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Simultaneous estimation of rosuvastatin calcium and ezetimibe in pharmaceutical formulation by RP-HPLC method with forced degradation studies

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ABSTRACT

A simple, specific, accurate and precise RP-HPLC method was developed and validated for the simultaneous estimation of Rosuvastatin Calcium and Ezetimibe in pharmaceutical formulation with forced degradation studies. The method was developed using Enable C 18G column (250 ×4.6 mm, 0.5 µm) with mobile phase consisted of acetonitrile and 1 % acetic acid in water at the ratio of 80:20 %v/v with a flow rate of 1 mL/min .UV detection was carried out at 252 nm. The retention time for Rosuvastatin Calcium and Ezetimibe were found to be 2.928 and 6.553 min respectively. The proposed method was validated for linearity, range, accuracy, precision, robustness, LOD and LOQ. Linearity was observed over a concentration range 0.5-250 µg/ml for Rosuvastatin Calcium (r^2 =0.9978) and 0.5-250 µg/ml for Ezetimibe (r^2 =0.9991). The % RSD for Intraday and Interday precision was found to be 0.56 and 0.36 for Rosuvastatin Calcium and 0.50 and 0.32 for Ezetimibe. The LOD and LOQ were found to be 0.04 µg/ml and 0.16 µg/ml for Rosuvastatin Calcium and LOD and LOQ were found to be 0.03 and 0.11 µg/ml for Ezetimibe respectively. Rosuvastatin Calcium and Ezetimibe were subjected to stress conditions of degradation including acidic, alkaline, oxidative, thermal and photolysis.

Key words: Rosuvastatin Calcium, Ezetimibe, RP-HPLC and Forced Degradation.

INTRODUCTION

Rosuvastatin Calcium. (Fig. 1) is a selective and competitive inhibitor of hydroxyl methyl glutaryl coenzyme A (HMG CoA) reductase, the rate- limiting enzyme that converts 3-hydroxyl-3-methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol. Rosuvastatin is a member of the class 'statins' and chemically designated as (3R, 5S, 6E) - 7 - [4 - (4 - fluorophenyl) - 2 - (N - methylmethanesulfonamido)- 6 - (propan - 2 - yl) pyrimidin - 5 - yl] - 3, 5 - dihydroxyhept - 6 -enoic acid . It is used for the treatment of Hyperlipidemia. It reduces levels of low-density lipoprotein, apolipoprotein B and triglycerides in the blood, while increasing levels of high-density lipoprotein in the management of hyper lipidaemias. Several analytical methods have been reported for the determination of Rosuvastatin Calcium either alone or in combination with other drugs in pure drug, pharmaceutical dosage forms and in biological samples using spectrophotometry [1-10], HPLC[11-20] , UPLC[21] ,HPTLC[22] ,Titrimetry[23] , Chemometric[24] methods have been reported for the determination of Rosuvastatin Calcium in pharmaceutical dosage forms.

Ezetimibe (Fig. 2) chemically designated as (3R, 4S) - 1 - (4 -fluorophenyl) - 3 - [(3S) - 3 - (4 - fluorophenyl) - 3 - hydroxypropyl]- 4 - (4 - hydroxyphenyl) azetidin - 2 - one (Figure 2). It is a selective cholesterol absorption inhibitor, used for the treatment of hyperlipidemia, which potentially inhibits the absorption of biliary and dietary cholesterol. Ezetimibe prevents intestinal absorption of cholesterol without affecting absorption of triglycerides, fatty acids, bile acids and fat-soluble vitamins. The drug is widely used in treatment of hypercholesterolemia and of sitosterolemia. Several analytical methods have been reported for the determination of Ezetimibe either alone or in combination with other drugs in pure drug, pharmaceutical dosage forms and in biological samples using HPLC[25-32],LC-MS[33-34], Voltammetry[35],Spectrofluorometric[36]and GC-MS[37].The combination of Rosuvastatin Calcium and Ezetimibe used to treat dyslipidemia, hyperlipidemia, hypercholesterolemia and to prevent cardiovascular disease including atherosclerosis. Various analytical methods were reported for simultaneous estimation of Rosuvastatin Calcium and Ezetimibe in pure drug, pharmaceutical formulations and biological fluids by spectrophotometric [38] and HPLC [39-47]. The developed method has long retention time, complex mobile phase composition and low linearity range. Therefore in the present study an attempt was made to develop a simple, precise, accurate RP-HPLC method with forced degradation studies for the analysis of Rosuvastatin Calcium and Ezetimibe in pharmaceutical formulation.

