Innovare
Academic Sciences

Original Article

SIMULTANEOUS ESTIMATION OF FAMOTIDINE AND RABEPRAZOLE SODIUM: METHOD DEVELOPMENT AND VALIDATION BY UV-SPECTROPHOTOMETRIC METHOD

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ABSTRACT

Objectives: Study aimed for the simultaneous estimation of Famotidine and Rabeprazole sodium at 263 nm, λ_{max} of Famotidine and 284 nm, λ_{max} of Rabeprazole sodium.

Methods: Method development and validation were done by UV spectrophotometric method.

Results: The method developed obeyed Beer-Lambert's law in the concentration range of 5-30 μg/ml for both famotidine and rabeprazole. The results of the analysis have been successfully validated statistically. The %RSD confirms the precision of the proposed method and Recovery studies show the accuracy of the method.

Conclusion: This method was simple, precise and accurate and was successfully applied to the determination of these drugs in the laboratory mixture.

Keywords: Famotidine, Rabeprazole, Beer-Lambert's Law, simultaneous estimation.

INTRODUCTION

Famotidine chemically 3-[[[2-[(Aminoiminomethyl) amino]-4-thiazolyl]methyl]thio]-N-(aminosulfonyl) propanimidamide is used in the treatment of gastric ulcer, stress ulcer and gastritis [1]. An extensive literature survey revealed titrimetry, HPLC, HPTLC and Spectrophotometric methods for the analysis of Famotidine in bulk and in formulations [2].

Rabeprazole sodium is a potent proton pump inhibitor that suppresses gastric acid secretion. It is used in the treatment of gastrooesophagial reflux disorder (GERD) and duodenal ulcer [3]. Chemically Rabeprazole is 2-({[4-(3-methoxypropoxy)-3-methylpyridin-2-yl] methane} sulfinyl)-1H-1,3 benzodiazole.
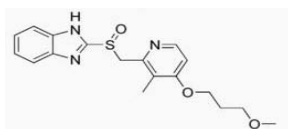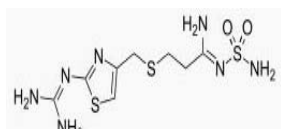

Fig. 1: Structure of Famotidine

Fig. 2: Structure of Rabeprazole

Literature Survey reveals that UV spectrophotometry and RP-HPLC methods have been developed for Rabeprazole in single and combined dosage forms [4].

Studies suggest proton pump inhibitors may not control the gastric acidity effectively during the night, especially in gastroesophageal reflux disease. It has therefore been suggested that H_2 receptor blockers should be added to the therapy [5]. However, no methods are yet reported for simultaneous estimation of Famotidine and Rabeprazole by simple spectrophotometric method. Hence the main purpose of the study was to develop a simple, accurate, reproducible, rapid and economical method for simultaneous estimation of Famotidine and Rabeprazole sodium in bulk and validating of method as per ICH norm.

MATERIALS AND METHODS

Drug

Famotidine was supplied by Zydus Cadilla and Rabeprazole sodium was supplied by Dr. Reddy's Laboratories, Hyderabad.

Reagents and chemicals

All other reagents were of analytical grade for Spectrophotometric method.

Instruments

Jasco V-630 UV spectrophotometer

Estimation of Famotidine and Rabeprazole by UV-Visible spectroscopy

Preparation of simulated gastric fluid pH 1.2

Accurately weighed 3.75 g of Potassium chloride was dissolved in distilled water and 3.71 ml of Conc. Hydrochloric acid was added to it. The final volume was made upto 1000 ml with distilled water.

Famotidine and Rabeprazole stock solution

An accurately weighed quantity of Famotidine equivalent to 100 mg was dissolved in 100 ml of simulated gastric fluid in 100 ml volumetric flask to get 1000 μg/ml. Similarly Rabeprazole equivalent to 100 mg was dissolved in 100 ml of simulated gastric fluid in 100 ml volumetric flask to obtain 1000μg/ml.

Study of spectra and selection of wavelength

Aliquot portions of stock solutions of Famotidine and Rabeprazole were diluted appropriately with simulated gastric fluid pH 1.2 to obtain concentration 10 μg/ml of each drug. The solutions were scanned in the range of 400-200 nm in 1 cm cell against blank.

The UV absorbance spectrum of Famotidine and Rabeprazole is shown in fig. 3 and fig. 4. From the spectrum the wavelengths selected for estimation of drugs were 263 nm as λ_{max} of Famotidine and 284 nm as λ_{max} of Rabeprazole.

Study of beer-lambert's law

Aliquots of the working stock solution of Famotidine and Rabeprazole were prepared with simulated gastric fluid of pH 1.2 to get concentrations in the range of 5-30 μg/ml for Famotidine and Rabeprazole. The absorbances of the resulting solutions were measured at their respective λ_{max}. A calibration curve as concentrations. Absorbance was constructed to study the Beer-Lambert's Law and regression equation.

Vierodt's simultaneous equation method

If a sample contains two absorbing drugs each of which absorbs at the λ_{max} of the other, it may be possible to determine both drugs by the technique of simultaneous equation method. This method analysis is based on the absorption of drugs at the wavelength maximum of the order. Quantification analysis of Drug1 and Drug2 in a binary mixture was performed with the simultaneous equation.

