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Research Article

DEGRADATION ESTIMATION OF ROSUVASTATIN CALCIUM IN PHARMACEUTICAL TABLET FORMULATION

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ABSTRACT

Objectives: The present objective was to undertaken the rosuvastatin calcium degradation in the tablets formulations with a rapid, economic, consistent, specific, and simple analytical procedure.

Methods: The analytical reversed-phase high-performance liquid chromatography (HPLC) was validated with mobile phase composition of methyl alcohol: Cyanomethane: water (45:35:20, v/v). The detection was achieved with a flow 1.0 mL/min using octylsilane column (250 × 4.6 mm, 5 µ), at 248 nm.

Results: The established analytical procedure of rosuvastatin calcium was validated statistically for reproducibility, accuracy, and specificity as per international conference on harmonization-guideline. The correlation coefficient was 0.999 with the linearity concentration range 140–260 µg/mL. The percentage recovery was achieved 99.86–106.12 and relative standard deviation% of precision was 0.599. The specificity was confirmed by excellent photolytic and thermal stability of rosuvastatin calcium. The degradation statistical recovery of rosuvastatin calcium in dry, wet, and thermal stage ware 99.25%, 99.52%, and 99.64%, respectively, validated. The developed peaks in the chromatograms of alkali, oxidation, and acid decomposition of rosuvastatin calcium were confirmed by screening the degradation peaks and the recovery percentage was found 23.16%, 85.59%, and 66.33%, respectively.

Conclusion: The stress conditions of rosuvastatin calcium in degradation study are successfully developed and it is also important in stability to determine the highest lipid lowering agent in the body that block the manufacturing of cholesterol. The stress conditions such as in aqueous acidic hydrolysis, oxidative, alkaline hydrolysis, thermal, and photolytic degradation study was validated with a simple, cost efficient, linear, accurate, selective, specific, and HPLC with a simple effortless mobile phase containing methyl alcohol, cyanomethane, and water.

Keywords: Chromatography, Aqueous acidic, Alkaline hydrolysis, Oxidative, Cost efficient, Thermal stability, Rosuvastatin calcium, Degradation.

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INTRODUCTION

Rosuvastatin calcium is used for hypercholesterolemia and cardiovascular disease. The statin salt with antilipidemic action is competitively inhibitor of hepatic 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase that catalyzed the transformation of HMG-CoA to precursor of cholesterol, in which cause decreases the hepatic cholesterol and triglyceride level and increase the consumption of low-density lipoprotein (bad cholesterol) [1-3]. Rosuvastatin calcium is chemically calcium; (*E*,3*R*,5*S*)-7-[4-(4-fluorophenyl)-2-[methyl(methylsulfonyl)amino]-6-propan-2-ylpyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate (Fig. 1).

On the market, 5, 10, 20, and 40 mg rosuvastatin calcium tablet is available and in this analytical work, a cost efficient simple isocratic high-performance liquid chromatography was reported for estimate from different tablet formulations. Almost all of the mobile phase preparation uses triethylamine, buffer, orthophosphoric acid, and THF in chromatographic method developed for quantification of rosuvastatin calcium [4-16]. The cost of determination is increase with the use of acute acid and buffer, which decrease the column life. Therefore, the proposed aim of this analytical work was for developing, validation and optimization of rosuvastatin calcium as per international conference on harmonization (ICH) guideline [17-20].

The specificity was evaluated by execution of different type of stress conditions such as in aqueous acidic hydrolysis, oxidative, alkaline hydrolysis, thermal, and photolytic degradation study of rosuvastatin calcium. However, this kind of degradation investigation was not found previously for analysis of rosuvastatin calcium in the tablets formulations.

In this analysis, we profitably developed simple economic, accurate, and routine analytical procedure for estimation of rosuvastatin calcium and its degradations.

METHODS

Instrument

The chromatographic development, validation, and separation was carried out for of this quantification method using Agilent Infinity II Technology 1260 having UV detector, multisampler (100 µL) loop and Quaternary pump. For the data collection and processing, OpenLab software was used for quantify the rosuvastatin calcium content.

Chromatographic environment

Chromatographic determination was carried out on octylsilane 4.6 mm × 25 cm, 5 µ column. For isocratic elution, a simple mixture of methyl alcohol: Cyanomethane: Water (45:35:20, v/v) ware use as mobile phase at 1 mL/min flow. The elution was observed at 248 nanometer by UV detector. The injection volumes 5 µL and oven temperature 30°C ware maintained throughout the analysis. The standard, sample, and mobile phase ware passes through 0.2 µm filter before injecting into the chromatographic condition. The chromatograms are shown in Figs. 2 and 3.

