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Research Article

SPECTROFLUORIMETRIC METHOD FOR DETERMINATION OF LAFUTIDINE IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

A simple and reproducible method was developed for the assay of Lafutidine from formulation. The solvent and wavelength of detection were optimized in order to maximize the sensitivity of the proposed method. The relative fluorescence intensity of Lafutidine was measured in 0.1 M sulphuric acid at an excitation and emission wavelength of 330 nm and 640 nm respectively. A linear calibration curve was obtained in the range of 0.5 µg/ml to10 µg/ml. The limit of detection and limit of quantification were found to be 0.048383µg/ml and 0.146616µg/ml, respectively. The proposed method was statistically validated and successfully applied for analysis of tablet dosage form.

Keywords: Spectrofluorimetry, Lafutidine, Validation

INTRODUCTION

Lafutidine (LAF) is chemically 2-[(2-furylmethyl)sulfinyl]-N-((2Z)-4-{[4-(piperidin-1-ylmethyl) pyridin-2-yl]oxy}but-2-en-1-yl) acetamide (Figure 1). It is not official in any pharmacopoeias. It is a second generation H2 receptor antagonist having multimodal mechanism of action. It not only suppresses gastric acid secretion, but also has cyto-protective properties by the virtue of its property to induce the collagen synthesis in the gastric mucosa. In addition to blocking the H2 receptors, it is also found to stimulate mucin biosynthesis and promote the restitution of damaged mucosa. It is indicated in hyperacidity, NSAID induced gastritis, gastric and duodenal ulcers and also used as preanesthetic medication. [1].

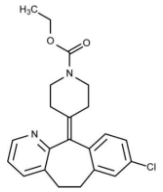

Fig. 1: Structure formula of LAF

The literature survey revealed that various methods of analysis for LAF individually or in combination with other drugs have been reported, which included UV [2-4], HPLC [5-8], HPLC- MS [9-12] and HPTLC [13] .There is no reported spectrofluorimetric method. The aim of the present work was to develop a simple spectrofluorimetric method for the determination of LAF in marketed Formulation.

MATERIALS AND METHODS

Instrumentation

All fluorescence measurements were done on a Perkin Elmer Spectrofluorimeter LS 55, with single quartz cell of 1 cm path length.

Chemicals and reagents

Acetonitrile, Methanol, Acetic Acid, Sodium Hydroxide, Sulphuric acid of AR grade was obtained from Loba chemicals, India.

Preparation of standard stock solution

10 mg of LAF was accurately weighed and transferred to 10 ml volumetric flask containing a few ml of diluent, i.e. 0.1 M Sulphuric acid. The mixture was made up to the mark with the diluent to yield a solution of concentration 1000µg/ml. Further dilution was done the get a working standard solution of concentration 10 µg/ml.

Method Development

Selection of diluent: LAF standard preparations were prepared in various mediums like water, dilute acetic acid, NaOH, Methanol, Ethanol, Acetonitrile, Acetic acid, Diethyl ether. The solutions were scanned to check the emission peaks.

Selection of Emission Slit Width: The standard solution of LAF was prepared and it was scanned with different excitation and emission slit width i.e. 5,7,10.

Calibration Curve for LAF

Appropriate aliquots of LAF working standard solution were taken in different 10 ml volumetric flask and further dilution was done to obtain final concentration of 0.5 to 10µg/ml of LAF. The calibration curve was constructed by plotting intensity versus concentration of the drug and regression equation was computed.

Method Validation

The method was validated for linearity, accuracy, precision and specificity, limit of detection, and limit and quantification as per ICH guidelines.

Accuracy

The accuracy of the method was assessed by determination of the recovery of the method at 3 different concentrations (50%, 100% and 150% concentration) by addition of known amount of standard to the sample solution. For each concentration three sets were prepared.

Precision

The repeatability of the method was evaluated by determining the absorbance of the standard solution of LAF six times repeatedly. The results are reported in terms of relative standard deviation. The intra-and inter-day precision for the determination of LAF was carried out in triplicate for 3 concentrations of the standard solution.

Limit of detection and quantification

LOD and LOQ were calculated using following equation as per ICH guidelines. LOD = 3.3 ×σ /S and LOQ = 10 ×σ /S, where σ is the standard deviation of response and S is the slope of the calibration curve.

Robustness

The robustness of the proposed method is demonstrated with minor change in the emission slit width (±1).

Solution Stability

Stability of the standard solution was evaluated after storing it for 24 hrs. The fluorescence intensity of the aged solution was evaluated by comparing with freshly prepared solution.

Analysis of marketed formulations

Lafudac (Unisearch) was procured from local market. Twenty tablets were weighed accurately and finely powdered. Tablet powder equivalent to 10 mg of LAF was accurately weighed and transferred to a 10 ml volumetric flask. Volume was made upto the mark with 0.1 M sulphuric acid. Further dilutions were made to prepare final concentration of 5 µg/ml of LAF. This solution was prepared six times and the intensity of each solution was determined at 640 nm and the concentration of drug in sample solution was determined from calibration curve.

