \times 10^{-4} \text{ M})$  concentrations of the linear range and on an intermediate concentration  $(2.36 \times 10^{-5} \text{ M})$ . A new pencil lead was employed for each voltammetric recording. RSD% values of 6.62, 2.37, and 1.21 were obtained for  $4.72 \times 10^{-7} \text{ M}$ ,  $2.36 \times 10^{-5} \text{ M}$ , and  $4.95 \times 10^{-4} \text{ M}$  famotidine, respectively. It must be emphasized that all RSD% values are within the accepted limits according to the respective concentration levels.<sup>39</sup>

## 2.2.3. Stability study

The stability of the famotidine solution for voltammetric analysis was investigated by recording DPV for several days after the preparation. Both pure famotidine and famotidine tablets (Zentiva) solutions were investigated. After preparation the solutions were stored in the refrigerator. It was observed that the peak intensity decreases significantly during the first 2 days after preparation and remains constant for several days (Figure 6). This observation leads to the conclusion that for the voltammetric analysis of famotidine it is necessary to prepare daily the stock solution of both pure famotidine or from tablets.



Figure 6. Variation with time of the DPV peak current for (a) a 2.36  $\times 10^{-4}$  M pure famotidine solution and (b) a  $1.18 \times 10^{-4}$  M famotidine from Zentiva tablets solution.

Famotidine structure presents more centers that could be involved in the observed decrease in the voltammetric peak. According to the literature data atmospheric oxygen or light can oxidize famotidine at the sulfur atoms, leading to pharmaceutically inactive sulfoxide derivatives.<sup>40</sup>

#### 2.2.4. Recovery studies and analytical applications on pharmaceutical preparations

The practical applicability of the developed DPV on PGE method for famotidine determination was tested on 2 types of famotidine tablets (*Famotidina ZENTIVA 20 mg* and *Famodin 20*) commonly available on the Romanian market. The famotidine content of the pharmaceutical preparations was evaluated using the

standard addition method. The solution to be analyzed was obtained from the pharmaceutical tablets of famotidine according to the procedure described in section 3.3.2. The DP voltammogram recorded for famotidine tablets solution presents only the peak characteristic for the famotidine oxidation (Figure 7), indicating the absence of any interference from the tablets' components. The intensity of this peak increased linearly with successive addition of famotidine stock solution. The corresponding peak currents were used to calculate the famotidine content of the *Famotidina ZENTIVA 20 mg* and *Famodin 20* tablets and to obtain the values of the % recoveries. For each sample 10 replicates were analyzed. The result for every replicate represents the average of 3 measurements (Table 4). The % recoveries are between 95.11% and 104.88% and between 95.43% and 104.19% for *Famotidina ZENTIVA 20 mg* and *Famodin 20* tablets, respectively. All the recovery values lie within the expected limits for these concentration levels.<sup>39</sup>



Figure 7. Differential pulse voltammograms obtained on PGE for a *Famotidina ZENTIVA 20 mg* tablets solution in PBS pH 6.81 before and after the 3 additions of 0.1 mL  $2.36 \times 10^{-3}$  M famotidine stock solution.

Sample	Famotidina ZENTIVA	Famodin HELCOR
Claimed content/(mg/tablet)	20	20
Found content by $(DPV \pm SD)/(mg/tablet)$	$19.85 \pm 0.51$	$20.31 \pm 0.76$
RSD/%	2.57	3.75
Relative error/%	0.76	1.54
Recovery		
Average $(R \pm SD)/\%$	$99.24 \pm 2.55$	$101.54 \pm 3.81$

Table 4. DPV on PGE results for quantitative determination of famotidine from tablets.

The relative error values below 2%, calculated considering as reference value the one declared by the producer, proved the good agreement between the results obtained using the proposed DPV method and the amounts claimed by the pharmaceutical manufacturers. Thus, it can be emphasized that employing the PGE comparable and reliable results are provided by the proposed DPV method.

In conclusion, the present paper describes for the first time the voltammetric behavior of famotidine on a disposable PGE electrode. Using the famotidine oxidation peak obtained on the PGE in PBS pH 6.81 a sensitive and rapid DPV method was developed for the quantitative determination of the investigated drug in the concentration range  $4.72 \times 10^{-7}$ – $4.95 \times 10^{-4}$  M famotidine. It must be emphasized that this linear range of over 3 orders of magnitude is larger than any other reported in the literature for the voltammetric determination of famotidine. The detection limit of the proposed method of  $1.51 \times 10^{-7}$  M is also one of the lowest reported in the literature for voltammetric methods employed for famotidine quantification. The use of the cheap disposable PGE eliminates the electrode cleaning step, resulting in a simple and rapid analysis method. Moreover, the new developed DPV on PGE method was successfully applied to the analysis of famotidine content of pharmaceutical tablets.

