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New Spectrophotometric Methods for the Quantification of an Anti-Peptic Ulcer Drug in Bulk and Tablets

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Abstract

Two simple, economical and reproducible fundamental and derivative UV spectrophotometric methods were developed and validated for determination of Famotidine in bulk and dosage form. Famotidine showed maximum absorption at 281 nm in phosphate buffer pH 7.5 while it has 282 nm as its absorption maxima in borate buffer pH 9.0. The linearity was determined in the concentration range of 30-80 µg/mL (r2 as 0.9993 & 0.9987) and 10-60 µg/mL (r2 as 0.9991 & 0.9995) for the fundamental and derivative methods in phosphate and borate buffers. The developed methods were validated as per ICH guidelines. Recovery studies gave satisfactory results indicating that none of the major additives/excipients interfered with the assay method. This method may be useful for routine laboratory analysis of famotidine.

Keywords: *Borate buffer pH 9.0, derivative, famotidine, fundamental, phosphate buffer pH 7.5, UV spectrophotometric, validation*

INTRODUCTION

Famotidine is a histamine H2 receptor antagonist that inhibits stomach acid production [1]. It is commonly used in the treatment of peptic ulcer disease and gastroesophageal reflux disease. Chemically Famotidine (Fig. 1) is 3-[[2-(diaminomethylideneamino)-1, 3-thiazol-4- yl] methylsulfanyl]-N'-sulfamoylpropanimidamide with a

molecular weight of 337.44 g/mol. It is very slightly soluble in water. Literature review reveals analytical methods like UV spectroscopy [2−10], colorimetry [11−18], spectrofluorimetry [19], HPLC [20−30], HPTLC [31], flow injection analysis [32, 33] and electrochemical analysis [34−36]. An attempt has been made to develop a simple, sensitive and economical UV spectroscopic method that can be used in routine analysis.

EXPERIMENTAL

Instrumentation

Double beam UV-Visible Spectrophotometer (UV-1800) Shimadzu (Japan) connected to computer located with software UV probe was employed with spectral band width of 1nm and wavelength accuracy of 0.3 nm with a pair of 10 mm path length matched quartz cells. For scanning, the wavelength range selected was 400 nm to 200 nm with medium scanning speed. All weights were taken using electronic balance (Shimadzu, Japan). All Experiments were performed at room temperature.

Chemicals and Reagents

Pure sample of Famotidine was supplied by Dr. Reddy's laboratories, Hyderabad and the commercial tablets were purchased from the local pharmacy. Potassium di hydrogen orthophosphate, boric acid and sodium hydroxide (AR grade) were procured from Qualigens and distilled water was used throughout the study.

Preparation of Phosphate Buffer pH 7.5

Phosphate buffer pH 7.5 was prepared by dissolving 45.36 gm of potassium di hydrogen orthophosphate in sufficient water to produce 1000 mL.

Preparation of Stock (1000 µg/mL) and Working Standard (100 µg/mL) Solutions

Accurately weighed about 25.0 mg of Famotidine was weighed and transferred to clean and dry volumetric flask, dissolved in methanol and made up the volume to 25 mL with the same solvent.

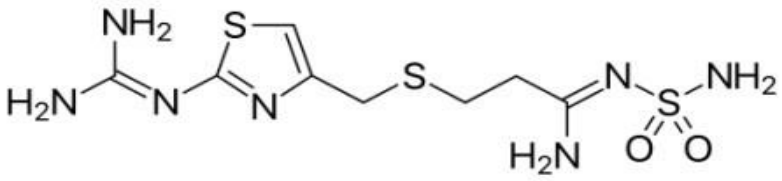

Figure 1: Chemical structure.

2.5 mL of the above solution was transferred to different 10 mL volumetric flasks and diluted with phosphate buffer pH 7.5 and borate buffer pH 9.0 separately. This solution was used for making series of dilutions for calibration curve. All solutions were freshly prepared before analysis.

