# HPLC-UV Method for Determination of Famotidine from Pharmaceutical Products

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*The aim of this study was to develop and validate a rapid, accurate, and exact method for the quantitative determination of famotidine in pharmaceutical products. The HPLC analyses were performed by using a mobile phase containing methanol:1% acetic acid solution=30:7 (v/v), at a flow rate of 0.4 mL/min.The total time of the method was 10 min, and the retention time of famotidine was 4.16 min. The detection was evaluated at λ=267 nm. The method has been validated by using different validation parameters. The linear response of the detector for famotidine peak area was observed at concentrations ranging from 0.1 to 0.0001 mg mL$^{-1}$ , resulting in a correlation coefficient of 0.99998. The values of the detection limit and of the quantification limit are 0.00048 mg mL$^{-1}$ and 0.00148 mg mL$^{-1}$, respectively. The method proposed allowed accurate (with a relative error of less than 2%) and precise (RSD values less than 2.0%) determination of famotidine content in pharmaceutical products and can be used for its rapid quantitative analysis.*

*Keywords: famotidine, HPLC-UV, pharmaceutical products*

Famotidine $C_8H_{15}N_7O_2S_3$ is a pharmaceutical substance that competitively blocks histamine H2 receptors, thus inhibiting gastric secretion, both by lowering the concentration of the acid and by decreasing the volume of the secretion [1, 2]. It is indicated for the treatment of gastric and duodenal ulcers and for other hypersecretion states, but also for the prevention of recurrent ulcers and for preventing the aspiration of gastric acid in general anesthesia (Mendelsson syndrome) [2]. Chemically known as 3-[[2-[(Aminoiminomethyl)amino]-4-thiazolyl] methyl]thio]-N-(aminosulfonyl)propanimidamide (M=337.45) [3], famotidine is available as pharmaceutical products: tablets, capsules, and powder for oral suspensions or injectable solutions.

There are numerous analytical [4-13], biochemical and quality control determinations throughout the lifecycle of any pharmaceutical product [5-7] to assess the stability of pharmaceutical substances, the concentrations of active substance, the period of validity, and pharmacological characteristics.

For the determination of famotidine in pharmaceutical preparations as well as in biological fluids, several types of analytical methods have been reported in the specialty literature: colorimetric [14-16], potentiometric [17], voltammetric [18], capillary electrophoresis [19-21], spectrophotometric [22-26], thin layer chromatography [27-29] and HPLC [30-36]. HPLC methods allow simultaneous determination of famotidine with other pharmaceutical substances in multicomponent preparations and in biological media [34, 36].

The purpose of this study is to develop and validate a rapid, accurate and exact HPLC method for the quantitative determination of famotidine in pharmaceutical products.

## Experimental part

Famotidine, both pure substance and film-coated tablets (40 mg), were provided by S.C. Helcor SRL. Baia Mare, Romania. Reagents used in the study were acquired from Merck and were of HPLC grade (methanol, HCl). An equipment HPLC Able&Jasco (Japan) equipped with NUCLEOSIL 100 C18 (5μm, 100×4.6 mm) column and BOR WIN 1.50 software was used for the analyses. All experiments were performed at +25°C, with (A) methanol and (B) 1 % acetic acid at a flow rate 0.4 mL/min, and the data were recorded at λ=267 nm. Stock solution of famotidine (1 mg mL$^{-1}$) was obtained by dissolving 0.01 g famotidine in 0.2 mL HCl aqueous solution 20%, 2 mL methanol, and distilled water. The stock solution was sequentially diluted to give the working solution a concentrations in the range 0.1-0.0001 mg mL$^{-1}$. In order to obtain the pharmaceutical sample, 10 tablets were grinded and homogenized, then the quantity equivalent to the mass of a tablet was dissolved in 5 mL methanol, 1 mL HCL 20% and distilled water to reach 100 mL. The solution was filtered.

## Results and discussions

### *Development of optimum mobile phase*

In order to develop a HPLC method, different ratios of methanol and water were tried to estimate famotidine. The best separation was obtained in the mobile phase composed of methanol (A) and 1% acetic acid aqueous solution (B) in the ratio of 30:70 (v/v), at a flow rate of 0.4 mL/min. The tested flow rate ranges were between 0.3-0.7 mL/min, and the selection of the best one was based on the peak parameters (height, asymmetry, tailing), baseline drift, and run-time (4.16 min) from a total of 10

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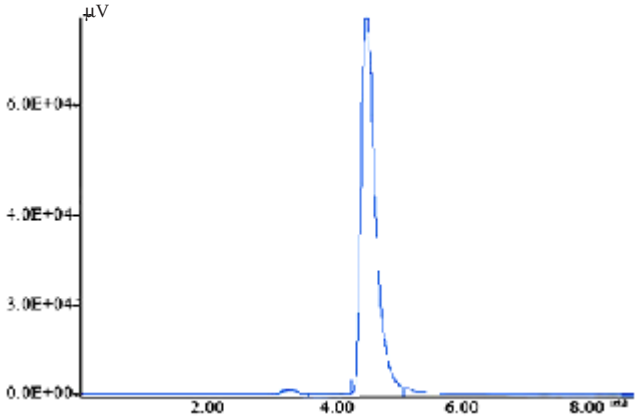


Fig. 1. Chromatogram of famotidine

minutes. Figure 1 presents the chromatogram for famotidine.

