Spectrophotometric simultaneous determination of lafutidine and domperidone in combined tablet dosage form by absorbance corrected method and first order derivative method

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ABSTRACT

Two simple, economical, precise and accurate methods are described for the simultaneous determination of Lafutidine (LAFU) and Domperidone (DOM) in combined tablet dosage form. The first method (Method A) is Absorption Corrected Method and second method (Method B) is First Order Derivative Spectrophotometry.The amplitudes at 258.0 nm and 299.85 nm in the Absorption Corrected Method and 301.87 nm and 276.18 nm in the first order derivative Spectrophotometry were selected to determine Lafutidine (LAFU) and Domperidone (DOM), respectively in combined formulation. Beer's law is obeyed in the concentration range of 2-10μg/ml for Lafutidine (LAFU) and 6-30 μg/ml for Domperidone (DOM) for both methods. The methods were validated by following the analytical performance parameters suggested by the International Conference on Harmonization (ICH).[20] All validation parameters were within the acceptable range. The % assay in commercial formulation was found to be in the range 99.12-100.2 % for Lafutidine (LAFU) and 98.52-99.25 % for Domperidone (DOM) by the proposed methods. The methods were validated with respect to linearity, precision and accuracy. Recovery was found in the range of 98.12-100.24% for Lafutidine (LAFU) and 99.53-100.34% for Domperidone (DOM) by absorbance corrected method and 98.32-99.24% for Lafutidine (LAFU) and 99.10-100.02% for Domperidone (DOM) by First Order Derivative. The methods developed are simple, economical, precise and accurate and can be used for routine quality control of analytes in combined tablets.

Key Words: Absorbance corrected, Derivative Spectrophotometry, Domperidone, Lafutidine.

INTRODUCTION

Lafutidine, a novel histamine H_2-receptor antagonis,exhibits gastro-protective action. Lafutidine, is chemically known as 2-[(2-furylmethyl) sulfinyl]-*N*-((2*Z*)-4-{[4-(piperidin-1-ylmethyl)pyridin-2-yl]oxy}but-2-en-1-yl)acetamide. Lafutidine, is known to exhibit potent protective activity in the gastrointestinal mucosa, in addition to gastric Anti-ulcer,anti-secretory action. Domperidone is a peripheral dopamine antagonist structurally related to the butyrophenones with antiemetic and gastroprokinetic properties. Domperidone effectively increases esophageal peristalsis and lower esophageal sphincter pressure (LESP). Domperidone is chemically known as 5-Chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)propyl]-4-piperidyl]-1,3-dihydro-2H-benzimidazol-2-one. Few analytical techniques such as spectrophotometry [1-6], HPLC [7-12], HPTLC[13], have been reported for DOM as single drug formulation in combination with other drugs. One HPLC Method [14],is available for LAFU for its estimation as single drug.Derivative Spectra and Absorbance Corrected Method, these methods are suitable for these drug. The method was validated for linearity, accuracy, precision, sensitivity, robustness, etc. in accordance with International Conference on Harmonization (ICH) guidelines.
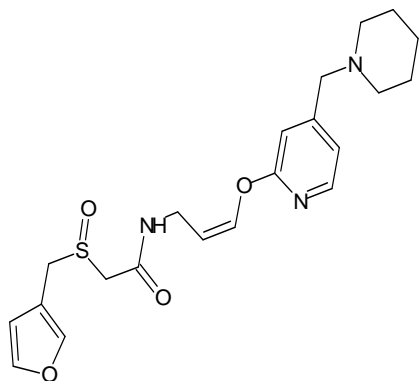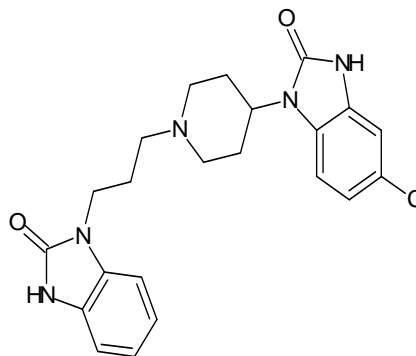
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FIG 1: Structure of Lafutidine

FIG 2: Structure of Domperidone

MATERIALS AND METHODS

Instrumentation
A double beam UV-Visible spectrophotometer (Varian Cary 100) with 10mm matched quartz cells was used.Electronic balance (Model Shimadzu AUW-220D) was used for weighing.