Preparation of Sample Solution (from tablets) 20 tablets of Famotidine (Famocid) were weighed, powdered and weight of powder equivalent to 10 mg of Famotidine was taken into a 10mL volumetric flask, dissolved in methanol, sonicated for 15 min and volume was made up to the mark with the same solvent and filtered. A solution of 100 µg/mL was prepared using phosphate buffer pH 7.5 and borate buffer pH 9.0 separately. The above solutions were suitably diluted to the required concentrations with phosphate buffer pH 7.5 and borate buffer pH 9.0.

Fundamental UV Spectrophotometric Method (D^o)

The drug solutions were scanned in the UV range (200-400nm) and the absorption spectra were recorded against the reagent blank. The absorbance was measured at 281 nm in phosphate buffer pH 7.5 and at 282 nm in borate buffer pH 9.0.

First Order Derivative UV

Spectrophotometric Method (D^1)

The spectra of all the drug solutions obtained in the zero order method were derivatized into first order spectra using the UV probe software and the derivative absorbance was measured at corresponding maxima and minima. The amplitude was calculated in the range of 269.23 nm to 302.2 nm in phosphate buffer pH 7.5 and 271. 23 nm to 304 nm in borate buffer pH 9.0.

Validation

The methods were validated [37] as per International Conference of Harmonization (ICH) guidelines for linearity, precision and accuracy.

Linearity

Aliquots of working standard solutions were suitably diluted with phosphate buffer pH 7.5 and borate buffer pH 9.0 and the absorbance of each solution was measured as per the method. Linearity plots were constructed for concentration v/s absorbance in D^0 and concentration v/s amplitude in D^1 methods.

Precision

The precision of the method was studied in terms of repeatability and intermediate precision. Replicate sample solutions of

20, 40 and 60 µg/mL famotidine were prepared in both the buffers and analysed for D0 and D1 on the same day and on different days. The absorbance, derivative absorbance was measured from which the assay and % RSD was calculated.

Accuracy

Accuracy was studied by standard addition method at three different levels (50, 100 and 150 %). The recovery and % RSD were calculated.

Assay

20 tablets of Famotidine (Famocid) were used to prepare the sample solutions. A solution of 100 µg/mL was prepared using phosphate buffer pH 7.5 and borate buffer pH 9.0 as per the above procedure. These solutions were suitably diluted to the required concentrations with phosphate buffer pH 7.5 and borate buffer pH 9.0 and assay was performed.

RESULTS AND DISCUSSION

Two simple and sensitive fundamental and first order derivative UV spectroscopic methods have been developed in phosphate buffer pH 7.5 (method A) and borate buffer pH 9.0 (method B). Several buffers and solvents have been used in the method optimization and the best optical characteristics were obtained with the selected phosphate buffer pH 7.5 and borate buffer pH 9.0. These methods were validated as per the ICH guidelines and the results are discussed below.

Linearity

The linearity was evaluated using different concentrations of standard solution. The Beer-Lambert's law was obeyed in the concentration range of 30 – 80 µg/mL in phosphate buffer pH 7.5 (D0 & D 1) and 10−60 µg/mL in borate buffer pH 9.0 (D0 & D1) as confirmed from the correlation coefficients. The corresponding spectra and linearity plots are given in Fig. 2a−2d, Fig. 3a−3d and the data is tabulated in Table 1.

Precision

Precision was studied in terms of intraday and interday0 precision. The results of the precision indicate that the methods are reliable. The % RSD for assay in D0 and D 1 was found to be 0.11-0.75 (intraday) and 0.05-1.02 (inter day) in both the buffers. The results are given in the Table 2a and 2b.

Accuracy

Accuracy was evaluated by standard addition method and the percent recovery calculated at 50, 100 and 150% levels of a pre analysed formulation solution were

obtained in the range of 99.2−101.3%. The % RSD was found to be 0.15−1.08. The results are given in Table 3.

