International Journal for Pharmaceutical Research Scholars (IJPRS)
ISSN No: 2277-7873
RESEARCH ARTICLE
V-2, I-1, 2013

Development and Validation of Derivative Spectroscopic Method for the Simultaneous Estimation of Lafutidine and Rabeprazole Sodium in Combined Dosage Form

Antala H[*1], Raval K[2] Dhudashia K[2], Patel N[3], Paghadar B[1]

[*] [1]*Department of Quality Assurance, Noble Pharmacy College, Junagadh, Gujarat, India*

[2]*Asst. Professor, Department of QA, Noble Pharmacy College, Junagadh, Gujarat, India*

[3]*Asst. Professor, Department of QA, B.M.Shah Pharmacy College, Modasa, Gujarat, India*

Manuscript No: IJPRS/V2/I1/00038, Received On: 25/02/2013, Accepted On: 28/02/2013

ABSTRACT

The Present manuscript describe simple, sensitive, rapid, accurate, precise and economical first derivative spectrophotometric method for the simultaneous determination of Lafutidine and Rabeprazole Sodium in combined Pharmaceutical dosage form. The derivative Spectrophotometric method was based on the determination of both the drugs at their respective Zero Crossing Point (ZCP). The First order derivative spectra was obtained in Methanol and the determinations were made at 284.2nm (ZCP of Rabeprazole Sodium) for Lafutidine and 272.8nm (ZCP of Lafutidine) for Rabeprazole Sodium. The linearity was obtained in the concentration range of 10-45 µg/ml for Lafutidine and 6-20 µg/ml for Rabeprazole Sodium. The mean recovery was 102.46 ± 1.19 and 100.61 ± 1.0 for Lafutidine and Rabeprazole Sodium, respectively. The method was found to be Simple, Sensitive, Accurate and Precise as per ICH guideline Q2B(R1). The Proposed method was successfully applied for the simultaneous estimation of both the drugs in commercial Pharmaceutical dosage form.

KEYWORDS

Lafutidine (LAF), Rabeprazole Sodium (RAB), Derivative spectrophotometry, Zero Crossing Point.

INTRODUCTION

Lafutidine is chemically 2-(furan-2-ylmethylsulfinyl)-N-[4-[4-(piperidin-1-ylmethyl) pyridin-2-yl]oxybut-2-enyl]acetamide. Lafutidine is not official in any pharmacopoeias. Lafutidine is the new generation H2-receptor antagonist. It blocks the production of acid by acid producing cells in the stomach and blocks histamine H_2-receptors in the stomach and prevents histamine mediated gastric acid secretion. It is indicated in hyperacidity, NSAID induced gastritis, gastric and duodenal ulcers and also used as preanesthetic medication. Apart from H2-receptor blockade activity, it has additional gastro protective action. Therefore not only inhibit acid secretion but also provide gastric mucosal protection.

Rabeprazole Sodium is chemically 2-[[[4-(3-Methoxypropoxy)-3-Methyl-2-Pyridinyl]-Methyl]Sulfinyl]-1H-Benzimidazole Sodium salt. Rabeprazole sodium (RBP) is a Potent Proton Pump inhibitor that suppress gastric acid secretion by specific inhibition of the gastric H+/K+-ATPase enzyme system at the secretory surface of the gastric parietal cell and is used in the treatment of Gastroeso phageal reflux disease (GERD) and duodenal ulcers. It has a faster onset of action and lower potential for drug interaction compared to Omeprazole.

***Address for Correspondence:**
Hiren Antala
Department of QA, Noble Pharmacy College,
Junagadh, Gujarat, India
E-Mail Id: hirenantala21@gmail.com

