UV-Spectrophotometric Determination for Simultaneous Estimation of Amlodipine Besylate and Telmisartan in Combination

K. P. Hirpara *, Dave V. M., Dr. S. D. Faldu, Dr. B. D. Patel
Smt. R.D.Gardi B.Pharmacy College, Nyara, Rajkot, India

ABSTRACT:

Two simple spectrophotometric methods have been developed for simultaneous determination of Amlodipine besylate and Telmisartan in tablet formulation. Method 1 is Absorbance correction method, which is based on determination of Amlodipine besylate at 362 nm using its absorptivity value and Telmisartan at 292 nm. Method 2 is based on Absorbance ratio in which wavelengths selected were 326 nm, an isoabsorptive point and 292 nm as λmax of Telmisartan. Linearity was observed in the concentration range of 0.5-20, 0.5-15.5 µg/ml for AMLB and 3-24, 3-24 µg/ml for TELM by method A and B respectively. The methods can be routinely adopted for quality control of these drugs in tablet. Recovery study was performed to confirm the accuracy of the methods. The methods were validated as per ICH guidelines.

KEY WORDS: Amlodipine Besylate, Telmisartan, UV-Spectrophotometric determination, validation

INTRODUCTION:

Amlodipine (as besylate, mesylate or maleate), chemically (Fig 1.) is 3-Ethyl-5-methyl (±) ‐2‐ ((2-aminoethoxy) methyl)-4- (2-chlorophenyl) ‐1, 4‐dihydro-6-methyl-3, 5-pyridinedicarboxylate benzenesulfonat1. Amlodipine is a dihydropyridine derivative with calcium antagonist activity2. It is used in the management of hypertension, chronic stable angina pectoris and prinzmetal variant angina1. Amlodipine acts by inhibiting the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle and also acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure3.

Telmisartan is a new angiotensin II receptor antagonist. It is chemically 4'-[(1, 4'-dimethyl-2'-propyl [2, 6'-bi-1H-benzimidazol]-1'-yl) methyl]-[1, 1'-biphenyl]-2-carboxylic acid3. The molecular structure of Telmisartan is shown in Figure 2.

Literature survey reveals few analytical methods for the determination of Amlodipine alone and in combination with other drugs in pharmaceutical preparations and biological fluids, viz. spectrophotometry4-10 HPLC11-45 and HPTLC15.

Also there are some analytical methods reported for determination of Telmisartan alone and in combination16-20.

However, there is no evidence in literature for simultaneous determination of Amlodipine Besylate and Telmisartan. Hence present work describes two spectrophotometric methods for estimation these two drugs simultaneously from tablet dosage form.
EXPERIMENTAL

Materials

Amlodipine Besylate reference standard was kindly donated by Intas Pharmaceuticals; Telmisartan reference standard was kindly donated by Torrent pharmaceuticals. The pharmaceutical formulation that is SARTAL-AM (INTAS PHARMACEUTICALS LTD.) was procured from the local market.

Hydrochloric acid: 8.5ml of concentrated hydrochloric acid Chemdias Corporation, Mumbai, India, (Sp. gr. 1.18) was diluted to 1000 ml with water, and used in spectrophotometric studies.

Instrumentation

Spectral and absorbance measurements were made on Helios alpha (Thermo Scientific) model - UVA 1002 E. Digital precision Balance (A series) Contech Model CA34 was used for weighing the samples.

Method

PREPARATION OF STANDARD STOCK SOLUTIONS OF AMLB AND TELM:

The stock standard solutions containing 1 mg/ml of amlodipine and Telmisartan were prepared by dissolving 100 mg of amlodipine and Telmisartan respectively in sufficient quantity of 0.1 N HCL and diluting up to the mark in a 100 ml volumetric flask with 0.1 N HCL.

ABSORPTION CORRECTION METHOD (METHOD 1)

Stock solutions of AMLB and TELM were diluted further with 0.1N HCl to get working concentrations (10µg/ml) of amlodipine and telmisartan for the spectrophotometric study. The diluted solutions were scanned over the wavelength range of 200-400 nm. From the overlain spectra (Figure-3), wavelengths 362 λmax of AMLB and 292 nm the λmax of TELM were selected for quantitation by proposed method. For studying Beer’s law, two series of different concentrations in range of 0.5-20 µg/ml for amlodipine and 3-24 µg/ml Telmisartan were prepared from stock solutions. The calibration curves were constructed at 292 and 362 nm respectively. The absorptivities (A1%, 1 cm) of both the drugs at both the selected wavelengths were determined. The quantitative determination of AMLB is carried out by using A(1%, 1 cm) value at a 362 nm where TELM, interfering substance does not have any absorption and quantitation of TELM is carried out by subtracting absorption due to AMLB, interfering drug in the overlapping region of spectrum, on the basis of its absorption ratio at two wavelengths.

ABSORPTION RATIO METHOD (METHOD 2)

The quantitation of AMLB and TELM by proposed method was done using the selected wavelengths, 292 nm was taken as λmax for TELM and 326 nm, an isoabsorptive point for estimation of AMLB, respectively. Series of different concentrations in range of 0.5-15.5 µg/ml for AMLB and 3-24 µg/ml TELM were prepared from stock solutions. The calibration curves were constructed and regression analysis (Table I), was carried out at 292 and 326 nm. The absorptivities (A1%, 1 cm) of both the drugs at both the wavelengths were determined. By using the following equations, one can easily find out the concentration of the individual drug in admixture at the two wavelengths.