RESULT

In this work an analytical Spectrofluorimetric method for assay of LAF in tablet formulation was developed and validated. 0.1 M Sulphuric acid as diluent was selected which gave sharp spectra of LAF. A peak at 330nm was obtained in the excitation mode, thus this wavelength was selected as the excitation wavelength. (Figure 2). The excitation and emission slit width was 5 and 10 respectively. The estimation was carried out by keeping the excitation wavelength as 330nm and then considering the fluorescent intensity at the emission wavelength of 650nm.

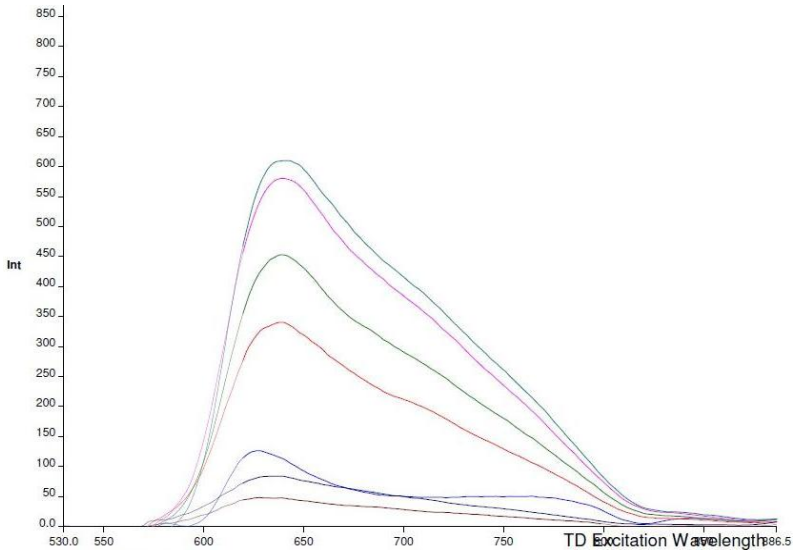

Fig. 2: Overlain spectra of LAF

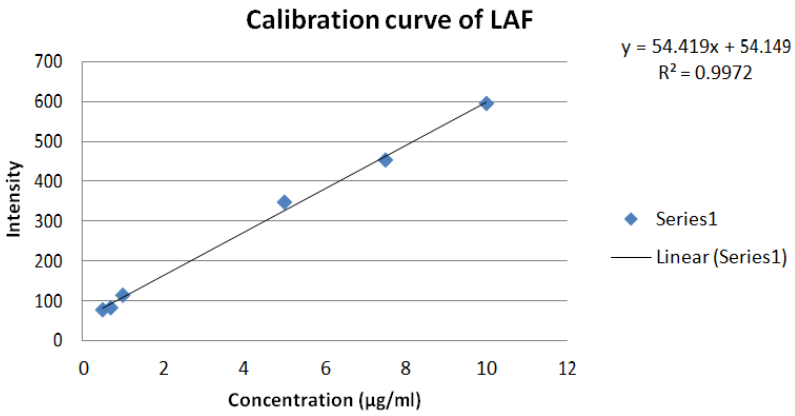

Fig. 3: Calibration curve of LAF

The calibration curve was found to be linear in the range of 0.5 to 10 µg/ml (Figure 3). The data of regression analysis of the calibration curve are shown in table 1.

Table 1: Regression analysis data of Calibration curve

Parameters	LAF
Linearity range ((µg/ml)	0.5 to 10
Regression equation	y = 54.419x + 54.149
Slope	54.419
Intercept	54.149
Correlation Coefficient	0.9972

The accuracy of the method was determined by calculating recoveries which were found to be 98.02% and 101.4%. The high values indicate that the method is accurate. Instrument precision was determined by performing injection repeatability test and the %RSD value for LAF were found to be 1.5. The RSD value indicates that the method is precise. The detection limit for LAF was 0.048 µg/ml while quantitation limit was 0.14 µg/ml. The validation parameters are summarized in table 2. The solution stability study revealed that LAF solution was stable for 48hrs without detectable degradation. The proposed method was applied to the determination of LAF in tablet dosage form. The result for LAF was comparable with the corresponding labelled amount (table 3).

Table 2: Summary of validation parameters

Parameters		LAF
Instrument Precision (%RSD)		1.51
Intraday(%RSD)		0.82 - 1.28
Interday(%RSD)		1.4 - 1.73
LOD (µg/ml)*		0.048
LOQ (µg/ml)*		0.14
Accuracy (%Recovery ± SD)	Level 1	100.14±1.84
	Level 2	99.31 ± 1.57
	Level 3	100.14 ± 1.09
%Assay ± SD		99.196 ± 1.44
Solution Stability (for 24hrs) (%)		98.57

Table 3: Assay of Tablet Dosage forms

Formulation	Actual Amount (mg)	Amount Found ± SD (mg)	% of Drug Found ± SD
Tablet (LAFUDAC)	10	9.91± 0.13	99.19 ± 1.44

DISCUSSION

This spectrofluorimetry method is newly developed and validated in large range. This is not time consuming method and also it is reproducible and repeatable.

CONCLUSION

This Spectroflourimetric method for assay of LAF in tablet dosage form was successfully developed and validated for its intended purpose. The method was shown to be linear, precise, and accurate. The sample recovery in tablet formulation was in good agreement with the label claim and thus suggested the validity of the method. So this method can be applied for routine analysis of LAF in its formulations.

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