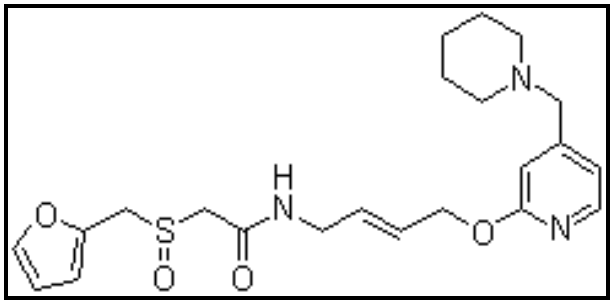

Figure 1: Chemical Structure of Lafutidine

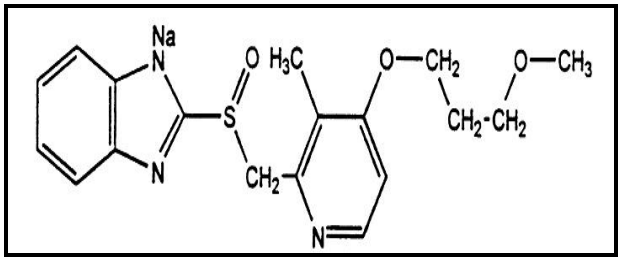

Figure 2: Chemical Structure of Rabeprazole Sodium

Literature survey[4,5,6,7,8,9,10] revealed that a number of analytical methods have been reported for the estimation of Lafutidine(LAF) and Rabeprazole Sodium(RAB) in individual and combination with other drugs are spectrophotometry, HPLC, RP-HPLC, HPTLC, but not even single method was reported for the simultaneous estimation of LAF and RAB in their combined dosage form.

MATERIALS AND METHODS

Instrument

Instrument used was an UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with a pair of 1 cm matched quartz cells. All weighing was done on Shimadzu analytical balance (Model AU-220).

Reagents and Chemicals

Pure drug samples of LAF and RAB were provided as a gift sample from Cadila Pharmaceuticals Ltd, Ahmedabad and Alkem Laboratories Ltd, Mumbai. Methanol LR was used as solvent. Calibrated glass wares were used throughout the work.

Marketed Formulation

The commercial formulation LAFUMAC *PLUS* (Macleods Pharmaceuticals Ltd., Mumbai) was purchased from Local pharmacy. Each Capsule contains 10mg Lafutidine and 20mg Rabeprazole Sodium.

Preparation of Standard Stock Solution

Accurately weighed quantity of LAF (100 mg) and RAB (100 mg) was transferred to two separate 100 ml volumetric flasks, dissolved in Methanol and diluted to the mark with same solvent. (Stock solutions: 1000µg/ml of LAF and 1000µg/ml of RAB).

Preparation of Working Standard Solution

100µg/ml of LAF solution was prepared by diluting 10.0 ml of stock solution with methanol in 100 ml volumetric flask up to the mark. 100µg/ml of RAB solution was prepared by diluting 10.0 ml of stock solution with Methanol in 100 ml volumetric flask up to the mark.

Selection of Wavelength for Analysis

1.0 ml of working standard solution of LAF (100µg/ml) and 2.0 ml of working standard solution of RAB (100µg/ml) was pipette out into two separate 10 ml volumetric flask and volume was adjusted to the mark with Methanol to get 10µg/ml of LAF and 20µg/ml of RAB. Each solution was scanned between 200-400 nm against methanol as a reagent blank for zero order spectra (figure 3). The first order derivative spectra of each solution were obtained using smoothing ($\Delta\lambda$ = 2, Scaling Factor = 25). The zero crossing points were found to be 272.8 nm and 284.2nm for LAF and RAB respectively (figure 4). Wavelengths selected for quantitation were 284.2 nm for Lafutidine (zero crossing point for Rabeprazole Sodium) and 272.8 nm for Rabeprazole Sodium (zero crossing point for Lafutidine).

Calibration Curves for LAF and RAB

Standard LAF solution from 10-45µg/ml were prepared by pipetting out, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0 and 4.5 ml of the working standard solution of LAF (100µg/ml) into series of 10 ml volumetric flasks and the volume was adjusted to mark with Methanol. Absorbance of each solution was measured at 284.2 nm using first order derivative spectrophotometry. A

calibration curve was prepared by plotting absorbance against respective concentration (figure 7). Standard RAB solution from 6-20µg/ml were prepared by pipetting out 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8 and 2.0ml of the working standard stock solution of RAB (100µg/ml) into series of 10ml volumetric flasks and the volume was adjusted to mark with Methanol. Absorbance of each solution was measured at 272.8 nm using first order derivative spectrophotometry. A calibration curve was obtained by plotting absorbance against respective concentration (figure 8).

