RESEARCH ARTICLE

An Improved Efficient Chromatographic Development and Validation for Quantitative Determination of Rosuvastatin Calcium and Cholecalciferol in Solid Pharmaceutical Tablets Dosage Forms

Kallol Jana,* Beduin Mahanti

School of Pharmacy, Techno India University, Salt Lake, Kolkata, West Bengal, India.

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ABSTRACT

The simple, reliable, sensitive and isocratic analytical chromatography was developed for the estimation, separation and validation of both the drugs rosuvastatin calcium and cholecalciferol in tablets dosage forms. Chromatographic elution was attained by C18 thermo, 250 x 4.6 mm column, with particle size 5 µm and 1.5 mL per minute flow rate using mobile phase as methanol : acetonitrile : triethanolamine (55:45:0.4%). Detection of both drugs were monitored at 265 nm. The retention time of rosuvastatin calcium and cholecalciferol were 1.336 and 6.031 minutes, respectively and overall chromatographic run time was approximately 20 minutes. The establishment of linearity was done in concentration of 70–130 µg/mL (r^2 = 0.995) and 7–13 IU (r^2 = 0.983), respectively in rosuvastatin calcium and cholecalciferol. The limit of detection (LoD) 0.88 and 0.11 and limit of quantification (LoQ) was 2.66 and 0.34 for rosuvastatin calcium and cholecalciferol, respectively. Accuracy (recovery) was between 94.34 to 103.51% and 100.82 to 102.46% for rosuvastatin calcium and cholecalciferol, respectively. The developed and validated chromatographic method was within the acceptable limits for both the drugs with precision, robustness, accuracy, ruggedness, and stability of the solution and the relative standard deviation was less then 2. The proposed chromatographic method is precise, accurate, rapid, time effective, simple, reproducible for routine quantitative estimation of both the drugs rosuvastatin calcium and cholecalciferol in solid pharmaceutical tablets dosage forms

Keywords: Rosuvastatin calcium, Cholecalciferol, limit of detection , limit of quantification, Validation.

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INTRODUCTION

The hypolipidemic drug rosuvastatin calcium is a salt of rosuvastatin, a statin that inhibits the conversion of 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) to the synthesis of free cholesterol (mevalonate) by HMG-CoA reductase enzyme. This leads increase low-density lipoprotein (LDL) receptor expression on liver.[1-3] It is chemically calcium salt of bis[(E)-7[4-(4-flurophenyl)-6-isopropyl-2-[methyl(methyl-sulphonyl) amino]pyrimidin-5-yl](3R,5S)-3,5dihydroxyhept-6enoicacid] (Figure 1).

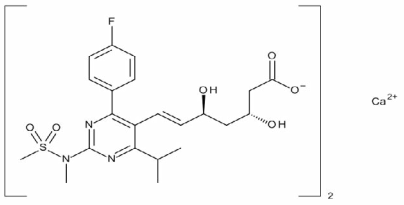

Figure 1: Rosuvastatin calcium

Cholecalciferol is fate soluble steroids most widely prescribed drug for cholecalciferol deficiency. Cholecalciferol synthesis on skin is done under the exposure of UV-B lights and influence the carrier mediated active calcium absorption from small intestine and duodenum.[4,5] The good food sources of cholecalciferol are oily fish, red meat, liver, egg yolks, and cheese.[6,7]. Chemically cholecalciferol is (3β,5Z,7E)-9,10-secocholesta- 5,7,10 (19)-trien-3-ol (Figure 2).

Rosuvastatin calcium when given in combination with cholecalciferol acts synergistically reduce LDL and total cholesterol levels. In combination, it also reduces the dosage requirement of rosuvastatin calcium. Cholecalciferol has mild hypolipidemic activity and also lessens the adverse effect of rosuvastatin calcium like myopathy.

