IJBPAS, September, 2024, 13(9): 4535-4542

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

OVERVIEW OF ANALYTICAL TECHNIQUES OF ROSUVASTATIN CALCIUM AND BEMPEDOIC ACID WITH THEIR COMBINATIONS

YADAV A[1*], MEHTA H[2] AND PARMAR K[3]

1: *Research Scholar, faculty of pharmacy, Parul Institute of Pharmacy and Research, Parul University, Vadodara, Gujarat-391760, India

2: Assistant Professor, Parul Institute of Pharmacy and Research, Parul University, Vadodara, Gujarat-391760, India

3: Assistant Professor, Parul Institute of Pharmacy and Research, Parul University, Vadodara, Gujarat-391760, India

***Corresponding Author: Ms. Aarti Yadav: E Mail:** aartiyadav1508@gmail.com

Received 18th July 2023; Revised 20th Sept. 2023; Accepted 10th Dec. 2023; Available online 1st Sept. 2024

https://doi.org/10.31032/IJBPAS/2024/13.9.8327

ABSTRACT

This review gives an overview of the different developed analytical methods and spectroscopic methods of Rosuvastatin calcium and Bempedoic acid in their combination with other drugs. The review implies different analytical methods like RP-HPLC, HPLC-UV, RP-UPLC, UV-VIS, and other methods reported to date. Rosuvastatin calcium belongs to the statin class of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibits. This medicine is used for the treatment of dyslipidemia and can help to reduce the level of "bad cholesterol" as well as the growth of atherosclerosis and the risk of heart disease. Bempedoic acid is a new lipid-lowering drug with a unique mechanism of action Bempedoic acid is used to cure heterozygous familial hypercholesterolemia and heart diseases and to lower cholesterol levels. Rosuvastatin calcium and Bempedoic acid are fixed-dose combinations and are significantly used to treat high cholesterol levels. This review provides a Summary of Work done on Rosuvastatin calcium and bempedoic acid alone or combined with other pharmaceutical drugs.

Keywords: HPLC, HPTLC, UV, Rosuvastatin calcium, Bempedoic acid

INTRODUCTION

Modern society, under Westernization, has transformed our way of life, which has influenced our dietary and health care. This is a rise in the prevalence of different illnesses such as diabetes, hypertension, and hyperlipidemia. Hyperlipidemia is a broad term for a range of illnesses defined by abnormally high levels of lipids and/or lipoproteins in the blood. It is also called hyperlipoproteinemia and is a major risk factor for heart attack.

The main factors affecting of hyperlipidemia are lifestyle changes (bad nutrition, smoking, and alcohol consumption). Obesity, diabetes, hypertension, and unhealthy lifestyle behaviors including smoking and drinking are all risk factors **[1]**.

Rosuvastatin calcium

Rosuvastatin calcium belongs to the lipid-lowering chemical class. It is a class of anticholesterenic. It is chemically bis[(E)-7-[4-(4-flurophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino] pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid]calcium salt . .It is sparingly soluble in water and methanol, slightly soluble in ethanol, and soluble in N, N-dimethyl formamide, acetone, and acetonitrile. It is a competitive inhibitor of HMG-CoA reductase, an enzyme that transforms 3-hydroxy-3-methylglutaryl-coenzyme-A to mevalonate, an initial form of cholesterol **[2]**. Used for the treatment of hyperlipidemia and dyslipidemia, it is also used to prevent coronary artery disease **[3]**. It has the appearance of an off-white and creamish crystalline powder. It is classified as an antihyperlipidemic medication **[4]**.

