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Development and validation of UV Spectroscopic method for simultaneous estimation of Lafutidine and Rabeprazole sodium in bulk and Pharmaceutical dosage form

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Abstract

A simple, rapid, accurate, precise, sensitive and economical UVspectrophotometric method has been developed for simultaneous estimation of Lafutidine and Rabeprazole sodium from bulk and pharmaceutical formulation. The λmax of Lafutidine and Rabeprazole sodium in Methanol was found to be 272.6nm and 283.8 nm respectively.The method is based Q-Absorption ratio method using two wavelengths, at 278.27nm(Isobestic point) and 283.8nm(λmax of Rabeprazole sodium). The parameters linearity, precision, accuracy, limit of detection and limit of quantitation, ruggedness were studied according to International Conference on Harmonization guidelines. The method follows linearity in the concentration range 5-30µg/ml and 10-60 µg/ml with correlation coefficient value R^2 0.9998 and 0.9998 for Lafutidine and Rabeprazole sodium, respectively. The proposed method was applied to pharmaceutical formulation and % amount of drug estimated 99.19 % was found in good agreement with the label claim. The accuracy of the method was checked by recovery experiment performed at three different levels i.e., 50%, 100% and 150 %. The % recovery was found to be in the range 99.09%– 100.18%. The low values of % R.S.D. are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intra-day, inter-day variations and repeatability. The % R.S.D. value less than 2 indicate that the method is precise. The above method was a cost-effective quality-control tool for routine analysis of Lafutidine and Rabeprazole sodium in bulk and in pharmaceutical dosage form.

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Key words:
Lafutidine, Rabeprazole sodium, Anti-ulcer, UV, Methanol.

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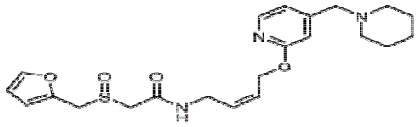
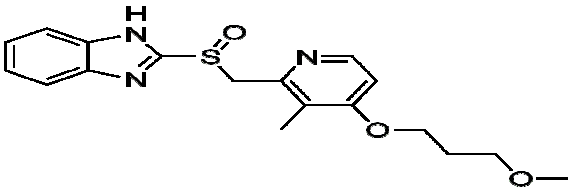
INTRODUCTION

Lafutidine is chemically 2-(furan-2-ylmethylsulfinyl)-N-[4-[4-(piperidin-1-ylmethyl)pyridin-2-yl]oxybut-2-ethayl]acetamide. Lafutidine is not official in any

pharmacopoeias. It is used as anti-ulcering agent as it is the new generation H2 receptor bloker. The structure of Lafutidine as below:



Rabeprazole sodium is 2-([4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]-1H benzimidazole sodium salt is an anti-ulcer drug in the class of proton pump inhibitors that reduce the production of acid by blocking the enzyme (hydrogen-potassium adenosine triphosphatase) in parietal cells and used to treat duodenal ulcers and erosive or ulcerative gastro esophageal reflux disease.The structure of Rabeprazole sodium as below:



The literature survey revealed that various methods of analysis for Lafutidine have been reported which include, LC-ESI-MS, HPLC-MS[6,7,8,9,10,11,12], Tandem MS.HPLC,LC-MS[13,14,15,16,17] and UV Spectroscopic method have been reported for Rabeprazole sodium.But no spectroscopic method have been reported for simultaneous estimation of Lafutidine and rabeprazole sodium in combined dosage form. In this report efforts are made to develop a simple, accurate, precise Q-Absorption ratio method to simultaneous determination of the Lafutidine and Rabeprazole sodium in combined dosage form.The following method was validated according to ICH norms.

Experiment

Chemical and Reagent:

Methanol was ued throughout UV Spectroscopic method development and validation.

Instrumentation:

UV-spectrophotometric method was performed on double beam UV-visible spectrophotometer (Shimadzu, model 1800) having two matched quartz cells with 1 cm light path.

Preparation of standard stock solution(100µg/ml):

Stock solutions were prepared by dissolving rabeprazole sodium and Lafutidine in Methanol as solvent to obtain a concentration of 1mg/1ml(1000ppm) for each compound. From this pipette out 10 ml of solution in another 100 ml volumetric flask and volume was made up with methanol to the mark to give final concentration of 100µg/ml.

