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DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR ESTIMATION OF ROSUVASTATIN CALCIUM SOLID DISPERSIONS TABLETS

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ABSTRACT

A simple, specific and precise reverse phase high performance liquid chromatographic (RP-HPLC) method was developed and validated for the estimation of Rosuvastatin Calcium solid dispersion tablets which were prepared in-house. A reversed phase C_{18}, 5 µm column having 100 x 4.6 mm i.d. in gradient mode, with mobile phase containing HPLC grade phosphate buffer: acetonitrile (55: 45 v/v) was used. The flow rate was 1 ml / min and effluents were monitored at 240 nm. Chromatogram showed a main peak of Rosuvastatin at retention time was 3.47 ± 0.001 min. The method was validated for linearity, accuracy, limit of detection and limit of quantitation etc. The limit of detection and limit of quantitation were found to be 0.12 µg / ml and 0.39 µg / ml respectively. Recovery study was found to be within the range. Proposed method can be successfully applied for the estimation of Rosuvastatin solid dispersion tablets.

Key words: RP-HPLC, Rosuvastatin Calcium, Validation, Solid dispersion tablets.

INTRODUCTION

Rosuvastatin calcium, a widely prescribed anti hyperlipidemic [1], exhibits low oral bioavailability due to its poor aqueous solubility. Its oral absorption is dissolution rate limited and it requires enhancement in solubility and dissolution rate for increasing its oral bioavailability. Researchers have attempted many technique for the same purpose out of that solid dispersion was very useful technique [2], but there was no evidence of quantification of such solid dispersion of Rosuvastatin thus the objective of the present study was to develop RP-HPLC method for quantification of prepared solid dispersions of Rosuvastatin calcium. This work also describes the validation parameters stated by the ICH guidelines [3,4] to achieve an analytical method with acceptable characteristics of suitability, reliability and feasibility.

MATERIALS AND METHODS

Starch, Talc, Magnesium stearate, PVP-K30 was procured from commercial source & Starch Phosphate was prepared in the laboratory, all others chemicals & glassware's used were of analytical grade.

Preparation of Solid Dispersions

Solid dispersions of Rosuvastatin and starch were prepared in 1:1, 1:1.5 & 1:2 ratios of drug: carrier by solvent evaporation method. Rosuvastatin calcium was dissolved in Methanol to get a clear solution. Starch phosphate was then added and dissolved. It was then triturated for 15 min for complete evaporation of Methanol and then dried at 55°C until dry. The dried mass was pulverized and sieved through mesh no. 100 [5, 6].

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Instrumentation

Analysis was performed with a Shimadzu (Japan) Chromatograph equipped with an LC-10 AD-*vp* solvent-delivery module, an SPD-10A UV–visible detector, and a Rheodyne model 7125 injector valve with 20-µL sample loop.

Chromatographic Conditions

Chromatographic analysis was performed on a Thermo Hypersil reversed phase C_{18} column with 100 x 4.6 mm i.d. and 5 µm particle size. The mobile phase consisted of phosphate buffer: acetonitrile (55: 45 v/v) and set at a flow rate of 1.0 ml/min. The mobile phase was degassed and filtered through 0.2 µm membrane filter before pumping into HPLC system. The eluent was monitored by UV detection at 240 nm.

Preparation of Solutions

Preparation of Standard Solutions

The stock solution of was prepared by dissolving accurately weighed quantity of 10 mg of the drug in 10 ml of methanol. From this stock solution, standard solution containing 100µg/ml of drug was prepared by suitably diluting the appropriate volume of stock solution with mobile phase. Different calibration standards were prepared by appropriate dilution of standard solution with mobile phase.

Preparation of Sample Solution

Prepared sample drug were accurately weighed, grounded, homogenized and portion of the powder equivalent to 10 mg of the drug was weighed accurately, transferred into a 100 ml volumetric flask and diluted up to mark with methanol. This solution was sonicated for 15 min and filtered through Whatman filter paper. Further dilution was done with mobile phase to get final concentration.

Method & Validation [7,8]

Linearity (Calibration Curve)

To carry out this study, six levels of concentration in the range 5–30 µg/ml were prepared. Each of the levels of concentration was prepared in triplicate. Calibration curve was constructed by plotting peak area against concentration and regression equation was computed.

Sensitivity

In order to estimate the limit of detection (LOD) and limit of quantitation (LOQ) values, the blank sample was injected six times and the peak area of this blank was calculated as noise level.

Accuracy

Accuracy of the method was determined on three concentration levels by recovery experiments. The recovery studies were carried out six times by spiked placebo recovery method and the percentage recoveries with standard deviations were calculated.

Precision

Precision is the measure of how close the data values are to each other for a number of measurements under the same analytical conditions. The three components of precision, i.e., repeatability (Intraday Variation), intermediate precision and reproducibility (Ruggedness), in accordance with ICH recommendations were performed.