Procedure

Preparation of standard

Accurately weighting 10 mg rosuvastatin calcium and take into a 50 mL volumetric flask. Add 30 mL mobile phase, sonicated to dissolve, and volume to 50 mL with mobile phase.

Sample preparation

Two different commercial brands of tablets were taken and average weight was calculated. Twenty tablets of each brand were crushed separately for fine particles. Accurately weighting equivalently 5 mg of rosuvastatin calcium powder of two brands separately into two 25 mL volumetric flask, sonicated for 30 min to dissolve completely with mobile phase.

Study of commercial formulation

The developed method was proposed for quantification of rosuvastatin calcium from Rosu-Rite-5 (MSN Laboratories PVT) and Rozucor-5(Torrent Pharma). The assay result is exhibited in Table 1 and indicates that the pharmaceutical excipients does not effect on quantification of rosuvastatin calcium from tablets formulation.

Method validation

System suitability

In the chromatography, system suitability is applied to confirm the reproducibility. The six replicates of standard solutions were injected and examine the different parameters and results are shown in Table 2. The relative standard deviation (RSD) was <2% and asymmetric was also <2% ware found in this simple isocratic method.

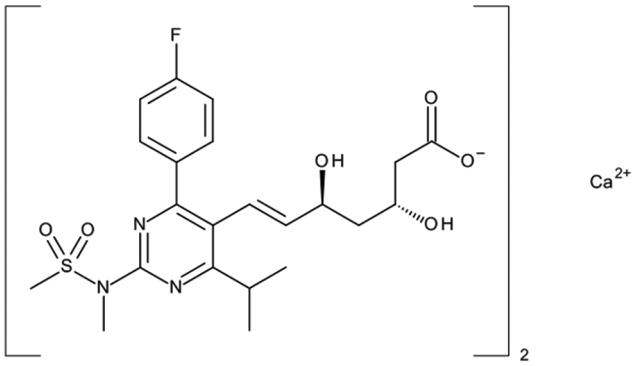

Fig. 1: Rosuvastatin calcium

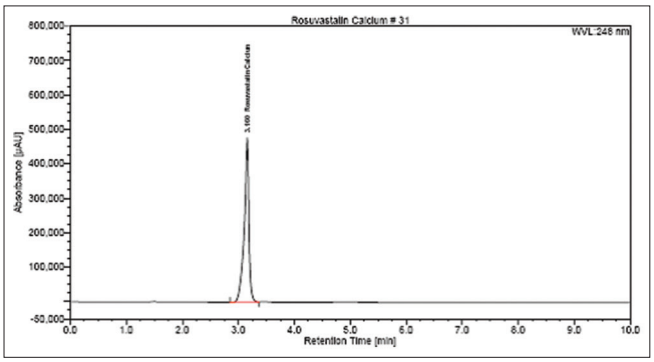

Fig. 2: Chromatogram of standard

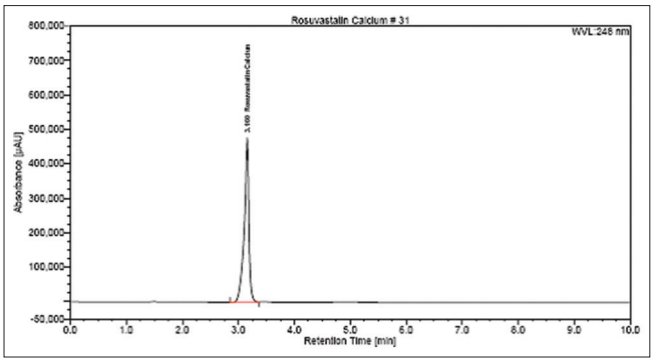

Fig. 3: Chromatogram of sample

Linearity

In the linearity study, test result of rosuvastatin calcium was directly proportional to its concentration within range 140–260 µg/mL. The least squares equation was confirmed by comparability of different levels peak area and the analyte concentration. In general, linear regression, slope, and y-intercept ware reported. The graphically calibration curves ware is represented in Fig. 4.

LOD and LOQ

As per the ICH guideline Q2R1, standard deviation response (σ) and slope(S) of the least squares equation were used to calculate the limit of detection and limit of quantification of rosuvastatin calcium. On the basis of standard deviation (σ), slope(S), limit of detection, and limit of quantification was calculated with the equation 3.3(σ)/S and 10(σ)/S, respectively. The outcome ware 0.02 µg/mL and 0.06 µg/mL, respectively, which are expressed in Table 3.