Preparation of sample stock solution(100µg/ml):

To measure the Lafutidine and Rabepazole sodium content of tablet (label claim 10 mg Lafutidine and Rabeprazole sodium 20mg per tablet, Lafumac plus capsule by Macleods Pharmaceuticals), twenty capsules were weighed, the mean weight was determined. A weight of the powder equivalent to10 mg Lafutidine and 20mg of Rabeprazole sodium were transferred to a 100 ml volumetric flask containing 50 ml Mehtanol and the mixture was sonicated for 20 min then made up to 100 ml with Methanol gives concentration of 100µg/ml and 200 µg/ml ,respectively . The solution was filtered and filtered solution was diluted to get concentration in ratio 10:20 as lafutidine and Rabeprazole sodium used throughout experiment.

UV-Spectroscopic method:

Q-Absorption ratio method

This method is applicable to the drugs that obey Beer's law at all wavelengths and the ratio of absorbance at any two wavelengths is a constant value, independent of concentration and path length.

The solutions of 20µg/ml and 10µg/ml for Rabeprazole sodium and Lafutidine were scanned in the wavelength range of 400 to 200nm to obtain overlain spectra (fig.3). Two wavelengths, 278.27nm as iso absorptive point and 283.8nm (λ_{max} of

Rabeprazole sodium) were selected for the formation of Q-absorbance ratio equation. The calibration curves were determined in the concentration range of 5-30µg/ml and 10-60µgml for Rabeprazole sodium and Lafutidine respectively. The absorptivity coefficients of each drug at both the wavelengths were determined. The concentration of the individual components, Cx and Cy can be calculated by using the following equations.

$Cx = (Q_M-Q_Y/Q_X-Q_Y) \times (A_1/ax_1)$

$C_Y = (Q_M-Q_X/Q_Y-Q_X) \times (A_2/ay_1)$

Where A_1 and A_2 are absorbance of sample solution at iso-absorptive point 278.27nm and 283.8nm λ_{MAX} ofRabeprazole sodium respectively, ax_1 and ax_2 are the absorptivities of the Lafutidine at 278.27nm and 283.8nm respectively and ay_1 and ay_2 are the absorptivities of the Rabeprazole sodium at 278.27nm and 283.8nm respectively.

Validation of UV-spectrophotometric method:

Linearity ans Range

Six aliquots of each drug solutions were taken from standard stock solution and transferred to 10ml volumetric flask to get a final concentration of 5, 10, 15, 20, 25 and 30µg/ml of Lafutidine and 10, 20, 30, 40, 50 and 60µg/ml of rabeprazole sodium and the volume was completed with the distilled water and each flask content was measured to determine the absorbance at all the selected wavelength. For Q-Absorption ratio method the wave lengths selected were 278.27nm (iso absorptive point) and 283.8nm (λ_{max} of Rabeprazole sodium). The absorbance at these two wavelengths for all standard solutions of both Lafutidine and Rabeprazole sodium were measured and the calibration curves and linear regression equation of Lafutidine and Rabeprazole sodium at 278.27nm and 283.8nm were determined.

Precision

In intraday study concentration of two drugs were calculated on the same day at an interval of one hour. In inter day study the concentration of drug contents were calculated on three different days study expresses with in laboratory variation in different days. In both intra and inter-day precision study for the methods %RSD were calculated.

Accuracy

Accuracy of the developed method was confirmed by doing recovery study as per ICH norms at three different concentration levels 50%, 100%, 150% and the values were measured at all wavelengths for Lafutidine and Rabeprazole sodium. This operation was done in triplicate. From the recovery study it was clear that the method is very accurate for quantitative estimation of Lafutidine and Rabeprazole sodium in capsule dosage forms as the statistical results were within the acceptance range.

Limit of Detection and Limit of Quantification

The limit of detection and limit of quantification of Lafutidine and Rabeprazole sodium by proposed methods were determined using calibration standards.LOD and LOQ were calculated as 3.3σ/S and 10σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of response.

