SPECTROPHOTOMETRIC DETERMINATION OF CETIRIZINE AND MONTELUKAST IN PREPARED FORMULATIONS

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ABSTRACT

The spectrophotometric method including first derivative (1D) ultraviolet spectrophotometry was developed for determination of Cetirizine as a long acting antihistamine and Montelukast as an antileukotriene in pharmaceutical dosage forms. The method was performed at 217 and 335 nm for Cetirizine and Montelukast respectively. The regression analysis data for the calibration plot showed good linear relationship in the concentration range of 2-20 μg/ml (R² = 0.9991) for Cetirizine and 6-28 μg/ml (R² = 0.9976) for Montelukast. The relative standard deviation <0.4 was obtained. The LODs were found to be 112 and 10.3 ng/ml for Cetirizine and Montelukast respectively. Statistical analysis proves that the method is reproducible and selective for the simultaneous determination of Cetirizine and Montelukast.

Keywords: Cetirizine, Monetlukast, First derivative Spectrophotometry, Quantitative Analysis.

INTRODUCTION

Montelukast (MON), figure 1a, is a potent leukotriene receptor antagonist used for the treatment of seasonal allergic rhinitis and asthma [1]. Its empirical formula is C35H36ClNO3S. Leukotriene inhibitors are a new pharmacological class of compounds for asthma management.

Various analytical methods have been reported for the assay of MON in the dosage forms or in plasma. Although most of them rely on the use of chromatographic methods such as HPLC [2-3]. HPLC with fluorescence detection [4] and HPTLC [5], other methods including capillary electrophoresis and voltametric determination were also used [6-7].

Cetirizine (CET), figure 1b, is a long acting antihistamine with some mast-cell stabilizing activity widely used in the comprehensive management of allergic rhinitis, the symptoms of which include itching, sneezing and nasal congestion. Its molecular formula is C21H27Cl3N2O3.

Literature reveals a variety of analytical methods for determination of CET such as HPLC [8-10], TLC [11], and spectrophotometry [12]. There are numbers of investigations that compare the efficacy and safety of CET and MON used for the treatment of pediatric perennial allergic rhinitis, seasonal allergic rhinitis and thyroid eye disease, alone and with combination [13-15]. The results of the studies demonstrate that combined MON/CET were more effective than CET alone in preventing eye itching rhinorrhea and nasal itching and delay appearance of AR symptoms [14-15].

No reports were in literature on the determination of MON and CET simultaneously. Here we describe the development of a rapid and simple second derivative spectrophotometric method for the determination of MON and CET. The proposed method is also useful for routine analysis of prepared formulations.

EXPERIMENTAL

Materials and Reagents

MON and CET standards were received as a gift from faculty of pharmacy, Tehran university. All the chemicals and reagents used were analytical and purchased from Merck.

Instrumentation

A double-beam UV-Visible spectrophotometer (Cary 100 CONC) connected to a compatible computer (software version 3.00) was used. The spectral bandwidth was 2 nm and the scanning speed was 600nm min⁻¹. The absorption spectra of solutions was recorded in 1-cm quartz cell over the range of 200-400 nm. The first derivatives of the measured spectra were obtained using accompanying software with Δλ= 4 nm.

Preparation of standard solutions

Stock standard solutions of MON and CET were prepared by dissolving 20 mg of each substances in 100 mL methanol. 0.5, 1, 2, 3, 4, 5, 6 and 7 mL of the stock standard solutions were diluted to 50 mL with methanol.

Preparation of sample solutions

Twenty tablets of MON and CET weighted, their mean weight was calculated and finely powdered. A portion of powder equivalent to sum of the mean weight of MON and CET were weighted and dissolved in 100 mL methanol. Then 10 mL of solution was diluted to 50 mL. The sample solution was filtered. Final concentrations of MON and CET were 10µg/ml and 20µg/ml respectively.

1D method

Absorption spectra of the standard solutions were recorded over the range of 200-400 nm. The second derivatives of the measured spectra were obtained. The values of the 1D amplitudes were measured at 217 nm (zero-crossing of MON) and 335 nm (zero-crossing of CET).

RESULTS AND DISCUSSION

The main instrumental parameters that affect the shape of derivative spectra are the wavelength increment (Δλ), wavelength scanning speed and smoothing. Generally the noise level decreases with an increase in Δλ. However if the value of Δλ is too large, the spectral resolution is very poor. Some values of Δλ were tested and Δλ=4 nm and wavelength scanning speed 600 nm min⁻¹ were selected. Proper selection of zero crossing point in derivative spectra completely eliminates the interference of unwanted component and thus concentration of two components can be easily calculated without prior separation of compounds from combined dosage form.

