Method Development and Validation of Simvastatin in Bulk and Pharmaceutical Dosage Forms by Using UV- Spectrophotometric Method

Shrikanth B S., Archana H G., Prathap S K. & Prajusha K P.
Department of Pharmaceutical Analysis,
Bharathi College of Pharmacy, Bharathinagara, K.M.Doddi, Maddur Taluk,
Mandya District, Karnataka, India – 571 422

Abstract: A simple, accurate and precise Zero order derivative spectroscopic method was developed and validated for the estimation of Simvastatin in bulk and Pharmaceutical dosage forms and has an absorption maximum at 241 nm in 0.1 M HCl. The Linearity was found to be in the concentration range of 2-12 μg/ml and the correlation coefficient was found to be 0.9997 and it has showed good linearity, reproducibility, precision in this concentration range. The regression equation was found to be Y = 0.0586 X + 0.0003. The % recovery values were found to be within 98.43 -99.36 % showed that the method was accurate. The LOD and LOQ were found to be 0.01952 and 0.1952 mcg / ml, respectively. The % RSD values were less than 2. The method has been validated according to ICH guidelines for linearity, accuracy, precision, robustness, ruggedness. Limit of detection and limit of quantitation. Proposed method was successfully applied for the quantitative estimation of Simvastatin in bulk and pharmaceutical dosage form.

Key words: Simvastatin, UV- Spectroscopy, 0.1M HCl, accuracy.

Introduction:

Simvastatin Statins are a group of 3-hydroxyl-3-methylglutaroyl-coenzyme A (HMG-CoA) reductase inhibitors used in heterozygotic hypercholesteremia and hyperlipidemia [1, 2]. Simvastatin (Figure 1) is a prodrug [2, 3] which is biotransformed in liver into an active form of simvastatin (β-hydroxyacid) by ring opening reaction of the lacton. Chemically, simvastatin is (1S,3R,7S,8S,8aR)-8-[2-[(2R,4R)-4-hydroxy-2H-pyran-2-yl]ethyl]-3,7-dimethyl-1,2,3,7,8,8a hexahydropyranalen-1-yl 2,2 dimethyl— butanoate. The inhibition of the HMGCoA causes a decrease in LDL, low density lipoprotein (20–40 %), triglycerides (10–20 %), while it increases HDL, high-density lipoprotein (5–15%) and LDL receptor expression [3, 4]. So, it is most commonly prescribed for the prevention of atherosclerosis and heart disease.

Figure.1: Chemical structure of Simvastatin

Literature Survey revealed that the drug has been estimated by few UV spectrophotometric [5,6], HPLC methods [7,8], and Voltammetry[9,10] has been reported so far.
The aim of present work was to develop and validate a novel, rapid, simple, precise, and specific UV-Spectrophotometric method for estimation of Simvastatin in its bulk and pharmaceutical dosage form.

Materials and Method:

Instrument:

UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software. All weights were taken on analytical balance.

Chemicals:

Simvastatin pure form was obtained as gifted sample from pharma industry and its pharmaceutical dosage form Simvastatin Tablets labelled claim 10 mg were purchased from local pharmacy.
Solvent:

0.1M HCl (prepared by dissolving 8.5ml in 1000ml of distilled water)

Selection of analytical wavelength:

Appropriate dilutions were prepared for drug from the standard stock solution and the solution were scanned in the wavelength range of 200-400 nm. It shows maximum absorbance at 241 nm.

Preparation of Standard stock solution:

Accurately weigh 100mg of Simvastatin was transferred into 100ml volumetric flask and dilated with 0.1M HCl up to the mark. From this pipette out 10ml into 100ml volumetric flask and diluted with 0.1M HCl up to the mark, from this solution pipette out 0.2, 0.4, 0.6, 0.8, 1.0, and 1.2 ml into 10ml individual volumetric flask and add 0.1MHCl up to the mark, this gives 2, 4, 6, 8, 10, and 12 µg/ml concentrations.

Preparation of Sample solution:

Twenty tablets were weighed and powdered, the tablet powder equivalent to 100mg of Simvastatin was transferred into 100ml volumetric flask then it was diluted with 0.1MHCl and made up to mark and the solution was filtered through. Whatmans filter paper no.41. From this pipette out 10 ml in a 100ml volumetric flask and make up the volume up to the mark with 0.1M HCl. From this solution pipette out 0.5 ml into 10ml volumetric flask and make up the volume with 0.1M HCl, this gives 3µg/ml concentrations.

Method validation: The method is validated according to the ICH guidelines [11,12,13]

Results and Discussion:

Method: UV- spectroscopy.

