Development and Validation of Analytical Method for Estimation of Telmisartan in Bulk and Marketed Formulation by UV-Spectrophotometer.

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ABSTRACT

We done work on development and validation of analytical method for estimation of telmisartan in bulk and marketed formulation by UV-spectrophotometer. In this simple, rapid, accurate, reproducible and economical methods have been described for telmisartan by using first and second order derivative method by UV visible spectrophotometer. For first order λmax of 313 and for second order λ max of 330. The concentration range over which the drugs obeyed Beer- Lambert’s law was found to be 2-12 µg/ml for Telmisartan. The developed UV spectroscopic methods were found suitable for determination of Telmisartan as bulk drug and in marketed solid dosage formulation without any interference from the excipients. It can therefore be concluded that use of these methods can save much time and money and it can be used in small laboratories with accuracy.

Keywords: Telmisartan, Method development, First and Second derivative spectroscopy.

INTRODUCTION

Telmisartan chemically is 2-{4-[(4-Methyl-6-(1-methyl-1H-1,3-benzodiazol-2-yl)-2-propyl-1H-1,3-benzodiazol-1-yl)methyl]phenyl}benzoic acid. It is an angiotensin II receptor antagonist, effective in the treatment of hypertension. It is also effective when used alone or in combination with other drugs for the treatment of high blood pressure. The pharmacokinetic properties of Telmisartan have been investigated in healthy volunteers after oral administration of the sample. Telmisartan and Hydrochlorothiazide we determined in tablets simultaneously by HPTLC and HPLC method. No validated UV spectrophotometric studies on Telmisartan individually in pharmaceutical preparations have been found in the literature.

RP-HPLC and LC–MS/MS and HPTLC for determination of Telmisartan with alone and with other drugs in combination have been reported. As the analysis is an important component in the formulation development of any drug molecule. Hence there is a need to develop a simple, sensitive, accurate, precise, reproducible method for the estimation of drug samples. Our main concern is development and validation of UV spectrophotometric method as per ICH guidelines.

Figure 1: Chemical Structure of Telmisartan

MATERIALS AND METHODS

A JASCO double beam UV–visible spectrophotometer, model: v-630, with a fixed band width (2 nm) and a pair of 1-cm quartz cell was used for spectral and absorbance measurements. Gift sample of Telmisartan was obtained from UMEDICA R &D Centre D-25/4, TTC Industrial Area, MIDC, Navi Mumbai. All chemicals and reagents were used of analytical grade and purchased from fine chemicals, Mumbai, India. Marketed formulation Telmisar tablet containing Telmisartan 20mg was used as sample; purchased from local pharmacy Pune. Calibration glassware’s were used throughout the work.

Preparation of Standard Stock Solution

Weigh accurately 10 mg of Telmisartan was transferred to 100 ml volumetric flask separately, dissolved in 40 ml Methanol by sonicator, sonicate up to 10 minute. The volume was adjusted with the same up to the mark to give final strength i.e. 100 µg/ml.

Selection of Wavelength for Analysis

Method A

Figure 2: First Order Derivative Spectra
By appropriate dilutions with methanol were prepared for each drug from the standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm and their spectra were overlaid. For first order derivative & second order derivative spectra at $N=1$, selected wavelength were 315nm and 330nm, which were selected for quantitation of Telmisartan respectively. Telmisartan shows zero crossing point at 315nm for first order.

Method B

By appropriate dilutions with methanol were prepared for each drug from the standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm and their spectra were overlaid.

**Figure 3: Second Order Derivative Spectra**

**Linearity**

Calibration curve constructed was linear over the selected range of 2-12 μg/ml for Telmisartan at $\lambda_{max}$ of 295. For first order $\lambda_{max}$ of 313 and for second order $\lambda_{max}$ of 330. Each concentration was repeated three times. The assays were performed according to experimental conditions and the linearity of the calibration graphs were validated by the high value of the correlation coefficient and the intercept value. The concentration range over which the drugs obeyed Beer- Lambert’s law was found to be 2-12 μg/ml for Telmisartan shown in Fig 4 & 5.

**Figure 4: Calibration Curve of First Order Derivative**

**Validation of the Method**

Marketed tablets containing 20mg Telmisartan were used. Ten tablets were weighed and average weight was calculated. The tablets were triturated to a fine powder. An accurately weighed quantity of powder equivalent to 10mg Telmisartan were transferred to 100 ml volumetric flask and dissolved in 40 ml of methanol solution by sonicating for 10 mins and volume was then adjusted up to 60 ml with methanol. The solution was filtered through Whatmann filter paper no. 41.

**Sensitivity**

The sensitivity of measurements of Telmisartan by the use of the proposed method was estimated in terms of the limit of quantification (LOQ) and limit of detection (LOD). The LOQ and LOD were calculated using equation LOD = 3.3 x n/b and LOQ = 10 x n/b, where, ‘n’ is standard deviation of the peak areas of the drugs (n = 3), taken as a measure of noise, and ‘b’ is the slope of the corresponding calibration curve.

