A Review on Ultraviolet Spectrophotometric Determination of Rosuvastatin Calcium in Marketed Formulation

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ABSTRACT
Three new simple, economic spectrophotometric methods were developed for quantitative estimation of Rosuvastatin Calcium in bulk formulation. First method includes determination of Rosuvastatin Calcium at absorption maxima 252 nm, second method applied was area under curve for analysis of Rosuvastatin Calcium in the wavelength range of 247-257 nm and third method was first order derivative. Beer law obeyed in the concentration range of 5-35 µg/ml for all three methods. The correlation coefficients were found to be 0.974, 0.982 and 0.982 by absorption maxima, area under curve and first order derivative spectra. Results of analysis were validated statistically and by performing recovery studies. The mean percent recoveries were found satisfactory for all three methods. The percentage label claim was found in the range of 100.48% to 101.05%. The proposed method was validated statistically and recovery studies.

Keywords: Rosuvastatin Calcium, Absorption maxima method, Area under curve method, Derivative spectroscopy.

INTRODUCTION
The chemical name for Rosuvastatin calcium is bis [(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enonic acid] calcium salt. It is a lipid-lowering drug1,2. It inhibits the enzyme 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase, the rate limiting enzyme that converts HMG-CoA to mevalonate a precursor of cholesterol and thereby checks the synthesis of cholesterol1,2. Extensive literature review reveals that several spectrophotometric, UV3–4,6,7,8, HPLC5,9,10,11,12 and HPTLC13,14 methods have been reported so far for determination of Rosuvastatin Calcium alone and its combination with other drugs. Therefore, it was thought worthwhile to develop simple, accurate and reliable spectrophotometric method for estimation of Rosuvastatin Calcium in bulk and in tablet dosage form using methanol as a solvent. All the chemicals used were of analytical grade. Spectral and absorbance measurement were made on Shimadzu Double beam UV-Visible spectrophotometer 1800 with 10 mm matched quartz cells.

MATERIAL AND METHODS
Procurement of Drug Sample
Rosuvastatin Calcium was obtained from Emcure Pvt Lmt, Bhosari, Pune.
Reagents and chemicals used
Methanol-AR was used as solvent.
Instrument Used
Shimadzu UV-1800 double beam spectrophotometer with 1 cm path length supported by Shimadzu UV-Probe software, version 2.35 was used for all spectrophotometric estimations. Shimadzu balance (BL-220H) was used for all weighing.

Standard stock solution
Solution containing 100 µg/ml of pure drug was prepared by dissolving 10 mg of Rosuvastatin calcium in sufficient methanol to produce 100 ml solution in volumetric flask. From this aliquot solution was pipetted out and diluted with methanol to obtained working standard stock solution of 100 µg/ml.

Analysis of the tablet formulation
Six tablets were accurately weighed and powdered. A portion of tablet powder equivalent to 100 mg of Rosuvastatin calcium was accurately weighed and transferred into a 100 ml volumetric flask and to this 25 ml of methanol added. The solution was Sonicated for 20 min and filtered through Whatman filter paper 41. The final volume was made up to 100 ml with methanol to obtained concentration of 1 mg/ml Rosuvastatin calcium. It was further diluted for the analysis, to obtained concentration in the range of 5-35 µg/ml. The results of the analysis of tablet formulation were found to be 100.48±0.29, 101.38±0.015 and 101.05±0.02 for absorption maxima, area under curve method and first order derivative spectra respectively.

Recovery
A recovery study was carried out by addition of known amount of standard drug in the preanalysed tablet formulation, in 80%, 100% and 120% of label claim. At each level of amount three determinations were performed.

Method I: Absorption maxima method
For selection of analytical wavelength 10 µg/ml solution of Rosuvastatin calcium was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400-200 nm. From the spectra λmax of Rosuvastatin calcium 252 nm was selected for the analysis (Figure 1 and Figure 2). The calibration curve was prepared in the concentration range of 5-35 µg/ml at 252 nm. By using calibration curve, the concentration of the sample solution was determined.

Fig. 1: Zero order UV-spectrum of Rosuvastatin Calcium
Method II: Area under curve method
For selection of analytical wavelength, 10 µg/ml solution of Rosuvastatin calcium was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400-200 nm. From the spectra of drug, area under the curve in the range of 247-257 nm was selected for the analysis (Figure 3). The calibration curve was prepared in the concentration range of 5-35 µg/ml at their respective AUC range. By using calibration curve, the concentration of the sample solution can be determined.
Method III: First order derivative spectroscopic method

In this method, 10 µg/ml solution of Rosuvastatin calcium was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400-200 nm. The absorption spectra obtained was derivatized to first order derivative spectra. The first order derivative spectra show maxima and minima at 238 nm and 205 nm respectively (Figure 4). The absorption difference is calculated which was directly proportional to the concentration of the standard solution. The calibration curve for Rosuvastatin calcium was plotted in the concentration range of 5-35 µg/ml and scanned in the Second order derivative spectra. The calibration curve of \(d^2A/d\lambda^2\) against concentration of drug showed linearity.