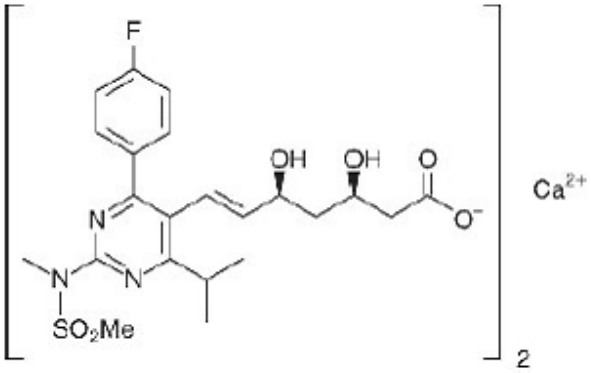

Fig 1. Structure of Rosuvastatin Calcium

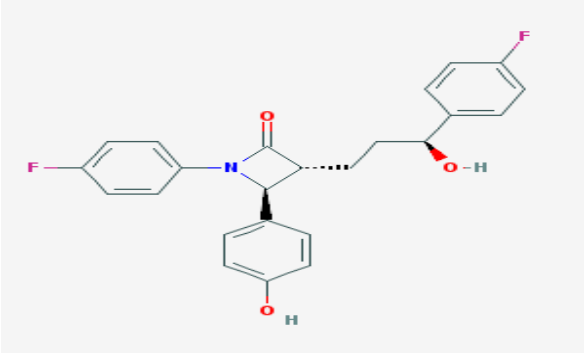

Fig 2. Structure of Ezetimibe

MATERIALS AND METHODS

Materials and Chemicals

Rosuvastatin Calcium and Ezetimibe standard were obtained as gifted sample from pharma industry. Rosuvastatin Calcium and Ezetimibe tablets (ROZAVEL- EZ) containing Rosuvastatin calcium 10 mg and Ezetimibe 10 mg were purchased from local pharmacy. HPLC grade water and acetonitrile was from MERCK India Ltd. HPLC grade methanol was from standard reagent pvt ltd Hyderabad. Analytical grade hydrochloric acid, sodium hydroxide, hydrogen peroxide, acetic acid, was from SD Fine chemicals Mumbai, India. Nylon membrane filters 0.2 µm and 0.45 µm were from PALL life sciences Mumbai, India. Ultrasonicator used was from LAB India Ltd Mumbai. p^H

meter was of Elico LI 120 make. UV Specctrophotometer was of Elico SL 210 model consisted of spectral treats software.

Instrumentation
The chromatographic system used for the method development and validation consisted of Shimadzu HPLC comprising of LC-20AD binary gradient pump, a variable wavelength programmable SPD-20A detector and an SCL 20A system controller. A Rheodyne injector 7725i fitted with a 20 µL loop was used and data were recorded and evaluated by use of LC solutions software version 5.0.

Chromatographic Conditions
Chromatographic analysis was performed on Enable C18 G column (250 x 4.6 mm i.d, 5µ) .The mobile phase consisted of acetonitrile and 1 % acetic acid in water at the ratio of 80:20 %v/v. The flow rate was 1 mL/min, injection volume was 20 µL and detection was carried out at 252 nm using a UV detector.

Preparations of Rosuvastatin Calcium and Ezetimibe stock solution
Stock solution of Rosuvastatin Calcium (1000 µg/ml) and Ezetimibe (1000 µg/ml) was prepared separately by transferring accurately weighed 50 mg of Rosuvastatin Calcium and 50 mg of Ezetimibe into a 50 ml volumetric flask and to it added a 20 ml methanol. The mixture was sonicated for 5 min to dissolve the drug and the solution was diluted up to the mark with methanol. To prepare a binary mixture of Ezetimibe and Rosuvastatin Calcium appropriate volume of standard solution was transferred into a 10 ml volumetric flask and diluted with mobile phase to get a solution containing 150 µg/ml of Ezetimibe and 150 µg/ml of Rosuvastatin Calcium.

