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Research Article

SIMULTANEOUS SPECTROPHOTOMETERIC ESTIMATION OF LAFUTIDINE AND DOMPERIDONE IN SOLID DOSAGE FORMS

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ABSTRACT

The research work intended to develop an accurate, simple, precise, sensitive and economical method for the estimation of Lafutidine (LF) and Domperidone (DP) in tablet dosage form by UV spectrophotometric method. UV spectrophotometric method includes simultaneous equations method (Method I) and Absorbance ratio method (Method II). For development of Method I wavelengths were selected for 274.0nm and 286.0 nm for estimation of LF and DP respectively. For method II, 286.0 nm λ max for DP and 255.0 nm iso-absortive point of LF and DP. The two drugs follow Beers- Lamberts law over the low concentration range of 2µg-12µg/ml for LF and 3-15µg/ml for DP. The percentage estimation of the drugs was found near to 100% representing the two methods. The recovery of the LF and DP were found near to 100%. Validation of the proposed methods was carried out for its accuracy, precision and specificity according to ICH guidelines. The proposed methods can be successfully applied in routine work for the determination of LF and DP in combined dosage forms.

Keywords: Lafutidine, Domperidone, UV spectroscopy, Simultaneous equations, Absorbance ratio.

INTRODUCTION

Lafutidine (LF) is chemically 2-[(2-Furanylmethyl)-sulfinyl]-N-[(2z)4-[[4-(1-piperidinylmethyl)-2-Pyridinyl] oxy]-2-butenyl]-acetamide[1]. It is used as H_2 antagonist. For estimating LF, LC–ESI–MS method[2] have been reported in bioequivalence study, LC–tandem mass spectrometry method[3] for the simultaneous determination of four H_2 antagonists in human plasma, UV simultaneous method[4]and derivative spectroscopymethod[5] for combined dosage form with rabeprazole sodium, RP-HPLC[6]method for LF in combination with other drugs.

Domperidone (DP) is chemically,5-chloro-1-[1-[3-[2,3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl]-4- 6eridinyl]1,3dihydro2H-ben-Imidazol-2-one[7].It used as peripheral dopamine antagonist. Literature survey reveals that RP-HPLC method[8], HPTLC method[9,10], Simultaneous estimation of spectrophotometric methods[11-14]have been reported for estimation domperidone in combined dosage forms with rabeprazole sodium, paracetamol, tramadatolHCl and pantoprazole except Lafutidine. Our study attempt to develop accurate, precise, specific, linear, simple, rapid, validated and low cost effective analytical method for Lafutidine and Domperidone in tablet dosage form by simultaneous UV spectroscopic methods. The methods has been and developed and validated based as per the ICH guidelines [15,16].

MATERIAL AND METHODS

Spectrophotometric analysis was carried out on a LABINDIA3000+ Series UV visible double beam spectrophotometer with fixed slit width 1nm attached to the computer with UV probe, version 5.2.0, UVWIN 5 spectrophotometer software for obtaining the spectra 1cm matched quartz cells and spectral bandwidth of 2nm. Pure drugs of Lafutidine and Domperidone were procured from The Madras Pharmaceuticals, Chennai. Methanol AR grade was used as solvent in this experiment. The commercial pharmaceutical formulation (lafaxid –D) tablet was procured from the local market.

Preparation of standard stock solutions

The standard stock solutions of 100µg/ml of LF and 100µg/ml of DP were prepared.10 mg of both the drugs were weighed, taken in 100 ml volumetric flask and dissolved in 80% methanol and then make up to the mark with methanol. Further dilutions were made to in 80 % methanol to obtain concentrations 10 µg/ml for LF and DP.

Selection of wavelength

LF and DP 10µg /ml solutions were prepared separately and λ_{max} of both drugs was scanned individually in the range of 200-400nm to determine the wavelength of maximum absorption for both the drugs. For estimation, two wavelengths were selected, 274nmfor LF and 286nm DP in the simultaneous equation method, and 255nm iso-absortive method in respective solvent.

Preparation of calibration curve

By Appropriate dilutions of two standard solutions with 80% methanol, solutions containing10 µg/ml of LF and DP were scanned separately in the range of 200-400 nm to determine the wavelength of maximum absorption for both the drugs. LF showed absorbance maxima at 274 nm, DP at 286 nm and 255nm (iso-absorptive). Beer lamberts concentration range was found to be LF 2-12 µg/ml and DP 3-15 µg/ml were selected and working calibration curves of both the drugs were plotted separately.

