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DEVELOPMENT AND VALIDATION OF HIGH-PERFORMANCE THIN LAYER CHROMATOGRAPHIC METHODFOR LAFUTIDINE IN BULK AND TABLET DOSAGE FORM

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Keywords:

Lafutidine, Ethyl acetate, Toluene, Methanol, Ammonia, HPTLC

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ABSTRACT: A simple, precise and sensitive High Performance Liquid Chromatographic method has been developed for the quantitative estimation of Lafutidinein bulk and tablet dosage form. The method was performed on Silicagel 60 F_{254} aluminum plate. A Camag HPTLC system comprising of Camag Linomat IV semiautomatic sample applicator, Camag TLC Scanner 3, Camag twin-trough chamber (10×10 cm) and Camag CATS 4 software, As mobile phase Ethyl acetate: Toluene: Methanol: Ammonia (6:2.5:1.5:0.1%v/v) was utilized to develop the Chromatographic method. Lafutidinegave separation at R_f value of 0.45±0.03 and scanned at 273 nm. The calibration curve response was observed between 400-1400ng/spot. The linear regression data showed good linear relationship with R^2 value of 0.99895. The method was validated in terms of repeatability, precision, accuracy, and specificity according to ICH guidelines. The LOD and LOQ were found to be 19ng/Spot and 59 ng/spot respectively. The developed method was successfully used for assay of Lafutidine in tablet formulation.

INTRODUCTION: Lafutidine, chemically 2-[(2-furylmethyl) sulfinyl]-N-((2Z)-4-{[4-(piperidin-1-ylmethyl) pyridin-2-yl] oxy} but-2-en-1-yl) acetamide **Fig. 1** is H2-receptor antagonist used in the treatment of peptic ulcer and gastro-esophageal reflux disease (GERD). Being histamine H_2receptor antagonist, it inhibits daytime (i.e., postprandial) as well as nighttime gastric acid secretion. It also has gastro protective activity that particularly affects mucosal blood flow.

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It elevates postprandial intragastric pH and increases plasma calcitonin gene-related peptide and somatostatin concentrations in humans [2, 3].

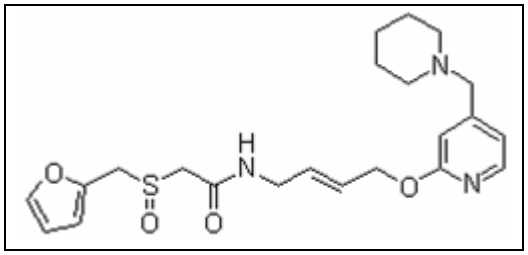

FIG. 1: STRUCTURE OF LAFUTIDINE

The literature reveals that there are some of the methods have been Determination of Lafutidine in human plasma by HPLC-MS, Determination of Lafutidine in human serum by HPLC-FD method and study of pharmacokinetics, Simple, sensitive and rapid LC-ESI-MS method for quantification of

Lafutidine in human plasma, Determination of Lafutidine in serum with reverse high performance liquid chromatography, Determination of residual organic solvent in Lafutidine by GC, Determination of related substance in Lafutidine by RP-HPLC, Determination of Lafutidine and its tablets by HPLC method, Determination of Lafutidine and its tablet by RP-HPLC, UV-spectroscopic method determination of Lafutidine in its tablet dosage form, Quantitative determination of Lafutidine in tablets by first order derivative spectrophotometry using area under curve. The purpose of this work was to develop and validate simple, specific, sensitive, accurate, precise, rapid and cost effective HPTLC method for the estimation of Lafutidine in bulk and its formulations.

MATERIALS AND METHODS:

Materials: Lafutidine working standard was procured as a gift sample from Ajanta Pharma. Ltd. Silica gel 60 F254 TLC plates (10×10 cm, layer thickness 0.2 mm) were used as stationary phase. Single component tablet formulations of Lafutidine (LAFUDAC 10 mg) manufactured by Unichem Pharma. Ltd. Mumbai were purchased from local market. Ethyl acetate, methanol and ammonia (MERCK) were used for mobile phase preparation and as solvent. A Camag HPTLC system comprising of Camag Linomat IV semiautomatic sample applicator, Camag TLC Scanner 3, Camag twin-trough chamber (10×10 cm), n Camag CATS 4 software, Hamilton syringe (100 µl), Shimadzu weighing balance, Sonicator were used during the study.

Preparation of Standard Solution of Lafutidine: Lafutidine (10 mg) was weighed accurately and transferred in 100 ml volumetric flask. It was dissolved in and diluted up to mark with methanol, contained 100µg of Lafutidine per ml of the solution.

Preparation of Sample Solution: Twenty tablets were weighed and finely powdered. The powder equivalent to Lafutidine (10 mg) was weighed accurately and mixed with methanol and sonicated for 10 minutes. The solution was diluted to 100 ml with methanol. The residue was washed thoroughly with methanol. The filtrate and washings were combined in a 100 ml volumetric flask and diluted to mark with methanol to obtain 100µg/ml.

Method and Chromatographic Condition: The chromatographic estimations were performed using following conditions.