**Author for Correspondence: janakallol@gmail.com*

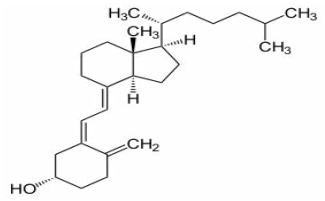

Figure 2: Cholecalciferol

Rosuvastatin calcium and cholecalciferol are available in tablet form containing 10 mg rosuvastatin calcium and 1000IU cholecalciferol. In this method of development work, economic, simple, first and isocratic chromatography was used to estimate the tablet formulations. In the most developed chromatography method was used buffer, Tetrahydrofolate (THF), ortho phosphoric acid and triethylamine in the mobile phase preparation to estimate the cholecalciferol and rosuvastatin calcium in tablet formulations[8-20] (Table 1). An acute use of buffer and acid decreases the column life, increasing estimation cost. The proposed developed research work was validated and optimized according to the international conference on harmonization (ICH) guideline.[21]

Aims and Objectives

The goal and objective of the developed research work was a cost effective, time effective, rapid, reliable, precise and simple chromatographic quantitative analysis of rosuvastatin calcium and cholecalciferol in pharmaceutical tablets dosage forms by using isocratic chromatography reverse-phase high performance liquid chromatography (RP-HPLC) within the acceptance limits.

MATERIAL AND METHODS

Methanol, acetonitrile and triethanolamine were procured from Merck. A gift sample of rosuvastatin was received from MSN Laboratories Pvt. Limited, Telangana, India. The cholecalciferol was purchased from USP. PTFE syringe filter (0.2 µm) and nylon filter (0.2 µm) were purchased from Millipore.

Equipment

The Shimadzu photodiode-array HPLC system SPD-M10A VP, binary pump (LC-10AT VP, LC-20AD), autosampler (SIL-20AHT) and column oven (CTO-10AS VP) with LC solution software.

Instrumentation

The chromatographic quantative analysis was done by C_{18} Thermo, 250 x 4.6 mm, 5 µm particle size column. The mobile phase was prepared by mixing the methanol: acetonitrile: triethanolamine in the ratio of 55:45:0.4%. The elution was done at 1.5 mL/minute and detection monitored at 265 nm. The maintained column temperature 35°C and injection volumes of sample was 20 µL. Filtered the mobile phase through a nylon filter (0.2 µm) before use.

Standard Preparation

Weigh about 25 mg of cholecalciferol accurately, dissolve with 70 mL of methanol and volume up to 100 mL with the same solvent (solution a). Weigh about 100 mg rosuvastatin calcium accurately, dissolve with 70 mL of methanol, add 1 mL of solution a, and volume up to 100 mL with the same solvent (solution b). Transfer 1.0 mL solution b and volume up 10 mL with methanol. Then it is filtered through 0.2 µm PTFE syringe filter. Chromatographic separation in tablets is shown Figure 3.

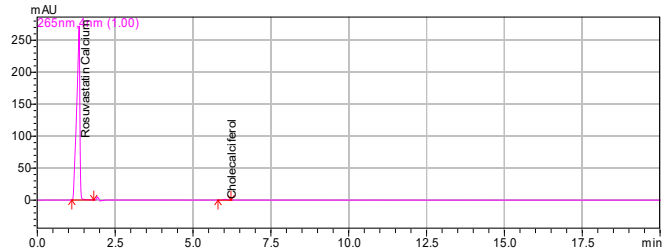

Figure 3: Chromatographic separation of Cholecalciferol and Rosuvastatin calcium

Sample Preparation

Two different brands each of 20 tablets were crushed. Weigh accurately 10 mg equivalent of rosuvastatin calcium, dissolve separately in methanol and volume up to 100 mL with the same solvent. Shake the solutions 5–10 minutes and then sonicate for 30 minutes. Then it is filtered through 0.2 µm PTFE syringe filter.

Quantification of Tablets

The proposed developed research work was to determination of rosuvastatin calcium and cholecalciferol in Rosave D 10 (Alembic Pharmaceuticals Limited) (Sample A) and Rosuvas D 10 (Sun pharma laboratories) (Sample B). The quantification of two brands were calculated with area comparison of the standard and sample. The assay % of the of rosuvastatin calcium and cholecalciferol is calculated Table 2.