Table 1: Application of the proposed method to the pharmaceutical dosage forms

Method	Lafutidine				Domperidone			
	Label claim (mg/tab)	Estimated Amount (mg/tab)	% of lable claim S.D (n=6)	% RSD	Label claim (mg/tab)	EstimatedAmount (mg/tab)	% of lable claim S.D (n=6)	% RSD
A	10	9.81	99.36±0.99	0.90	30	29.60	98.79±0.73	0.007
B	10	10.03	100.31±0.25	0.24	30	29.80	99.61±0.30	0.30

Average of six determinations, mean ± standard deviation

Analysis of tablet formulation

Twenty tablets were weighed and average weight was calculated. The tablets were crushed to obtain fine powder. The powder equivalent to 0.078gm was transferred to 100ml volumetric flask, 80 % methanol added, ultrasonicated for 10 minutesto dissolve and volumes was made up to mark with 80% methanol. The solution

was then filtered through a whatmann filter paper (No 41). Further dilute the final solution was 10µg/ml of LF and 30 µg/ml of DP. The concentration of both LF and DP were determined by measuring the absorbance of the sample at 274nm and 286nm as A_1 and A_2 respectively (method A, simultaneous equation method) 255 nm and 286 nm (method B, absorbance ratio method). Concentration of sample solution was determined. Results of the analysis of the formulation are reported (Table no:1).

Method A. Simultaneous equation method

Two wavelengths selected for the method are 274nm and 286nm that are absorption maxima of LF and DP respectively in 80 percent methanol. The absorbances were measured at the selected wavelengths and absorptivities (A1%, 1cm) for both the drugs at both wavelengths were determined as mean of three independent determinations. Concentrations in the sample were obtained by using following equations

$$\text{At } \lambda 1 \; A_1 = ax_1\, bcx + ay_1 bcy \text{ (274 nm)}$$

$$\text{At } \lambda 2 \; A_2 = ax_2 bcx + ay_2 bcy \text{ (286 nm)}$$

$$Cx = \frac{A_2\, ay_1 - A_1\, ay_2}{ax_2 ay_1 - ax_1\, ay_2}$$

$$CY = \frac{A_1\, ay_1 - A_2\, ay_2}{ax_2\, ay_1 - ax_1\, ay_2}$$

Where A_1 and A_2 are absorbances of sample at 274 nm and 286 nm respectively, ax_1 and ax_2areabsorptivities of LF and ay_1 and ay_2 are absorptivities of DP at λ1 and λ2 respectively. C X and C Y are concentrations of LF and DP respectively. Figure 1 represents the overlain spectra of both the drugs in 1: 1 ratio and the criteria for obtaining maximum precision (i.e. absorbance ratio (A2/A1)/ax2/ax1 and ay2/ay1) by this method were calculated and found to be outside range of 0.1-2.0 which is satisfied for both the LF and DP.

Method B: Absorption ratio method (Q- Analysis)

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

The solutions of 10µg/ml each of LF and DP were scanned wavelength range of 400 -200 nm to obtain the overlain spectra (Figure1). Two wavelengths are selected 255nm iso- absorptive point and 286nm that are maxima absorption DP of Q- absorbance equation. The calibration curves were determined in the concentration range 2-12µg/ml for LF and 3-15µg/ml of Dp drug. The absorptivity co-efficient of each drug at both wavelengths were determined. The concentration of individual components calculated by following equations,

For Lafutidine,

$$Cx = \frac{Qm-Qy}{Qx-Qy} \times \frac{A1}{ax1}$$

For Domperidone,

$$CY = \frac{Qm-Qx}{Qy-Qx} \times \frac{A1}{ay1}$$

Where, Cx = concentration of LF

Cy = concentration of DP

A1 = Absorbance of sample at iso- absorptive wavelength at 255nm

ax1 = absorptivity of LF at iso- absorptive wavelength 255nm

ay1 = absorptivity of DP at iso- absorptive wavelength 255nm

$$Qm = \frac{\text{Absorbance of sample solution at 255nm}}{\text{Absorbance of sample solution at 286nm}}$$

$$Qx = \frac{\text{Absorptivity of LF solution at 255nm}}{\text{Absorptivity of LF solution at 286nm}}$$

$$Qy = \frac{\text{Absorptivity of DP solution at 255nm}}{\text{Absorptivity of DP solution at 286nm}}$$

Recovery studies

To ascertain the accuracyof the proposed methods, recovery studies were carried at three different levels (80%, 100%, and 120%).The percent recovery for LF and DP, by these methods are presented in Table no: 2.