Analysis of Rosuvastatin Calcium and Ezetimibe in combined dosage form
Accurately weighed about twenty tablets and average weight of tablet was determined. The tablets were transferred into mortar and triturated to a fine powder form. An a liquate of the powder equivalent to 50 mg of Ezetimibe and 50 mg of Rosuvastatin Calcium was transferred into a 50 ml volumetric flask .To it 20 ml HPLC grade methanol was added and sonicated for 5 min to dissolve the drugs. The content of the flask was kept for 10 min at laboratory temperature and diluted up to mark with HPLC grade methanol this gives a concentration of Ezetimibe 1000 µg/ml and Rosuvastatin Calcium 500 µg/ml. The above solution was filtered through 0.2 µ membrane filter. The 1.5 ml of the filtrate was transferred into a 10 ml volumetric flask and diluted with mobile phase to get a concentration of 150 µg/ml and 150 µg/ml for Ezetimibe and Rosuvastatin Calcium respectively.

Method Validation
The method was validated for accuracy, precision, linearity, specificity, robustness, limit of detection, limit of quantitation.

Linearity
Linearity was performed by preparing standard solutions of Ezetimibe and Rosuvastatin Calcium at different concentration levels. Ezetimibe was prepared in the concentration range of 0.5-250 µg/mL and 0.5-250 µg/mL for Rosuvastatin Calcium. Twenty micro litres of each concentration from both drug solutions was injected in duplicate into the HPLC system. The response was carried out at 252 nm and the corresponding chromatograms were recorded from these mean peak areas were calculated. The calibration curve was plotted by taking concentration on x-axis and peak areas on y-axis for both the drugs.

Accuracy
The accuracy of the method evaluated by standard addition method in which a known amount of standard drug was added to the fixed amount of pre-analyzed tablet solution. Percent recovery of Ezetimibe and Rosuvastatin Calcium was calculated at three concentration levels of 80%, 100% and 120%. The solutions were analyzed in triplicate at each level. The percent recovery and %RSD at each level was calculated.

Precision
Precision of the method was evaluated as system precision and method precision.

To study the system precision, six replicate standard solutions of Ezetimibe and Rosuvastatin Calcium were analysed. The percent relative standard deviation (%RSD) was calculated for both Ezetimibe and Rosuvastatin Calcium.

Method precision of the analytical method was carried out on six preparations from the tablet formulation and percentage amount of Ezetimibe and Rosuvastatin Calcium in the tablet formulation was calculated. The intraday and interday precision study were conducted for both Ezetimibe and Rosuvastatin Calcium. The mean % assay value, standard deviation and percent relative standard deviation was calculated.

Limit of detection (LOD) and Limit of quantitatation (LOQ)
LOD was measured by serially diluting the standard solutions of Ezetimibe and Rosuvastatin Calcium and determining the concentration was response of sample peaks are three times the noise peak .LOQ was measured by serially diluting the standard solutions of Ezetimibe and Rosuvastatin Calcium and determining the concentration was response of sample peaks are ten times the noise peak.

Robustness
Robustness of the method was determined by making slight changes in composition of organic phase ± 5% , flow rate by ± 0.1 ml/min and detection wavelength by ± 2 nm.

Specificity
The specificity of the proposed method was determined against blank and placebo applications. Here mobile phase was used as blank and excipients like starch, lactose, magnesium stearate were used as placebo.

Forced Degradation studies
Different stress conditions were used for the forced degradation studies of formulation .These was also used to evaluate the specificity of the method. All the samples were diluted with mobile phase and filtered through 0.2 µ membrane filter.

