A COMPARATIVE REVIEW OF DIFFERENT ANALYTICAL METHOD /TECHNIQUES FOR DETERMINATION OF ROSUVASTATIN CALCIUM WITH VARIOUS COMBINATION

1] Aditi .P. Gade* 2] Dinesh .N. Gaikwad*, 3] Dr.Prasanna.A.Datar, 4] Dr.Rajkumar Shete

DEPARTMENT OF PHARMACEUTICAL QUALITY ASSURANCE DEPARTMENT
RAJGAD DNYANPEETH COLLEGE OF PHARMACY BHOR,PUNE

ABSTRACT:

This review comprehensively covers the analytical methods developed for the quantification of Rosuvastatin Calcium, a prominent statin drug. It addresses various techniques, including High-Performance Liquid Chromatography (HPLC), High-Performance Thin-Layer Chromatography (HPTLC), UV-Visible Spectrophotometry, Liquid Chromatography-Mass Spectrometry (LC-MS), and Method validation criteria are discussed, providing insights into the reliability of these methods for routine analysis in pharmaceutical quality control .The primary focus is on optimizing these methods to ensure precise, accurate, and reliable determination of Rosuvastatin Calcium in pharmaceutical formulations.

Keywords:

Rosuvastatin Calcium, HPLC, HPTLC, UV Spectroscopy, LC-MS, Method Development, Analytical Validation

INTRODUCTION:

Rosuvastatin

Rosuvastatin is a statin used for treating hyperlipidemia and reducing cardiovascular risk by inhibiting HMG-CoA reductase, a key enzyme in cholesterol biosynthesis. This inhibition lowers low-density lipoprotein (LDL) cholesterol levels, reducing the risk of cardiovascular diseases. In addition to its lipid- lowering effects, rosuvastatin has anti-inflammatory and potential neuroprotective properties, making it beneficial for both cardiovascular and neurological health.Rosuvastatin Calcium (RSV) belongs to a class of drugs known as HMG-CoA reductase inhibitors, commonly referred to as statins. It is mainly used to treat hyperlipidemia and lower the risk of cardiovascular diseases such as heart attacks and strokes. Rosuvastatin selectively inhibits the enzyme HMG-CoA reductase, which plays a pivotal role in the cholesterol biosynthesis pathway. By reducing LDL cholesterol, it helps prevent the development of atherosclerosis. Rosuvastatin is considered more potent than other statins like Atorvastatin and Simvastatin, offering superior efficacy at lower doses.[1-3]

Drug Profile [4-6] Structure of rosuvasatin calcium made by chemspace

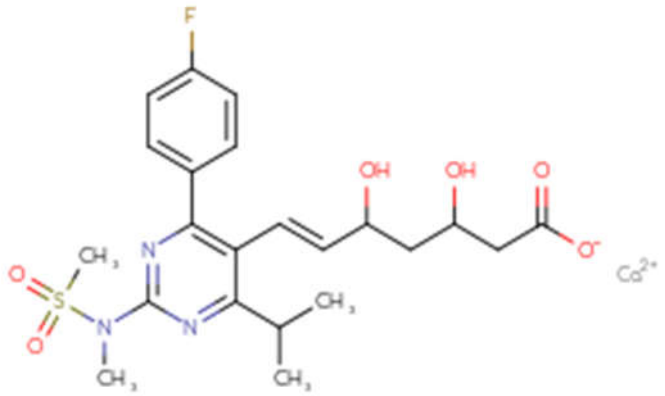

Fig:2 Structure of rosuvasatin calcium

Table1 :

Generic Name:	Rosuvastatin Calcium
Class:	HMG-CoA reductase inhibitor (Statin)
Chemical Formula:	C44H54CaF2N6O12S2
Molecular Weight:	481.54 g/mol
empirical formula	C22H28FN3O6S

Dosage Forms:	Tablets: 5 mg, 10 mg, 20 mg, 40 mg
Administration Route:	Oral
Half-Life:	Approx. 19 hours
Bioavailability:	~20% (increases when taken with food)
Chemical Name:	(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-methyl-5-pyrimidinyl]-3,5-dihydroxy-6-oxo-2,3-dihydro-1H-pyrrole-1-carboxylic acid
Molecular Structure:	It contains a pyrimidine ring connected to a fluorophenyl group and a carboxylic acid functional group.
Appearance:	White to off-white crystalline powder
Odor:	Odorless
Solubility:	Poorly solvable in water,Soluble in

	methanol and ethanol
Melting Point:	174–176°C
pKa (Acidity Constant):	4.6 (for the carboxylic acid group)
Density:	1.34 g/cm³

