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**Original Research Article**

# Analytical Method Development and Validation for the Estimation of Rosuvastatin Calcium in Raw Material and Tablet Formulation by UV Spectrometric Method

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**Abstract:** Statins are the treatment of choice for controlling hypercholesterolemia in patients with cardiovascular risk. Although all statins are HMG-CoA reductase inhibitors, they possess different chemical structure, pharmacokinetic profile and lipid modifying efficacy. From the published literature, it is known that Rosuvastatin calcium is more effective in lowering bad cholesterol and raising good cholesterol compared to rest of statins. Extensive analytical methods for the determination of Rosuvastatin are more complex, expensive and time-consuming. So the present study is focused on development and validation of a reliable, simple and economic method for the estimation of Rosuvastatin Calcium in bulk and formulation. Analytical method development being a vital part of pre-formulation and formulation, research and development obviates the need to develop reliable and economical methods for the estimation of drugs in bulk and formulation. UV Spectroscopy is one of the earliest and widely used methods in drug analysis despite the availability of chromatographic and hyphenated techniques. A simple, precise, sensitive, accurate and economical method has been developed for the estimation of Rosuvastatin Calcium in bulk and formulation. The drug exhibits an absorption maximum at a wavelength of 240nm with 0.1N sodium hydroxide as solvent. Beer's law is obeyed in the concentration range of 1-6µg/ml and percentage purity is found to be 98.90%. LOD and LOQ values are found to be 0.603 and 0.830µg/ml. The developed method is validated statistically as per ICH guidelines and the results obtained are within acceptance criteria related to linearity, accuracy and precision.
**Keywords:** Rosuvastatin Calcium, Sodium Hydroxide, Hypercholesterolemia, Accuracy, Precision.

## INTRODUCTION

Rosuvastatin calcium is used as an anti-hyperlipidemic, which is a HMG-CoA reductase inhibitor, a rate-limiting enzyme in cholesterol biosynthesis. It is used in the treatment of dyslipidemia, which is effective at low doses and its half-life is more compared to other statins. Chemically it is, calcium salt of (3R,5S,6e)-7-(4-(4-Fluorophenyl)-6-(1-methylethyl)-2-(ethyl(methylsulfonyl)amino)-5-pyrimidinyl)-3,5-dihydroxy-6-heptenoic acid (fig:1) and molecular formula is $(C_{22}H_{27}FN_3O_6S)_2Ca$ [1]. Extensive literature survey reveals that a few spectrometric [2-9] were available for the estimation of Rosuvastatin calcium in bulk and formulations. The objective of the present study is to develop a new simple, sensitive, accurate, rapid and economic method for the estimation of Rosuvastatin Calcium in bulk and tablet formulation.

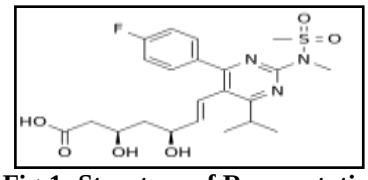


**Fig-1: Structure of Rosuvastatin**

## MATERIALS AND METHODS:

### Instrument

Spectrophotometric analysis was performed using double beam UV-Visible spectrophotometer (LABINDIA 3000) with 1cm pathlength supported by UV-WIN Software.

### Chemicals

Rosuvastatin Calcium was obtained as gift sample from APOTEX Labs, Bangalore, analytical grade Sodium Hydroxide (S.D FINE chemicals) and distilled water (AR Grade) were used for analysis. Roseday tablets 10mg (USV Limited) were purchased from a local pharmacy.

## METHOD

### Determination of lambda max

Solution of Rosuvastatin Calcium was prepared using 0.1N NaOH and scanned on UV-Visible spectrometer between 200-400nm against 0.1N NaOH as blank.

**Preparation of standard stock**

The standard solution of Rosuvastatin Calcium (1000µg/ml) was prepared by dissolving 10mg of accurately weighed rosuvastatin calcium in sufficient volume of 0.1N NaOH.

**Preparation of working standard**

Working standard (10µg/ml) was prepared by diluting 0.1ml of standard stock solution (1000µg/ml) with 0.1N NaOH.

**Preparation of calibration standards**

Accurately 1-6ml of working standard solution of Rosuvastatin Calcium was transferred to a series of 10ml volumetric flasks and the volume was made upto the mark with 0.1N NaOH to produce 1-6µg/ml solutions and the absorbance of the resulted solutions was measured at 240nm. The calibration curve was constructed by plotting absorbance against concentration.