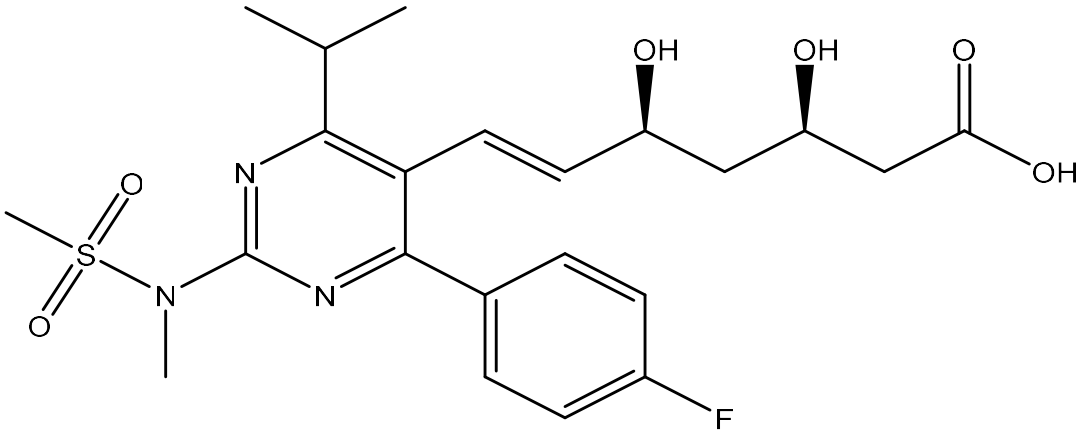

Figure 1: Chemical structure of Rosuvastatin calcium

Bempedoic acid

Bempedoic acid is a drug used to treat high cholesterol (high blood cholesterol levels). Bempedoic acid has approval for the treatment of hypercholesterolemia and hence the most well-tolerated statin medication in individuals with heterozygous hypercholesterolemia or existing atherosclerotic cardiovascular disease who require extra LDL cholesterol lowering. Muscle spasms, discomfort in the back or within the limb, gout, and gastrointestinal disorders such as diarrhea are the most common side effects in clinical trials **[5]**. Bempedoic Acid is a class of (ACL) adenosine triphosphate citrate lyase) inhibitors used once daily in statin-resistant patients to decrease LDL cholesterol levels. Bempedoic acid also called -hydroxy-2,2,14,14-tetramethylpentadecanedioic acid, is a prodrug released in the liver **[6]**.

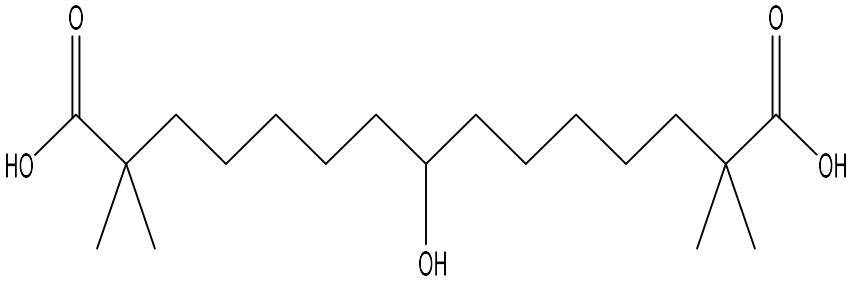

Figure 2: Chemical Structure of bempedoic acid

Analytical Methods for Determination of Rosuvastatin calcium and bempedoic acid in single and combined with other drugs.

This review describes different analytical methods such as HPLC, HPTLC, UV-VIS Spectrophotometric, UPLC, and other methods performed for the mentioned drugs.

