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Development and Validation of difference Spectrophotometric method for the estimation of Famotidine in bulk and Pharmaceutical dosage Form

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Abstract

A simple, accurate, precise, reproducible and an economical difference spectrophotometric method has been developed for the estimation of famotidine in bulk and pharmaceutical dosage form. This spectrophotometric method is based on the principle that famotidine shows two different forms in acidic and basic medium that differ in the absorption spectra in acidic and basic medium. The maxima and minima in the difference spectra of famotidine were found to be at 290.60 nm and 259 nm in basic and acidic medium, respectively. The method obeys Beer-Lambert's law in the concentration range of 5 - 30 µg/ml (r^2 = 0.9995). The proposed method was validated as per ICH Q2 (R1) analytical method validation guidelines. The proposed method is suitable for the routine quality control analysis of famotidine in pharmaceutical dosage form.

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Famotidine, difference spectrophotometric method, 0.1 N HCl, 0.1 N NaOH

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INTRODUCTION

Chemically, famotidine (FAM) (Figure 1) known as 3-([2-(diamino- methylene amino) thiazol-4-yl] methylthio)-N′-sulfamoylpropanimidamide is a histamine H_2 receptor antagonist used in the treatment of peptic ulcer and gastro esophageal reflux disease [1,2].

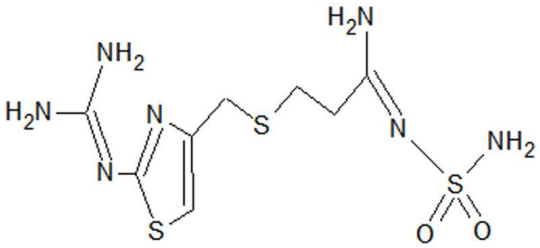

Figure 1: Structure of FAM

Indian Pharmacopoeia [2], British Pharmacopoeia [3], European Pharmacopoeia [4] and United States Pharmacopoeia [5] described titrimetric method for the estimation of FAM in bulk form whereas, liquid chromatographic method was described for the assay of tablet, injection and oral suspension of FAM. Few methods have been described in the literature for the estimation of FAM as single formulation which include spectrophotometric [6-9], spectrofluorimetric [10, 11], HPLC [12-17], flow injection analysis [18], HPTLC [19]. Also numerous methods have been developed for the estimation of FAM in multicomponent formulation which includes spectrophotometric [20-25], HPLC [26, 27], flow injection analysis [28] and HPTLC [29-31].

The selectivity and accuracy of spectrophotometric analysis of sample containing absorbing interference may be markedly improved by the technique of difference spectrophotometry[32]. The essential feature of difference spectrophotometric assay is that the measured value is the difference in absorbance (ΔA) between two equimolar solutions of the analyte in different chemical forms which exhibit different spectral characteristics [32].

No difference UV spectrophotometric method has been reported for estimation of famotidine. Therefore, an attempt has made to develop a simple, accurate, rapid and precise spectrophotometric method for the determination of famotidine in bulk and tablet dosage form.

MATERIALS AND METHOD

Chemicals and reagents

FAM was obtained as gift sample from Centurion Laboratories, Baroda, India. Analytical grade chemicals and distilled water were used during experimentation.

Instrument

A Shimadzu UV-1700 Pharma Spec UV-Visible spectrophotometer (UV probe 2.21 software) with a pair of 1.0 cm matched quartz cells was used for the measurement of absorbance.

Selection of solvent

About 0.1 M HCl and 0.1 M NaOH was selected as solvent to study spectral characteristics of FAM.

Preparation of standard solution

Stock solution of FAM (100 µg/ml) was prepared in 0.1 M HCl and 0.1 M NaOH separately. Appropriate volume of above stock solution was diluted up to 10.0 ml and the resulting solution (10 µg/ml) was used as working solution.