**Preparation of sample solution**

Ten tablets of Roseday each containing 10mg of Rosuvastatin calcium were weighed accurately and made into a fine powder. The tablet powder equivalent to 10mg of rosuvastatin calcium was weighed accurately and transferred into a 10ml volumetric flask, 4ml of 0.1N NaOH was added, mixed well and sonicated for 10mins using ultrasonicator. The volume was made upto the mark with the same solvent to get 1000µg/ml.

Rosuvastatin 10µg/ml sample solution was prepared by diluting 0.1ml of 1000µg/ml of the stock solution with 0.1N NaOH. Accurately 3ml of 10µg/ml solution was transferred to 10ml volumetric flask and made upto the mark with 0.1N NaOH to get 3µg/ml of Rosuvastatin and the absorbance of the prepared solution was measured at 240nm.

**Validation of the Developed Method**

The developed method was validated for accuracy, precision, linearity, limit of detection, limit of quantitation and robustness as per ICH guidelines [10].

**Accuracy**

Accuracy of the developed method was established by recovery studies at three different levels 80, 100 & 120% of the sample in triplicate.

**Precision**

Intra-day precision was determined for calibration standards at three different time-points and inter-day precision on three different days.

**Linearity**

Linearity of the developed method was developed between 1-6µg/ml. Accurately 1ml to 6ml of 10µg/ml solution was transferred to a series of 10ml volumetric flasks and the volume was made upto the mark with 0.1N NaOH to get 1µg/ml to 6µg/ml of Rosuvastatin and the absorbance of the prepared solutions was measured at 240nm against blank. The calibration curve was constructed by plotting absorbance Vs concentration. The regression equation of the calibration curve was Y = mX+c

**Limit of Detection**

Limit of Detection was determined on the basis of slope and standard deviation of the calibration curve.

$$\mathbf{LOD = 3.3\ \sigma/S}$$

Where, σ = standard deviation of Y intercept of regression lines

S = slope of the calibration curve

**Limit of Quantitation**

Limit of Quantitation was determined on the basis of slope and standard deviation of the calibration curve.

$$\mathbf{LOQ = 10\ \sigma/S}$$

Where, σ = standard deviation of Y intercept of regression lines

S = slope of the calibration curve

**RESULTS AND DISCUSSION**

The present study was focused on development of a new spectrometric method for the analysis of Rosuvastatin in bulk drug and tablet dosage form. Spectrophotometric analysis was performed using double beam UV-Visible spectrophotometer (LABINDIA 3000) with 1cm pathlength supported by UV-WIN Software. For the method development suitable solvent, concentration of the drug and detection wavelength were studied and selected.

The solvent selected for the study was 0.1N NaOH and the drug showed absorption maxima at 240nm [fig 2]. The concentration range of the drug selected for linearity was 1-6µg/ml [table1 and figure: 3]. The calibration curve of Rosuvastatin calcium was found to be linear from 1-6µg/ml with correlation co-efficient value of 0.999 indicating that good correlation exists between peak area and the concentration [fig 3]. The proposed method showed molar absorptivity of 2.98 x $10^4$ lt/mole/cm.

To further assess the accuracy and reliability of the method, recovery experiments were performed by applying the standard-addition technique (80, 100 & 120% of the sample). The recovery was assessed by determining the agreement between the measured standard concentration and added known concentration to the sample. The results of recovery studies were 97.44-102.52, which indicate that the developed method was accurate [table.2]. High recovery values indicate that the developed method was free from interference of the excipients used in the tablet formulation.

The method was validated for intra-day and inter-day precision [table3]. %RSD for inter-day and intra-day precision was less than 2, which indicates that the developed method was precise. The results of the assay were comparable with the corresponding labeled amounts [table 4]. Detection limit for Rosuvastatin calcium was 0.603µg/ml and quantitation limit was 0.830µg/ml [table 5]; suggest that the developed method can be used for the estimation of Rosuvastatin even in micrograms accurately. Therefore, the proposed method is accurate and specific for the estimation of Rosuvastatin calcium in bulk and tablet dosage form.