MON possesses a very large absorption in the UV region while CET exhibits a low absorption in the same region (figure 2). The 1D value at 217 nm (zero crossing of MON) has been used for quantitation of CET and the 1D value at 335 nm (zero crossing of CET) has been used for quantitation of MON (figure 3). the plots of the absolute values of second derivative at 335 nm against concentrations of

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MON showed a linear relationship in the range of 6-28 µg ml⁻¹. For CET, the linearity range was in the range of 2-20 µg ml⁻¹ (table 1). The LODs were found to be 10.3 and 112 ng ml⁻¹ for MON and CET respectively. The LOQs were found to be 34.33 and 373.33 ng ml⁻¹ for MON and CET respectively, which indicate the good sensitivity of the method.

**Precision**

The intra-day and inter-day variations for determination of MON and CET were carried out five times in the same day and five consecutive days. Low values of the %RSD (0.4%) suggested an excellent precision of the method (table 2).

**Accuracy**

Accuracy of method was studied by applying the method to samples which known amount of MON and CET corresponding to 50, 100 and 150% of drug label claims had been added. Five determinations were performed for each level. Percent recovery for MON and CET was found in the range of 98.73% to 100.90% (table 3).

**Analysis of prepared formulation**

The method was applied to the determination of MON and CET in samples solutions. The amounts (%) of two drugs (table 4) were calculated by use of linear equation obtained from the calibration curves. The % recovery of MON and CET were well within the limits (label claim ± 5%).

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![Fig. 1: Chemical structures of Montelukast (a) and Cetirizine (b).](image1)

![Fig. 2: UV absorption spectra of CET (4 µg ml⁻¹) and MON (10 µg ml⁻¹) in methanol.](image2)

![Fig. 3: First derivative spectra of CET and MON in methanol.](image3)
Table 1: Characteristic parameters for linear regression equation of MON and CET of the first derivative method

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MON</th>
<th>CET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linearity range (µg ml⁻¹)</td>
<td>6-28</td>
<td>2-20</td>
</tr>
<tr>
<td>Regression equations (Y)*</td>
<td>( Y = 0.0001 + 0.2901X )</td>
<td>( Y = 0.0003 + 0.8021X )</td>
</tr>
<tr>
<td>First regression coefficient (b)</td>
<td>0.2901</td>
<td>0.8021</td>
</tr>
<tr>
<td>Standard deviation of the first regression coefficient (S_b)</td>
<td>19.32×10⁻²</td>
<td>18.15×10⁻²</td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>0.0001</td>
<td>0.0003</td>
</tr>
<tr>
<td>Standard deviation of the Intercept (S_a)</td>
<td>1.07×10⁻⁴</td>
<td>1.01×10⁻⁴</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.9991</td>
<td>0.9976</td>
</tr>
<tr>
<td>Standard error of estimation</td>
<td>3.01×10⁻³</td>
<td>2.83×10⁻³</td>
</tr>
</tbody>
</table>

\( Y = a + bX \) Where X is the concentration of the drug in µg ml⁻¹ and Y is the amplitude at the specified wavelength.

Table 2: Precision of 1D method (n=5)

<table>
<thead>
<tr>
<th>Drug</th>
<th>% label claim estimated (mean ±rds)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inter-day</td>
</tr>
<tr>
<td>MON</td>
<td>99.87 ± 0.37</td>
</tr>
<tr>
<td>CET</td>
<td>99.46 ± 0.12</td>
</tr>
</tbody>
</table>

Table 3: Accuracy of 1D method (n=5)

<table>
<thead>
<tr>
<th>Level [%]</th>
<th>Theoretical content</th>
<th>Amount added [mg]</th>
<th>Mean amount found [mg]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MON</td>
<td>CET</td>
<td>MON</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>2.5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>7.5</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 4: Determination of MON and CET in sample solutions

<table>
<thead>
<tr>
<th>Amount (µg ml⁻¹)</th>
<th>Recovery (mean* ±RSD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MON</td>
<td>100.13±0.72</td>
</tr>
<tr>
<td>CET</td>
<td>99.5±1.10</td>
</tr>
</tbody>
</table>

*Average of five determinations

CONCLUSION

The proposed 1D method provides simple, accurate and reproducible quantitative analysis for simultaneous determination of MON and CET in tablets. The 1D method has some advantages over other methods (e.g. HPLC) such as a short analysis time, easiness and good accuracy.

REFERENCES