Preparation of sample solution

Twenty tablets of each brand of FAM (TOPCID® 40 tablet and FAMOTIN® 40 tablet) were weighed accurately and powdered finely. A quantity of tablet powder equivalent to 10 mg of FAM was accurately weighed and transferred into two separate 100 ml volumetric flask, 10 mL of 0.1 M HCl and 0.1 M NaOH was added in to respective flask and the content was ultrasonicated for 20 min. The volume was made up to the mark with same solvent and mixed well. The solution was further filtered using Whatman filter paper to remove any unwanted particulate matter. The filtered solution was further appropriately diluted with respective solvent to finally produce sample solution of concentration 10 µg/ml for analysis. The amount of FAM present in the sample solution was determined using the calibration curve of standard drug.

METHOD VALIDATION

The method was validated according to ICH Q2 (R1) guidelines for parameters like linearity, accuracy, precision, LOD, LOQ and specificity of the analyte [33]

Linearity

Aliquot portions of 0.5 – 3.0 ml of FAM stock solution was separately transferred into 10.0 ml volumetric flask. The volume was adjusted to the

mark with 0.1M HCl and 0.1M NaOH so as to obtain a series of concentrations ranging from 5-30 µg/ml as reference and sample solution, respectively. The difference spectrum for famotidine was recorded by placing reference and sample solution of FAM in reference and sample cell, respectively. The difference in absorbance at wavelength between 290.60 nm (maxima) and 259 nm (minima) was calculated to find out the amplitude. Calibration curve was plotted by taking concentration of FAM (µg/ml) on X-axis and amplitude (ΔA) on Y-axis. The overlain difference UV absorption spectra of FAM (5 – 30 µg/ml) is shown in Figure 2.

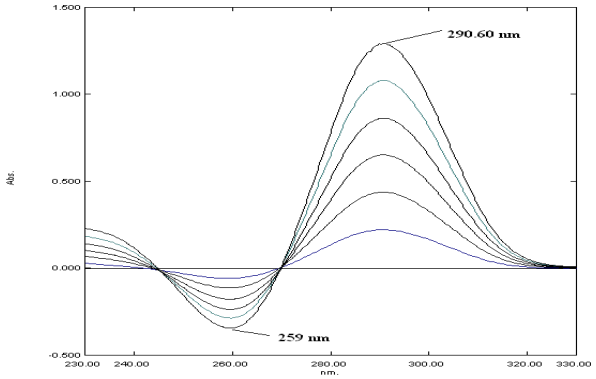

Figure 2: Overlain difference UV absorption spectrum of FAM

Accuracy

The accuracy of the proposed method was determined by recovery study. The known amount of pure FAM was spiked to pre-analyzed tablet dosage form of FAM (TOPCID® 40 tablet and FAMOTIN® 40 tablet). Analysis of FAM was carried out at three concentration levels such as 80%, 100% and 120% within the specified linearity and range.

The % recovery by proposed method was calculated using the formula as below.

$$\% \text{ recovery} = \frac{E}{T + P} \times 100$$

Where,

E: Total amount of drug estimated (µg/ml)

T: Amount of drug taken from pre-analyzed tablet dosage form (µg/ml)

P: Amount of pure drug added (µg/ml)

Precision

Precision was studied to find out intra and inter-day variations in the test method of FAM. The repeatability study (intra-day precision) was performed by analyzing the sample of FAM repeatedly within the day. The inter-day precision study was performed by analyzing the sample of FAM repeatedly at different days. Six determinations of working standard solution of FAM were performed. The results were expressed as % RSD.

