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Research Article

Simultaneous Estimation of Lafutidine and Domperidone by Ultraviolet Spectroscopy

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A simple, accurate, and precise method for simultaneous estimation of Lafutidine and Domperidone in combined-dosage form have been described. The method employs formation and solving of simultaneous equations using 279 and 284 nm as two analytical wavelengths. This method allows the simultaneous determination of Lafutidine and Domperidone in concentration ranges employed for this purpose with the standard deviation of <1.0% in the assay of tablet.

1. Introduction

Lafutidine (LAF) is (furan-2-ylmethylsulphinyl)-N-[(Z)-4-[4-(piperidinyl-methyl)-pyridin-2-yl) oxybut 2-enyl] acetamide (Figure 1) [1]. It is freely soluble in methanol, whereas it is practically insoluble in water. It is a second generation histamine H_2-receptor antagonist used as an antiulcerative agent [2]. Domperidone (DOP) is chemically 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl) propyl]-piperidin-4-yl]-1,3-dihydro-2*H*-benzimidazol-2-one (Figure 2) used as an antiemetic drug [3, 4]. A combination of these drugs, DOP (10 mg) and LAF (10 mg) is available as tablets for clinical practice. This unique combination has comprehensive acid control and prokinetic action which ensures better control and relief from reflux, gastric ulcers, and associated gastrointestinal (GIT) disorders. Many methods like HPLC[4,5], HPTLC[7], and LCMS[9] [5–9] have been described in the literature for the determination of DOP and LAF individually or in combination with others. However, there is no spectroscopic method reported for the simultaneous determination of these drugs either as active pharmaceutical ingredient or from dosage forms. The present work describes a simple, precise, and accurate simultaneous ultraviolet spectrophotometric method for simultaneous estimation of LAF and DOP in combined dosage forms.

2. Experimental

2.1. Materials and Methods. UV/Vis double beam spectrophotometer, model-Shimadzu UV 1800 PC with 1 cm quartz cells was used. Standard bulk drug samples of LAF (99.45% pure) and DOP (99.67% pure) were provided as gift samples by Ajanta Pharmaceuticals Ltd, Mumbai, India and Cipla Ltd., Mumbai, India, respectively. The pharmaceutical dosage form used in this study was Lafaxid D tablets with a declared content of 10 mg LAF and 10 mg DOP USP per tablet (Zuventis healthcare Ltd., Mumbai).

2.2. Preparation of Solutions. LAF and DOP standard stock solution (0.5 mg/mL) was prepared by transferring accurately weighed 50 mg portion of each drug in 100 mL volumetric flask, dissolved in 50 mL of methanol and volume was made up with distilled water to give concentration of 500 μg/mL.

2.3. Methodology. Selection of analytical wavelengths was done by taking pure samples of LAF and DOP which were separately dissolved in methanol to give two solutions of 25 and 50 μg/mL, respectively. They were scanned in the wavelength range of 200–400 nm. From the overlain spectra (Figure 3), wavelengths 279 and 284 nm were selected for

Table 1: Determination of precision.

Sample number	Assay of lafutidine and domperidone as % of labeled amount			
	Analyst I (Intra-day precision)		Analyst II (Inter-day precision)	
	LAF	DOP	LAF	DOP
(1)	99.72	99.28	99.77	99.65
(2)	99.93	99.52	99.97	99.86
(3)	99.78	99.02	99.71	99.29
(4)	99.90	99.35	99.88	99.22
(5)	99.48	99.65	99.51	99.49
(6)	99.20	99.31	99.25	99.75
Mean	99.67	99.35	99.68	99.54
SD	0.28	0.26	0.24	0.24

Table 2: Determination of accuracy by percentage recovery method.