Accuracy

In the accuracy, analytical determination was express with recovery of rosuvastatin calcium between true conventional value or founded value and reference accepted value in the formulation. The reference material was spiked with known concentration to the pre-analyzed tablet and the experimental work was performed with injection of accuracy 80%, 100%, and 120% level. The chromatographic recovery of this method is represented in Table 4.

Specificity/forced degradation

The specificity studies were conducted through acid, alkali, oxidative, and photolytic degradations of rosuvastatin calcium in the force

Table 1: Evaluation of rosuvastatin calcium in tablet formulation

Trade name	Assay %
Rosu-Rite-5 (MSN Laboratories PVT)	100.16
Rozucor-5(Torrent Pharma)	98.84

Table 2: System suitability

System suitability parameters	Rosuvastatin calcium (%)
Retention time	3.160
Theoretical plates	9576
Linear dynamic range	140–270 mg/mL
R^2 value	0.999
L O D	0.02 (µg/mL)
L O Q	0.06 (µg/mL)
Tailing factor	0.77
Specificity	Specific
Recovery	99.86–106.12
Inter-day	100.76
Intra-day	99.70
RSD %	0.12

RSD: Relative standard deviation

Table 3: LOD and LOQ

y-intercepts	Slope S	LOD and LOQ	
12,200	37,040		
12,490	37,027	3.3σ	10 σ
SD: 205.06097	SD: 9.192388155	LOD =	LOQ = ------- = 0.06
Mean: 12345	Mean: 37033.5	------ = 0.02	S
		S	

decomposition investigation. The main peak was survey with the exposition of the samples with this said condition. The method was successfully separated the decomposed peaks from the reference peak, as shown in Fig. 5. It was also confirmed by recovery of the active ingredient from the degradations, as shown in Table 5.

Acid degradation

Accurately weighting 10 mg of rosuvastatin calcium in a reflux condenser and reflux at 70° for 5 h with 1 mL 5(N)HCl and take into volumetric flask. Add 30 mL mobile phase, sonicate for complete dissolution and volume to 50 mL with the same solvent and injected into the chromatographic condition. The chromatographic response is represented in Fig. 6.

Alkaline degradation

Accurately weighting 10 mg of rosuvastatin calcium in a reflux condenser and reflux at 70° for 5 h with 1 mL 5(N) NaOH and take into volumetric flask. Add 30 mL mobile phase, sonicate for complete dissolution and volume to 50 mL with the same solvent and injected into the chromatographic condition. The chromatographic response is represented in Fig. 7.

Oxidative degradation

Accurately weighting 10 mg of rosuvastatin calcium in a reflux condenser, add 1 mL 30% H_2O_2 and reflux at 70° for 2 h and take into volumetric flask. Add 30 mL mobile phase, sonicate for complete dissolution and volume to 50 mL with the same solvent and injected into the chromatographic condition. The chromatographic response is represented in Fig. 8.

Photolysis

Accurately weighting 10 mg of rosuvastatin calcium into two separate 50 mL volumetric flask and kept at 254 nm in a UV cabinet in dry and wet condition for 2 h. Add 30 mL mobile phase, sonicate for complete dissolution and volume to 50 mL with the same solvent and injected into the chromatographic condition. The chromatographic responses are represented in Figs. 9 and 10.

Thermal degradation

Accurately weighting 10 mg of rosuvastatin calcium into a 50 mL volumetric flask and kept an oven 70° for 6 h. Add 30 mL mobile phase, sonicate for complete dissolution and volume to 50 mL with the same solvent and injected into the chromatographic condition. The chromatographic response is represented in Fig. 11.

Table 4: Recovery of rosuvastatin calcium

Concentration	Results (%)
80	106.12
100	99.86
120	102.77

Table 5: Forced degradation recovery

Test	Recovery%	Degradation%
Degradation in acid	66.33	33.67
Degradation in alkali	23.16	76.84
Degradation in oxidation	85.59	14.41
Degradation in photolysis (dry stage)	99.25	0.75
Degradation in photolysis (wet stage)	99.52	0.48
Thermal degradation	99.64	0.36