Stationary phase, precoated silica gel 60 F254 aluminum sheets (10×10 cm) (pre-washed with methanol. and dry in air); mobile phase, Ethyl acetate: Toluene: Methanol: Ammonia (6:2.5:1.5:0.1 v/v); chamber saturation time, 20 min; wavelength of detection, 273 nm.

Chromatographic Separation: Aliquots of 4, 6, 8, 10, 12 and 14µl of standard or sample solution was applied on TLC plate. The plate was dried in air and developed up to45 mm at using mixture of Ethyl acetate: Toluene: Methanol: Ammonia (6:2.5:1.5:0.1% v/v) as mobile phase in Camag twin-trough chamber previously saturated with mobile phase for 20 min. The plate was removed from the chamber and dried. Photometric measurements were performed at 273 absorbance/reflectance mode with Camag TLC Scanner 3 with CATS4 software.

Calibration Curve of Standard Lafutidne: Standard Lafutidine solution (4, 6, 8, 10, 12,14µl) was spotted on precoated TLC plate, using semiautomatic spotter The TLC plate was developed and photometrically analyzed as described under chromatographic separation. The calibration curve was prepared by plotting peak area vs. concentration (ng/spot) corresponding to each spot **Fig. 2.**

Quantification of Lafutidinein Tablet Formulation: Six µl of sample solution (100 µg/ml) was applied on prewashed TLC plate, developed and scanned as described in chromatographic separation. The amount of Lafutidine present in sample solution was determined by fitting area values for peak corresponding to Lafutidine into the equation of line representing calibration curve for Lafutidine.

RESULTS AND DISCUSSION: In present work HPTLC method was developed for estimation of Lafutidine pure powder and its pharmaceutical formulation. HPTLC method is cost-effective and less time consuming. Lafutidine is soluble in methanol; therefore methanol was selected as solvent.

The formulation was dissolved in methanol with sonication for 10 min to assure complete release of drug from the formulation matrix. The method was validated in terms of linearity, inter-day and intra-day precision, repeatability of measurement of peak area as well as repeatability of sample application, accuracy and specificity. The limit of detection and limit of quantification were also determined.

The intra-day precision was determined by analyzing standard solutions in the concentration range of 400-800 ng/spot three times on the same day, while inter-day precision was determined by analyzing corresponding standards for 3 days over a period. Repeatability of sample application was assessed by spotting 4 µl of drug solution six times on a TLC plate, followed by development of plate and recording the peak area for six spots. The percent RSD for peak area values of Lafutidine was found to be 0.2031. Repeatability of measurement of peak area was determined by spotting 4 µl of Lafutidine solution on a TLC plate and developing the plate.

The spot was scanned six times without changing the position of the plate, and percent RSD for measurement of peak area of Lafutidine was 0.1315. To confirm the specificity of the proposed method, the solution of the formulation was spotted on the TLC plate, developed and scanned. It was observed that the excipients present in the formulation did not interfere with the peaks of Lafutidine. In order to determine detection and quantification limit, Lafutidine concentrations of 400-800ng/ml solution was scanned three times and graph of average response (peak area) verses concentration of Lafutidine was plotted. From that standard deviation of intercept and mean of slope was calculated.

Detection limit was calculated by (3.3×S.D. of intercept/mean of slope) and quantification limit was calculated by (10× S.D. of intercept/mean of slope).

Recovery studies of the drugs were carried out for accuracy parameters. These studies were carried out at three levels, i.e., multiple level recovery studies. Sample stock solution from Tablet formulation of 100 µg/ml of Lafutidine was prepared. Dilutions were made and recovery studies were performed. The analyzed samples were spiked with extra 50, 100, and 150% of the standard Lafutidine and the mixture was analyzed by the proposed method. Percentage recovery was found to be within limits. The assay values for the marketed formulations were found to be within limits. The low RSD value indicated the suitability of the method for routine analysis of Lafutidine in pharmaceutical dosage forms. The HPTLC technique described is simple, precise, specific and accurate, and the statistical analysis proved that the method is reproducible and selective for the analysis of Lafutidine in bulk drug and tablet formulations