Analysis of Marketed Formulation

Twenty Capsules were weighed and content crushed to obtain a fine powder. An accurately weighed powder equivalent to about 10mg of LAF and 20mg of RAB was transferred to 100 ml volumetric flask and the volume was made up to the mark using Methanol as solvent. The solution was sonicated for 20minutes. The solution was filtered through whatman Filter Paper No.42. First few ml of filtrate were discarded. 10 ml of the solution from above filtrate was diluted to 100 ml with Methanol. The absorbance of the resulting solution was measured using first order derivative spectrophotometry at 284.2 nm for LAF and 272.8 nm for RAB. The concentration of each drug was calculated using equation of straight line. (Table.7)

METHOD VALIDATION[3]

Linearity and Range

Aliquots of standard stock solutions of LAF and RAB were taken in volumetric flasks and diluted with Methanol to get final concentrations in range of 10-45µg/ml for LAF and 6-20µg/ml for RAB. This calibration range was prepared five times and absorbances were measured at respective wavelengths for each drug separately. (Table.1) (figure 5, 6)

Precision

Precision of the method was determined by performing interday variation, intraday variation and method repeatability studies. In inter day precision, the absorbance of standard solutions of LAF (15, 30 and 45µg/ml) and RAB (6, 12 and 18µg/ml) were measured on Three consecutive days. In intraday variation the absorbances were measured Three times in a day. Repeatability study, one concentration of both the drugs was measured Six times. (Table.2, 3, 4)

Recovery Studies

To study the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels. A known amount of drug was added to preanalyzed Capsule powder and percentage recoveries were calculated. (Table.5, 6)

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

LOD and LOQ were calculated from the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the six replicate determinations of same conc. (15 µg/ml of LAF and 12 µg/ml of RAB), standard deviation (SD) of the responses was calculated. From these values, the parameters Limit of Detection (LOD) and Limit of Quantitation were determined on the basis of standard deviation and slope of the regression equation.

$$LOD = (3.3 \times SD) / Slope$$

$$LOQ = (10 \times SD) / Slope$$

RESULTS AND DISCUSSION

The proposed method was validated as per ICH guideline Q2B (R1). The plot of absorbances versus respective concentrations of LAF and RAB were found to be linear in the concentration range of 10-45µg/ml and 6-20µg/ml respectively with correlation coefficient 0.998 at 284.2 nm and 0.998 at 272.8 nm (as shown in Table. 1 and Figure 5,6,7,8.) Precision was calculated as repeatability, intraday and interday variations and %RSD (Relative Standard Deviation) was found to be in the range (Table 2, 3, 4). The accuracy of method was determined at 80, 100 and 120% level. The mean recovery was 102.46 ± 1.19 and

100.61 ± 1.0 for Lafutidine and Rabeprazole Sodium, respectively (Table.5, 6).

The derivative spectrophotometric method can be successfully used for simultaneous estimation of LAF and RAB in their combined Capsule dosage form. Marketed Capsules were analyzed and results obtained were within the range (Table 7).

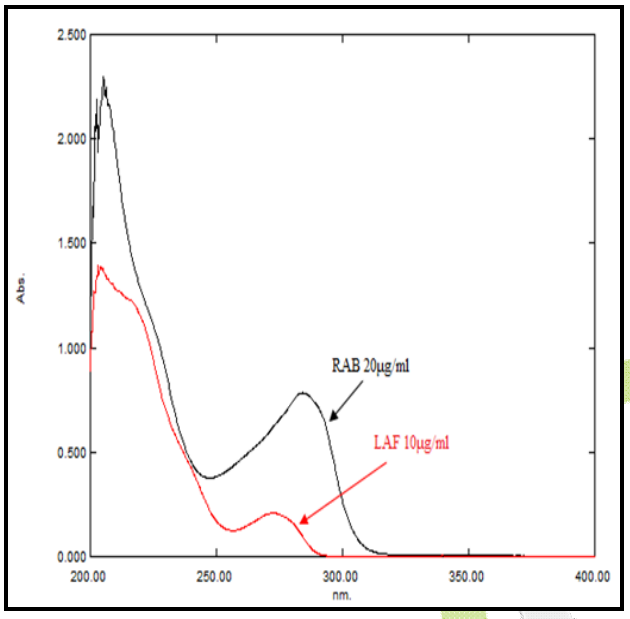

Figure 3: Overlain Zero order spectra of LAF (10µg/ml) and RAB (20µg /ml) in methanol.