Ingredient	*Tablet amount (μg/mL)	Level of addition (%)	*Amount added (μg/mL)	*Total amount taken from tablet (μg/mL)	Amount recovered (μg/mL)	% Recovery	Average % Recovery
Lafutidine	10.00	80	8.4	18.4	18.34	99.67	100.1 ± 0.07611
	10.00	100	10.2	20.20	20.13	99.65	
	10.00	120	12.23	22.23	22.45	100.98	
Domperidone	10.00	80	8.3	18.3	18.26	99.78	99.18
	10.00	100	10.4	20.4	20	99.10	
	10.00	120	12.6	22.6	22.1	98.67	

*Amount equivalent to pure drug.

the formation of simultaneous equations. For constructing a calibration curves, two series of different concentrations in range of 10–150 μg/mL for LAF and 5–40 μg/mL for DOP were prepared from stock solutions. The calibration curves were plotted at 279 and 284 nm. The absorptivities (A1%, 1 cm) of both the drugs at both the wavelengths were determined. These calculated values were the mean of five independent determinations. The absorbance and absorptivities values at the particular wavelengths were calculated and substituted in the Cramer's rule to obtain the concentrations:

$$Cx = \frac{A_2 ay_1 - A_1 ay_2}{ax_2 \cdot ay_1 - ax_1 \cdot ay_2},$$
$$Cy = \frac{A_1 ax_2 - A_2 ax_1}{ax_2 \cdot ay_1 - ax_1 \cdot ay_2}. \quad (1)$$

Cx and Cy are concentration of LAF hydrochloride and DOP, respectively, (in gram/100 mL) in sample solution. The validity of formed equations was checked by preparing five mixed standards, measuring their absorbances at respective wavelengths and comparing these with the absorbances calculated using above formed equations.

2.4. Estimation from Tablets. The pharmaceutical dosage form used in this study was Lafaxid D tablets with a declared content of 10 mg LAF and 10 mg DOP USP per tablet (Zuventis healthcare Ltd, Mumbai).

Twenty tablets of brand Lafaxid D tablets were weighed and finely powdered. Accurately weighed tablet powder equivalent to 10 mg was taken in 100 mL volumetric flask. 20 mL of methanol was added and sonicated for 5 min. The volume was made to mark with distilled water. Aliquot

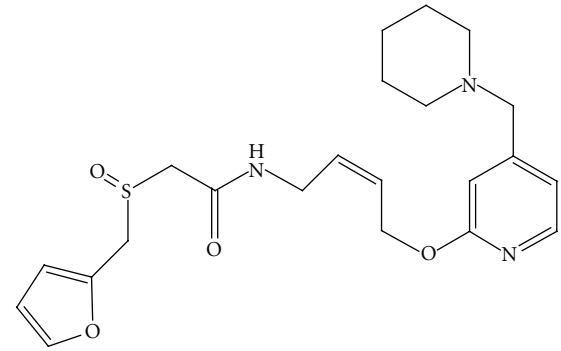

Figure 1: Structure of lafutidine.

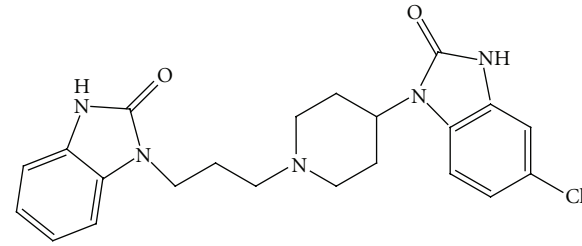

Figure 2: Structure of domperidone.

Table 3: Summary of validation parameters.