Linearity:

The working standard solution were diluted serially with 0.1MHC1 to obtain the range of 2-12 µg/ml. a calibration curve for Simvastatin was obtained by measuring the absorbance at the λmax of 241nm and absorbance values are shown in Table.1 and Calibration graph were presented in Fig.2. Statistical parameters like slope, intercept, coefficient of correlation, and Sandel sensitivity were determined and presented in Table.2.

Table.1: Results of calibration curve at 241 nm by zero order Spectroscopy

<table>
<thead>
<tr>
<th>Sl. no</th>
<th>Concentration in (µg/ml)</th>
<th>Absorbance**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>0.117</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>0.235</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>0.356</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>0.462</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>0.582</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>0.709</td>
</tr>
</tbody>
</table>
Precision:
Precision of the method was studied as intra-day and inter-day precision. Intra-day precision was determined by analyzing the 2, 4, 6, 8, 10 and 12µg/ml concentration for three times in same day. Inter-day precision was determined by analyzing the same concentration of solution daily for three days. Precision results are shown in Table 3.

Table 3: Determination of precision results for Simvastatin at 241 nm by zero order derivative spectroscopy.

<table>
<thead>
<tr>
<th>Concentration (µg/ml)</th>
<th>Intra-day Absorbance ±SD**</th>
<th>% RSD</th>
<th>Inter-day Absorbance ±SD**</th>
<th>% RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.1178±0.00057</td>
<td>0.483</td>
<td>0.127±0.001528</td>
<td>1.197</td>
</tr>
<tr>
<td>4</td>
<td>0.234±0.002</td>
<td>0.008</td>
<td>0.235±0.0002</td>
<td>0.851</td>
</tr>
<tr>
<td>6</td>
<td>0.353±0.0036</td>
<td>1.019</td>
<td>0.336±0.00208</td>
<td>0.617</td>
</tr>
<tr>
<td>8</td>
<td>0.448±0.003606</td>
<td>0.804</td>
<td>0.472±0.002517</td>
<td>0.532</td>
</tr>
<tr>
<td>10</td>
<td>0.577±0.003215</td>
<td>0.557</td>
<td>0.589±0.0002</td>
<td>0.339</td>
</tr>
<tr>
<td>12</td>
<td>0.705±0.00041</td>
<td>0.581</td>
<td>0.6816±0.001528</td>
<td>0.224</td>
</tr>
</tbody>
</table>

Accuracy:
To assess the accuracy of the proposed method, recovery studies were carried out at three different levels i.e., 50%, 100% and 150%. In which the formulation concentration was kept constant and varied pure drug concentration. Accuracy results were shown in Table 4.

Table 4: Determination of accuracy results for Simvastatin by Zero order derivative spectroscopy.

<table>
<thead>
<tr>
<th>Spiked levels</th>
<th>Amount of sample (µg/ml)</th>
<th>Amount of standard (µg/ml)</th>
<th>Amount recovered(µg/ml)</th>
<th>% Recovery ±SD**</th>
<th>% RSD</th>
</tr>
</thead>
</table>

Fig.2: Linearity curves for Simvastatin at 241 nm by zero order Spectroscopy

Table 2: Regression parameters for Simvastatin by zero order spectroscopy

<table>
<thead>
<tr>
<th>Regression parameters</th>
<th>Simvastatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>2-12</td>
</tr>
<tr>
<td>max</td>
<td>241 nm</td>
</tr>
<tr>
<td>Regression equation</td>
<td>Y=0.0586x+0.0003</td>
</tr>
<tr>
<td>Slope (b)</td>
<td>0.0586</td>
</tr>
<tr>
<td>Intercept(a)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Correlation coefficient (r²)</td>
<td>0.9997</td>
</tr>
</tbody>
</table>

y = 0.0586x - 0.0003
R² = 0.9997
**Average of six determinations**

**Limit of detection and Limit of Quantitation:**

The LOD and LOQ of the present method were calculated based on standard deviation of the Response and slope of linearity curve. LOD and LOQ values of Simvastatin were found to be 0.01952 μg/ml and 0.1952 μg/ml.

**CONCLUSION:**

Thus, the developed method was found easy, simple, accurate, precise, selective and economical for the routine estimation of Simvastatin in bulk and pharmaceutical dosage form.

**ACKNOWLEDGEMENT:**

We like to thanks management, principal, teaching and non-teaching staff of Bharathi College of pharmacy for their continuoes co-operation and support.

**REFERENCES:**

11. ICH, Q2A Text on Validation of Analytical Procedures; 1994.
12. ICH, Q2B Validation of Analytical Methodology; 1996.
13. ICH, Q2 (R1) Validation of Analytical Procedures: text and methodology; 2005.