Results and discussions

Linearity and range

The linearity of Q- Absorption ratio method was found to be 5-30µg/ml with correlation coefficients of 0.9998 and0.999 at 278.27nm and 283.8nm respectively, the calibration data with %RSD for the method shown in (table-4) and calibration curves are shown in (figure 5, 6, 7, 8, 9 and 10).

Precision

The precision of the method was expressed in terms of % relative standard deviation (%RSD). The %RSD values found to be less than 2 for intra-day and inter-day precision, which indicate that the proposed

method is precise for analysis. The result is expressed in Table 1 and Table 2.

Accuracy

Accuracy of the methods was confirmed by doing recovery studies from marketed formulation at three concentration levels of standard addition. The %recoveries found for Q-Absorption ratio method was found to be 99.09-100.18 and 99.57-99.82 for Lafutidine and Rabeprazole sodium, respectively as shown in table 3.

Limit of Detection and Limit of Quantification

For Q-Absorption ratio method the limit of detection found to be 0.3991 at (278.27nm),0.3694 at (283.8nm) and 1.113at(278.27nm), 1.145 at(283.8nm) for Lafutidine and Rabeprazole sodium, respectively, the limit of quantification found to be 1.2095 at (278.27nm) and 1.1194 at (283.8nm), 2.412 at (278.27nm) and 2.172 at (283.8nm) for both Lafutidine and Rabeprazole sodium as shown in table 9.

Analysis of marketed preparation (Lafumac Plus®) by UV Spectroscopic method

The percentage of Lafutidine and Rabeprazole sodium in the estimated formulation was found to be 98.70% and99.55% as shown in table 5.

CONCLUSION

The present work describes a new, simple,cost effective, accurate, precise method.It is concluded that the described methods have the potential for the application in the quality control laboratory.