Reagents and chemicals
Pure drug sample of LAFU, % purity 99.60 and , DOM % purity 100.2 was kindly supplied as a gift sample by Emcure Pharmaceutical Pvt.Ltd. Pune, India.These samples were used without further purification. Tablet used for analysis was Lafaxid-D manufactured by Emcure Pharmaceutical Pvt. Ltd. Pune.containing LAFU 10 mg and DOM 30 mg per tablet.

Preparation of Standard Stock Solutions and Calibration Curve
Standard stock solutions of pure drug containing 1000 μg/mL of LAFU and DOM were prepared separately in methanol. Standard stock solutions were further diluted with methanol to get working standard solutions of analytes in the concentration range of 2-10 μg/mL and 6-30μg/mL of Lafutidine (LAFU) and Domperidone (DOM), respectively and scanned in the range of 200-400nm. First derivative amplitudes of spectrum, by using the above mentioned procedures, were used to prepare calibration curves for both the drugs. Beer's law obeyed in the concentration range of 2-10 μg/ml for LAFU and 6-30 μg/ml for DOM by both the methods.

Preparation of Sample Solution and Formulation Analysis
Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 10 mg of LAFU(DOM 30mg) was weighed and dissolved in the 30 mL of methanol with the aid of ultrasonication for 10 min and solution was filtered through Whatman paper No. 41 into a 100mL volumetric flask,volume was made up to the mark with methanol. The solution was suitably diluted with methanol to get 10μg/mL LAFU and 30 μg/mL of DOM. Percent labeled claim and standard deviation (S.D) was calculated and the results are presented in Table 1.

Recovery studies
The accuracy of the proposed methods were checked by recovery studies, by addition of standard drug solution to preanalysed sample solution at three different concentration levels (50 %, 100 % and 150 %) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 10 μg/ml of LAFU and 30μg/ml of DOM for both the methods.

Precision of the Method
Method repeatability was determined by six times repetitions of assay procedure. For intra-day precision method was repeated 5 times in a day and the average % RSD was determined.Similarly the method was repeated on five different days for inter-day precision and average %RSD was determined (Table 1). Precision of analyst was determined by repeating study by another analyst working in the laboratory.

Specificity
Specificity is a procedure to detect quantitatively the analyte in the presence of component that may be expected to be present in the sample matrix. Commonly used excipients in tablet preparation were spiked in a pre-weighed quantity of drugs and then absorbance was measured and calculations done to determine the quantity of the drugs.

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Robustness:
The robustness of the proposed methods was tested by changing parameters such as wavelength range and slit width etc. None of these variables significantly affected the absorbance of the drugs indicating that the proposed methods could be considered as robust.

Limit of Quantification (LOQ) and Limit of Detection (LOD)
The LOD and LOQ of lafutidine and domperidone by proposed methods were determined using calibration standards. LOD and LOQ were calculated as $3.3a\sigma/S$ and $10\sigma/S$ respectively, where S is the slope of the calibration curve and σ is the standard deviation of response. The results of the same are shown in Table 1.
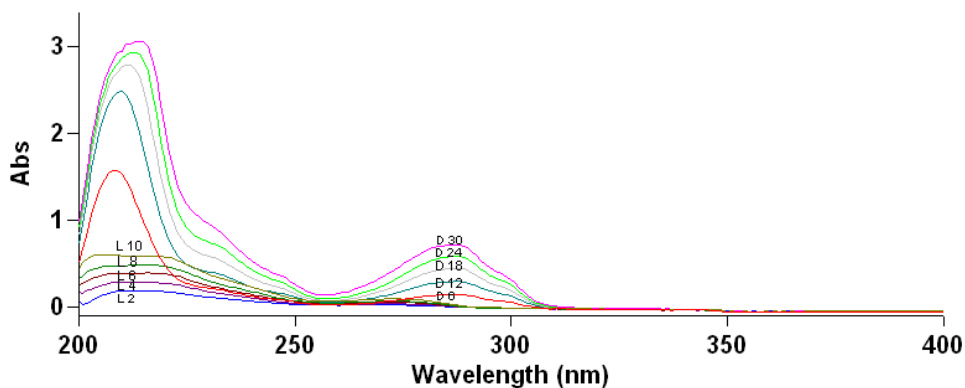
RESULTS AND DISCUSSION