Therapeutic Uses

Rosuvastatin is widely used for managing hyperlipidemia and reducing cardiovascular risk. It has also been investigated for its potential neuroprotective effects, which could offer therapeutic benefits in neurodegenerative disorders

Pharmacological Classification

Rosuvastatin, on the other hand, belongs to the statin class and is a potent HMG-CoA reductase inhibitor. It is widely used to lower cholesterol levels and reduce the risk of cardiovascular disease (Husain et al., 2019) (Calza, 2009).[7-8]

Market Availability

Rosuvastatin is available in multiple strengths, including 5 mg, 10 mg, 20 mg, and 40 mg tablets. It is frequently prescribed for hypercholesterolemia and cardiovascular risk reduction, particularly in Asian populations

Literature review : HPLC, HPTLC and other techniques.
Reported method for rosuvastatin calcium and with combination of other samples

1] **Palacharla,(2019) Aspirin, rosuvastatin, ezetimibe, and clopidogrel** are the four active components that can be determined in a shorter amount of time using a single HPLC approach. The HPLC technique was created and approved. 3.5 µ HPLC column, X-terra C18 100 × 4.6 mm, acetonitrile (mobile phase B), and KH2PO4 buffer (mobile phase A) were utilised. For separation, the following parameters were used: 230 nm, 1.0 mL/min flow rate, 20 µ injection volume, and room temperature in the column oven. At 0 minutes, mobile phase-B 13%, at 4 minutes, at 8 minutes, 44%, at 14 minutes, 57%, at 17 minutes, 57%, at 20 minutes, and at 25 minutes, 13%, is the gradient program.
As directed by ICH, method validation was carried out with accuracy, precision, linearity, specificity, robustness, and ruggedness. According to the satisfactory validation results, this technology can be used for routine drug product manufacture.[12]

2] **Pisal,(2018) Aspirin, Rosuvastatin, And Clopidogrel**
Using a BISCOF HPLC C18 column (250 mm ×4.6, 5 µm) and a mobile phase made of water at pH 2.51 with 0.1% (v/v) orthophosphoric acid (OPA): acetonitrile in a 50:50 ratio, at a flow rate of 1 ml/min, the isocratic approach produced satisfactory chromatographic separation in the current work. The UV-visible detector was used to track the effluents at 237 nm.It was discovered that the retention times for clopidogrel, rosuvastatin, and aspirin were 16.6 minutes, 7.6 minutes, and 4.3 minutes, respectively. Seven-point calibration curves for linearity were generated for aspirin, rosuvastatin, and clopidogrel in a concentration range of 1–7 µg/ml, with correlation coefficients of 0.999, 0.9989, and 0.9988, respectively. The high recovery rates (99%–101%) suggest that the precision is adequate. The precision study's low percent relative standard deviation (% RSD) findings demonstrate how accurate the methodology is. As advised by the ICH, stability was assessed in the current investigation using an RP-HPLC method for the combination by oxidising the medicines together under a variety of stress conditions, including acid, base, and neutral hydrolysis, as well as thermal and photolytic stress.[13]

3] **Chirag B,(2010) Rosuvastatin Calcium (RC)** in pharmaceutical dosage forms, a straightforward, accurate, exact, and specific reverse phase high performance liquid chromatographic (RP-HPLC) approach was created and validated. HPLC-grade acetonitrile: potassium dihydrogen orthophosphate (50:50 v/v, pH 3) was employed in the mobile phase of a Thermo hypersil reversed phase C18, 5 µm column with 100 x 4.6 mm i.d. in gradient mode. The effluents were seen at 243 nm, and the flow rate was 0.5 ml/min.