Fig. 1: Absorption maxima of Lafutidine

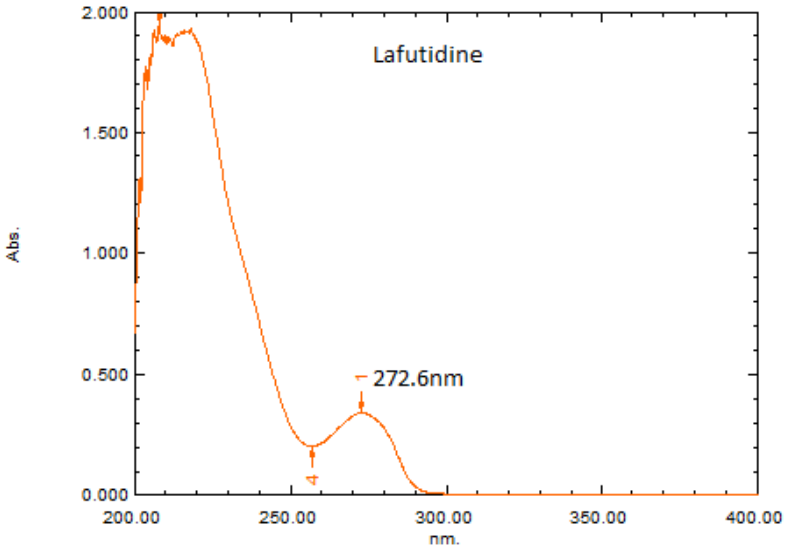


Fig 2: Absorption maxima of Rabeprazole sodium

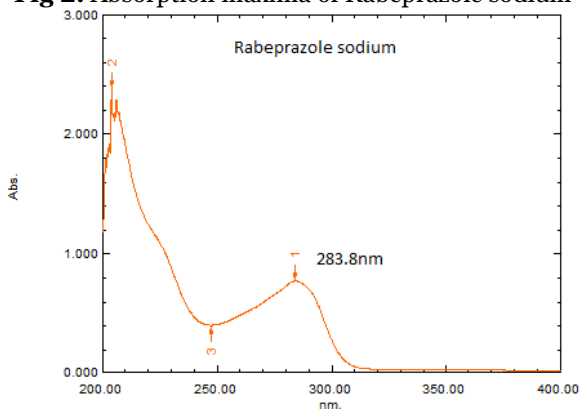


Fig 3: Overlay spectra of Lafutidine and Rabeprazole sodium

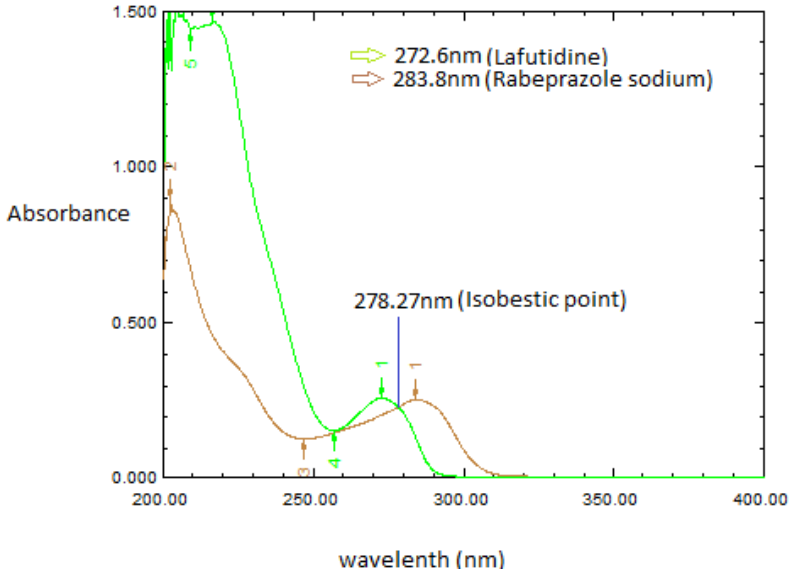


Fig 4: Linearity curve of sample

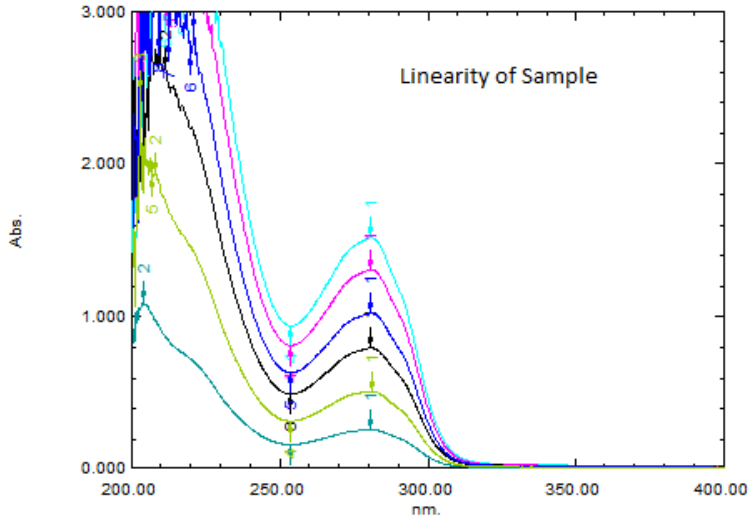


Fig. 5: Calibration Curve and linear regression equation for Lafutidine