Analysis of laboratory mixture by proposed method

In order to see the feasibility of the proposed method for simultaneous estimation Famotidine and Rabeprazole in pharmaceutical formulations, the method was first tried for the estimation of the drugs in standard laboratory mixture.

Accurately weighed quantities of Famotidine and Rabeprazole sodium 100 mg taken in 100 ml volumetric flask and dissolved in simulated gastric fluid of pH 1.2 by vigorous shaking. The suitable dilution was made to get a final concentration of about 10 µg/ml famotidine and 10 µg/ml rabeprazole. The absorbances of the resulting solutions were measured at 263 nm and 284 nm in 1 cm cell against a blank. Amount of each drug was determined using simultaneous equation as following:

$$C_X = \frac{A_1 ay_2 - A_2 ay_1}{ax_1 ay_2 - ax_2 ay_1} \dots\dots\dots\dots (Equ. 1)$$

$$C_y = \frac{A_2 ax_1 - A_1 ax_2}{ax_1 ay_2 - ax_2 ay_1} \dots\dots\dots\dots (Equ. 2)$$

Where,

A1 and A2 are absorbance of Sample solution of Drug1 and Drug2 respectively.

ax_1 = Absorptivity of Drug1 at A1 nm

ax_2 = Absorptivity of Drug 1 at A2 nm

ay_1 = Absorptivity of Drug 2 at A1 nm

ay_2 = Absorptivity of Drug 2 at A2 nm

Validation of proposed method

Validation of an analytical method is the process to establish that the performance characteristics of the developed method meet the requirements of the intended analytical application. The UV method was validated in terms of accuracy, precision, LOD, LOQ, linearity and sensitivity.

Linearity

It was determined by measuring the absorbance of various concentrations of both drugs Famotidine and Rabeprazole at their own respective λ_{max} and at the λ_{max} of other drug. The response was plotted against concentration of the analyte. Linearity of the calibration curve was demonstrated by applying the least square regression analysis to the plot obtained.

Accuracy

To determine accuracy of the proposed method, three different levels of drug concentrations were prepared from independent stock solution and analyzed. Accuracy was assessed as the mean percentage Bias.

Precision

Intra-day and inter-day variation was taken to determine intermediate precision of the proposed method. Different levels of drug concentrations in triplicates were prepared three different times in a day and studied for intra-day variation. The same drug concentrations were prepared on three different days to study inter-day variation. %Relative standard deviation (%RSD) were calculated which should be less than 2%.

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

LOD was determined using the relation 3.3 σ/s where 'σ' is the standard deviation of the response and 's' is the slope of the calibration curve.

The standard deviation of the response can be obtained either by measuring the standard deviation of the blank response or by calculating the residual standard deviation of the regression line or by calculating the standard deviation of the y-intercept of the regression line, i.e. the standard error of the estimate. Similarly, LOQ was determined using the relation 10 σ/s.

RESULTS

An attempt has been made to develop a simple, sensitive, reproducible, fast and economic analytical method for the simultaneous estimation of Famotidine and Rabeprazole in bulk form using Simultaneous equation method. This method uses the absorbance at two selected wavelengths. One is the λ_{max} of Famotidine and other being the λ_{max} of Rabeprazole. From the stock solution, working standard solutions of Famotidine and Rabeprazole were prepared by appropriate dilution and were scanned in the entire UV range to determine the λ_{max} of both the drugs.