S. No.	Title	Description	Ref.no
1	Development and validation of new RP-HPLC method for estimation of Rosuvastatin calcium in pharmaceutical dosage forms	Stationary phase: Thermo scientific C8 (250×4.6mm,5µm) columns Mobile phase: Methanol: Acetonitrile: Water (40:40:20v/v/v/) Flow rate:1.0ml/min Detection: 248nm Retention time: 3.427 min	[7]
2	Stability indicating new RP-HPLC method for determination of Rosuvastatin calcium in pure and tablet dosage forms	Stationary phase: Agilent Eclipse XDC(4.6mm× 50mm,5µm) column Mobile phase: Sodium dihydrogen phosphate: Acetonitrile (50:50v/v) Flow rate:1.2 mL/min Detection: 245 nm Retention time:3.684min	[8]
3	Development of RP HPLC method for estimation of Rosuvastatin calcium by Quality by design	Stationary phase: Shimadzu C18(250×4.6mm, 5um)column Mobile phase: Methanol: Water (90:10 v/v) Flow rate: 0.9 ml/min Detection: 243nm Retention time: 2.6 min	[9]
4	Development and Validation for Simultaneous Estimation of Rosuvastatin Calcium and	Stationary phase: Princeton C18 (250×4.6mm, 5µ) column Mobile phase:Water: Methanol (20:80v/v) Flow rate: 1.0 ml/min	[10]

	Clopidogrel Bisulfate in Pharmaceutical Dosage Form by Reverse Phase-High Performance Liquid Chromatography	**Detection: 240nm** **Retention time:** **Rosuvastatin calcium-2.844 min** **Clopidogrel bisulfate -4.388 min**	
5	**Validated RP-HPLC method for simultaneous determination of Rosuvastatin calcium and Ezetimibe in pharmaceutical dosage form**	**Stationary phase: Enable C18 (250mm ×4.6mm,5µm) column** **Mobile phase: Acetonitrile: water (75:25v/v)** **Flow rate: 0.6ml /min** **Detection: 252nm** **Retention time:** **Rosuvastatin calcium -2.931min** **Ezetimibe-6.631 min**	**[11]**
6	**Development validation of HPTLC method for simultaneous estimation of Rosuvastatin calcium and Aspirin in capsule dosage form**	**Stationary phase: silica gel 60 F254** **Mobile phase:n-hexane : Acetone: Ethylacetate: Formic acid (6:3:1:0.2v/v/v/v)** **Detection: 245 nm** **Flow rate: 0.1ml/min** **RF:** **Rosuvastatin calcium -0.31±0.02min** **Aspirin - 0.60±0.02min**	**[12]**
7	**Simultaneous Estimation of Rosuvastatin calcium and Fenofibrate in bulk in tablet dosage form by UV spectroscopy and RP –HPLC**	**Stationary phase: LUNA C18 (25 mm ×46 mm,5µm) column** **Mobile phase: Acetonitrile: Methanol: Water (50:40:10 v/v/v)** **Flow rate: 0.5ml/min** **Detection: 252 nm** **Retention time:** **Rosuvastatin calcium- 2.60±0.03min** **Fenofibrate - 7.34±0.03 min**	**[13]**
8	**RP-HPLC method development and validation for simultaneous estimation of telmisartan, Rosuvastatin calcium, Amlodipine Besylate in combination**	**Stationary phase: LUNA C18 (250mm×4.6mm,5 µm)column** **Mobile phase: Methanol : Acetonitrile(60: 40 v/v)** **Flow rate:1.0ml/min** **Detection: 242nm** **Retention time:** **Rosuvastatin calcium -2.67 min** **Amlodipine besylate -4.70min** **Telmisartan-7.44min**	**[14]**
9	**Spectrophotometric Estimation of Rosuvastatin Calcium and Glimepiride in Tablet Dosage Form**	**Detection:** **Rosuvastatin calcium:241 nm** **Glimepiride:231 nm** **Concentration range: 10-22µg/ml** **Linearity:** **Rosuvastatin calcium-99.04%** **Glimepiride :100.94%**	**[15]**
10	**Method Development and Validation for Multicomponent Analysis of Rosuvastatin Calcium and Losartan Potassium in Bulk Drug by RP-HPLC**	**Stationary phase: C18 (250mm ×4.6mm,5µm)column** **Mobile phase: Acetonitrile: Methanol: water(20:25:55 v/v/v)** **Flow rate: 0.1 ml/min** **Detection: 233 nm** **Retention time:** **Rosuvastatin calcium-3.55 min** **Losartan potassium- 4.64 min**	**[16]**
11	**Development and validation of HPTLC method for simultaneous estimation of Fenofibrate and Rosuvastatin in tablet dosage form**	**Stationary phase: silica gel 60F254** **Mobile phase : Toluene:Chloroform:n-butanol:Formic acid (6:2:1.5:0.5 v/v/v/v)** **Flow rate:1.5ml/min** **Detection:261 nm** **Rf:** **Fenofibrate- 0.73 ± 0.02 min** **Rosuvastatin- 0.43 ± 0.02 min**	**[17]**
12	**Development and validation of UV spectrophotometric method for simultaneous estimation of propranolol hydrochloride and Rosuvastatin calcium in bulk drug and pharmaceutical dosage form**	**Detection: Propranolol hydrochloride - 289 nm** **Rosuvastatin calcium-243 nm** **Solvent: Methanol** **Concentration range: Propranolol hydrochloride -2-40 µg/ml** **Rosuvastatin calcium-2-42 µg/ml**	**[18]**
13	**Development and validation of RP-HPLC method for estimation of Rosuvastatin calcium solid dispersion tablets**	**Stationary phase: Aquasil** **C18 (100×4.6mm,5µm)coulmn** **Mobile phase: phosphate buffer: acetonitrile (55: 45 v/v)** **Flow rate:1ml/min** **Detection: 240nm** **Retention time: 3.47 ± 0.001 min**	**[19]**