**Fig.4: First order derivative Overlaid Spectra of Rosuvastatin Calcium**

Method Validation

The proposed methods were validated as per ICH guidelines.[15, 16]

**Linearity**

From standard stock solution of 100 µg/ml of Rosuvastatin calcium 0.5, 1.0, 1.5, 2.0, 2.5, 3.0 & 3.5 ml were transferred into series of 10 ml volumetric flasks to obtain concentration range of 5 to 35 µg/ml for Rosuvastatin calcium (Table 1).

**Table 1. Statistical parameters of linearity of Rosuvastatin calcium**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Absorption Maxima</th>
<th>Area Under Curve</th>
<th>First Order Derivative Spectroscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer’s law range</td>
<td>5-35 µg/ml</td>
<td>5-35 µg/ml</td>
<td>5-35 µg/ml</td>
</tr>
<tr>
<td>Coefficient of Correlation (r^2)</td>
<td>0.974</td>
<td>0.982</td>
<td>0.982</td>
</tr>
<tr>
<td>Slope(m)</td>
<td>0.046</td>
<td>0.022</td>
<td>0.001</td>
</tr>
<tr>
<td>Intercept(c)</td>
<td>0.091</td>
<td>0.006</td>
<td>0.002</td>
</tr>
</tbody>
</table>

\(Y=mx+c\)

**Accuracy and precision**

Precision of the method was evaluated by using tablet powder equivalent to 100% of the label claim of Rosuvastatin calcium. Method repeatability was obtained from R.S.D. value by repeating assay of four replicates of single concentration three times in a same day.
Intermediate precision was assessed by assay of four replicates of single concentration of Rosuvastatin calcium on three consecutive days. The accuracy of the methods was assessed by recovery studies at three different levels, 80%, 100% and 120%. The values of standard deviation and recovery studies were found satisfactory (Table 2).

Table 2. Results of analysis of Rosuvastatin calcium in tablet formulation and recovery studies

<table>
<thead>
<tr>
<th>Method</th>
<th>Label Claim mg/tab</th>
<th>% Label claim*</th>
<th>% Recovery*</th>
<th>S.D.</th>
<th>% RSD</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption Maxima</td>
<td>10 mg</td>
<td>100.48</td>
<td>99.80</td>
<td>±0.2949</td>
<td>0.2939</td>
<td>0.1296</td>
</tr>
<tr>
<td>Area Under Curve</td>
<td>10 mg</td>
<td>101.38</td>
<td>100.50</td>
<td>±0.0150</td>
<td>0.0147</td>
<td>0.0067</td>
</tr>
<tr>
<td>First Order Derivative</td>
<td>10 mg</td>
<td>101.05</td>
<td>102.92</td>
<td>±0.0200</td>
<td>0.0197</td>
<td>0.0089</td>
</tr>
</tbody>
</table>

*denotes n=4    CRESTOR-10 mg (Astra Zeneca Pharma Limited, Bangalore)
S.D. = Standard Deviation, %RSD = % Relative Standard Deviation, SEM = Standard Error of Mean

Limit of detection and limit of quantitation
The detection limit and quantitation limit was computed for lower limit of detection and minimum quantity of analyte measured and was found to be satisfactory by proposed spectrophotometric methods.

RESULTS AND DISCUSSION
The methods discussed in the present work provide a convenient and reliable way for quantitative determination of Rosuvastatin calcium in bulk and marketed formulation. Wavelengths of maximum absorbance for Rosuvastatin calcium 252 nm were selected for analysis by Absorption maxima method (Method I). In area under curve method (method II) quantitative determination was carried out at wavelength range 247-257 nm (For Rosuvastatin Calcium). In First order derivative spectroscopic method (method III) quantitative determination was carried out at wavelength range maxima and minima at 238 nm and 205 nm respectively (for Rosuvastatin Calcium). Linearity for Rosuvastatin Calcium was observed in the concentration range of 5- 35µg/ml for all three methods. The results of the analysis of tablet formulation were found to be 100.48±0.29, 101.38±0.015 and 101.05±0.02 for absorption maxima, area under curve method and first order derivative spectra respectively. Percent drug found for in marketed formulation, by all three methods, was found in the range of 100.48 to 101.05%. Percent recovery for Rosuvastatin Calcium by all the methods was found in the range of 99.80 % to 102.92 % with standard deviation well below 2 indicating accuracy of the methods. Intra-day and Inter-day precision studies were carried out by analyzing marketed formulation, by all the methods, three times on the same day and on three different days, respectively. Standard deviation and coefficient of variance for intra-day and inter-day precision studies was satisfactorily low indicating high degree of precision and reproducibility of proposed methods.

CONCLUSION
The developed new three methods proved to be simple in procedure and it produced more accurate results. Hence all three methods effective for the routine analysis of Rosuvastatin calcium in bulk and tablet dosage form.

REFERENCES


15. ICH, Q2A; Text on Validation of Analytical Procedure-October, International Conference on Harmonization, Geneva; 1-5 (1994)