**Repeatability**

Repeatability was determined by analyzing 10μg/ml concentration Telmisartan solution for to the preanalysed sample solutions, a known amount of standard stock solution was six times.

**Accuracy**

Added at different levels 80%, 100% and 120%. The solutions were reanalyzed by proposed method.

**Precision**

Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 10μg/ml of Telmisartan solutions. For three times in the same day. Inter-day precision was determined by analyzing the 8μg/ml of Telmisartan solutions daily for three days over the period of week.

**RESULTS AND DISCUSSION**

**Method Validation**

The proposed method was validated as per ICH guidelines. The solutions of the drugs were prepared as
per the earlier adopted procedure given in the experiment.

**Linearity Studies**

The linear regression data for the calibration curves showed good linear relationship over the concentration range 2-12 mg/ml for Telmisartan. The result is expressed in Table 1.

**Sensitivity**

The LOD and LOQ for Telmisartan for method A and B; shown in Table 2.

**Repeatability**

Repeatability was determined by analyzing 10µg/ml concentration of Telmisartan. For six times and the % amount with % R.S.D.

**Accuracy**

The solutions were reanalyzed by proposed method; results of recovery studies are reported in Table 3.

**Precision**

The precision of the developed method was expressed in terms of % relative standard deviation (% RSD). These result shows reproducibility of the assay.

The % R.S.D. values found to be less than 2, so that indicate this method precise for the determination of both the drugs in formulation shown in Table 2 and Table 4.

**Table 1: Optical Characteristics of Telmisartan**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Telmisartan (295nm)</th>
<th>Telmisartan (315 Nm)</th>
<th>Telmisartan (330nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zero Order</td>
<td>First Order</td>
<td>Second Order</td>
</tr>
<tr>
<td>Slope*</td>
<td>0.872</td>
<td>0.0027</td>
<td>0.0004</td>
</tr>
<tr>
<td>Intercept*</td>
<td>0.018</td>
<td>0.0004</td>
<td>0.0006</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.995</td>
<td>0.997</td>
<td>0.998</td>
</tr>
<tr>
<td>Linearity Range µg/ml</td>
<td>2-12</td>
<td>2-12</td>
<td>2-12</td>
</tr>
</tbody>
</table>

*Average of Six Determinations

**Table 2: Summary of Validation Parameter**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameter</th>
<th>Method A (First Order Derivative)</th>
<th>Method B (Second Order Derivative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Linearity (R²)</td>
<td>0.997</td>
<td>0.998</td>
</tr>
<tr>
<td>2</td>
<td>Accuracy (% Recovery ± *SD)</td>
<td>99.77 ± 0.3700</td>
<td>99.59 ± 0.1135</td>
</tr>
<tr>
<td>3</td>
<td>Range (µg/ml)</td>
<td>2-12</td>
<td>2-12</td>
</tr>
<tr>
<td>4</td>
<td>Repeatability (% Mean ± *SD)</td>
<td>100 ± 0.00021</td>
<td>99.5 ± 0.00040</td>
</tr>
<tr>
<td>5</td>
<td>Reproducibility (% Mean±)</td>
<td>98.13 ± 0.00021</td>
<td>100.3 ± 0.00012</td>
</tr>
<tr>
<td>6</td>
<td>*LOD</td>
<td>0.2566</td>
<td>3.31</td>
</tr>
<tr>
<td>7</td>
<td>*LOQ</td>
<td>0.7777</td>
<td>10.12</td>
</tr>
</tbody>
</table>

*Average of Six Determinations

**Table 3: Determination of Accuracy by Percentage Recovery Method for Telmisartan**

<table>
<thead>
<tr>
<th>Method</th>
<th>Tablet Amount (µg/ml)</th>
<th>Amount Added (µg/ml)</th>
<th>Level Of Addition</th>
<th>Percentage Recovery (%)</th>
<th>Average (% Recovery *S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Order</td>
<td>10</td>
<td>8</td>
<td>80%</td>
<td>99.58</td>
<td>99.77 ± 0.3700</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>10</td>
<td>100%</td>
<td>100.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>12</td>
<td>120%</td>
<td>99.54</td>
<td></td>
</tr>
<tr>
<td>Second Order</td>
<td>10</td>
<td>8</td>
<td>80%</td>
<td>99.64</td>
<td>99.59 ± 0.1135</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>10</td>
<td>100%</td>
<td>99.46</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>12</td>
<td>120%</td>
<td>99.67</td>
<td></td>
</tr>
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</table>

*Average of Six Determinations
CONCLUSION

The results of our study indicate that the proposed UV spectroscopic methods are simple, rapid, precise and accurate.

The developed UV spectroscopic methods were found suitable for determination of Telmisartan as bulk drug and in marketed solid dosage formulation without any interference from the excipients.

Statistical analysis proves that, these methods are repeatable and selective for the analysis of Telmisartan.

It can therefore be concluded that use of these methods can save much time and money and it can be used in small laboratories with accuracy.

Acknowledgement: The authors are thankful to UMEDICA R &D Centre D-25/4, TTC Industrial Area, MIDC, Navi Mumbai for providing the drug.

REFERENCES