Acidic conditions
Weighed accurately about twenty tablets and triturated it to a fine powder form. An a liquate of the powder equivalent to 50 mg of Ezetimibe and 50 mg of Rosuvastatin Calcium was transferred into a 50 ml volumetric flask. To this added a 20 ml of diluent and sonicated for 10 min to dissolve the drug completely. Then 10 ml of 1N HCl was added to it, refluxed for 12 hr at 60 ^{0}C, cooled to room temperature, neutralized with 1N NaOH and diluted up to the mark with the diluent. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipetted 1.5 ml of the above filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent

Alkaline conditions
Weighed accurately about twenty tablets and triturated it to a fine powder form. An a liquate of the powder equivalent to 50 mg of Ezetimibe and 50 mg of Rosuvastatin Calcium was transferred into a 50 ml volumetric flask. To this added a 20 ml of diluent and sonicated for 10 min to dissolve the drug completely. Then 10 ml of 1N NaOH was added to it, refluxed for 6 hr at 60^{0}C , cooled to room temperature, neutralized with 1N HCl and diluted up to the mark with the diluent. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipetted 1.5 ml of the above filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent

Oxidative degradation
Weighed accurately about twenty tablets and triturated it to a fine powder form. An a liquate of the powder equivalent to 50 mg of Ezetimibe and 50 mg of Rosuvastatin Calcium was transferred into a 50 ml volumetric flask. To this added a 20 ml of diluent and sonicated for 10 min to dissolve the drug completely. Then 5 ml of 3 % hydrogen peroxide was added, refluxed for 10 hr at 60 ^{0}C , then cooled to room temperature and diluted up to the mark with diluents. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipetted 1.5 ml of the above filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent.

Thermal degradation
Weighed accurately about twenty tablets and triturated it to a fine powder form. The powder sample was subjected to thermal stress at 80 ^{0}C for about 7 days. An a liquate of the powder equivalent to 50 mg of Ezetimibe and 50 mg of Rosuvastatin Calcium was transferred into a 100 ml volumetric flask. To this added a 20 ml of diluent and sonicated for 10 min to dissolve the drug completely the diluted up to mark with diluents. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipetted 1.5 ml of the above filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent.

Photolytic Degradation

Weighed accurately about twenty tablets and triturated it to a fine powder form. The powder sample was subjected to UV light in a photostability chamber for about 7 days. An a liquate of the powder equivalent to 50 mg of Ezetimibe and 50 mg of Rosuvastatin Calcium was transferred into a 50 ml volumetric flask. To this added a 20 ml of diluent and sonicated for 10 min to dissolve the drug completely the diluted up to mark with diluents. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipetted 1.5 ml of the above filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent.

RESULTS AND DISCUSSION

Optimization of chromatographic conditions

In the present work an analytical method based on RP-HPLC using UV detector was developed and validated for simultaneous estimation of Ezetimibe and Rosuvastatin Calcium in pharmaceutical formulation. The selection of analytical conditions was based on the chemical nature of Ezetimibe and Rosuvastatin Calcium. A systematic study of various factors were undertaken by varying one parameter at a time and keeping all other conditions constant for development of analytical method. Both Ezetimibe and Rosuvastatin Calcium were soluble in polar solvents therefore RP-HPLC was chosen. The selection of stationary phase has been done on the basis of back pressure, resolution, peak shape, theoretical plates and day to day reproducibility in retention time resolution between Ezetimibe and Rosuvastatin Calcium peaks. After evaluating all these factors Enable C18 G column (250 x 4.6 mm i.d, 5µ) was chosen for the analysis. For optimization of mobile phase preliminary trials were conducted under isocratic conditions using mobile phases composed of mixture of solvents like water, methanol, actonitrile and 1 % acetic acid in water in different combination. A mixture of acetonitrile and 1 % acetic acid at a ratio of 80:20 % v/v was found to be most suitable of all the combinations since the chromatographic peaks obtained were have good system suitability parameters. The Flow rate of mobile phase was optimized based on resolution between chromatographic peaks and minimal solvent consumption. The flow rate of mobile phase was changed from 0.5-2 ml/min. It was found from trials that 1 ml/min flow rate was ideal for successful elution of both drugs. For selection of analytical wavelength standard solutions of both drugs were scanned in wavelength range of 200-350 nm. A detection wavelength of 252 nm was selected. The chromatogram of sample was shown in Fig. 3