The primary RC peak on the chromatogram at retention time was 3.333 ± 0.004 minutes. For the estimation of RC, the limits of detection and quantification were determined to be 0.14 µg/ml and 0.46 µg/ml, respectively. The range of RC recovery was determined to be between 98.50 to 100.17 percent. The suggested approach was effectively used to measure RC quantitatively in pharmaceutical kinds of dose. [9]

4] **Drashti A. Mandale,(2021)- Rosuvastatin And Tenegliptin**
Occasionally, people with Type 2 diabetes also have elevated blood pressure and cholesterol. Multidrug therapy in a single dose regimen is necessary for these disorders, which can lead to several problems.

A gradient high performance reverse phase liquid chromatography method for the estimation of rosuvastatin and tenegliptin in bulk drug samples and synthetic mixtures was developed and validated in the current study using a Luna C18 100A0 (250mm × 4.6mm i.d. 5 µm) column maintained at 25°C and UV detection at 240 nm. At a rate of 1.0 milliliters per minute, the chemicals were eluted gradiently. Teneligliptin and Rosuvastatin had respective average retention durations of 2.583 and 5.458 minutes. [24]

5] **Mahmoud M. Sebaiy ,(2020) Rosuvastatin, simvastatin, and olmesartan in bulk** and dose forms can be determined using a straightforward and sensitive spectrophotometric approach that uses methyl orange and
bromate-bromide-as:reagents.
Materials and procedures: A predetermined amount of methyl orange is used to treat drugs with known excesses of insitu produced bromine, and the absorbance at 510 nm is used to measure the amount of residual un-reacted bromine. The quantity of each medicine that reacted is correlated with the amount of bromine that was eaten. Numerous analytical criteria, including the impact of acidity, bromate-bromide volume, and time on absorption, have been assessed, and the findings have been verified in accordance with ICH guidelines. Results: In the range of 6–11 µg/mL for rosuvastatin, 1–3.50 µg/mL for simvastatin, and 2–7 µg/mL for olmesartan, Beer's rule was followed. [25]

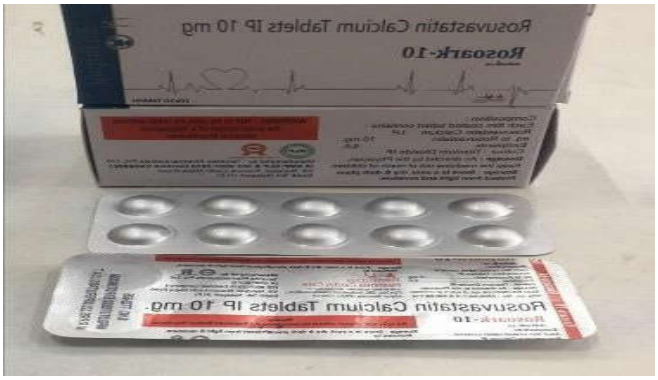

Figure 2: Rosuvastatin(source)

Table 2 : HPLC Analysis Parameters for Rosuvastatin [14-15]

Parameter	**Rosuvastatin**	**Authors**
Instrument Type	HPLC	Dhoru et al. (2023),
Column	**Agilent Inertsil ODS C18** (250 × 4.6 mm, 5 µm).	Dhoru et al. (2023)

Mobile Phase	Methanol and water (**pH = 3** adjusted with **10% Orthophosphoric Acid**) (70:30 v/v)	Dhoru et al. (2023)
Flow Rate	0.8 mL/min.	Dhoru et al. (2023)
Retention Time	7.41 min.	Dhoru et al. (2023)
Detection Wavelength	244 nm.	Dhoru et al. (2023)
Validation Parameters	Linearity range: **5-15 µg/mL**, R^2 = 0.998.	Dhoru et al. (2023)
Alternative Methods	UV spectrophotometry as an alternative approach.	Attimarad et al. (2024)

Table 3:Drug Combination of Rosuvastatin [16-18]

Combination	Column	Mobile Phase	Flow Rate (mL/min)	Detection Wavelength (nm)	Retention Time (min)	Ref
Rosuvastatin + Fenofibrate	Kinetex C18 (5 µm, 4.6×150 mm)	Phosphate buffer (pH 3.0):Methanol (25:75 v/v)	1.0	254	1.997,3.232	17
Rosuvastatin	Zorba	Buffer (pH	1.2	254	1.6,2.5	16

+ Clopidogrel	x- SB C18 (150 mm	3.0):Methanol (60:40 v/v)				