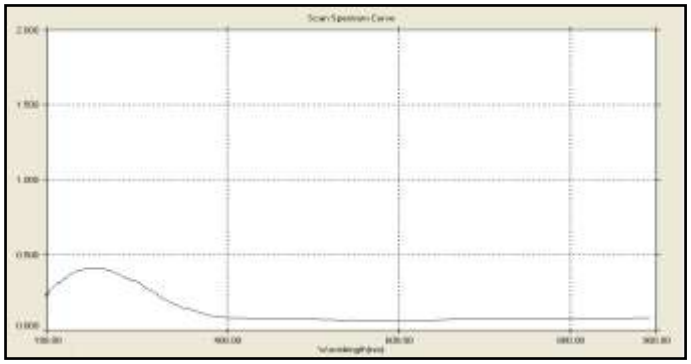

**Fig-2: UV Spectrum of Rosuvastatin Calcium**

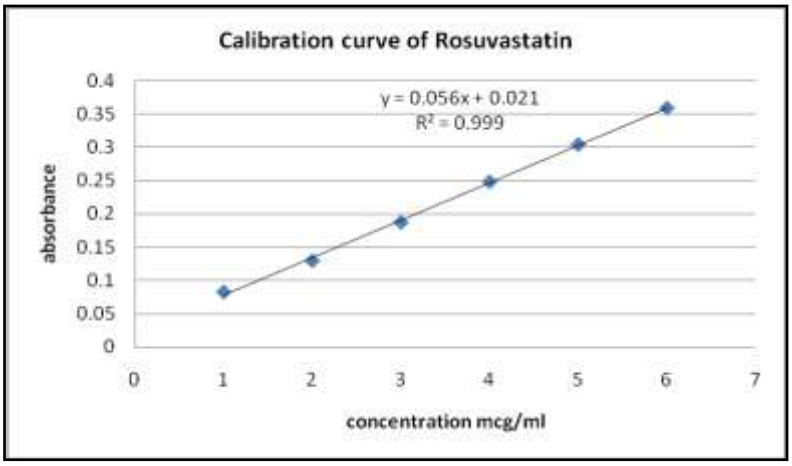


**Fig-3: Calibration Curve of Rosuvastatin**

**Table-1: Linearity Data of Rosuvastatin:**

| S.NO. | Conc. (µg / ml) | Absorbance at 240nm |
|---|---|---|
| 1 | 1 | 0.082 |
| 2 | 2 | 0.129 |
| 3 | 3 | 0.187 |
| 4 | 4 | 0.248 |
| 5 | 5 | 0.304 |
| 6 | 6 | 0.359 |

**Table-2: Recovery data of Rosuvastatin by proposed UV method:**

| Brand name | Amount of sample (µg / ml) | % of Spiked sample | Amount of drug added (µg / ml) | Amount Recovered | % Recovery ± SD |
|---|---|---|---|---|---|
| Roseday | 2 | 80 | 1.6 | 3.508 | 97.44 ± 0.18 |
| Roseday | 2 | 100 | 2 | 4.101 | 102.52 ± 0.54 |
| Roseday | 2 | 120 | 2.4 | 4.332 | 98.45 ± 0.27 |

***mean of three determinations**

**Table-3: Precision data of Rosuvastatin by proposed method**

| Conc mcg / ml | Inter-day Absorbance Mean** ± SD | % RSD | Intra-day Absorbance Mean** ± SD | % RSD |
|---|---|---|---|---|
| LQC (1mcg/ml) | 0.084 ± 0.0015 | 1.817 | 0.082 ± 0.000577 | 0.704 |
| MQC (4mcg/ml) | 0.249 ± 0.001 | 0.401 | 0.248 ± 0.001154 | 0.465 |
| HQC (6mcg/ml) | 0.358 ± 0.0015 | 0.418 | 0.360 ± 0.000577 | 0.160 |

****mean of six determinations**

**Table-4: Results of Analysis of the tablet dosage form**

| S.No | Formulation | Label claim (mg/tab) | Amount found (mg) (n=4) Mean ± SD | Assay | %RSD |
|---|---|---|---|---|---|
| 1 | Roseday | 10mg | 9.89 ± 0.00115 | 8.90% | 1.402 |

**Table-5: Optical Characteristics and precision data of Rosuvastatin:**

| Parameter | UV method |
|---|---|
| $\lambda_{max}$ (nm) | 240 |
| Beer's law limits (µg/ml) | 1-6 |
| Sandell's sensitivity (mcg / $cm^2$ -0.001 absorbance units) | 0.0121 |
| Molar absorptivity (Litre.$mole^{-1}$.$cm^{-1}$) | 2.98 x $10^4$ |
| Regression equation (Y) | y = 0.0563x + 0.0211 |
| Slope (b) | 0.0563 |
| Intercept (a) | 0.0211 |
| Correlation coefficient($r^2$) | 0.999 |
| % RSD* | < 2% |
| Limit Of Detection (µg/ml) | 0.603 |
| Limit Of Quantitation (µg/ml) | 0.830 |

## CONCLUSION

The developed method was found to be simple, rapid, accurate, precise, economic, sensitive and easy to perform analysis. Hence, the method could be used in routine quality control of Rosuvastatin calcium in raw material and tablet formulation.

## ACKNOWLEDGEMENTS

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