Sr. no.	Parameter	LAF	DOP
(1)	Absorption maxima (nm)	279	284
(2)	Linearity range (μg/mL)	10–100	5–40
(3)	Standard regression equation	$y = 0.818x + 0.208$	$y = 1.552x - 0.036$
(4)	Correlation coefficient (r^2)	0. 999	0.997
(5)	Molar absorptivity	2608	11480
(6)	A (1%, 1 cm)	$\lambda_1 = 60.52$ $\lambda_2 = 56.08$	$\lambda_1 = 279$ $\lambda_2 = 304$
(7)	Accuracy (% recovery ± SD)	99.18	
(8)	Precision (% CV)	0.5684	
(9)	Limit of quantitation (μg/mL)	2.08	0.479
(10)	Limit of detection (μg/mL)	6.11	1.45

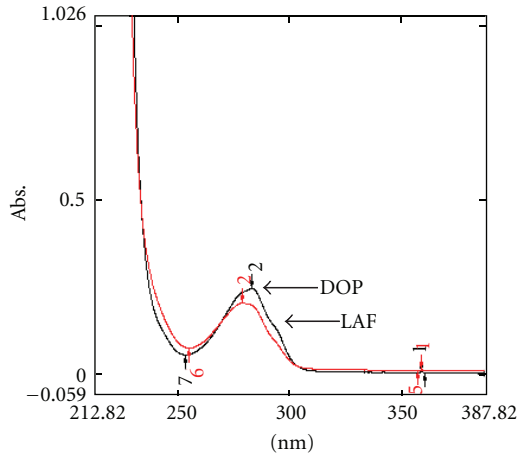

Figure 3: Overlain spectra of LAF and DOP (400–200 nm).

portion of this solution was further diluted to achieve final concentration of 25 μg/mL for LAF and DOP. The absorbances were noted at respective wavelengths. The concentration of each drug in tablet formulation was determined using above methods.

3. Result and Discussion

The overlain spectra of LAF and DOP in the concentration ratio of 1 : 1 showed that the peaks are resolved, thus satisfactory criteria for obtaining maximum precision based on absorbance ratios. The criteria being the ratios (A_2A_1/aX_2aX_1) for drug Y and (aY_2aY_1/A_1A_2) for drug X should lie outside the range of 0.1–2.0 where A_1 and A_2 represent absorbance of tablet solution at λ_1 and λ_2, aX_1 and aX_2 represent absorptivities of X at λ_1 and λ_2, and aY_1 and aY_2 denote absorptivities of Y at λ_1 and λ_2, respectively. In the present contest, the above criteria was found to be satisfing for LAF (X) and DOP (Y) where λ_1 is 279 nm and λ_2 is 284 nm. In overlain spectra, LAF shows two distinct peaks, one at around 230 and the other at 279 nm. The peak at 279 nm was found to be prominent hence for simultaneous equations method; the peak was used for determination of LAF. Since only one prominent peak exists for DOP at 284 nm, the same was used for its determination. Absorbance was determined at the both wavelengths.

Calibration curves were plotted and regression analysis was carried out. The linearity range of LAF was found to be 10–100 μg/mL and for DOP 5–40 μg/mL. The absorpitivity was then calculated and substituted in (1) along with absorbance values to obtain concentration of drugs.

3.1. Validation. LOD and LOQ were calculated, in accordance with ICH guidelines, as $3.3r/S$ and $10r/S$, respectively, where r is the standard deviation of the response (y-intercept) and S is the slope of the calibration plot. To study intraday variation, six mixed standard solutions containing LAF (50 μg/mL) and DOP (50 μg/mL) were prepared and absorbance was taken. All the solutions were analyzed on the same day to record any intraday variation in the results. To study interday variation, analysis of three mixed standard solutions of the same concentration was performed on different days (Table 1).

3.2. Recovery Studies. To check the accuracy of the method, recovery was measured by addition of standard drug solution at three different levels (80, 100, and 120%) to preanalyzed sample solution (Table 2).

By observing the validation parameters (Table 3), the method was found to be specific, accurate, precise, repeatable, and reproducible. Hence, this method can be employed for routine analysis of tablet for assay as well as dissolution testing.

4. Conclusion

Simple, new, simultaneous UV spectroscopic method was developed and validated. The proposed method is accurate, precise, reproducible, and economical and can be successfully used for routine analysis of simultaneous estimation of lafutidine and domperidone.

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