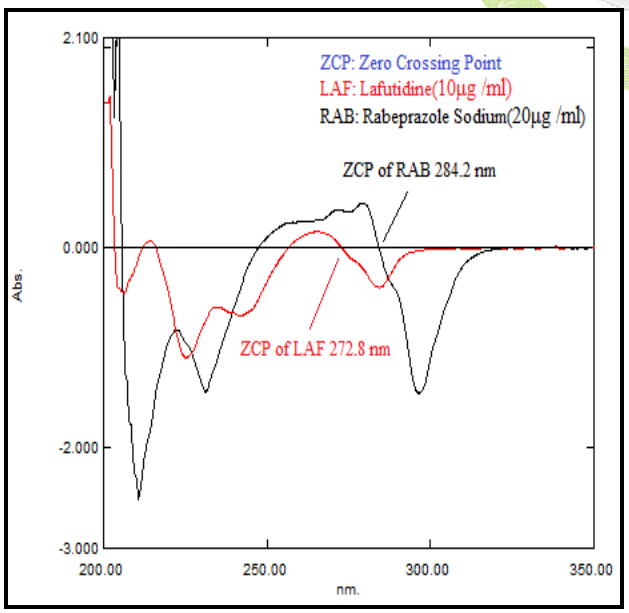

Figure 4: Overlain First order Derivative spectra of LAF (10µg/ml) and RAB (20µg /ml) in Methanol.

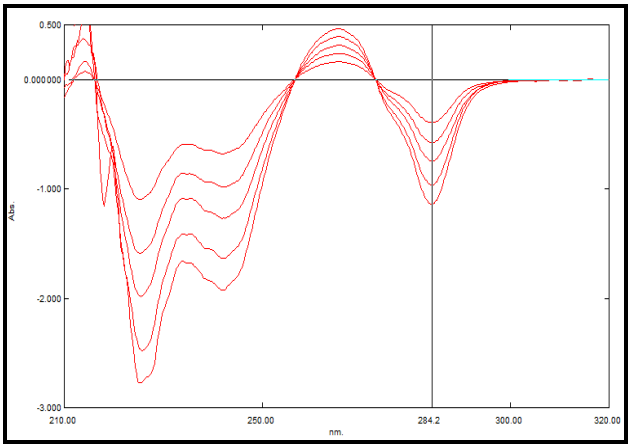

Figure 5: Overlain First order Derivative spectra of LAF (10-30µg/ml) at 284.2 nm (ZCP of RAB) in Methanol.

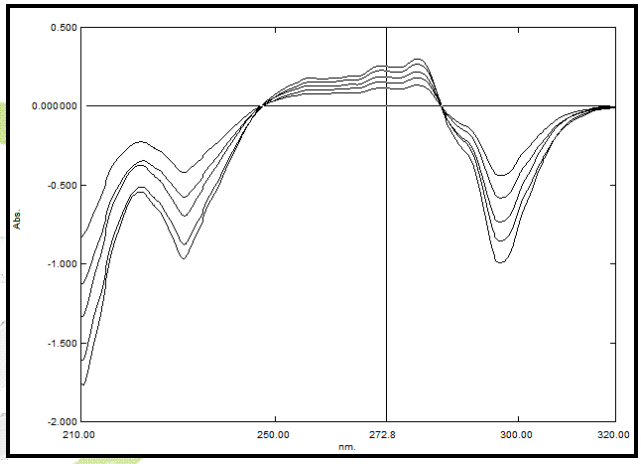

Figure 6: Overlain First order Derivative spectra of RAB (6-20µg/ml) at 272.8 nm (ZCP of LAF) in Methanol.

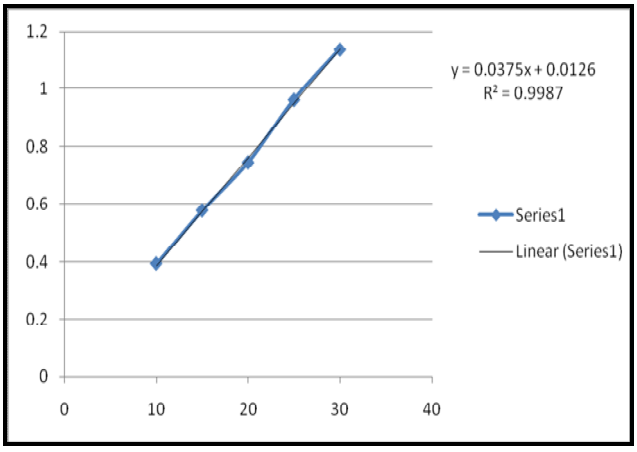

Figure 7: Calibration curve of standard LAF at 284.2nm by first order derivative spectrophotometry.