14	**Novel and stability indicating HPLC method for Ezetimibe, Rosuvastatin, and Atorvastatin in tablets form**	**Stationary phase: Agilent ZorbaxSBC18(150mm×4.6 mm,5µm) column Mobile phase :KH2PO4: Acetonitrile (50:50v /v) Flow rate: 1.0ml/min Detection: 230nm Retention time: Ezetimibe -15.3 min, Rosuvastatin - 9.0 min Atorvastatin -17.1 min**	**[20]**
15	**Stability indicating RP UPLC for simultaneous quantification of bempedoic acid and ezetimibe in bulk pharmaceutical formulations**	**Stationary phase: Acquity C18 (50mm ×21mm,1.7µm)column Mobile phase: Methanol: Acetonitrile: Water (50:30:20v/v/v) Flow rate: 0.5 ml/min Detection: 260nm Retention time: Bempedoic acid -1.827 min Ezetimibe-3.577 min**	**[21]**
16	**A novel HPLC method developed for the estimation of bempedoic acid and ezetimibe in bempedoic acid and ezetimibe pharmaceutical dosage forms of tablets**	**Stationary phase: Ascentis C18 (150mmx 4.6mm,5µm)column Mobile phase: Potassium dihydrogen phosphate; Acetonitrile (50:50v/v) Flow rate:1.0ml/min Detection: 230nm Retention time: Bempedoic acid -2.240 min Ezetimibe -2.956 min**	**[22]**
17	**Simultaneous Determination of Bempedoic Acid and Ezetimibe in Rat Plasma Using HPLC–PDA and its application to a pharmacokinetic study**	**Stationary phase: X-bridge C18(150mm×4.6mm,3.5µm)column Mobile phase: Formic acid: acetonitrile (40:60v/v) Flow rate: 1ml/min Detection: 236nm**	**[23]**
18	**Development and validation of a novel cleaning validation and assay method for simultaneous estimation of rosuvastatin and fenofibrate by RP –HPLC**	**Stationary phase: agilentzorbax RP-Cyano (250mm×4.6mm,5µm)column Mobile phase: Potassium dihydrogen phosphate buffer (OPA):Methanol: Acetonitrile (45:33:22v/v/v) Flow rate: 1.5ml/min Detection: 252nm Retention time: Rosuvastatin-3.6min Fenofibrate- 10.01 min**	**[24]**
19	**Method Development and validation for the Simultaneous Estimation of Rosuvastatin calcium and Amlodipine in Bulk and its Formulation using Reverse –Phase High reverse-performance Liquid Chromatography**	**Stationary phase: Aqusil C18 (4.6mm×250mm,5µm)column Mobile phase: Acetonitrile: Phosphate buffer: Methanol (30:60:10 v/v/v) Flow rate: 1ml/min Detection: 251nm**	**[25]**