RESULTS AND DISCUSSION

HPLC Method Validation and Optimization

For the development of mobile phase different composition and ratio was tried, including methanol: water (10:90), acetonitrile: water (50:50) and flow rate variation but peak shape was not so good. Wavelength scanning was done in between 200–400 nm. Primary development was done with C18, C8 and normal phase columns. The good separation and quantification were attained by C_{18} thermo, 250 x 4.6 mm column, with particle size 5 µm and 1.5 mL/minute flow rate using mobile phase as methanol: acetonitrile: triethanolamine (55:45:0.4%). Detection of both drugs were monitored at 265 nm. This selected developing method allows a sharp peak with good retention time and without tailing.

Method Validation

The developed analytical chromatographic method was validated with system suitability, accuracy, method precision, system precision, linearity, recovery, solution stability, limit of detection (LoD), limit of quantification (LoQ), robustness and ruggedness as per international conference on harmonization (ICH) guidance for industry.[22-24]

Table 1: Methods comparison.

Rosuvastatin Calcium						
S. No.	*Mobile phase*	*Column*	*Wave length*	*Injection Volume µL*	*Flow rate (mL/min)*	*Retention time*
1	KH_2PO_4 (Potassium dihydrogen phosphate):Methanol = (30:70)	RP-18 150 X 3.0 mm (5µm)	234 nm	20	1.0	5.969
2	0.02 M phosphate buffer pH 6.8: Acetonitrile = (60: 40)	C-18, 100 x 4.6 mm, (3µm)	242 nm	20	0.6	3.424
3.	Acetonitrile :THF: Water (pH 3.0) = (68:12:20)	C-18, 250 x 4.6 mm, (5µm), 50°	251 nm	10	0.5	5.4
4.	KH_2PO_4 (Potassium dihydrogen phosphate):Acetonitrile = (50:50) pH 3.0 by phosphoric acid	C-18, 100 x 4.6 mm, (5µm)	243 nm	20	0.5	3.33
5.	Methanol : pH 5.5 ammonium di-hydrgen orthophosphate buffer 0.02 M (75:25)	C-18, 250 x 4.6 mm, (5µm)	272 nm	20	1.0	4.18
6.	Acetonitrile:water pH 3.5 by phosphoric acid =(40:60)	C-8, 150 x 4.6 mm, (5µm)	242 nm	20	1.5	5.2
7.	Acetonitrile : water (75: 25)	C-18, 250 x 4.6 mm, (5µm)	252 nm	20	0.6	8.0
8.	Sod. dihydrogen orthophosphate buffer 0.78 % w/v pH 4.8 : acetonitrile =(50:50)	C-18, 250 x 4.6 mm, (5µm)	241 nm	20	1.0	4.72
9.	Buffer pH4.5 (0.05 M sod.dihydrogen phosphate) : Acetonitrile = (50:50)	C-8, 250 x 4.6 mm, (5µm)	245 nm	10	1.2	3.684
10.	Water pH 2.6: acetonitrile = (30:70)	C-18, 150 x 4.6 mm, (5µm)	220 nm	20	1.0	1.89
11.	Phosphate buffer pH 2.8 : Acetonitrile =(65:35) pH 3.8 by triethylamin	C-18, 250 x 4.6 mm, (5µm)	252 nm	20	1.0	2.147
12.	(Methanol : Acetonitrile) : 0.1% Formic acid (82.8 : 9.2 : 8 v/v)	C-8, 250 x 4.6 mm, (5µm),	265 nm	10	1.2	1.777
As per IP 2018	Ammonium acetate buffer : Acetonitrile: THF = (585:360: 50)	C-18, 250 x 4.6 mm, (5µm)	248 nm	20	1.5	5.600
Developed method	Methanol : Acetonitrile : Triethanolamine (55:45:0.4%,v/v).	C_{18} Thermo, 250 x 4.6 mm, (5µm)	265 nm	20	1.5	1.336
Cholecalciferol						
1.	Methanol : Acetonitrile (50:50 v/v).	C-8, Eurosphere 100-5 250 x 4.6 mm, (5 µm)	265 nm	50	1.0	5.0
2.	(Methanol : Acetonitrile) : 0.1% Formic acid (82.8 : 9.2 : 8 v/v)	C-8, 250 x 4.6 mm, (5 µm),	265 nm	10	1.2	7.423
Developed method	Methanol : Acetonitrile : Triethanolamine (55:45:0.4%,v/v).	C_{18} Thermo, 250 x 4.6 mm, (5 µm)	265 nm	20	1.5	6.031