Table 1: Linearity Study

Sr No.	Concentration (µg/ml)	Absorbance at 284.2 nm	Concentration (µg/ml)	Absorbance at 272.8 nm
1	10	0.393	6	0.115
2	15	0.577	8	0.151
3	20	0.746	10	0.186
4	25	0.962	12	0.224
5	30	1.139	14	0.253

Table 2: Intra-Day Precision Study

LAF Concentration (µg/ml)	Absorbance* ± S.D.	%RSD	RAB Concentration (µg/ml)	Absorbance* ± S.D.	%RSD
15	0.5936 ± 0.001155	0.19	6	0.1016 ± 0.00058	0.56
30	1.17 ± 0.001732	0.15	12	0.212 ± 0.001	0.47
45	1.7286 ± 0.001732	0.10	18	0.3173 ± 0.00058	0.18

*****Average of Three determination

S.D. = Standard Deviation

RSD= Relative Standard Deviation

Table 3: Inter-Day Precision Study

LAF Concentration (µg/ml)	Absorbance* ± S.D.	%RSD	RAB Concentration (µg/ml)	Absorbance* ± S.D.	%RSD
15	0.5976 ± 0.002309	0.39	6	0.10366 ± 0.001528	1.47
30	1.180 ± 0.01044	0.88	12	0.21133 ± 0.002517	1.19
45	1.745 ± 0.01345	0.77	18	0.321 ± 0.003606	1.12

*****Average of Three determination

Table 4: Repeatability Study

LAF Concentration (µg/ml)	**Absorbance* ± S.D.**	**%RSD**	**RAB Concentration (µg/ml)**	**Absorbance* ± S.D.**	**%RSD**
15	0.59633 ± 0.003327	0.56	12	0.211833 ± 0.001329	0.63

*****Average of Six determination

Table 5: Recovery Study of Lafutidine

	Level of Recovery	**Amt. of Drug taken (µg/ml)**	**Amt. of Std. drug taken (spiked amt.) (µg/ml)**	**% Recovery* ± S.D.**	**%RSD**
Lafutidine	80%	10	11.2	103.2± 0.28	0.27
	100%	10	14.0	103.09± 0.42	0.40
	120%	10	16.8	101.09± 1.94	1.90

*Average of Three determination

Table 6: Recovery Study of Rabeprazole Sodium

	Level of Recovery	**Amt. of Drug taken(µg/ml)**	**Amt. of Std. drug taken (spiked amt.) (µg/ml)**	**% Recovery* ± S.D.**	**%RSD**
Rabeprazole Sodium	80%	10	6.4	100.49 ± 1.06	1.06
	100%	10	8.0	101.67 ± 1.44	1.41
	120%	10	9.6	99.67 ± 0.94	0.94

*Average of Three determination

Table 7: Results of simultaneous estimation of LAF and RAB in Marketed Formulation.

BRAND NAME:	**Drugs**	**Label Claim (mg)**	**Amount Found (mg)**	**% Label Claim***	**S.D.**	**%RSD**
LAFUMAC *PLUS*	LAF	10	10.37	103.74 %	1.06	1.02
	RAB	20	19.72	98.58 %	0.71	0.72

Table 8: Results of Validation Parameters

SR No.	PARAMETERS	LAFUTIDINE	RABEPRAZOLE SODIUM
1	Zero Crossing Point	272.8nm	284.2nm
2	Range	10-45 µg/ml	6-20 µg/ml
3	Linearity	R^2= 0.998	R^2= 0.998
4	Precision a)Intraday b)Interday c)Repeatability	%RSD 0.10-0.19 0.39-0.88 0.56	%RSD 0.18-0.56 1.12-1.47 0.63
5	Accuracy	%RSD 0.27-1.90	%RSD 0.94-1.41
6	Limit of detection (LOD)	0.297	0.258
7	Limit of Quantification (LOQ)	0.899	0.782
8	Assay	103.7%	98.6%