Famotidine have λ_{max} at 263 nm and Rabeprazole at λ_{max} 284 nm. A series of standard solutions were prepared for both Famotidine and Rabeprazole and absorbances of solutions were recorded at 263 nm and 284 nm to plot a calibration curve of absorbance versus concentration. Regression equation and Absorptivity values of Famotidine and Rabeprazole were determined at selected wavelengths are presented in table 1.
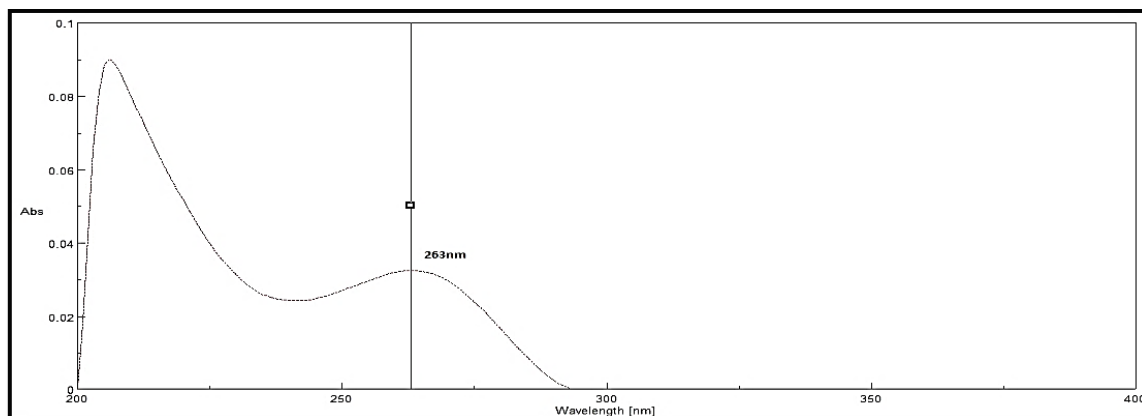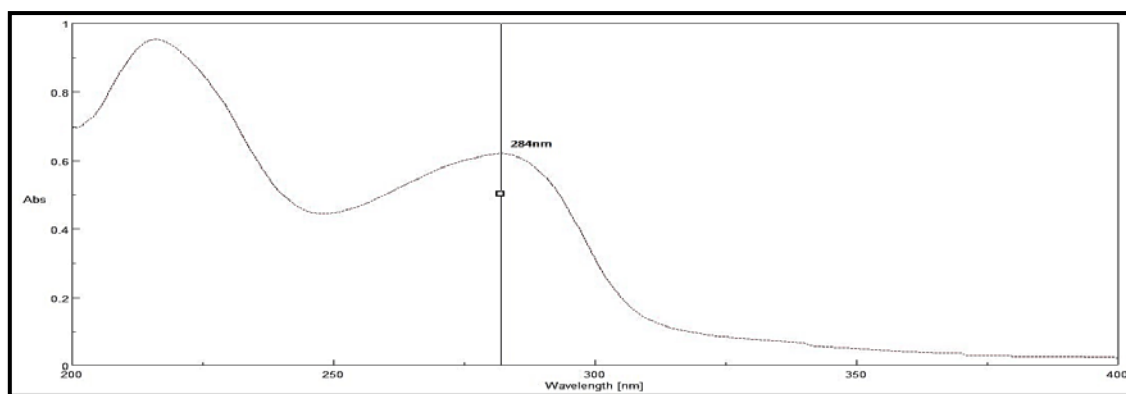

Fig. 3: Spectrum of Famotidine

Fig. 4: Spectrum of Rabeprazole

Table 1: Result of analytical method development in SGF pH 1.2

Parameter		Famotidine		Rabeprazole	
		At 263 nm	At 284 nm	At 263 nm	At 284 nm
Absorptivity		330.75	200.73	366.505	346.55
Regression equation	Slope	0.0299	0.0161	0.0345	0.0343
	Intercept	0.0276	0.0356	0.0171	0.0038
Correlation coefficient (r^2)		0.9968	0.9865	0.9979	0.9998

The concentration of two drugs in the mixture was calculated by using the equation (1) and (2). The percentage purity of Famotidine and Rabeprazole in Laboratory mixture is shown in the table 2.

Using the %RSD of the absorbance of six replicate injections of the drug, the precision of the spectrophotometer system was determined.

Table 2: Determination of Famotidine and Rabeprazole in Laboratory mixture

Mixture content	Label content (µg)	Amount found (µg)	%Amount*	±SD*
Famotidine	10	9.96	99.60	±0.050
Rabeprazole	10	9.84	98.40	±0.032

*Mean of six readings

Inorder to prove the validity and applicability of the proposed method, studies were carried out as per ICH Guidelines and their

results are presented in table 3. LOD and LOQ values for Famotidine and Rabeprazole are stated in table 3.

Table 3: Validation ofthe proposed method

Parameter		Famotidine at 263 nm	Famotidine at 284 nm	Rabeprazole at 263 nm	Rabeprazole at 284 nm
Beer's Law Limit (µg/ml)		5-30	5-30	5-30	5-30
LOD (µg/ml)		1.927	1.55	0.3535	0.3807
LOQ (µg/ml)		5.839	4.72	1.0719	1.1535
Precision	Interday	0.14-0.29	0.07-0.34	0.25-0.59	0.2-0.71
(%RSD)	Intraday	0.16-0.33	0.23-0.38	0.18-0.21	0.1-0.27
Accuracy (% Bias)		0.02-0.15	0.1-0.14	0.07-0.11	0.08-0.19

DISCUSSION

UV Spectrophotometric method was successfully developed and validated for the combination of Famotidine and rabeprazole. The calibration curves were found to be linear in the concentration range under study. The Correlation coefficient of these drugs was found to be close to 1.00, indicating good linearity the % RSD in both intraday and interday precision study was found to be less than 2 which indicates the precision of the method. Satisfactory results were obtained with %RSD value less than 2 %; thus confirming the accuracy and precision of the proposed method.

CONCLUSION

The proposed method was proved to be simple, accurate, precise, sensitive, rapid, reproducible and economical for the simultaneous estimation of Famotidine and Rabeprazole sodium in combined

Laboratory mixture. The % RSD. values were found to be less than 2% as required by ICH guidelines, which indicates the accuracy of methods; thus this method can be used for routine simultaneous determination of Famotidine and Rabeprazole in bulk drug and can be used to carry out the simultaneous estimation in the dosage form.

ACKNOWLEDGEMENT

Authors are thankful to Zydus Cadilla and Dr. Reddys Laboratories for providing samples of Famotidine and Rabeprazole respectively.

CONFLICT OF INTERESTS

Declared None.

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