Rosuvastatin + Telmisartan	Kinetex C18 (5 µm, 4.6×150 mm)	Ammonium phosphate monobasic buffer (pH 3.0):Methanol (30:70 v/v)	1.0	242	2.2, 4.3	18

Combination Table 4 for Analytical Techniques (RPHPLC,HPTLC, LC-MS,) for Rosuvastatin Calcium

No.	Technique and Combination	Column	LOD	LOQ	Mobile Phase	Wavelength (nm)	Ref
1	RPHPLC Rosuvastatin	Thermo hypersil reversed phase C18, 5 µm column having 100 x 4.6 mm	0.14	0.46	HPLC grade Acetonitrile : Potassium dihydrogen orthophosphate (50 : 50 v / v, pH 3)	243 nm	[9]
2	Stability-Indicating RP-HPLC method Telmisartan And Rosuvastatin	Oyster ODS3 (150×4.6 mm, 5 µm)	TLS - 1.1066 RST 0.6932	TLS- 3.3532 RST 2 .1005	10 mM phosphate bufer with 1.1 g octane-1-sulfonic acid sodium salt having pH 2.5 (adjusted with 5% OPA) and acetonitrile, with a proportion of 500:500, v/v	242.0 nm	[10]

3	Stability Indicating HPTLC Rosuvastatin Calcium	Merck TLC plates precoated with silica gel 60 F254 (10 cm × 10 cm with 250 µm layer thickness)	9.24 ng/band	28.02 ng/band	Toluene: Ethyl acetate: Methanol (5: 3: 2, v/v/v)	242 nm	[11]
4	LC Method Simultaneous Estimation of Rosuvastatin Calcium and Olmesartan Medoxomil	Symmetry C18 column (4.6mm×150 mm, particle size 5.0µm)	ROS-0.05µg/mL OLM - 0.89µg/mL,	ROS-0.15µg/mL and OLM-2.6µg/mL	Buffer: Acetonitrile: Tetrahydrofuran In The Ratio Of (71:25:4 V/V/V)	248 nm	[23]

Table 5 :Reported analytical liquid chromatography–mass spectrometry methods in mixture with further drugs in biological examples

No.	Drug and Combination	Matrices	Flow rate (mL/min)	Stationary phase	Mobile Phase	Detection	Ref
1	Rosuvastatin	Human plasma	1 mL/min	Phenomenex Luna C18 column (150 £ 4.6 mm, 5 mm)	2% formic acid: MeOH (20:80 v/v)	LC–MS/MS ESIC MRM 482 >258	[19]
2	Ezetimibe And Rosuvastatin	Human plasma	1 mL/min	Luna C18 column (150 £ 4.60 mm, 5 mm)	0.1% (v/v) formic acid:MeOH (20:80 v/v)	LC–MS/MS ESI¡ SIM 480	[20]
3	Rosuvastatin Calcium	Human plasma	1 mL/min	Luna C18 column (150 £ 4.6 mm, 5 mm)	MeOH:0.2% formic acid in water (70:30 v/v)	LC–MS/MS ESIC MRM 482.2 >258.2	[21]

4	Rosuvastatin Calcium and Amlodipine	Plasma]	0.75 mL/min	Zorbax SB C18 column (50 £ 4.6 mm, 3.5 mm)	0.1% formic acid in 5 mM ammonium acetate:MeOH:ACN (20:20:60 v/v/v)	LC–MS/MS ESIC MRM 482.1 >258.3	[22]

Conclusion:

The current review covered the wide range of analytical methods used to assess rosuvastatin calcium .Rosuvastatin calcium in bulk and in combination with other pharmaceutical formulations have been evaluated using a variety of techniques, such as HPLC, HPTLC, UV/Vis-Spectroscopy, LC-MS, etc.

This review and included tables offers a clear comparison of the analytical methods for Rosuvastatin blends with a variety of drugs. The detailed parameters contribution in understanding how different combinations require custom-made analytical approaches.

Rosuvastatin is frequently used with other statins to treat various cardiovascular diseases. It can be used with other medications, such as Vildagliptin (for diabetes), Ezetimibe (for cholesterol management), or even statins like Atorvastatin or many drug, to enhance lipid control. These combinations' efficacy is determined by a variety of parameters, including pharmacokinetics, safety profiles, and possible medication interactions**.**

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