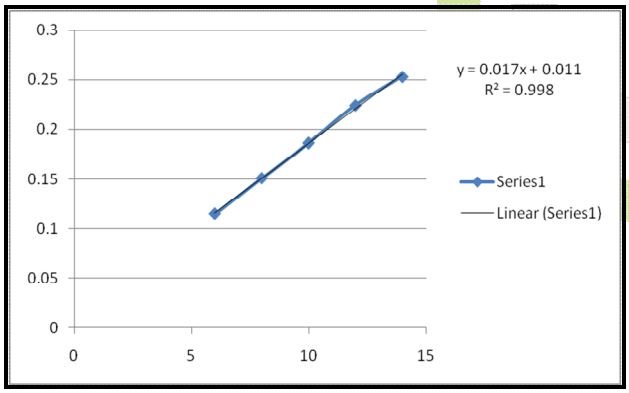

Figure 8: Calibration curve of standard RAB at 272.8 nm by first order derivative spectrophotometry.

CONCLUSION

The proposed method gives accurate and precise results for determination of LAF and RAB in marketed Capsule formulation and is easily applied for routine analysis. The method is simple, accurate, precise and rapid. The proposed method was successfully applied for the estimation of these drugs in commercial dosage form.

ACKNOWLEDGEMENT

The Authors are thankful to Cadila Pharmaceuticals Ltd and Alkem Laboratories Ltd for providing standard drug samples and also to Mr. Saurabh Lokhnde, Mr. Tushar Mahajan and Mr. Bhaumik Bhatt for their valuable support in this research work.

REFERENCES

1. Richardson P, Hawkey C and Stack W, “Proton pump inhibitors- pharmacology and rationale for use in gastrointestinal disorders”, Drugs, 1998, 56(3), 307-35.
2. The Merck Index - An encyclopedia of chemicals, drugs and biologicals, published by Merck Research Laboratories, 14th edition, Lafutidine, (5347), 926.
3. The International Conference on Harmonization-Guidelines Q2(R1), Validation of Analytical Procedures: Text and Methodology, 2005.

4. Sumithra M, Shanmuga P, Srinivasulu K, "Analytical Method Development and Validation of Lafutidine in Tablet dosage form by RP-HPLC", Int. J. ChemTech, 2011, 3, 1403-1407.

5. Shefali R, Jigar P, Sagar S, Dr. Mandev P, "Development and Validation of Spectrophotometric method for Simultaneous estimation of Lafutidine and Domperidone in combined dosage form by area under curve method", International Journal of Drug Development & Research, 2012, 257-262.

6. Ravishkumar R, Pinkal H, Chinmay D, Krupali S, Hardik N, "Development and Validation of UV Spectrophotometric method for estimation of Lafutidine in bulk and Pharmaceutical dosage form", International Journal of Drug Development & Research, 2012, 4, 325-329.

7. Mallikarjuna M, Somashekar S, Rajesh Kumar P, Shanta Kumar S, "Physico-chemical characterization, UV spectrophotometric analytical method development and validation studies of Rabeprazole Sodium", Journal of Chemical and Pharmaceutical Research, 2010, 2(3), 187-192.

8. Halder A, Mandal B, Sridevi R, Navalgund S, "Validated RP-HPLC method for rabeprazole and its stability studies", NSHM Journal of Pharmacy and Healthcare Management, 2011, 02, 76-82.

9. Padmalatha M, Snehalath T , Ramya S, Kanakadurga M, "A simple and validated RP-HPLC method for the simultaneous estimation of Rabeprazole and Levosulpiride in bulk and pharmaceutical dosage forms", International Research Journal of Pharmaceutical and Applied Sciences, 2012, 2(2), 99-106.

10. Wei-Dong C, Yan L, Hao Li, Ye Xiong, Xiao-Dong L, Guang-Ji W, Lin Xie, "Simple, sensitive and rapid LC–ESI–MS method for the quantitation of lafutidine in human plasma: Application to pharmacokinetic studies", Journal of Pharmaceutical and Biomedical, 2006, 41(1), 256-260.

11. Dewan B, Chimata R, "An open-label, randomized, crossover bioequivalence study of Lafutidine 10 mg under fasting condition", World J Gastrointest Pharmacol Ther, 2010, 1, 112-118.

12. Sun X, Tian Y, Zhang Z, Chen Y, "A single LC–tandem mass spectrometry method for the simultaneous determination of four H2 antagonists in human plasma", J Chromatogr B Analyt Technol Biomed Life Sci, 2009, 877, 3953-3959.