CONCLUSION

As per the review, it was concluded that for Rosuvastatin calcium and Bempedoic acid, different analytical methods and spectroscopy methods are available for single–single drugs. From the review, it was observed that still, there are no developed analytical methods available in combination with Rosuvastatin calcium and Bempedoic acid. Thus, it is concluded that to develop analytical methods on RP-HPLC in this combination of Rosuvastatin Calcium and Bempedoic acid. The developed methods were simple, accurate precise, and reproducible in nearly all methods of RP-HPLC and UV absorbance which provide with best available reliability, repeatability, and sensitivity.

REFERENCES

[1] Attar T, Gharge V, Review Article on Hyperlipidemia, International Journal of

Pharmaceutical Research and Applications, 6(6), 2021, 468-471.

[2] Donthula S, Kumar MK, Teja GS, Kumar M, Janapati YK, A new validated RP-HPLC method for determination of Rosuvastatin calcium in bulk and pharmaceutical dosage form.DerPharmaciaLetter, 3(3), 2011, 350-356

[3] Dumasiya Mr., Bhatt Kk, Patel b, Joshi nk, Development and validation of stability indicating RP-HPLC method for estimation of Rosuvastatin calcium and Aspirin in combined dosage form, An international journal of pharmaceutical science, 1(3), 2012, 2421-2439.

[4] Patel B, Jadav A, Solanki H, Parmar S, Parmar V, Captain A, Development and validation of a derivative spectroscopic method for the simultaneous estimation of rosuvastatin calcium and fenofibrate in tablet, International Journal of Pharma Research & Review, 2(7), 2013, 1-6.

[5] Vejendla A, Talari S, Ramu G, Rajani C, Characterization of novel stress degradation products of Bempedoic acid and Ezetimibe using UPLC–MS/MS: development and validation of stability-indicating UPLC method, Future Journal of Pharmaceutical Sciences, 7, 2022, 1-3.

[6] Kasa Maheshwari, Satla Shobha Rani, Validated method for the simultaneous estimation of bempedoic acid and ezetimibe in bulk and tablet formulation by RP-HPLC method, World Journal of Pharmaceutical Science, 10(09) 2022, 33-41. https://doi.org/10.54037/WJPS.2022.100903

[7] Jana K, Mahanti B, Development and Validation of a new improved RP-HPLC Method for estimation of Rosuvastatin calcium in Pharmaceutical dosage form, Research Journal of Pharmacy and Technology, 13(6), 2022, 2886-2892.

[8] Hassouna ME, Salem HO, Stability indicating new RP-HPLC method for the determination of rosuvastatin calcium in pure and tablet dosage forms, International Journal of Applied Pharmaceutical and Biological Research,2(2), 2017, 11- 27.

[9] Lode RV, Lohe NS, Kosalge SB, Pimpalshende SV, Urade PK, Development of RP-HPLC Method for Estimation of Rosuvastatin Calcium by Quality by Design Approach, International Journal of Research Publication and Reviews, 2(9), 2021,1141-1152.

[10] Pimple A, Kakde R, Development and validation for simultaneous estimation of Rosuvastatin calcium and Clopidogrel bisulfate in pharmaceutical dosage form by reverse phase-high performance liquid chromatography, International Journal of

Pharmacy and Biological Sciences, 10(2), 2020, 296-303.

[11] Swathi S, Kumar HT, Rao PK, Validated RP-HPLC method for simultaneous determination of Rosuvastatin calcium and Ezetimibe in the pharmaceutical dosage form, International Journal of Pharmacy And Pharmaceutical Science, 7(4), 2015, 209-213.