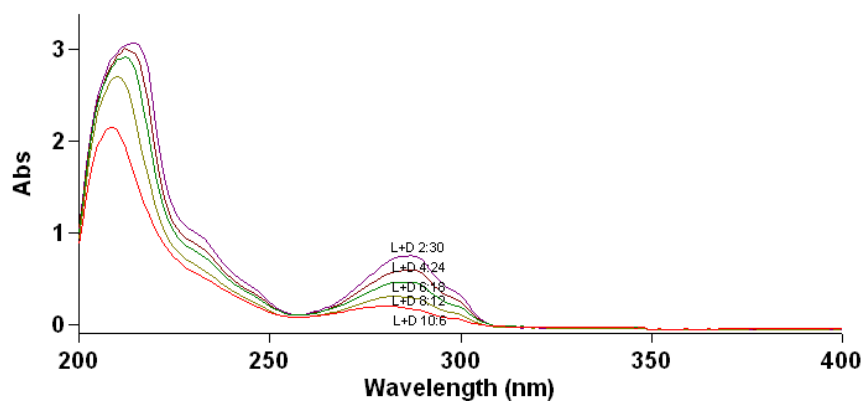**Fig 3:Simple Overlay Spectra Of Lafutidine and Domperidone(Absorbance corrected)**

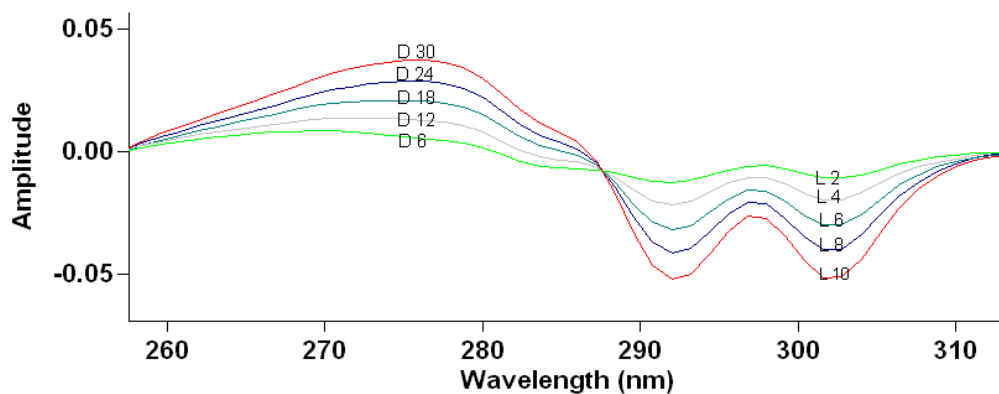**Fig 4:Simple Overlay Derivative spectra of LAFU+DOM**

Fig 5: Derivative spectra of LAFU+DOM

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Method A: Absorption Corrected Method

λ max of LAFU and DOM was determined by scanning the drug solution in UV Spectrophotometer in the range 200 - 400 nm at 0.5 band width and 600 nm/min scan speed and was found to be at 258.02 nm and 299.85 nm respectively.To construct Beer's plot for LAFU and DOM, stock solutions of 1000 µg/ml of both the drugs were prepared in methanol and working standard dilutions were made in methanol using stock solution of 1000 µg/ml. Also Beer's plot was constructed   for LAFU and DOM   in solution mixture at different concentration levels. Both the drugs followed linearity individually and in mixture within the concentration range 2-10 µg/ml and 6-30 µg/ml for LAFU and DOM, respectively.