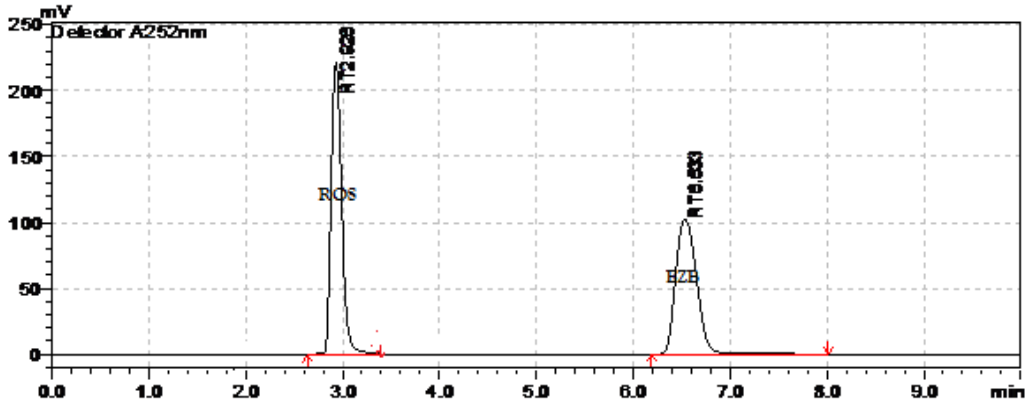

Fig 3. Chromatogram of Rosuvastatin Calcium and Ezetimibe

Method Validation

Linearity was studied by preparing standard solutions at different concentration levels. The linearity ranges for Rosuvastatin Calcium and Ezetimibe were found to be 0.5-250 µg/mL and 0.5-250 µg/mL respectively. The linear regression equation for Rosuvastatin Calcium was found to be 137338x -299929 with correlation coefficient 0.9978. The linear regression equation for Ezetimibe was found to be 92951x -198182 with correlation coefficient 0.9991. The calibration table for Rosuvastatin Calcium and Ezetimibe was shown in Table 1 and Table 2 respectively. The calibration curve of Rosuvastatin Calcium and Ezetimibe were shown in Fig. 4 and Fig. 5 respectively.

Table 1. Linearity data for Rosuvastatin Calcium

Level	Concentration of Rosuvastatin Calcium(µg/mL)	Mean peak area
Level-1	0.5	67885
Level-2	50	6675300
Level-3	100	12480657
Level-4	150	21000463
Level-5	200	26701520
Level-6	250	34346502
Slope		137338
Intercept		-299929
Correlation Coefficient		0.9978

Table 2. Linearity data for Ezetimibe

Level	Concentration of Ezetimibe(µg/mL)	Mean peak area
Level-1	0.5	48653
Level-2	50	4465300
Level-3	100	9058453
Level-4	150	13295900
Level-5	200	18341209
Level-6	250	23361253
Slope		92951
Intercept		-198182
Correlation Coefficient		0.9991

