SIMULTANEOUS SPECTROPHOTOMETRIC 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 is o-absorptive 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-Furanyl)methyl]-sulfanyl-N-[2(3H-Imidazol-1-yl)]propyl]-4-teridinyl]-2-Pyridinyl]oxo-2-butenyl]-acetamide[1]. It is used as H₂ 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 H₂ antagonists in human plasma, UV simultaneous method[4] and derivative spectrophotometry method[5] for combined dosage form with rabeprazole sodium, RP-HPLC(m) method for LF in combination with other drugs.

Domperidone (DP) is chemically 5-chloro-1-[3-[2,3-dihydro-2-oxo-1H-benimidazol-1-yl] propyl]-4-teridinyl][3dihydro2H-benimidazol-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, tramadaloHCl and pantoprazole except Lafutidine. Our study attempt to develop accurate, precise, specific, linear, simple, rapid, validated and cost effective analytical method for Lafutidine and Domperidone in tablet dosage form by simultaneous UV spectrophotometric methods. The methods has been and developed and validated based as per the ICH guidelines [1,5,16].

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 10µg/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, 274nm for LF and 286nm DP in the simultaneous equation method, and 255nm is o-absorptive method in respective solvent.

Preparation of calibration curve

By Appropriate dilutions of two standard solutions with 80% methanol, solutions containing 10 µg/ml of LF and DP were scanned separately in the range of 200-400nm to determine the wavelength of maximum absorption for both the drugs. LF showed absorbance maxima at 274 nm, DP at 286 nm and 255 nm (iso-absorptive). Beer lamberts concentration range was found to be LF 2-12 µg/ml and DP 3-15 µg/ml and working calibration curves of the drugs were plotted separately.

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

<table>
<thead>
<tr>
<th>Method</th>
<th>Lafutidine</th>
<th>Domperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Label claim (mg/tab)</td>
<td>Estimated Amount (mg/tab)</td>
</tr>
<tr>
<td>A</td>
<td>10</td>
<td>9.81</td>
</tr>
<tr>
<td>B</td>
<td>10</td>
<td>10.03</td>
</tr>
</tbody>
</table>

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 minutes 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 10 µg/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 274 nm and 286 nm as A₁ and A₂ respectively (method A, simultaneous equation method) 255 nm and 286 nm (method B, absorption 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 274 nm and 286 nm 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 following equations

\[
\begin{align*}
A_{\lambda 1} = & ax_1 \cdot bcx + ay_1 \cdot bcy \\
A_{\lambda 2} = & ax_2 \cdot bcx + ay_2 \cdot bcy
\end{align*}
\]

\[
\begin{align*}
C_x = & \frac{A_{\lambda 2} \cdot ay_2 - A_{\lambda 1} \cdot ay_1}{ax_2 \cdot ay_2 - ax_1 \cdot ay_1} \\
C_y = & \frac{A_{\lambda 2} \cdot ax_2 - A_{\lambda 1} \cdot ax_1}{ax_2 \cdot ay_2 - ax_1 \cdot ay_1}
\end{align*}
\]

Where, A₁ and A₂ are absorbances of sample at 274 nm and 286 nm respectively, ax₁ and ax₂ are absorptivities of LF 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 10 µg/ml each of LF and DP were scanned wavelength range of 400 -200 nm to obtain the overlain spectra (Figure1). Two wavelengths are selected 255 nm iso-absorptive point and 286 nm that are maxima absorption DP of Q-absorbance equation. The calibration curves were determined in the concentration range 2-12 µg/ml for LF and 3-15 µg/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,

\[
C_x = \frac{Q_m \cdot Q_y \cdot X_1}{Q_x \cdot Q_y \cdot ay_1}
\]

For Domperidone,

\[
C_y = \frac{Q_m \cdot Q_x \cdot ay_1}{Q_x \cdot Q_y \cdot ay_1}
\]

Where, Cx = concentration of LF

Qy = Absorbance of sample solution at 255nm

Qx = Absorptivity of LF at iso-absorptive wavelength 255nm

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

Recovery studies

To ascertain the accuracy of 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.

<table>
<thead>
<tr>
<th>Amount added (µg/ml)</th>
<th>Method A</th>
<th>Method B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amount recovered</td>
<td>% Recovery± S.D.</td>
</tr>
<tr>
<td>LF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8µg/ml (80%)</td>
<td>8.15</td>
<td>80.82±0.74</td>
</tr>
<tr>
<td>10µg/ml (100%)</td>
<td>9.93</td>
<td>99.36±0.99</td>
</tr>
<tr>
<td>12µg/ml (120%)</td>
<td>12.01</td>
<td>120.16±0.50</td>
</tr>
<tr>
<td>DP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8µg/ml (80%)</td>
<td>24.01</td>
<td>80.55±0.51</td>
</tr>
<tr>
<td>10µg/ml (100%)</td>
<td>29.63</td>
<td>98.79±0.73</td>
</tr>
<tr>
<td>12µg/ml (120%)</td>
<td>32.01</td>
<td>120.47±0.65</td>
</tr>
</tbody>
</table>

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 found to be satisfactory and the results are presented in Table no:2

Table 3: Regression data of validation parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Lafutidine Method A</th>
<th>Lafutidine Method B</th>
<th>Domperidone Method A</th>
<th>Domperidone Method B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beers law limit (µg/ml)</td>
<td>2-12</td>
<td>2-12</td>
<td>3-15</td>
<td>3-15</td>
</tr>
<tr>
<td>Molar absorptivity (lit/mole/cm)</td>
<td>3204.7043</td>
<td>4676.3207</td>
<td>6605.621</td>
<td>6307.4957</td>
</tr>
<tr>
<td>Correlation coefficient(r)</td>
<td>0.999/0.998</td>
<td>0.997/0.998</td>
<td>0.998/ 0.997</td>
<td>0.999/0.997</td>
</tr>
<tr>
<td>Regression equation Slope</td>
<td>0.026(at274nm)</td>
<td>0.042(at255nm)</td>
<td>0.020(at274nm)</td>
<td>0.013(at255nm)</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.020(at286nm)</td>
<td>0.020(at286nm)</td>
<td>0.017(at286nm)</td>
<td>0.020(at286nm)</td>
</tr>
<tr>
<td>LOD (µg/ml)</td>
<td>1.2(at274nm)</td>
<td>0.8(at255nm)</td>
<td>1.2(at274nm)</td>
<td>0.9(at255nm)</td>
</tr>
<tr>
<td>LOQ (µg/ml)</td>
<td>3.7(at274nm)</td>
<td>2.6(at255nm)</td>
<td>2.8(at274nm)</td>
<td>2.8(at255nm)</td>
</tr>
<tr>
<td>Precision</td>
<td>99.3±0.1</td>
<td>100.90±0.55</td>
<td>98.1±0.80</td>
<td>98.00±0.72</td>
</tr>
<tr>
<td>Interday precision</td>
<td>±1.15</td>
<td>±0.55</td>
<td>±0.25</td>
<td>±0.72</td>
</tr>
<tr>
<td>Intraday precision</td>
<td>±1.15</td>
<td>±0.55</td>
<td>±0.81</td>
<td>±0.71</td>
</tr>
</tbody>
</table>

CONCLUSION
The proposed UV spectrophotometric methods showed good agreement at estimated concentrations of both the active ingredients with declared labels claims. Both the estimated methods were showed 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.

REFERENCES
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7. The Merck Index, 14th edn. The Merck Research Laboratories publishers, USA, 2006;578.