Method B: Derivative Method

The method involves obtaining the first derivative spectra of the series of the solution of mixtures of LAFU + DOM in ascending and descending concentration. From the observations of the derivative spectrum, derivative amplitudes responsible for LAFU and DOM were selected and wavelength for each amplitude was noted. These wavelengths were further confirmed by checking the first order derivative amplitude of the mixed standard solutions of these drugs in the given ratio. Mixed standard solutions were prepared in the range of 2-10 µg/ml and 6-30 µg/ml for LAFU& DOM respectively were used for the study. Wavelengths 301.87 nm and 276.18 nm were selected for the quantification of LAFU in LAFU + DOM mixture and DOM in LAFU + DOM mixture, respectively . Under experimental conditions described, calibration curve, assay of tablets and recovery studies were performed. A critical evaluation of proposed method was performed by statistical analysis of data where slope, intercept, correlation coefficient is shown in Table 1. As per the ICH guidelines, the method validation parameters checked. Beer's law is Obeyed in the concentration range of 2-10 µg/ml for LAFU and 6-30 µg/ml for DOM by method A & B, with correlation coefficient > 0.999 for both the drugs. The proposed methods were also evaluated by the assay of commercially available tablet containing LAFU and DOM. The results of formulation analysis are presented in Table 1. For LAFU, the recovery study results ranged from 99.12 to 100.2% with % RSD values ranging from 0.98 to 0.56 % for proposed the methods. For DOM, the recovery results ranged from 98.52 to 99.25 %, with % RSD values ranging from 0.65 to 0.79% for proposed the methods. Results of recovery studies are shown in Table 2. The accuracy and reproducibility is evident from the data as results are close to 100 % and standard deviation is low.

Table 1: Optical characteristics of the proposed methods and result of formulation analysis

Parameter		Lafutidine		Domperidone	
		Method A	**Method B**	**Method A**	**Method B**
wavelength (nm)		258.02	301.87	299.85	276.18
Beer's law limit (µg/mL)		2-10	2-10	6-30	6-30
Regression Equation*	**Slope (m)**	0.00533	0.00516	0.0109213	0.001351
	Intercept (c)	0.009365	-0.0066	-0.011012	-0.00379
Correlation coefficient (r)		0.996	0.999	0.999	0.999
Precision (%RSD)	**Repeatability (n=5)**	0.75	0.96	1.12	0.64
	Intra-day(3x5 9)))times0)0))	0.52	0.82	0.68	0.98
	Inter-day(3x5 days)	0.92	1.20	0.59	1.24
Formulation Analysis (% Assay, %RSD), n=6		99.12, 0.56	100.2,0.98	98.52, 0.65	99.25, 0.79
LOD	**(µg/mL)**	0.5234	0.6735	0.7489	1.0258
LOQ	**(µg/mL)**	2.1215	1.962	3.0253	2.2475
Ruggedness (%RSD)	**Analyst I**	1.08	0.95	0.55	0.64
	Analyst II	0.87	1.14	0.47	0.83

RSD = Relative Standard Deviation, Y = mX + c, where Y is the absorbance and X the concentration (µg/mL)*

Table 2: Accuracy result for LAFU & DOM

Recovery Level	Analyte name	Amount Spiked (µg/mL)	% Mean Recovery, % RSD, n=6	
			Method A	**Method B**
50%	LAFU	10	98.12, 0.65	98.32, 0.84
	DOM	37	99.53, 0.76	99.10, 0.45
100%	LAFU	20	99.50, 1.02	98.70, 0.56
	DOM	76	98.14, 0.79	99.42, 0.89
150%	LAFU	30	100.24,1.21	99.24, 0.98
	DOM	112	100.34,1.08	100.02,0.94

CONCLUSION

The validated spectrophotometric methods employed here proved to be simple, economical, precise and accurate. Thus it can be used as IPQC test and for routine simultaneous determination of LAFU and DOM in tablet dosage form.

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