For estimation of AMLB:

\[
C_x = \frac{Q_M - Q_Y}{A_1X \cdot a_{x1}} \text{………………………….. (1)}
\]

And for estimation of TELM:

\[
C_y = \frac{Q_M - Q_X}{A_1Y \cdot a_{y1}} \text{………………………………(2)}
\]

Where,

\(C_x\) and \(C_y\) are concentrations of AMLB and TELM respectively (g/1000 ml in final solution),

\(Q_x\) = the ratio of absorptivity of AMLB at 292 and 326 nm.

\(Q_y\) = the ratio of absorptivity of TELM at 292 and 326 nm.

\(Q_M\) = the ratio of absorbance of mixture at 292 and 326 nm.

\(A\) = the absorbance of mixture at isoabsorptive point.

\(a_{x1}\) = the absorptivity value of AMLB at isoabsorptive point.

\(a_{y1}\) = the absorptivity value of TELM at isoabsorptive point.
ASSAY

An amount equivalent to two tablets (5 mg of amlodipine and 40 mg of telmisartan) was taken into a 100 ml volumetric flask and shaken for about 10 min with 5 ml of 0.1 N HCl, diluted up to the mark with 0.1 N HCl. The contents of the flask were filtered using a Whatman No. 40 filter paper. Aliquot portion of the filtrate was further diluted with 0.1 N HCl to achieve a concentration of 5 μg/ml of amlodipine and 40 μg/ml Telmisartan respectively (on labeled claim basis). The above solution was analyzed for the content of AMLB and TELM using the methods described above.

RESULTS AND DISCUSSION

For absorption correction method, the overlain spectra of both the drugs showed the λmax of 292 nm for TELM and 362 nm for AMLB where TELM does not show a significant absorption. Hence these wavelengths were selected for estimation of AMLB and TELM. Absorbances were determined at both the wavelengths. AMLB and TELM obeyed linearity in the concentration range of 0.5-20 μg/ml and 3-24 μg/ml respectively. The absorptivity was then calculated and along with absorbance, these values were submitted in the equations 1 and 2 to obtain concentration of drugs. Both the methods were successfully used to estimate the amounts AMLB and TELM in marketed tablet formulation containing amlodipine 5 mg and telmisartan 40 mg. The results obtained were comparable with the corresponding labeled amounts (Table II). The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. The accuracy of the method was determined by performing recovery studies by standard addition method in which preanalyzed samples were taken and standard drug was added at three different levels. By observing the validation parameters (Table III), accuracy, intra-day and inter-day precision expressed as %RSD, reproducibility (% RSD), specificity, linearity (correlation coefficient) and range, both the methods were found to be specific, accurate, precise, repeatable, and reproducible. Hence, both methods can be employed for routine analysis of tablets for assay.
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Method 1</th>
<th>Method 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMLB</td>
<td>TELM</td>
<td>AMLB</td>
</tr>
<tr>
<td>Linearity Range (µg/ml)</td>
<td>0.5-20</td>
<td>3-24</td>
</tr>
<tr>
<td>Correlation coefficient (R²)</td>
<td>At 362 nm</td>
<td>At 362 nm</td>
</tr>
<tr>
<td></td>
<td>0.9995</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>At 292 nm</td>
<td>At 292 nm</td>
</tr>
<tr>
<td></td>
<td>0.9997</td>
<td>0.9991</td>
</tr>
<tr>
<td>Precision (% C.V.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Repeatability (n=3)</td>
<td>0.312 ± 0.03</td>
<td>0.10 ± 0.049</td>
</tr>
<tr>
<td>2. Intraday (n=3)</td>
<td>0.571 ± 0.21</td>
<td>0.273 ± 0.52</td>
</tr>
<tr>
<td>3. Interday (3 days)</td>
<td>0.851 ± 0.22</td>
<td>0.521 ± 0.30</td>
</tr>
<tr>
<td>Ruggenedness</td>
<td>0.0203 ± 0.00503</td>
<td>0.017 ± 0.00102</td>
</tr>
<tr>
<td>Accuracy(% Recovery)</td>
<td>98.75-100.55</td>
<td>99.54-100.33</td>
</tr>
<tr>
<td>Limit of Detection (µg/ml)</td>
<td>0.0542</td>
<td>0.178</td>
</tr>
<tr>
<td>Limit of Quantitation (µg/ml)</td>
<td>0.178</td>
<td>0.541</td>
</tr>
<tr>
<td>Reproducibility</td>
<td>Reproducible</td>
<td>Reproducible</td>
</tr>
<tr>
<td>Specificity</td>
<td>Specific</td>
<td>Specific</td>
</tr>
</tbody>
</table>

Method 1 = Absorbance Correction Method and Method 2 = Absorbance Ratio Method
% C.V. = Coefficient of Variation

CONCLUSION
Both the methods for the determination of Amlodipine Besylate and Telmisartan have been developed and validated. The methods rely on the use of simple and cheap chemicals and techniques and provide sensitivity comparable to that achieved by sophisticated and expensive technique like HPLC, HPTLC. Thus these can be used as alternatives for rapid and routine determination of bulk sample and tablets.

ACKNOWLEDGEMENTS
The authors are thankful to INTAS PHARMACEUTICAL and Torrent Pharmaceuticals, Ahmedabad, India for providing gift sample of Amlodipine Besylate and Telmisartan for research. The authors are highly thankful to Smt R. D. Gardi College of Pharmacy, Gujarat Technological University, Rajkot, India for providing all the facilities to carry out the work.

REFERENCES