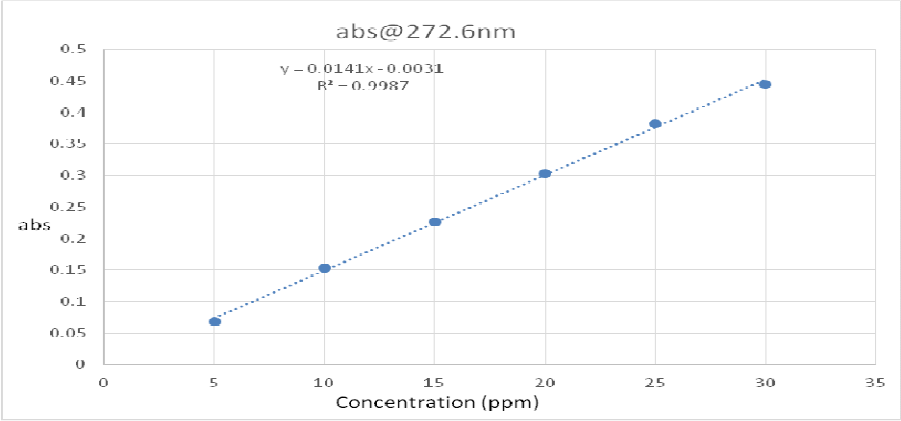


Fig 5: Calibration Curve and linear regression equation for Lafutidine

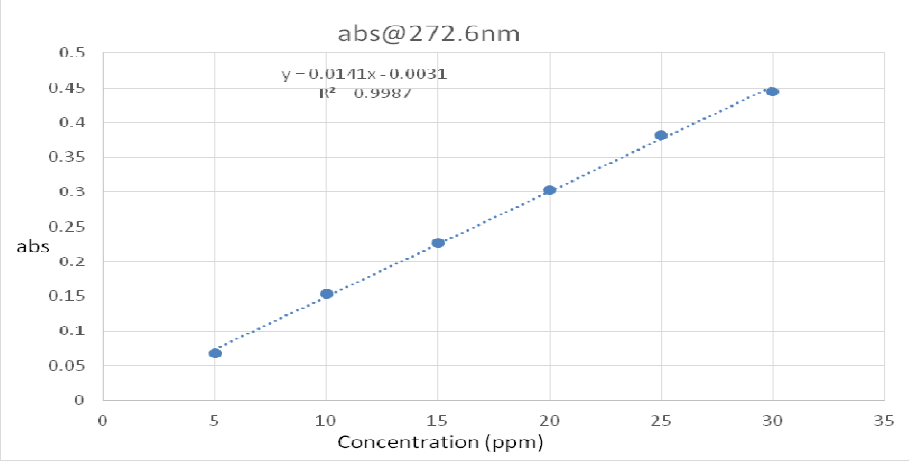
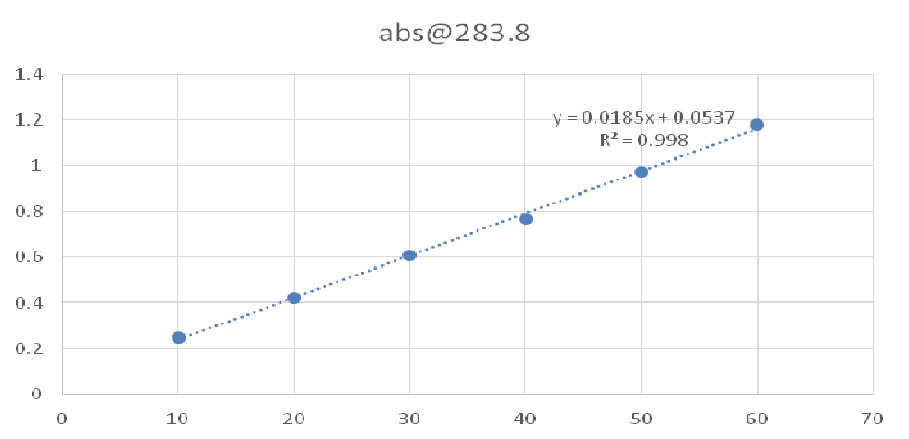


Fig 6: Calibration Curve and linear regression equation for Rabeprazole sodium



Calibration curve for Q-Absorption ratio method:

Fig 7: Calibration curve for Lafutidine at 278.27nm (Iso-absorptive point)