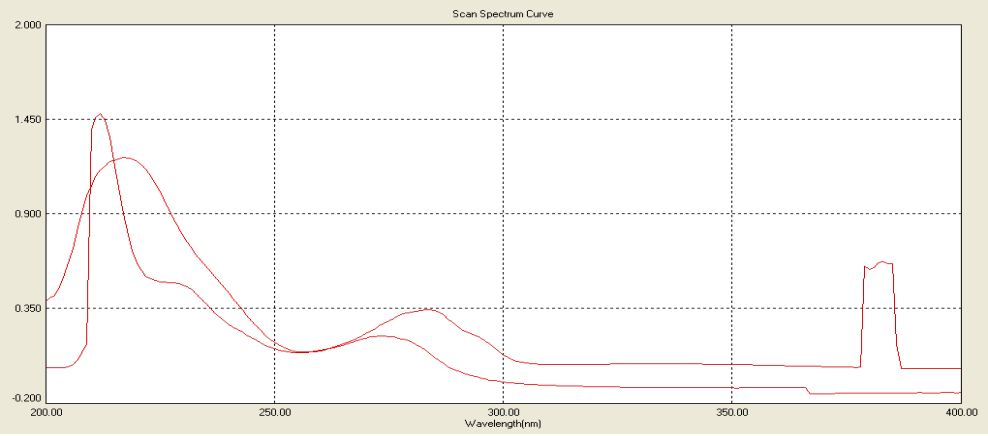

Fig. 1: Overlain spectra

Table 2: Determination of percentage recovery in proposed method

Amount added (µg/ml)	Method A		Method B	
	Amount recovered	%Recovery± S.D.	Amount recovered	%Recovery ± S.D.
LF				
8µg/ml (80%)	8.15	80.82±0.74	8.06	80.63±1.8
10µg/ml (100%)	9.93	99.36±0.99	10.11	101.10±0.60
12µg/ml(120%)	12.01	120.16±0.50	12.04	120.46±0.41
DP				
8µg/ml (80%)	24.01	80.55 ±0.51	8.02	80.23±1.06
10µg/ml (100%)	29.63	98.78±0.73	9.93	99.43±0.71
12µg/ml(120%)	32.01	120.47±0.65	12.01	120.83±0.83

S.D* for standard deviation, the results of three absorption (n=3)

RESULTS AND DISCUSSION

Precision

Assay of the method precision (inter day, intraday) was evaluated by carrying out three independent assays of test samples of LF and DP. The intermediate precision(inter day precision) of the method was evaluated by was employed with spectral band width of 0.1nm and wavelength with automatic wavelength corrections with a pair of 1cm UV matched quartz cells.

Accuracy

Accuracy of the method was studied by recovery experiments. The recovery experiments were performed by adding known amounts to tablet samples. The recovery was performed at three different sample concentrations (at80%, 100%, 120% level). The recovery samples were prepared; three different concentrations of the samples were prepared for each level. Then the solutions were analyzed, and the results of recovery studies were found to be satisfactory and the results are presented in Table no: 2

Linearity

The linearity drug measurement was evaluated by analyzing different concentration of the standard solution of LF and DP. For both the methods, the Beer-Lamberts concentration range was found to be 2-12µg/ml and 3-13µg/ml for LF and DP, respectively. The calibration graphs were obtained by plotting the absorbance various the concentration data and were treated by linear regression analysis (Table no:3). The correlation co-efficient (r^2) for LF and DP were determined.

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

The limit of Detection (LOD) and the limit of Determination (LOQ) oftheLF and DP were derived by calculating the signal to-noise ratiousing the following equations as per in ICH guidelines.LOD=3.3xσ/S;LOQ=10xσ/S

Where σ=standard deviation of the response and S=slope of calibration curve. The LOD and LOQ are presented inthe Table no: 3.

Table 3: Regression data of validation parameters

Parameters	Lafutidine		Domperidone	
	Method A	Method B	Method A	Method B
Beers law limit (µg/ml)	2-12	2-12	3-15	3-15
Molar absorptivity (lit/mole/cm)	2304.7043	4676.3207	6605.621	6307.4957
Correlation coefficient(r)	0.999/0.998	0.997/0.998	0.998/ 0.997	0.999/0.997
Regression equation Slope	0.026(at274nm)	0.042(at255nm)	0.020(at274nm)	0.013(at255nm)
	0.020(at286nm)	0.020(at286nm)	0.017(at286nm)	0.020(at286nm)
Intercept	0.002(at286nm)	0.003(at255nm)	0.002(at274nm)	0.002(at255nm)
	0.004(at286nm)	0.004(at286nm)	0.002(286nm)	0.002(at286nm)
LOD(µg/ml)	1.2(at274nm)	0.8(at255nm)	1.2(at274nm)	0.9(at255nm)
	1.2(at286nm)	1.2(at286nm)	2.7(at286nm)	2.8(at286nm)
LOQ(µg/ml)	3.7(at274nm)	2.6(at255nm)	2.8(at274nm)	2.8(at255nm)
	3.7(at286nm)	3.7(at286nm)	2.7(at286nm)	2.6(at286nm)
Precision	99.33±1.1	100.90±0.55	98.91±0.80	98.80±0.72
Interday precision	±1.1	±0.59	±0.25	±0.72
Intraday precision	±1.15	±0.55	±0.81	±0.71

CONCLUSION

The proposed UV spectrophotometric methods showed good agreement at estimated concentrations of both the active ingredients with declared labels claims. Both the estimatedmethods wereshowed good recoveries close to 100% and % coefficient variation was less than 2.0% for both LF and DP. The developed methods were simple, accurate, precise reproducible, economical, which would be used to estimate LF and DP in their combined tablet dosage form in routine analysis.

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