ABSTRACT

Four new simple, accurate and precise spectrophotometric methods have been developed for simultaneous determination of telmisartan and amlodipine in pharmaceutical dosage form. Method A involves formation and solving of simultaneous equation using 299nm and 364nm as two wavelengths. Method B involves formation of Q-absorbance equation at 339nm (iso absorptive point) and at 299nm ($\lambda_{max}$ of telmisartan). Method C involves first order derivative method for simultaneous estimation of these two drugs. Method D involves the AUC for first order derivative spectrum. Both the drugs obey the Beer’s law in the range 5-50µg/mL for amlodipine and 5-40µg/mL for telmisartan. The results of analysis have been validated statistically and by recovery studies.

Keywords: Telmisartan (TEL); Amlodipine (AML); Simultaneous equation; Q-absorbance; Area under curve; Derivative spectrophotometry.

INTRODUCTION

Telmisartan is 42 -[1,42 -Dimethyl-22 -propyl-[2,62 -bi-1H-benzimidazole]-12 -yl][1,12 -biphenyl]-2 -carboxylic acid 1. Telmisartan is a new angiotensin II receptor antagonist for the treatment of essential hypertension usually given in combination with amlodipine. Amlodipine besylate is 3-Ethyl 5-methyl(4RS)-2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate benzenesulphonate2 and is used as calcium antagonist. The Literature survey of these two drugs revealed that some spectrophotometric, RP-HPLC, HPTLC methods have been developed for estimation of individual drugs and in combination with other drugs and in plasma3-18. No method has been developed for the simultaneous estimation of telmisartan and amlodipine in formulations.

EXPERIMENTAL

Instrumentation

All spectral measurements were made on Shimadzu UV-VIS spectrophotometer – 1650 with 1mm matched quartz cells.

Preparation standard stock solution

An accurately weighed quantity of 25mg each of TEL and AML were separately taken in a 50mL volumetric flask, dissolved in ethanol and made up to volume using ethanol to get 500µg/mL respectively.

Preparation of sample solution

The average weight of 20 tablets was determined and finely powdered. The powder equivalent to 40mg of TEL was taken in 50mL volumetric flask and dissolved in 25mL of ethanol, shaken well for 15 minutes and then made up to volume with ethanol. The solution was then filtered through Whatman filter paper No. 41, the first few mL of the filtrate was discarded and remaining solution was used for further analysis.

ASSAY PROCEDURE

Method A: Simultaneous equation method

Aliquots of the standard stock solutions were transferred to a series of 50mL volumetric flask and suitably diluted with distilled water to give varying concentrations ranging from 1-5µg/mL for AML and 8-40µg/mL for TEL and the solutions were scanned in the spectrum mode from 400-200nm using distilled water as blank. The absorption maximum for AML and TEL are shown in Fig. 1. Two wavelengths selected for formation and solving of simultaneous equation18 were 299nm and 364nm. The absorptivity coefficient of both drugs was determined at selected wavelengths. A set of two simultaneous equations18 thus framed were:

$$A_1 = 122.99 C_1 + 0.68325 C_2 - I$$
$$A_2 = 9.505 C_1 + 460.16 C_2 - II$$

Where, $A_1$ and $A_2$ are absorbance of sample solutions at 364nm and 299nm, respectively. $C_1$ and $C_2$ are concentration of AML and TEL, respectively in sample solution in g/L. Aliquots of sample solution were diluted suitably and absorbance of the final dilutions was measured at 364nm and 299nm respectively. The concentration of two drugs in sample was calculated using above framed simultaneous equations-I and II. The validity of above framed equation was checked by
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preparing five mixed standards using pure sample of
two drugs, measuring their absorbance at respective
wavelengths and calculating concentration of two
components. The results of validation studies were
found satisfactory.