*Linearity and calibration*

The linearity of the method was determined by injecting standard solutions of five different concentrations, in the range 0.1-0.0001 mg $mL^{-1}$, as it is shown in table 1.

**Table 1**
LINEARITY OF STANDARD INJECTED SOLUTION OF FAMOTIDINE

| No. crt. | Concentration [mg $mL^{-1}$] | Peak area |
|---|---|---|
| 1 | 0.01 | 11454227 |
| 2 | 0.005 | 5769175 |
| 3 | 0.001 | 1213298 |
| 4 | 0.0005 | 566149 |
| 5 | 0.0001 | 120214 |

The calibration curve could be represented by the regression equation

$$y=1145x+0.19 (r=0.99998, n=5) \quad (1)$$

where $x$ is the concentration of famotidine in mg $mL^{-1}$ and $y$ is the peak area. Repeatability was given by three times determinations of each stock solution in the same day and also in different days. The accuracy was evaluated by analyzing three different concentrations of famotidine (0.003, 0.008, 0.015 mg $mL^{-1}$ respectively).

**Table 2**
DATA RELATED TO FAMOTIDINE'S DETERMINATION IN PHARMACEUTICAL PRODUCTS ANALYZED

| Intraday analyses | | Interday analyses | |
|---|---|---|---|
| Conc. [mg $mL^{-1}$] | RSD (%) | Conc. [mg $mL^{-1}$] | RSD (%) |
| 0.01 | 0.29 | 0.01 | 0.38 |
| 0.05 | 0.20 | 0.05 | 0.96 |
| 0.001 | 0.49 | 0.001 | 1.14 |
| 0.005 | 0.33 | 0.005 | 0.83 |
| 0.0001 | 0.17 | 0.0001 | 0.51 |

The results obtained for validating the famotidine determination method from pharmaceutical products are exhibited in table 2.

We determined the relative standard deviation (RSD) both for the analyses performed in the same day and in different days. The values of RSD range from 0.17 % to 0.49 % for the intra-day analyses and from 0.38 % to 1.14 % for inter-day analyses. We have to mention here that the obtained values are below 2% which is required for a method of pharmaceutical product quantification (table 2).

Thereafter, in order to evaluate the precision of the method we prepared three solutions of different concentrations of famotidine (0.003, 0.008 and 0.015 mg $mL^{-1}$) and we calculated the relative error. The results are depicted in table 3.

LOD (0.00048 mg $mL^{-1}$) and LOQ (0.00148 mg $mL^{-1}$) were calculated by using the equations (2) and (3), where $\sigma$ is the standard deviation of the lowest standard concentration, and S is the slope of the standard curve:

$$LOD=3.3\sigma/S \quad (2)$$

$$LOQ=10\sigma/S \quad (3)$$

LOD and LOQ values confirm that the method is precise.

*Famotidine's determination from pharmaceutical products*

The quantitative analyses of the tablets was evaluated by using the presented method and the data are shown in table 4.

**Table 3**
DATA RELATED TO PRECISION OF THE METHOD

| Concentration of famotidine in solutions [mg $mL^{-1}$] | Intraday analyses | | Interday analyses | |
|---|---|---|---|---|
| | Measured concentration [mg $mL^{-1}$] | Relative error % | Measured concentration [mg $mL^{-1}$] | Relative error % |
| 0.003 | 0.0031 | ±3.33 | 0.0032 | ±6.66 |
| 0.008 | 0.0079 | ±1.25 | 0.0081 | ±1.25 |
| 0.015 | 0.0148 | ±1.33 | 0.0147 | ±2.0 |

| Product | Concentration [mg $mL^{-1}$] | | Relative error (%) |
|---|---|---|---|
| | Drug | Found | |
| Tablet 1 | 0.00392 | 0.003834 | ±2.0 |
| Tablet 2 | 0.0040 | 0.003969 | ±0.775 |

**Table 4**
PRECISION OF THE METHOD FOR PHARMACEUTICAL PRODUCTS

## Conclusions

A fast HPLC-UV method for determination of famotidine was developed.

From the point of view of analytical performance, this analytical method is accurate and precise (with relative error smaller than 2 %). Also, the method is very suitable to be used at the determination of famotidine from pharmaceutical products containing it in the form of tablets, capsules, and powder for oral suspensions or injectable solutions.

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