## 3. Experimental

#### 3.1. Apparatus

An electrochemical system (potentiostat/galvanostat) Autolab PGSTAT 12 was used for the voltammetric recordings. The employed voltammetric cell contained a Ag/AgCl (3 M KCl) reference electrode, a Pt wire as auxiliary electrode, and a working electrode consisting of a glassy carbon electrode (GCE) having a surface area of 12.56 mm<sup>2</sup> (4 mm diameter) or a pencil-graphite electrode (PGE) with a surface area of 15.86 mm<sup>2</sup> (0.5 mm diameter and 1.0 cm height). The surface area of the PGE was calculated according to the formula  $\pi r^2 + 2\pi rh$ , where r is diameter/2 = 0.25 mm and h is the height of the PGE immersed in the solution to be analyzed. For each measurement, 10 mL of the solution to be analyzed was introduced into the voltammetric cell.

Before each recording the GCE was polished with alumina powder, rinsed with distilled water, and dried. The PGE, consisting of a 1-cm-long graphite pencil lead 0.5 HB, was realized as previously described.<sup>11-13</sup>

A Consort P901 Scientific Instrument  $pH/mV/^{\circ}C$  – meter (Belgium) equipped with a combined pH-glass electrode was employed for the pH measurements of the analyzed solutions.

#### 3.2. Reagents and solutions

Famotidine,  $H_2SO_4$  (98.0%, ACS reagent),  $CH_3COOH$  ( $\geq 99.7\%$ , ACS reagent),  $H_3BO_3$  (1 g/tablet),  $H_3PO_4$  (85 wt. % in  $H_2O$ ), NaOH (pellets), Na<sub>2</sub>HPO<sub>4</sub>×2H<sub>2</sub>O, and KH<sub>2</sub>PO<sub>4</sub> (p.a. ACS reagent) were purchased from Sigma-Aldrich.

Pharmaceutical preparations consisting of famotidine tablets containing 20 mg of active principle per tablet, namely *Famotidina ZENTIVA 20 mg* produced by S.C. Zentiva S.A., Romania and *Famodin 20* manufactured by AC HELCOR SRL, Romania were purchased from a local pharmacy. According to the producers' declaration both investigated pharmaceutical preparations contain only famotidine as active principle and common excipients.

 $H_2SO_4$  solutions of different concentrations, acetate buffer solution (ABS) pH 4.06, phosphate buffer solution (PBS) pH 6.81 and pH 7.30, and Britton–Robinson buffers (BRB) with pH values in the range 2.21– 11.58 were used as supporting electrolytes in the voltammetric cell. A stock solution of 2.36 × 10<sup>-3</sup> M famotidine was daily freshly prepared by dissolving under ultrasonication the appropriate weighed amount of analyte in deionized water. When not used, the solution was stored in the refrigerator. More diluted solutions with concentrations from 2.36 × 10<sup>-7</sup> to 9.9 × 10<sup>-4</sup> M famotidine used for the voltammetric measurements were obtained from the stock solution by diluting with the appropriate supporting electrolyte to the mark of 10-mL volumetric flasks.

## 3.3. Procedures

## 3.3.1. Voltammetric measurements

Electrode activation by electrochemical pretreatment was performed by cyclic voltammetry in 1 M  $H_2SO_4$ . The potential was cycled 10 times from -500 mV to 3000 mV.

Cyclic voltammograms (CVs) were recorded from 300 to 1500 mV at a scan rate of 100 mV/s if not stated otherwise.

Differential pulse voltammetry (DPV) was performed in the potential range 400 to 1100 mV using the following optimized instrumental parameters: modulation amplitude 25 mV, step potential 4.95 mV, interval time 0.1 s, and modulation time 0.05 s. The experiments were carried out at room temperature ( $25.0 \pm 0.2 \circ C$ ).

## 3.3.2. Analysis of pharmaceutical preparations

Twenty tablets from each of the 2 pharmaceuticals (Famotidina ZENTIVA 20 mg and Famodin 20) were accurately weighed and ground with a pestle in a porcelain mortar in order to obtain a fine powder. A quantity of this powder equivalent to 0.0200 g of famotidine was accurately weighed, transferred into a 50-mL volumetric flask, dissolved in approximately 30 mL of deionized water, swirled and sonicated for 30 min, and then diluted to the mark with deionized water. The thus obtained sample was filtered using Blue Ribbon Quantitative Whatman filter paper. An aliquot of the filtrate was further 100-fold diluted with the proper supporting electrolyte (PBS pH 6.81) so that the famotidine concentration in the solution to be analyzed would be within the linear range of the developed DPV method. The standard addition method was applied for the evaluation of the famotidine tablets' content. DP voltammograms were recorded for the diluted famotidine tablet sample solution (10 mL) before and after 3 successive additions of 0.1 mL of  $2.36 \times 10^{-3}$  M famotidine stock solution. The concentrations of added famotidine in the voltammetric cell were  $2.34 \times 10^{-5}$  M,  $4.36 \times 10^{-5}$  M, and  $6.87 \times 10^{-5}$  M after each of the 3 additions. For a set of measurements the corresponding peak currents recorded before and after each addition were 0.40  $\mu$ A,  $1.61 \ \mu$ A,  $2.32 \ \mu$ A, and  $3.76 \ \mu$ A, respectively. These peak currents were further used to calculate the % recoveries of famotidine from the Famotidina ZENTIVA 20 mg and Famodin 20. The obtained results represent the average of 3 measurements for each sample.

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