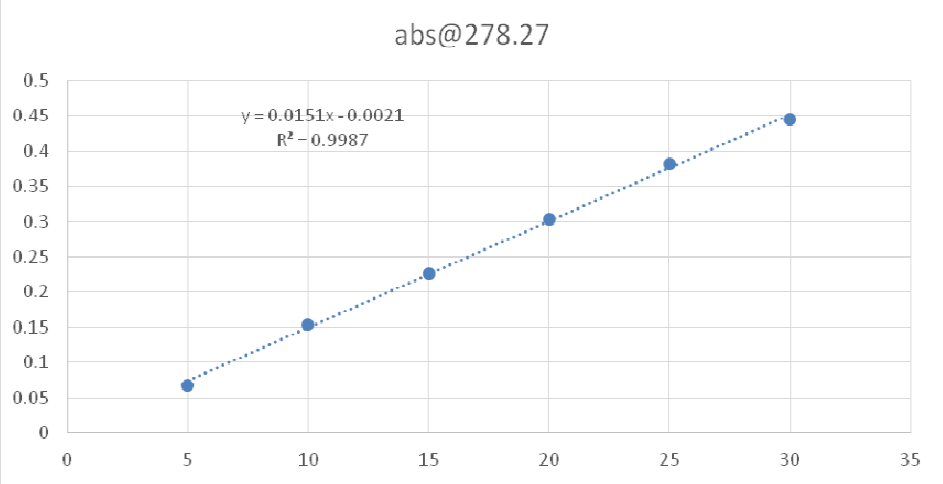


Fig 8: Calibration curve for Lafutidine at 283.8nm (λmax of Rabeprazole sodium)

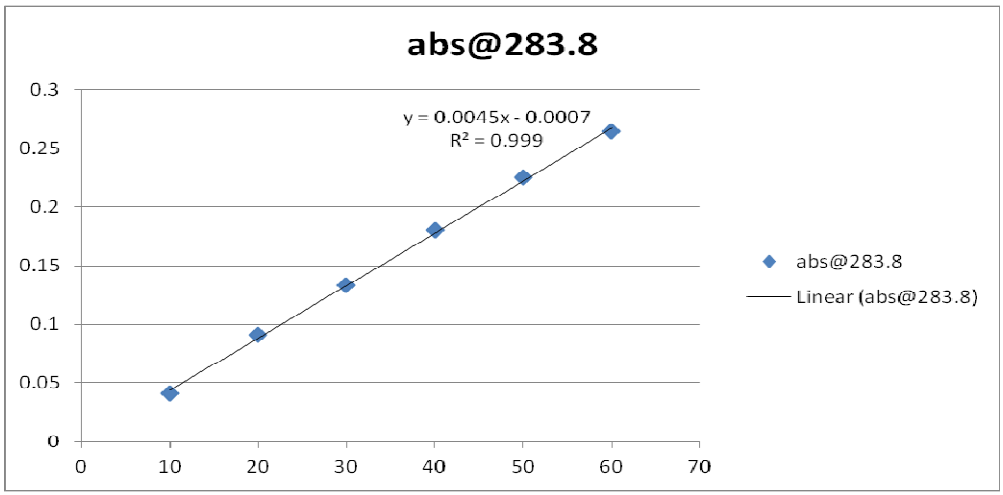


Fig 9: Calibration curve for Rabeprazole sodiumm at 278.27nm (Iso-absorptive point)

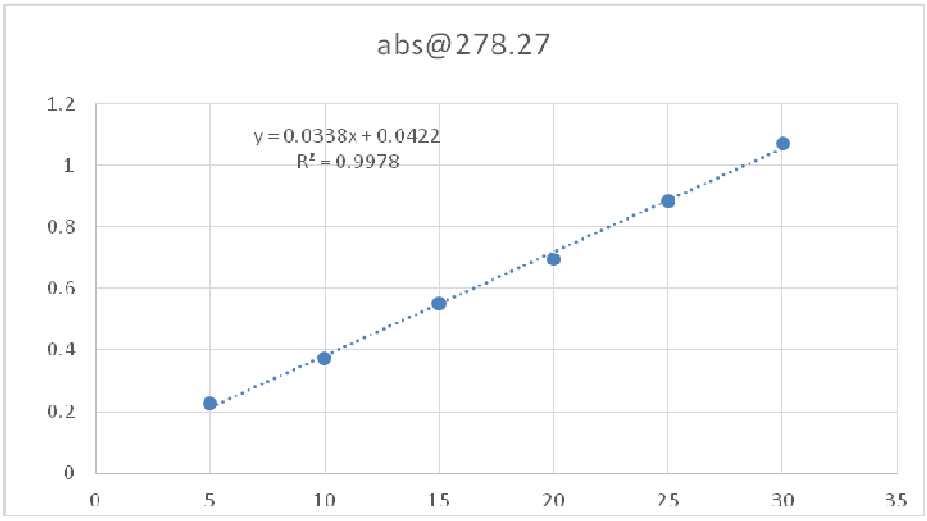
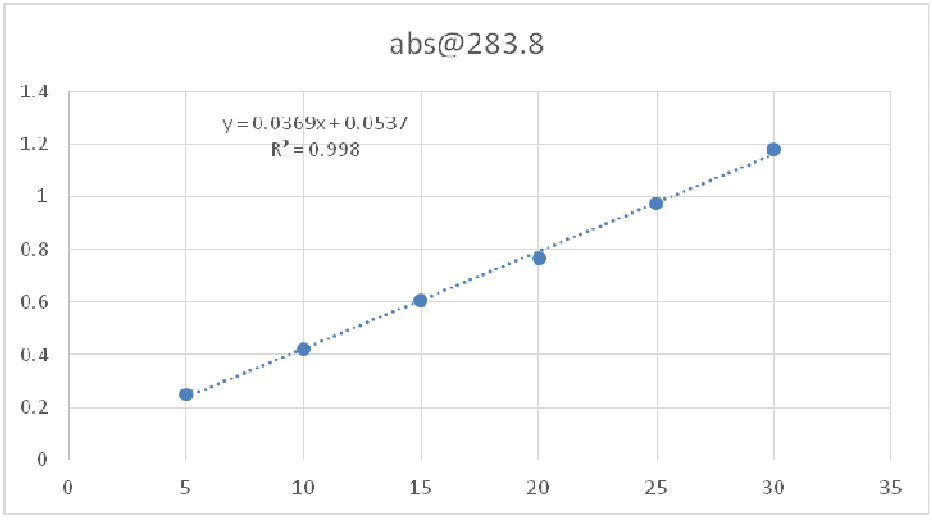