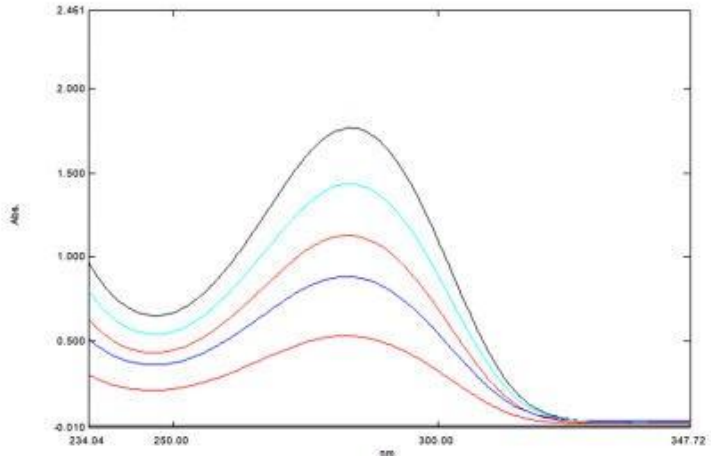

Figure 2a: D^0 spectra in phosphate pH 7.5.

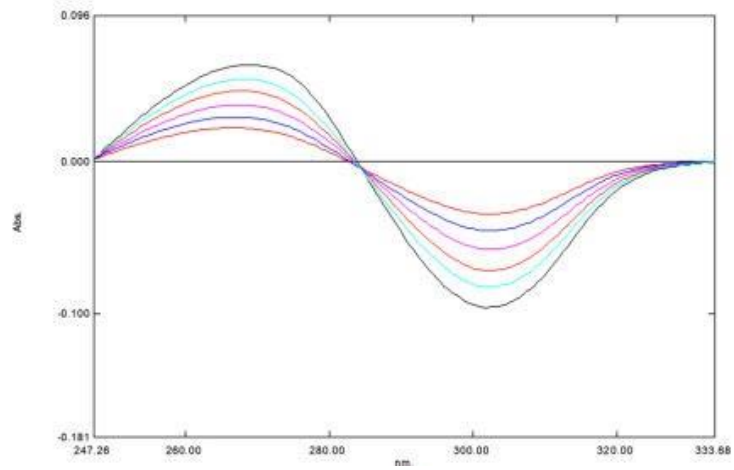

Figure 2b D^1 spectra in phosphate pH 7.5.

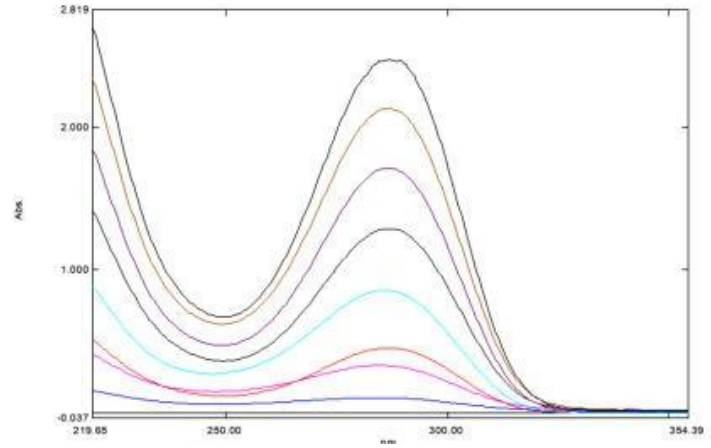

Figure 2c: D^0 spectra in borate pH 9.0.