**Method B : Q- absorbance method**

Aliquots of the standard stock solution were transferred
to a series of 50mL volumetric flask and suitably diluted
to give varying concentrations ranging from 1-5µg/mL
for AML and 8-40µg/mL for TEL and the solutions were
scanned in the spectrum mode from 400-200nm using
distilled water as blank. From the overlain spectra,
(Fig. 1) the wavelengths 339nm (isoabsorptive point)
and 299nm (λ<sub>max</sub> of TEL) were selected for formation of
Q-absorbance equation<sup>20</sup>. The absorptivity values
(A1%, 1cm) of each drug at iso absorptive point were
determined. The absorptivity of AML and TEL at 339nm
was 76.04 and 10.62 respectively. The concentration
of each drug in tablet formulation was determined by
substituting the absorbance and absorptivity values in
the following equations:

\[
C_x = (Q_m - Q_x/Q_y - Q_x) \times A/a_x
\]

\[
C_y = (Q_m - Q_y/Q_x - Q_y) \times A/a_y
\]

where, \(C_x\) is the concentration of AML, \(C_y\) is the
concentration of TEL, \(Q_m\) is the ratio of absorbance of
sample at selected wavelengths, \(Q_x\) is the ratio of
absorptivity of AML, \(Q_y\) is the ratio of absorptivity of
TEL, \(a_x\) is \(A(1\%, 1\text{ cm})\) of AML at 339nm, \(a_y\) is \(A(1\%,
1\text{ cm})\) of TEL at 339nm.

**Method C: First derivative spectrophotometry**

Mixed standards of AML and TEL were prepared in the
ratio 1:8 of AML and TEL ranging from concentration
0.5-3µg/mL and 4-24µg/mL of AML and TEL
respectively and scanned in the range of 200-400nm.
Similarly the sample solutions were also scanned. The
normal spectra obtained were derivatized for the first
order<sup>21</sup>. The overlain spectra of mixed standards of TEL
and AML are shown in Fig. 2. The amplitude were
measured from 225-240nm for AML and from 282-318
for TEL. The amount of AML and TEL in marketed
sample was computed from the calibration curve
obtained by plotting the amplitude versus concentration
for AML and TEL individually.

**Method D: AUC for first derivative**

The mixed standard solutions of AML and TEL were
scanned between 200-400nm using distilled water as
blank. The primary spectra so obtained were
derivatised for the first order. The area under curve<sup>22</sup>
in the first order spectrum between 231.2-253.2nm for
AML and 295-354nm for TEL (Fig. 3) were measured
by using the inbuilt software. The amount of AML and
TEL in marketed sample was computed from the
calibration curve obtained by plotting the area versus
centration for AML and TEL individually.

**Recovery Studies**

To ensure the accuracy and reproducibility of the results
obtained, recovery experiments were performed by
adding known amounts of pure drug to the previously
analyzed formulation samples and these samples were
reanalyzed by the proposed method.
RESULTS AND DISCUSSION

The optical characteristics such as RSD, regression equation, correlation coefficient, slope and intercept for the two methods were calculated and the results are summarized in Table 1. The amount, % label claim and % of recovery studies obtained by the proposed methods are presented in Table 2. Interference studies revealed that the excipients and additives did not interfere. Hence these methods are most economic, simple, sensitive and accurate and can be used for the simultaneous determination of AML and TEL in pharmaceutical preparations.

Table 1. Optical characteristics and validation of the proposed methods

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Method A</th>
<th>Method B</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSD (%)</td>
<td>2.20</td>
<td>2.30</td>
</tr>
<tr>
<td>Linear Regression</td>
<td>5.48</td>
<td>4.80</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>0.99</td>
<td>0.98</td>
</tr>
<tr>
<td>Slope</td>
<td>4.34</td>
<td>4.23</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.33</td>
<td>0.34</td>
</tr>
<tr>
<td>% Label Claim</td>
<td>100.4</td>
<td>100.2</td>
</tr>
<tr>
<td>% Recovery</td>
<td>100.8</td>
<td>100.1</td>
</tr>
</tbody>
</table>

Table 2. Results of tablet formulation and recovery studies

<table>
<thead>
<tr>
<th>Method</th>
<th>Drug</th>
<th>Low Level (mg)</th>
<th>High Level (mg)</th>
<th>% Label Claim</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>80</td>
<td>100</td>
<td>120</td>
<td>99.8</td>
<td>101.1</td>
</tr>
<tr>
<td>B</td>
<td>5.0</td>
<td>5.4</td>
<td>5.8</td>
<td>100.6</td>
<td>100.2</td>
</tr>
<tr>
<td>C</td>
<td>0.5</td>
<td>0.4</td>
<td>0.6</td>
<td>100.8</td>
<td>100.3</td>
</tr>
</tbody>
</table>

* Average of three determinations, † After spiking the sample
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