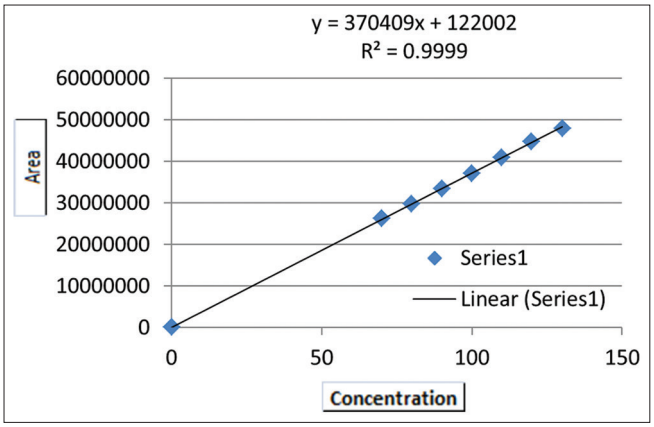

Fig. 4: Standard curve

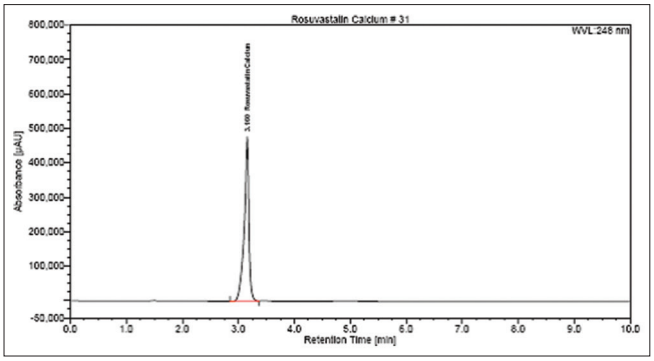

Fig. 5: Rosuvastatin calcium

RESULTS AND DISCUSSION

The present high-performance liquid chromatographic analytical technique was successfully undertaken to developed and quantify the rosuvastatin calcium at 248 nm using octylsilane column (250 × 4.6 mm, 5 µ). In this quantification method, asymmetrical peak was obtained with composition of methyl alcohol: Cyanomethane: Water (45:35:20, v/v) when used as mobile phase preparation. The peak was appearing very short retention time at 3.160 min with a flow