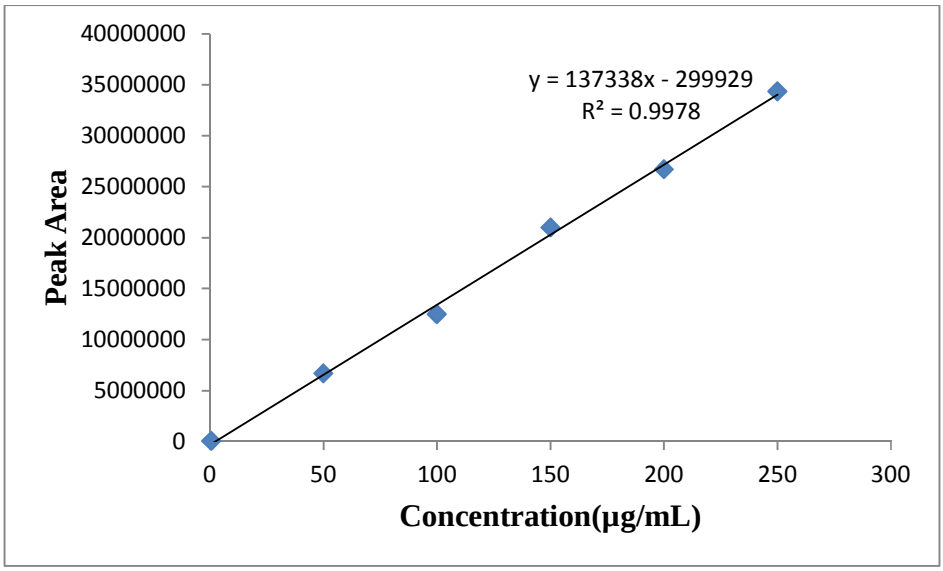

Fig 4. Linearity plot of Rosuvastatin Calcium

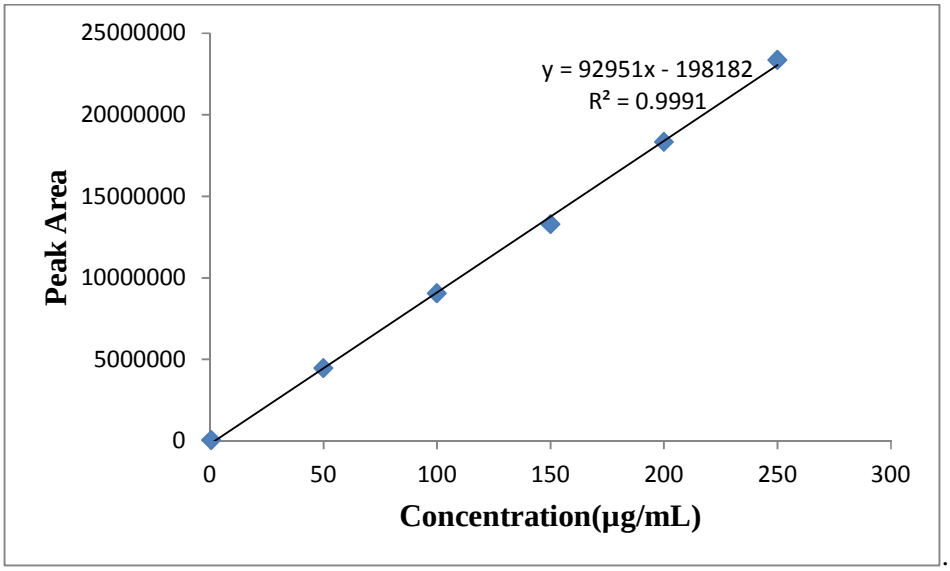

Fig 5. Linearity plot of Ezetimibe

Accuracy

The percent recovery of Ezetimibe and Rosuvastatin Calcium was found to be 99.86-100.33 % and 99.63-100.19%.This indicates the accuracy of the method. The results are shown in Table 3 & 4.

Table 3. Accuracy results of Ezetimibe

Accuracy level (%)	Amount taken(µg/mL)	Amount found(µg/mL)	% Recovery	Mean Recovery	% RSD
80	120	120.23	100.19	100.28	0.24
	120	120.69	100.57		
	120	119.89	100.09		
100	150	150.26	100.17	99.86	0.28
	150	149.48	99.65		
	150	149.68	99.78		
120	180	180.35	100.19	100.33	0.15
	180	180.94	100.52		
	180	180.55	100.30		

Table 4. Accuracy results of Rosuvastatin Calcium

Accuracy level (%)	Amount taken(µg/mL)	Amount found(µg/mL)	% Recovery	Mean Recovery	% RSD
80	120	119.04	99.20	99.63	0.45
	120	119.53	99.60		
	120	120.11	100.09		
100	150	150.69	100.46	99.88	0.53
	150	149.15	99.43		
	150	149.63	99.75		
120	180	179.88	99.93	100.19	0.29
	180	180.97	100.53		
	180	180.21	100.11		

Precision

System precision

The %RSD for Ezetimibe was found to be 0.949 and for Rosuvastatin Calcium was found to be 1.6 which are within the acceptance criteria of not more than 2.0 indicates the precision of the method. The results are shown in Table 5.