Table 2: Assay % of Two Different Brands

Different Brands	*Rosuvastatin calcium* ***(% w/w)***	*Cholecalciferol* ***(IU)***
Sample-A (Alembic Pharmaceuticals) Limited Limited)	102.79	1014.0
Sample-B (Sun pharma laboratories)	101.26	1018.8

System Suitability

Six replicates of standards were used to determine system suitability and give the reproducibility of analytical data. tailing factor, R^2 value, linearity, retention time, theoretical plates, LoD (mg/mL) and LoQ (mg/mL) parameters were determined in the standard drug solutions and RSD (relative standard deviation) is less then ± 2% (Table 3). Hear Tailing factor is less than 2, peak is sharp, and clear base line separation.

Table 3: System suitability Parameters

	Rosuvastatin calcium	*Cholecalciferol*
Linearity	70-130 µg/mL	7-13 IU
R^2 value	0.995	0.983
Retention time	1.336	6.031
Theoretical plates	2445.155	9557.641
Tailing Factor	0.962	0.958
LOD (mg/mL)	0.88	0.11
LOQ (mg/mL)	2.66	0.34
RSD%	0.26	1.85

Table 4: Rosuvastatin calcium % recovery study

	Sample A	*Sample B*	*Mean*
80%	94.51	94.67	94.34
	94.21	93.97	
100%	100.10	99.43	100.07
	100.63	100.11	
120%	102.96	103.74	103.51
	103.79	103.52	

Table 5: Cholecalciferol % recovery study

	Sample A	*Sample B*	*Mean*
80%	101.07	102.09	102.22
	102.40	103.29	
100%	101.31	101.42	102.46
	102.83	104.24	
120%	99.75	101.16	100.82
	101.75	100.58	

Accuracy

Accuracy was done for rosuvastatin calcium and cholecalciferol recovery from pre-analyzed tablets formulation with standard drugs addition, 80,100 and 120% concentrations and calculated the recovery of each drug by comparing with each level of the standard concentration (Table 4 and 5).

Precision

The intraday and inter-day precision were studied by six replicates of sample from the same lot of tablets formulation was used and the sample was prepared as same manner as describe in sample preparation.

The result is shown in Table 6 and 7 respectively. The RSD% was found less than 2 for both the drugs in inter-day and intraday precision.

Linearity

Rosuvastatin calcium peak area was linear in 70–130 mg/mL in two replicates and gives two good slope, intercept and correlation value in the calibration curve Y= 18696 X - 15101. R^2=0.995 and Y= 18852 X - 8045. R^2=0.996, respectively (Figure 4).

Table 6: Comparison of Intraday Precision

Sl. No.	*Rosuvastatin calcium %*		*Cholecalciferol %*	
	Sample A	*Sample B*	*Sample A*	*Sample B*
Set-1	102.79	101.26	101.40	101.88
Set-2	98.96	101.01	102.51	104.97
Set-3	102.16	100.44	105.73	104.97
Set-4	99.70	101.76	100.80	104.30
Set-5	100.61	99.82	102.59	100.87
Set-6	98.96	100.43	103.38	102.59
RSD%	1.6278	0.6879	1.685	1.677

Table 7: Inter-day Precision.

Day-1	*Rosuvastatin calcium %*		*Cholecalciferol %*	
	Sample A	*Sample B*	*Sample A*	*Sample B*
Set-1	102.79	101.26	101.40	101.88
Set-2	98.96	101.01	102.51	104.97
Set-3	102.16	100.44	105.73	104.97
Set-4	99.70	101.76	100.80	104.30
Set-5	100.61	99.82	102.59	100.87
Set-6	98.96	100.43	103.38	102.59
RSD%	1.6278	0.6879	1.685	1.677

Day-2	Rosuvastatin calcium %		Cholecalciferol %	
	Sample A	Sample B	Sample A	Sample B
Set-1	104.68	105.86	101.02	102.28
Set-2	105.79	104.83	101.99	101.34
Set-3	104.45	104.29	100.81	100.70
Set-4	103.17	104.25	99.42	100.42
Set-5	104.16	104.21	100.49	100.45
Set-6	104.21	104.91	100.53	100.97
RSD%	0.8148	0.6060	0.8295	0.6971

Day-3	*Rosuvastatin calcium %*		*Cholecalciferol %*	
	Sample A	*Sample B*	*Sample A*	*Sample B*
Set-1	101.64	101.83	100.90	100.84
Set-2	103.78	102.25	103.14	101.38
Set-3	102.14	103.76	101.27	102.68
Set-4	101.99	103.92	101.19	102.91
Set-5	101.78	103.31	100.55	102.19
Set-6	102.34	102.70	101.43	101.64
RSD%	0.7595	0.8164	0.8887	0.7804

To be continued...