Fig 10: Calibration curve for Rabeprazole sodium at 283.8nm (λmax of Rabeprazole sodium)



Precision:

Table 1: Intraday study

Sr. No.	Concentration(µg/ml)	Absorbnce*±Mean SD (n=3)		%RSD	
		@278.27 nm	@283.8nm	@278.27nm	@283.8nm
1	5	0.1355±0.01296	0.1446±0.0081	0.7808	0.2396
2	20	0.548±0.02049	0.578±0.0466	0.3058	0.3492
3	30	0.820±0.01311	0.869±0.0132	0.1301	0.131

Table 2: Interday study

Sr. No.	Concentration(µg/ml)	Absorbnce*±Mean SD (n=3)		%RSD	
		@278.27nm	@283.8nm	@278.27nm	@283.8nm
1	5	0.131±0.0173	0.139±0.0264	1.0561	0.8090
2	20	0.54±0.1021	0.57±0.1489	1.5414	1.1236
3	30	0.81±0.1814	0.849±0.2605	1.8424	1.9908

Table 3: % Recovery (Accuracy) of developed method

Preanalysed sample solution(ppm)	Spiking concent-ration (ppm)	Amount recovered(ppm)* (n=3)		%Recovery		%RSD	
		at 278.27nm	at 283.8nm	at 278.27nm	At 283.8nm	at 278.27nm	at 283.8nm
20	10	0.8207	0.8682	99.27	99.21	0.94	1.02
20	20	1.0966	1.1616	99.09	99.57	0.74	0.78
20	30	1.3740	1.4473	100.18	99.80	0.85	0.89

Table 4: Data showing linearity of developed method,LOD and LOQ

Parameter	Lafutidine	Rabeprazole sodium
λmax	272.6nm	283.8nm 278.27nm(Iso-absorptive point)
Beer's-law limit (ppm)	5-30 ppm	10-60 ppm
Correlation coefficient	0.9987(at 278.27nm) 0.999(at 283.8nm)	0.998(at 278.27nm) 0.998(at 283.8nm)
Slope	0.0076(at 278.27nm) 0.0226(at 283.8nm)	0.0338(at 278.27nm) 0.0185(at 283.8nm)
LOD	0.3991 1.1131	0.3694 1.1450
LOQ	1.0295 2.4120	1.1194 2.1720

Table 5: Results of analysis of capsule dosage forms containing Lafutidine and Rabeprazole sodium

Q-Absorption ratio method	Lafutidine	Rabeprazole sodium
Lable claim	10mg	20mg
Estimated content	9.87	19.91
%Assay	98.7	99.55
SD	0.029	0.021
%RSD	1.26	1.85

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