Limit of detection (LOD) and limit of quantitation (LOQ)

LOD and LOQ of FAM by developed analytical method was calculated using the formula mentioned below.

$$\text{LOD} = \frac{3.3 \times \sigma}{S}$$

$$\text{LOQ} = \frac{10 \times \sigma}{S}$$

Where,

σ: Standard deviation of the response

S: Slope of calibration curve

RESULT AND DISCUSSION

The aim of present work is to develop a simple, accurate, precise, reproducible and an economical difference UV spectrophotometric method to determine the amount of FAM present in pharmaceutical dosage form. The values were presented as amplitude (ΔA) of FAM in two different chemical forms exhibiting different spectral properties. The difference spectrum of FAM in 0.1M NaOH was recorded by taking 0.1M HCl solution as reference. The typical difference spectrum has shown characteristic maxima at 290.60 nm and minima at 259 nm.

Analysis of pharmaceutical dosage form

The assay result of TOPCID® 40 tablet and FAMOTIN® 40 tablet was found to be 99.09 ± 0.43 and 99.04 ± 0.94 respectively (Table 1).

Table 1: Analysis of pharmaceutical dosage form

Dosage form	Label claim (mg)	Amount estimated (mg)	Percent purity ± %RSD (n = 5)
TOPCID® 40 Tablet	40	39.63	99.09 ± 0.43
FAMOTIN® 40 Tablet	40	39.61	99.04 ± 0.94

Linearity

The proposed spectrophotometric method has shown linear relationship in the concentration range of 5 - 30 µg/ml (r^2 = 0.9995) for FAM (Table 2, Figure 3).

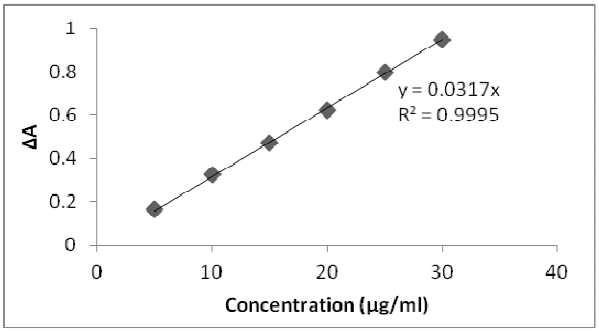

Figure 3: Linearity of FAM

Table 2: Optical characteristics and validation of proposed method.

Parameters	Values
λ_{maxima} (nm)	290.60
λ_{minima} (nm)	259
Linearity range (µg/ml)	5-30
Correlation coefficient	0.9995
Slope	0.0317
Limit of detection (µg/ml)	0.4435
Limit of quantitation (µg/ml)	1.3307
Precision (n = 6)	
Inter-day precision	1.30
Intra-day precision	1.93

Accuracy

The mean % recovery in TOPCID® 40 tablet and FAMOTIN® 40 tablet was found to be 99.17 ± 0.47 and 99.22 ± 0.59, respectively (Table 3).

Table 3: Results of accuracy study

Dosage form	Content of drug (mg)	Excess drug added %	% Recovery ± % RSD (n = 3)
TOPCID® 40 Tablet	40	80	99.45 ± 0.11
		100	99.21 ± 0.94
		120	98.84 ± 0.37
Mean			**99.17 ± 0.47**
FAMOTIN® 40 Tablet	40	80	98.56 ± 0.15
		100	99.24 ± 0.99
		120	99.87 ± 0.64
Mean			**99.22 ± 0.59**

Precision

The result of inter-day precision was expressed as % RSD and it was found to be 1.30. The result of intra-day precision was expressed as % RSD and it was found to be 1.93. The % RSD value indicates the good precision of the method (Table 2).

Limit of detection (LOD) and limit of quantitation (LOQ)

The LOD and LOQ was found to be 0.4435 µg/ml and 1.3307 µg/ml for FAM (Table 2).

CONCLUSION

The result of the developed method for determination of FAM indicates that the method was accurate, precise and reproducible. The method is economical as compared to other reported analytical method. Hence this method can be used for routine analysis of commercially available formulation of FAM. The method is suitable for the determination of the FAM in tablet formulation without interference from commonly used excipients. The solvents used for the proposed method were inexpensive and simple to prepare. The method could be used in a quality control laboratory for routine drug analysis.

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