	Rosuvastatin calcium %		*Cholecalciferol %*	
	Sample A	*Sample B*	*Sample A*	*Sample B*
Day-1	102.79	101.26	101.40	101.88
	98.96	101.01	102.51	104.97
	102.16	100.44	105.73	104.97
	99.70	101.76	100.80	104.30
	100.61	99.82	102.59	100.87
	98.96	100.43	103.38	102.59
Day-2	104.68	105.86	101.02	102.28
	105.79	104.83	101.99	101.34
	104.45	104.29	100.81	100.70
	103.17	104.25	99.42	100.42
	104.16	104.21	100.49	100.45
	104.21	104.91	100.53	100.97
Day-3	101.64	101.83	100.90	100.84
	103.78	102.25	103.14	101.38
	102.14	103.76	101.27	102.68
	101.99	103.92	101.19	102.91
	101.78	103.31	100.55	102.19
	102.34	102.70	101.43	101.64
RSD%	1.9144	1.7437	1.4164	1.4219

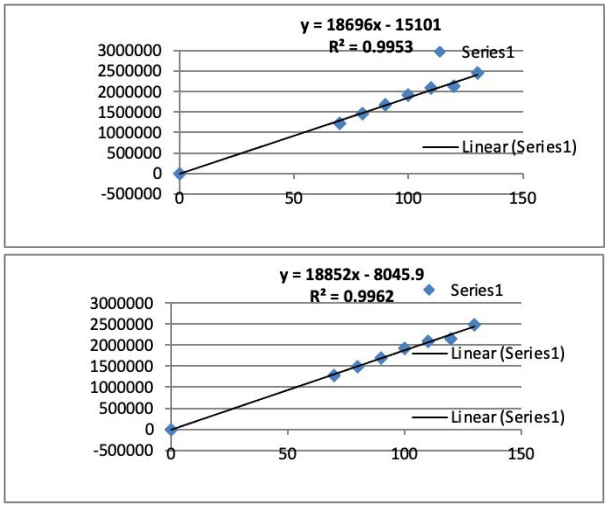

Figure 4: Calibration Curve of Rosuvastatin calcium

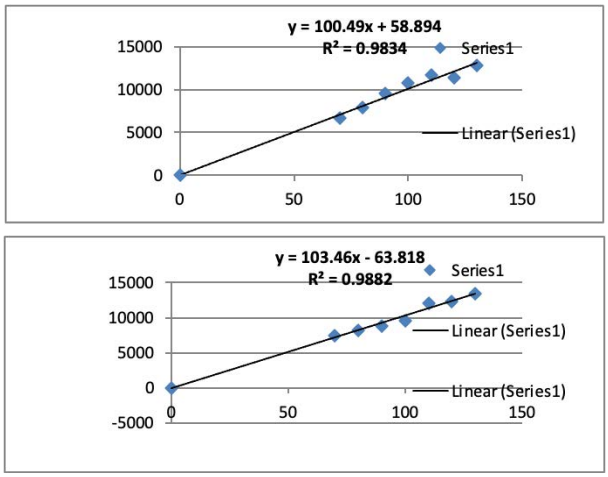

Figure 5: Calibration Curve of Cholecalciferol

Cholecalciferol peak area was linear in 7-13 IU in two replicates and gives two good slope, intercept and correlation value in the calibration curve Y= 100.4 X+ 58.89. R^2=0.983 and Y= 103.4 X-63.81. R^2=0.988 respectively (Figure 5).