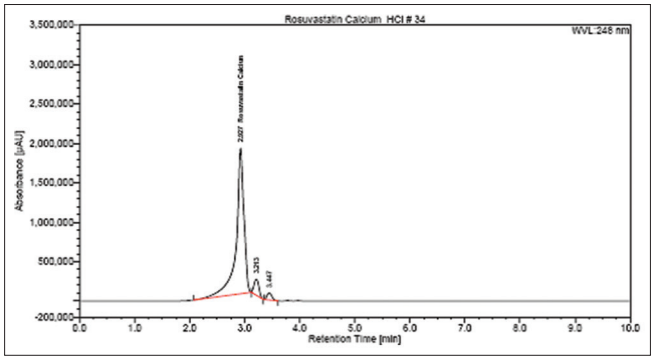

Fig. 6: Acid degradation

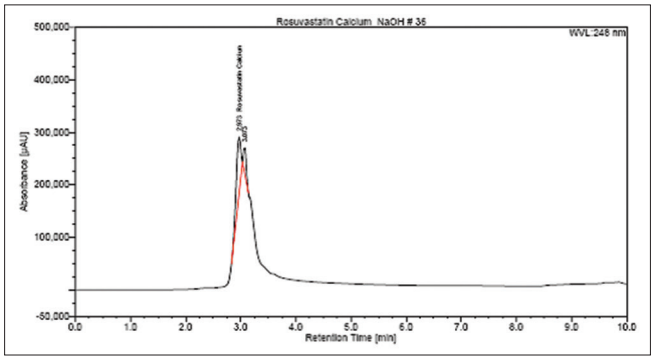

Fig. 7: Alkali degradation

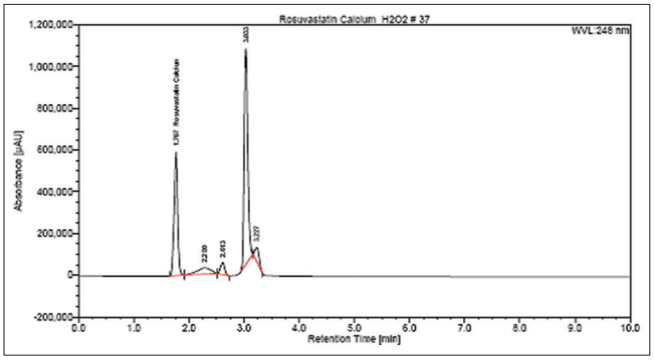

Fig. 8: Oxidative degradation

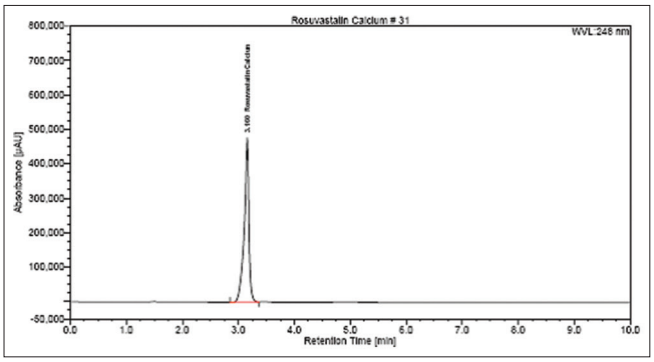

Fig. 9: Dry stage

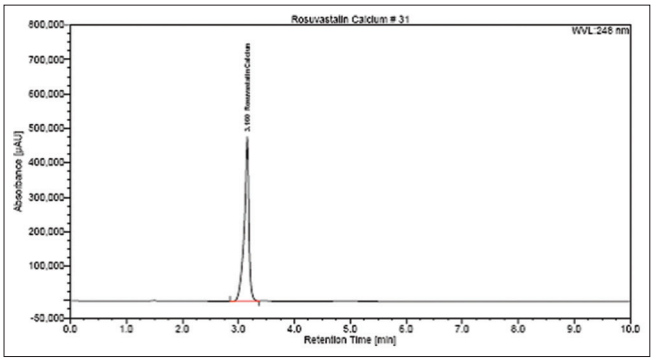

Fig. 10: Wet stage

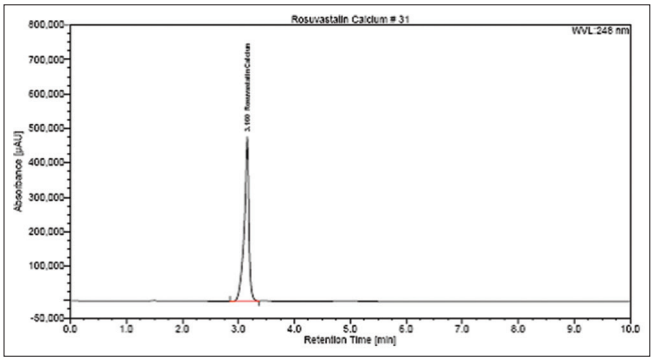

Fig. 11: Thermal degradation

1.0 mL/min. The cost of the developed chromatographic method was decrease and increase the life time pump was accomplish with the use of methyl alcohol, cyanomethane, and water as mobile phase. The reference and degradation product peaks were eluted within 10 min, which acknowledge the large number of estimation should be achieved with very short time. The stability indicative method was separating successfully degradation peaks and the recovery of rosuvastatin calcium was in between 99.86% and 106.12% (Table 2). In the standard curve, linear line was passes through the origin with 140–260 mg/mL concentration range (Fig. 4). In this experimental condition, limit of detection and limit of quantification were established 0.02 and 0.06 mg/mL, respectively. As the part of robustness, deliberately changes the conditions of chromatographic method which was developed in quantification, enclose column temperature (28 and 32°), detection nanometers (246 and 250 nm), and pump flow (1.1 and 0.9 mL/min.). The principle and robustness samples all-inclusive RSD percentage were found <2.0%. Hence, the proposed recommended method was strongly robust, fast, simple, precise, cost effectively and accurate. It also acknowledges that, the continuous used of non-identical excipients in the tablets preparation dose not clog up the chromatographic condition for quantification of rosuvastatin calcium in its commercial formulations.

In the force degradation study, rosuvastatin calcium was stable in thermal and photolytic exposure except in acid, alkali hydrolysis, and oxidation (Table 5). On acidic hydrolysis decomposition, peaks were found at 3.213 min and 3.447 min (Fig. 7). On alkaline hydrolysis, peak was developed at 3.073 min (Fig. 8). On oxidation with H_2O_2, degradation peaks were found in 2.280 min, 2.613 min, 3.033 min, and 3.227 min (Fig. 9). The stability indicative power of rosuvastatin calcium with this experimental method is not affected with different tablets excipients and degradation products, which may be developed in stability.

CONCLUSION

In industry, chromatographic experiment was perfect for estimation of rosuvastatin calcium in tablets preparations. For the current good manufacturing practices and Food Drug Administration, this analytical development is cost-effective, first, simple, highly accurate, scientific, sensitive, and stability indicating. This method was also confirmed to its superiority to the reported analytical procedures. Therefore, in the pharmaceutical, this analytical technique should be used for routine quantification and stability study of rosuvastatin calcium in tablet formulation.

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CONFLICTS OF INTEREST

The authors have no competing interests to declare that are relevant to the content of this article.

AUTHORS FUNDING

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