Table 5. System precision results for Ezetimibe and Rosuvastatin Calcium

Injection No.	Peak Area of Ezetimibe	Peak Area of Rosuvastatin Calcium
1	13295900	21000463
2	13309873	21383521
3	13127439	21739147
4	13098310	21222749
5	13269432	21979234
6	13438216	21628492
Mean	13256528	21492268
SD	125912	358603
%RSD	0.949	1.6

Method Precision

The %RSD for Intraday and Interday precision assay results of six preparations for Ezetimibe were found to be 0.50 and 0.32 respectively which are within the acceptance criteria of not more than 2.0 indicates the precision of method. The %RSD for Intraday and Interday precision assay results of six preparations for Rosuvastatin Calcium were found to be 0.56 and 0.36 respectively which are within the acceptance criteria of not more than 2.0 indicates the precision of the method. The results are shown in Table 6.

Table 6. Method precision results for Ezetimibe and Rosuvastatin Calcium

Set	Ezetimibe(%Assay)		Rosuvastatin Calcium(%Assay)	
	Intraday(n=6)	Interday(n=6)	Intraday(n=6)	Interday(n=6)
1	100.45	99.85	100.76	100.04
2	99.86	99.43	100.25	99.66
3	100.14	99.67	100.38	99.39
4	100.06	99.54	99.89	100.28
5	100.78	100.12	100.46	99.81
6	99.28	100.23	99.11	99.47
Mean	100.09	99.80	100.14	99.77
SD	0.5134	0.3196	0.5796	0.3408
%RSD	0.50	0.32	0.56	0.36

Limit of detection and Limit of quantitatation

The LOD and LOQ were found to be 0.04 µg/mL and 0.16 µg/mL for Rosuvastatin Calcium and the LOD and LOQ for Ezetimibe were 0.03 µg/mL and 0.11 µg/mL respectively.

Robustness

To evaluate the robustness of the developed method, small deliberate variations in optimized method parameters were made. The effect of change in flow rate , change in composition of mobile phase and detection wavelength on retention time, tailing factor and theoretical plates were studied. The method was found to be unaffected by small changes in flow rate, change in pH, change in composition of mobile phase and detection wavelength as shown in Table 7 and Table 8.

Table 7. Robustness results for Rosuvastatin Calcium

Conditions	% Assay	System Suitability parameters	
		Theoretical Plates	Tailing Factor
Flow Rate 0.8 mL/min	100.48	3465	1.24
Flow Rate 1.2 mL/min	100.11	3217	1.47
Mobile Phase- ACN(90): 1 % AA(10)	100.45	3363	1.31
Mobile Phase- ACN(70): 1%AA(30)	100.63	3261	1.34
Wavelength 254 nm	99.87	3107	1.31
Wavelength 250 nm	100.16	3316	1.35

Table 8. Robustness results for Ezetimibe

Conditions	% Assay	System Suitability parameters	
		Theoretical Plates	Tailing Factor
Flow Rate 0.8 mL/min	100.24	4469	1.19
Flow Rate 1.2 mL/min	100.74	4313	1.26
Mobile Phase- ACN(90): 1 % AA(10)	100.36	4178	1.21
Mobile Phase- ACN(70): 1%AA(30)	100.34	4214	1.21
Wavelength 254 nm	100.47	4139	1.20
Wavelength 250 nm	100.18	4209	1.21

Specificity

Specificity is the ability to unequivocally assess the analyte in the presence of components that may be expected to be present. Typically, these might include impurities, degradants or matrix. Specificity of an analytical method is its ability to accurately and specifically measure the analyte of interest without interference from blank or placebo. The peak purities of Rosuvastatin Calcium and Ezetimibe were assessed by comparing the retention times of standard Rosuvastatin Calcium and Ezetimibe and the sample, and good correlation was obtained between the retention time of the standard and sample. Placebo and blank were injected and there were no peaks. There is no interference of degradation peaks on drug peaks hence, the method is specific. The specificity results are shown in Table 9.