RESULTS AND DISCUSSION

Analysis of drug sample was performed and a precise method was established for the determination of solid dispersion sample. Chromatogram showed a main peak of Rosuvastatin at retention time 3.47 ± 0.001 min. The method was validated for linearity, accuracy, limit of detection, limit of quantitation & precision etc.

Linearity (Calibration Curve)

To carry out this study, six levels of concentration in the range 10–50 µg/ml were prepared. Each of the levels of concentration was prepared in triplicate. Calibration curve was constructed by plotting peak area against concentration and regression equation was computed (Figure 1). The result shows excellent linear correlation between peak area and concentration.

Sensitivity

In order to estimate the limit of detection (LOD) and limit of quantitation (LOQ) values, the blank sample was injected six times and the peak area of this blank was calculated as noise level. The LOD was calculated as three times the noise level while approximately three times the LOD gave the LOQ, The limit of detection and limit of quantitation were found to be 0.12 µg / ml and 0.39 µg / ml respectively.

Accuracy

Accuracy of the method was determined on three concentration levels by recovery experiments. The recovery studies were carried out six times by spiked placebo recovery method and the percentage recoveries with standard deviations were calculated. The method was found to be sufficiently accurate and shown in Table 1.

Precision

Precision is the measure of how close the data values are to each other for a number of measurements under the same analytical conditions. The three components of precision, i.e., repeatability (Intraday Variation), intermediate precision and reproducibility (Ruggedness), in accordance with ICH recommendations, were determined as follows & results are shown in Table 2.

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Repeatability (Intraday Variation)

Six injections of sample solution were analyzed on the same day at different time intervals. % RSD were found to be within range.

Intermediate precision (Interday Variation)

Six injections of sample were analyzed on the consecutive days and determined the intermediate precision. Both intraday and interday precision studies are described in Table 2.

Reproducibility (Ruggedness)

The reproducibility of the method was checked by determining precision on the same instrument, but by a different analyst, the method was found to be reproducible with optimum % recovery.

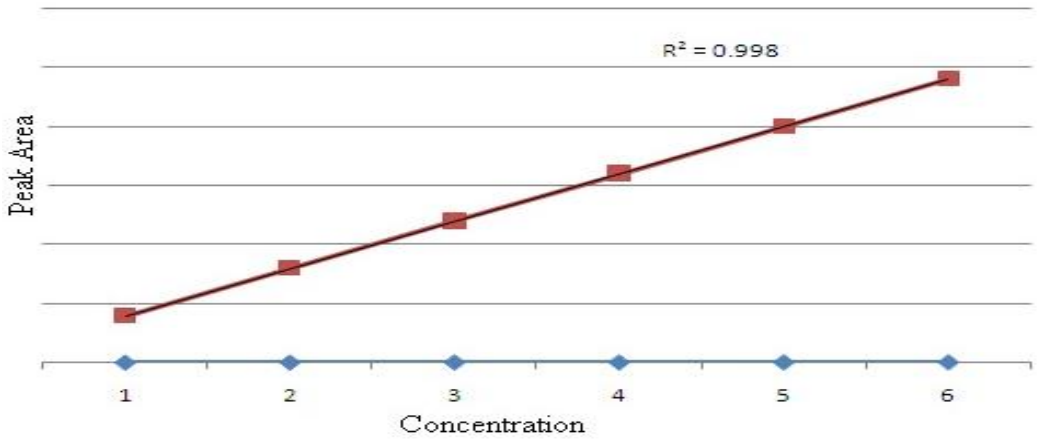
Table 1. Recovery Studies

Amount of pure drug added (%)	Amount of drug found (µg/ml)	% RSD
50	9.13	0.108
100	20.07	0.358
150	30.04	0.206

Table 2. Precision Studies

%RSD		Ruggedness studies	Recovery (%)	
			Analyst I	Analyst II
0.186	0.117	Brand I	99.22 ± 0.24	99.55 ± 0.31
		Brand II	100.37 ± 0.37	99.15 ± 0.24

Figure 1. Calibration curve (Linearity Graph)



CONCLUSION

The Rosuvastatin persist poor solubility and bioavailability hence it's desirable to formulate some more soluble preparation like solid dispersion, even many researchers have attempted for the same also and estimation of such formulation is also very important this article describe a convenient, rapid, accurate, precise and economical RP - HPLC method for estimation of Rosuvastatin solid dispersions. The assay provides a linear response across a wide range of concentrations and it utilizes a mobile phase which can be easily prepared. The proposed method is simple, fast, accurate and precise for the quantification of Rosuvastatin solid dispersions. Thus proposed method can be successfully applied for the estimation of Rosuvastatin solid dispersion tablets.

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