Solution Stability

When the samples solution was stored at normal room temperature for 12 hour and analyzed with 2,4,6,10,12 hour interval, the degradation was not observed in rosuvastatin calcium and cholecalciferol. The % of RSD is less than 2.0. Hence it was concluded that both the rosuvastatin calcium and cholecalciferol solution were stable for 12 hours in normal room temperature Table 8.

Ruggedness

Ruggedness was done by different laboratory analysts, different laboratories, interval of days, and different laboratory equipments (Table 9).

Robustness

Robustness was studies by deliberate changes in analytical condition of assay parameters. The change parameters were

Table 8: Solution stability

Time	*Rosuvastatin calcium area*		*Cholecalciferol area*		*Acceptance criteria*
	Sample A	*Sample B*	*Sample A*	*Sample B*	
2 hours	1935874	1938479	10552	10667	
4 hours	1937771	1941129	10521	10688	
6 hours	1930888	1932274	10566	10710	
10 hours	1933479	1936669	10527	10666	% of RSD is ≤2.0
12 hours	1933479	1938837	10527	10617	
Mean	1934298.2	1937477.6	10538.6	10669.6	
SD	2622.743163	3313.41135	19.424212	34.486229	
% of RSD	0.14	0.17	0.18	0.32	

Table 9: Comparison of intermediate precision of rosuvastatin calcium and cholecalciferol

Sl.no.	Rosuvastatin calcium %		Cholecalciferol %	
	Sample A	Sample B	Sample A	Sample B
Set-1	105.26	105.26	102.98	103.00
Set-2	105.57	107.62	103.12	105.23
Set-3	105.11	105.21	102.93	102.79
Set-4	104.38	104.23	102.05	101.93
Set-5	104.68	104.96	102.59	102.49
Set-6	105.38	105.84	102.92	103.65
Mean	105.06	105.52	102.77	103.18
RSD%	0.4282	1.0932	0.3807	1.1174

methanol composition (± 5%), temperature (± 2°) and flow (± 0.1 mL). The detection nanometer was set at 263 and 267 (± 2 nm) (Table 10).

LoD and LoQ

These approach was studied of calibration curve using linearity of 70-130 mg/mL and 7-13 IU for rosuvastatin calcium and cholecalciferol, respectively by using slope, intercept standard deviation. A linear graph was plotted and correlation coefficient was determined. LoD=3.3σ/slop, LoQ=10σ/slop and σ=Y-intercept standard deviation (Table 11).

The goal and objective of the develop research work was for separation and quantification of rosuvastatin calcium and cholecalciferol from the complex tablets matrix with critical concentration range. In this work a simultaneous improved efficient chromatographic development was done

Table 10: Change of methanol concentration (± 5%), temperature (± 2°), flow (±0.1 mL) and detection nanometer (± 2)

Rosuvastatin calcium				*Cholecalciferol*			
methanol : acetonitrile : triethanolamine (57.8:42.2:0.4,v/v)		methanol : acetonitrile : triethanolamine (52.3:47.7:0.4,v/v)		methanol : acetonitrile : triethanolamine (57.8:42.2:0.4,v/v)		methanol : acetonitrile : triethanolamine (52.3:47.7:0.4,v/v)	
Sample A	106.16%	Sample A	104.08%	Sample A	106.25%	Sample A	105.87%
Sample B	103.33%	Sample B	101.70%	Sample B	105.45%	Sample B	103.54%

Rosuvastatin calcium				*Cholecalciferol*			
Wavelength = 263		Wavelength = 267		Wavelength = 263		Wavelength = 267	
Sample A	101.63%	Sample A	102.15%	Sample A	102.29%	Sample A	104.31%
Sample B	100.76%	Sample B	105.10%	Sample B	101.41%	Sample B	105.88%

Rosuvastatin calcium				*Cholecalciferol*			
Column Temperature = 33°		Column Temperature = 37°		Column Temperature = 33°		Column Temperature = 37°	
Sample A	99.77%	Sample A	99.58%	Sample A	100.38%	Sample A	100.01%
Sample B	102.89%	Sample B	100.36%	Sample B	103.43%	Sample B	100.98%