Table 9. Specificity results of the method

Name of solution	Retention Time
Blank	No peaks
Placebo	No peaks
Ezetimibe	6.553 min
Rosuvastatin Calcium	2.928 min

Analysis of commercial formulation

The proposed method was applied for the determination of Rosuvastatin Calcium and Ezetimibe in marketed formulations available (ROZAVEL- EZ TABLETS). The % recovery was found to be 100.8±0.94 and 99.70±0.46 for Rosuvastatin Calcium and Ezetimibe respectively. The results are shown in Table 10.

Table 10. Analysis of Rosuvastatin Calcium and Ezetimibe in commercial formulation

Formulation	Labelled claim(mg)		Amount found*(mg)		%Recovery*±%RSD	
	Rosuvastatin Calcium	Ezetimibe	Rosuvastatin Calcium	Ezetimibe	Rosuvastatin Calcium	Ezetimibe
ROZAVEL- EZ TABLETS	10	10	10.08	9.97	100.8±0.94	99.70±0.46

**Average of three determinations*

Results of Forced degradation studies

Under acidic conditions Rosuvastatin Calcium degraded to 14.26 % and Ezetimibe degraded to 20.24 % .In these stress conditions there is a appearance of four degradant peaks at retention times of 0.801 min, 1.222 min, 1.983 min and 4.153 min. In basic conditions Rosuvastatin Calcium degraded to 16.46 % and Ezetimibe degraded to 26.93 %. Under these conditions there is a appearance of four degradation peaks on chromatogram at retention times of 1.725 min, 2.355 min, 2.752 min and 5.521 min respectively. In oxidative conditions Rosuvastatin Calcium degraded to 16.52 % and Ezetimibe to 24.83 %. Though both the drugs degraded to significant extent in this condition but there is no appearance of degradant peaks on chromatogram. In thermal conditions Rosuvastatin Calcium degraded to 9.32 % and Ezetimibe degraded to 5.08 %. The two degradant peaks appear at retention times of 2.315 and 4.121 min respectively on chromatogram. In photolytic conditions Rosuvastatin Calcium degraded to 5.42 % and Ezetimibe degraded to 6.63 % .The two degradant peaks appear at retention times of 1.601 min and 4.122 min. The system suitability parameters for all degradation studies was shown in Table 11.

Table 11. Forced degradation studies of Ezetimibe and Rosuvastatin Calcium

Stress Conditions	%Drug Recovered	% Drug decomposed	Retention Time (min)	Theoretical Plates	Tailing Factor
Ezetimibe					
Control Sample	99.70	----	6.553	4465	1.20
Acid Degradation (1 N/60°C/12 hr)	79.44	20.24	6.621	3486	1.15
Alkaline Degradation (1 N/60°C/6 hr)	71.77	26.93	6.484	4421	1.34
Oxidative Degradation (3 % H_2O_2/60°C /10 hr)	74.83	24.83	6.832	4323	1.16
Thermal Degradation (80 °C/7 days)	94.59	5.08	6.542	4243	1.11
Photolytic Degradation (1.2 million lux hours/7 days)	93.07	6.63	6.638	4467	1.23
Rosuvastatin Calcium					
Control Sample	100.8	---	2.928	3366	1.30
Acid Degradation (1 N/60°C/12 hr)	87.52	12.26	2.968	2865	1.52
Alkaline Degradation (1 N/60°C/6 hr)	84.30	16.46	3.310	3174	1.32
Oxidative Degradation (3 % H_2O_2/60°C /10 hr)	84.22	16.52	3.114	3426	1.31
Thermal Degradation (80 °C/7 days)	91.36	9.32	2.838	3421	1.30
Photolytic Degradation (1.2 million lux hours/7 days)	95.32	5.42	2.832	3235	1.31

CONCLUSION

The proposed method for the simultaneous estimation of Rosuvastatin Calcium and Ezetimibe validated as per the ICH guidelines and it is simple, specific and reliable. The data generated from the forced degradation studies enabled the evaluation of Rosuvastatin Calcium and Ezetimibe stability under a variety of ICH recommended conditions. These data are valuable for the safety and potency assessment of a drug product. Furthermore, this simple and rapid RP-HPLC method can also be used successfully for the determination of Rosuvastatin Calcium and Ezetimibe in pharmaceutical formulations without any interference from the excipient.

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