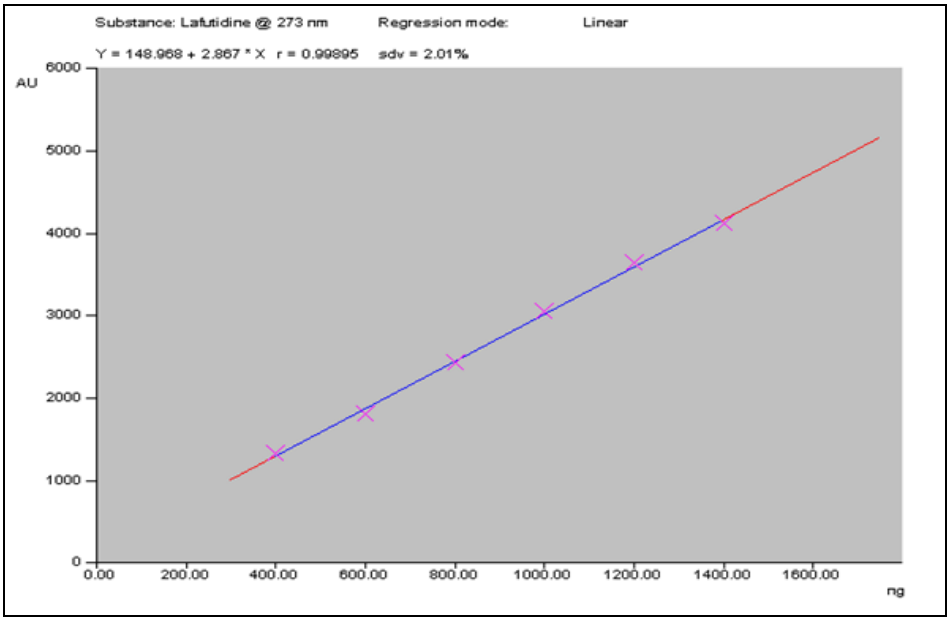

FIG. 2: CALIBRATION CURVE OF LAFUTIDINE

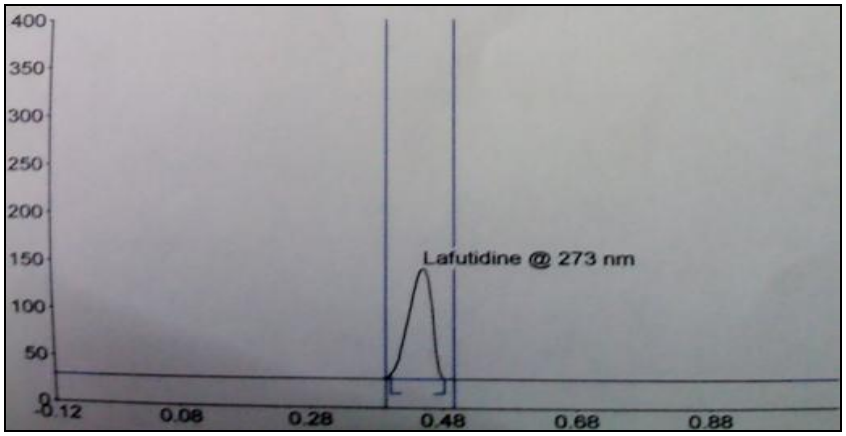

FIG. 3: CHROMAROGRAM OF LAFUTIDINE

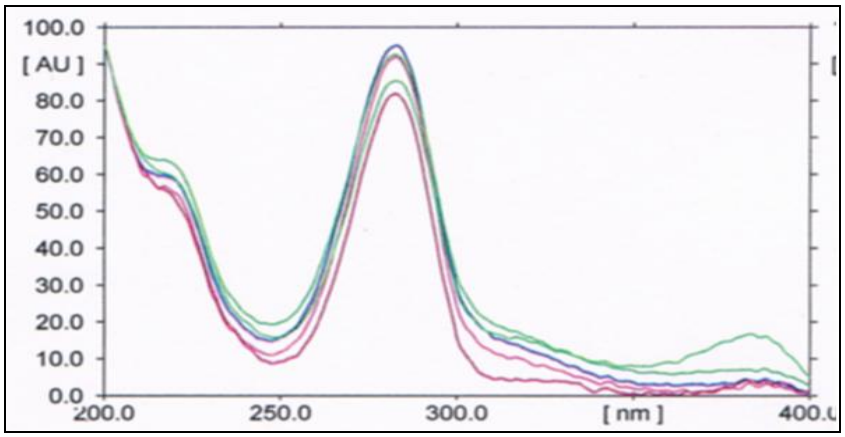

FIG. 4: UV SPETRA OF LAFUTIDINE

TABLE 1: ACCURACY OF LAFUTIDINE

%spiking	Tablet concentration (ng)	Spiked (ng)	Area obtained	Actual area	%recovery	%RSD
0	400	0	1325.4	1327.4	99.84±0.37	0.2541
50	400	200	1801.6	1807.9	99.65±0.19	0.1482
100	400	400	2420.3	2427.4	99.70±0.45	0.1576
150	400	600	3049.6	3052.4	99.90±0.35	0.1945

TABLE 2: MARKETED PRODUCT ANALYSIS

Drug	Label claim	Amount found	%RSD (n = 3)	%recovery
Lafutidine (LAFUDAC)	10mg	9.945	0.0414	99.45%

TABLE 3: VALIDATION PARAMETER OF LAFUTIDINE

Parameter	Data
Linearity	400-1400ng/spot
Correlation coefficient	0.99895
Slope	148.968
Intercept	2.887
Repeatability of measurement(n=6)	0.1315
Repeatability of sample application(n=6)	0.2031
Interday precision(n=3)	0.05-0.30
Intraday precision(n=3)	0.10-0.393841
Accuracy	99.76-99.90%
Limit of detection(ng/spot)	19
Limit of quantification(ng/spot)	59

CONCLUSION: The developed HPTLC technique is precise, specific and accurate. The developed method was validated based on ICH guidelines. Statistical analysis proves that the method is repeatable and selective for the analysis of Lafutidine as a bulk drug and in Pharmaceutical formulations.

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CONFLICTS OF INTEREST: Nil

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