Rosuvastatin calcium				Cholecalciferol			
Flow = 1. 4 mL		Flow = 1. 6 mL		Flow = 1. 4 mL		Flow = 1. 6 mL	
Sample A	100.33%	Sample A	103.61%	Sample A	101.28%	Sample A	103.95%
Sample B	102.41%	Sample B	101.12%	Sample B	103.55%	Sample B	101.52%

and validate for quantitative determination of both the drugs in solid pharmaceutical tablets dosage forms. The proposed time-effective chromatographic method was precise, accurate, rapid, simple and the separation was done by C_{18} thermo, 250 x 4.6 mm column, with particle size 5 µm and 1.5 mL per minute flow rate using mobile phase as methanol: acetonitrile: triethanolamine (55:45:0.4 %) with symmetrical two sharp peak and have clear base line separation. For mobile phase preparation, buffer was used in less quantity for the column's longevity, decreasing the analysis cost. Both drugs' detection were monitored at 265 nm and overall elution was done within 20 minutes. The rosuvastatin calcium and cholecalciferol were easily extract from tablets dosage forms due to solubility in methanol. The standard, sample solutions were found to be stable in methanol. The developed analytical chromatographic method was validated as per ICH and USP guidance for industry.

Linearity was determine for rosuvastatin calcium in 70-130 mg/mL with good slope, intercept and correlation value and regration equations were Y= 18696 X - 15101. R^2= 0.995 and Y= 18852 X - 8045. R^2= 0.996, respectively in two replicates. X is concentration of drug in mg/mL and Y is area of the peak by absorbance.

To determine linearity of cholecalciferol, calibration graph was obtained by plotting concentration against peak area. Linearity was in the concentration range 7-13 IU/mL.

Table 11: LoD, LoQ

Rosuvastatin calcium					
LOD(Limit of detection)=	3.3 σ S	= 0.88	LOQ(Limit of quantification)=	10 σ S	= 2.66

Cholecalciferol					
LOD(Limit of detection)=	3.3 σ S	= 0.11	LOQ(Limit of quantification)=	10 σ S	= 0.34

	Rosuvastatin calcium		*Cholecalciferol*	
Sl.no.	Slope S	y-intercepts	Slope S	y-intercepts
Set-1	18696	15101	100.4	58.89
Set-2	18852	8045	103.4	63.81
SD	110.3086579	4989.3454	2.121320344	3.4789654
Mean	18774	11573	101.9	61.35

The regration equation was Y= 100.4 X+ 58.89. R^2= 0.983 and Y= 103.4 X-63.81. R^2= 0.988, respectively. where X is concentration of drug in IU per mL and Y is area of the peak by absorbance.

In the assay for rosuvastatin calcium, the RSD of the same day (intra-day) 1.6278% for sample A, 0.6879% for sample B and different days (inter-day) 1.9144% for sample A, 1.7437% for sample B. The mean values of intermediate precision were 105.06% for sample A, 105.52% for sample B, RSD 0.4282% for sample A, 1.0932% for sample B respectively.

For the assay of cholecalciferol, the RSD of the same day (intra-day) 1.685% for sample A, 1.677% for sample B and different days (inter-day) 1.4164% for sample A, 1.4219% for sample B. The intermediate precision of cholecalciferol were 102.77% for sample A, 103.18 % for sample B, RSD 0.3807% for sample A, 1.1174% for sample B, respectively.

CONCLUSION

The chromatographic method was developed and validated successfully for quantitative determination of rosuvastatin calcium and cholecalciferol in solid pharmaceutical tablets dosage forms. The efficient time effective simple isocratic chromatographic method is precise, accurate, rapid, reproducible for routine quantitative estimation of both the drugs in solid pharmaceutical tablets dosage forms. The mobile phase is so simple because methanol, acetonitrile and triethanolamine is use, which elute drugs very shortly and decreases the mobile phase consumption. The volume of triethanolamine is use with very less amount, which increases the longevity of column and decrease the analysis cost. The advantage of developed method is that it represents fast, cost effective, simple analytical procedure and conveniently separates rosuvastatin calcium and cholecalciferol and meet the parameters as per ICH guidance for industry. Both drugs' recovery are free from complex tablets matrix and easily extracted from tablets matrix by using methanol. So this method is used to quantitatively analyze the rosuvastatin calcium and cholecalciferol in solid pharmaceutical tablet formulations.

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