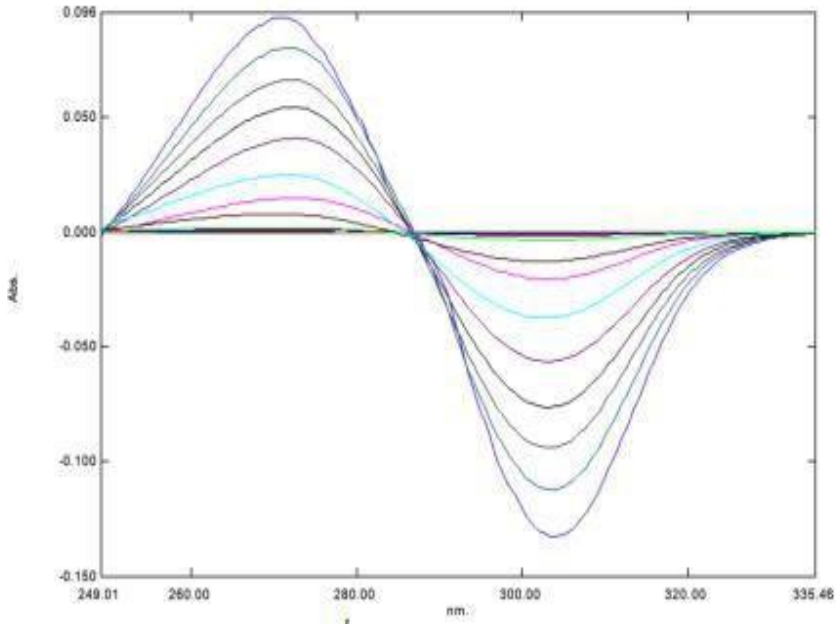

Figure 2d: D^1 spectra in borate pH 9.0.

Table 1: Data for linearity

Phosphate Buffer pH 7.5			Borate Buffer pH 9.0		
Conc. (µg/mL)	Absorbance	Amplitude	Conc. (µg/mL)	Absorbance	Amplitude
30	0.8845	0.056	10	0.4514	0.034
40	1.1328	0.075	20	0.8555	0.062
50	1.4317	0.095	30	1.2826	0.097
60	1.7627	0.118	40	1.7096	0.131
70	2.0230	0.138	50	2.129	0.161
80	2.3534	0.159	60	2.4721	0.193

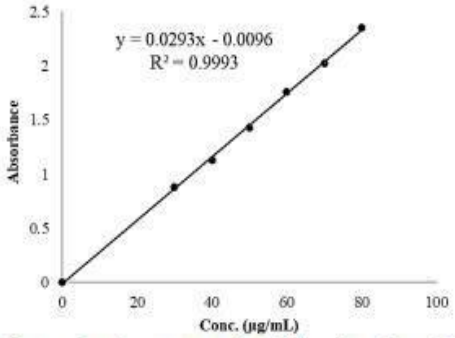

***Figure 3a:** Linearity plot (D^{II}), phosphate 7.5.*

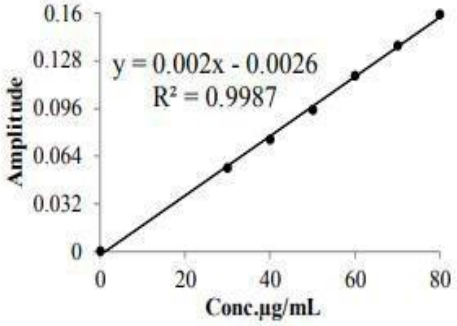

***Figure 3b:** Linearity plot (D^1), phosphate 3.5.*

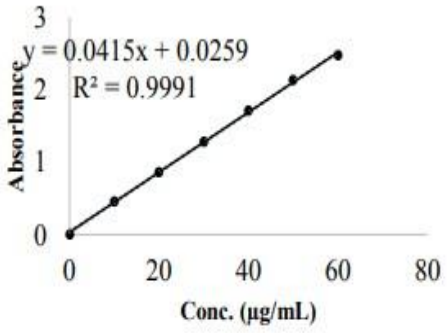

Figure 3c: Linearity plot (D^0), borate 9.0.

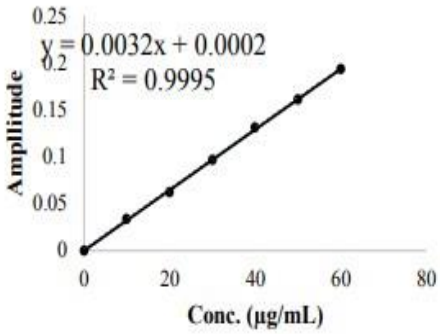

Figure 3d: Linearity plot (D^1), borate 9.0.

Table 2a: Precision data in phosphate buffer pH 7.5.