[12] Tank PH, Vadalia KR, Dedania ZR, Development and validation of HPTLC method for simultaneous estimation of Rosuvastatin calcium and Aspirin in capsule dosage form, International Journal of Pharmaceutical Science Research, 3(10), 2012, 3867-3870.

[13] Karunakaran A, Subhash V, Chinthala R, Muthuvijayan J, Simultaneous estimation of Rosuvastatin calcium and Fenofibrate in bulk and tablet dosage form by UV-spectrophotometry and RP-HPLC, Stamford Journal of Pharmaceutical Sciences, 4(1), 2011,58-63.

[14] Mistry RP, Shah C, Jat R, RP-HPLC method development and validation for simultaneous estimation of telmisartan, Rosuvastatin calcium, and Amlodipine besylate in combination, Folia Medica, 64(1), 2022, 103-109.

[15] Afroz A, Haque T, Talukder MU, Islam SM, Spectrophotometric estimation of Rosuvastatin calcium and Glimepiride in tablet dosage form, Asian Journal of Pharmaceutical Analysis, 1(4), 2011, 74-78.

[16] Kumar P, Ankalgi AD, Kaushal P, Ashawat MS, Method development and validation for multicomponent analysis of rosuvastatin calcium and losartan potassium in bulk drug by RP-HPLC, Journal of Drug Delivery and Therapeutics, 15(10), 2020, 76-84.

[17] Kalyankar GG, Ghariya VV, Bodiwala KB, Lodha SR, Joshi SV, Development and validation of HPTLC method for simultaneous estimation of Fenofibrate and Rosuvastatin in tablet dosage form, Journal of Pharmacy and Applied Sciences, 3(1), 2016, 1-7.

[18] Shinde NG, Aloorkar NH, Development and validation of UV spectrophotometric method for simultaneous estimation of propranolol hydrochloride and rosuvastatin calcium in bulk drug and pharmaceutical dosage form, International Journal of Applied Pharmaceutics, 4(5), 2015, 55-59.

[19] Hazra K, Chowdary A, Devgan M, Shukla R, Sarkar B, Suryawanshi A, Development and validation of RP-HPLC method for estimation of Rosuvastatin calcium solid dispersions tablets, Asian Journal of Pharmaceutical Research, 4(3), 2014, 122-125.

[20] Vanaja M, Reddy YN, Sreeramulu J, Novel and stability indicating HPLC method for Ezetimibe, Rosuvastatin, Atorvastatin in tablets form, Caribbean Journal of Sciences and Technology, 8(1), 2020, 01-24.

[21] Yarra US, Gummadi S, Stability indicating RP-UPLC method for simultaneous quantification of bempedoic acid and ezetimibe in bulk and pharmaceutical formulations, Future Journal of Pharmaceutical Sciences, 7, 2021,1-9.

[22] Reddy R, Jadi S, A novel HPLC method developed for the estimation of bempedoic acid and ezetimibe in bempedoic acid and ezetimibe pharmaceutical dosage forms of tablets, Research Journal of Chemistry and Environment, 26(3), 2022, 94-101.

[23] Karla VR, Raghasudha M, Chitta R, Simultaneous determination of bempedoic acid and ezetimibe in rat plasma using HPLC–PDA and its applications to a pharmacokinetic study, Chemistry Africa, 5(4), 2022, 917-927.

[24] Celina N, Anushka B, Development And Validation of A Novel Cleaning Validation and Assay Method For Simultaneous Estimation of Rosuvastatin And Fenofibrate By RP-HPLC, World journal of pharmaceutical Research, 7(3), 2018, 1454-1465.

[25] Peddapalli H, Method Development and Validation for the Simultaneous Estimation of Rosuvastatin and Amlodipine in Bulk and its Formulation using Reverse-phase High-Performance Liquid Chromatography, Asian Journal of Pharmaceutics, 12(04), 2018, 1-6.