Conc. (µg/mL)	Intraday Precision		Interday Precision	
	D^0	D^1	D^0	D^1
	*Assay (%w/w) ± SD, % RSD			
20	102.17 ± 0.76, 0.75	101.3 ± 0.57,0.56	103.6 ± 0.61, 0.61	101.1 ± 1.04,1.02
40	103.9 ± 0.36,0.34	101.5 ± 0.46,0.45	104.7 ± 0.180.18	101.3 ± 0.15,0.15
60	103.7 ± 0.45, 0.38	101.3 ± 0.57,0.56	104.1 ± 0.900.86	101.5 ± 0.5,0.49

**Mean of three determinations*

Table 2b: Precision data in borate buffer pH 9.0.

Conc. (µg/mL)	Intraday Precision		Interday Precision	
	D^0	D^1	D^0	D^1
	*Assay (%w/w) ± SD, % RSD			
20	101.6 ± 0.76, 0.75	99.5 ± 0.40, 0.40	102.2 ± 0.8, 0.76	99.7 ± 0.40, 0.40
40	103.1 ± 0.12, 0.11	101.5 ± 0.75, 0.73	104.0 ± 0.11, 0.11	100.5 ± 0.45, 0.42
60	103.7 ± 0.23, 0.22	99.64 ± 1.13, 1.14	104.1± 0.05, 0.05	99.4 ± 0.96, 0.96

**Mean of three determinations.*

***Table 3:** Recovery studies.*

Level (%)	Phosphate buffer pH 7.5		Borate buffer pH 9.0	
	D^0	D^1	D^0	D^1
	*Recovery ± SD, % RSD			
50	99.4 ± 0.15, 0.15	100.2 ± 0.57, 0.57	99.2 ± 0.45, 0.45	99.7 ± 0.23, 0.23
100	100.2 ± 0.92, 0.91	101.1 ± 57, 0.52	100.7 ± 0.72, 0.71	101.3 ± 0.95, 0.96
150	101.2 ± 0.69, 0.68	101.3 ±0.57, 0.56	101.4 ± 0.44, 0.44	100.9 ± 1.08, 1.08

**Mean of three determinations*

Assay The developed methods were also applied for the determination of Famotidine in commercial tablets. There was no interference from the excipients as observed from the assay as stated against the label claim and the results are given in Table 4.

Table 4: Assay in tablets.

Method		Brand	Label claim (mg)	*Amount obtained (mg)	*Assay (% w/w) ± SD
Phosphate buffer pH 7.5	D^0	FAMOCID	40.0	39.9	99.75 ± 0.82
	D^1			40.2	100.5 ± 0.76
Borate buffer pH 9.0	D^0			40.5	101.25 ± 0.83
	D^1			39.7	99.25 ± 1.04

**Mean of three determinations*

Table 5: Summary of optical and validation parameters.

Parameters	Phosphate buffer pH 7.5		Borate buffer pH 9.0	
	D^0	D^1	D^0	D^1
Range (µg/mL)	30 – 80	30 – 80	10 – 60	10 – 60
Regression equation	y = 0.0293x-0.0096	y = 0.002x-0.0026	y = 0.0415x + 0.0259	y = 0.0032x + 0.0002
Correlation coefficient (r^2)	0.9993	0.9987	0.9991	0.9995
Intraday precision (% RSD)	0.34-0.75	0.45-0.56	0.11-0.75	0.40-1.14
Inter day precision (% RSD)	0.18 - 0.86	0.15-1.02	0.05-0.76	0.40-0.96
Accuracy (% RSD)	0.15 – 0.91	0.52-0.57	0.44 – 0.71	0.23-1.08
Sandell's sensitivity (µg/cm^2/0.001)	0.034	-	0.022	-
Molar Absorptivity (L. $mol.^{-1}$ cm^{-1})	9793.3	-	14464.4	-
LOD (µg/mL)	1.235	2.83	0.872	0.309
LOQ (µg/mL)	4.081	9.37	2.879	1.021

CONCLUSION

Two simple and economical UV spectrophotometric methods were proposed for the determination of famotidine with reasonable precision and accuracy. Validation parameters justify this method for application to quantification of Famotidine in pure and dosage form. Moreover, the methods are free from interference by common additives and excipients making them specific for the assay and evaluation of Famotidine in pharmaceutical dosage form.

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