ORIGINAL ARTICLE

A Stability-Indicating Ultra-Performance Liquid Chromatography Method Development and Validation for the Simultaneous Estimation of Rosuvastatin and Bempedoic Acid in Bulk and Pharmaceutical Dosage Form

H. Neelofar[1], D. Ranganayakulu[2]

[1]Assistant Professor, Department of Pharmaceutical Analysis, Sri Padmavathi School of Pharmacy, Tiruchanoor, JNTUA, Ananthapuram, Andhra Pradesh, India, [2]Professor & Principal, Department of Pharmacology, Sri Padmavathi School of Pharmacy, Tiruchanoor, JNTUA, Ananthapuram, Andhra Pradesh, India

Abstract

Aim: This study aimed to develop and validate a rapid, accurate, and stability-indicating ultra-performance liquid chromatography (UPLC) method for the simultaneous estimation of Rosuvastatin and Bempedoic acid in bulk and pharmaceutical dosage form. **Materials and Methods:** Chromatographic separation was achieved using an Acquity UPLC BEH C18 column (50 mm × 1.1 mm, 1.7 µm) with a mobile phase consisting of Acetonitrile: Ammonium formate pH-3.0/OPA in a ratio of 20:80 v/v, at a flow rate of 0.2 mL/min. Detection was carried out at 240 nm. The method was validated in accordance with ICH Q2(R1) guidelines for system suitability, linearity, precision, accuracy, specificity, robustness, limit of detection, and limit of quantitation. Forced degradation studies were performed under acidic, basic, oxidative, thermal, and photolytic conditions to evaluate the stability-indicating nature of the method. **Results and Discussion:** Rosuvastatin and Bempedoic acid were well resolved with retention times of 0.627 and 1.254 min, respectively. The method demonstrated excellent linearity ($r^2 > 0.999$), with acceptable precision (%relative standard deviation < 2%), recovery (98–102%), and robustness. Significant degradation was observed under acid and oxidative stress, while the method successfully resolved all degradation peaks from the analytes. **Conclusion:** The developed UPLC method is sensitive, reliable, and stability-indicating. It is suitable for routine analysis and quality control of Rosuvastatin and Bempedoic acid in combined dosage forms.

Key words: Bempedoic acid, forced degradation, method validation, rosuvastatin, stability-indicating method, ultra-performance liquid chromatography

INTRODUCTION

Pharmaceutical formulations that include two or more active pharmaceutical ingredients (APIs) in a single dosage form are known as fixed-dose combinations, or FDCs. WHO (2003). FDCs are essential to contemporary pharmacotherapy, especially when it comes to treating chronic and complex illnesses. Improved patient adherence, less pill burden, streamlined treatment plans, and possibly additive or synergistic therapeutic effects are their main benefits. FDCs are frequently used to treat diseases such as dyslipidemia, HIV/AIDS, TB, hypertension, and type 2 diabetes.[1-3]

A thorough grasp of each drug's pharmacokinetic and pharmacodynamic profiles is necessary for the creation of an FDC. To guarantee effectiveness, safety, and chemical compatibility within a single formulation, factors such as absorption, metabolism, elimination, and possible drug-drug interactions must be carefully considered.[2,3] Elevated

Address for correspondence:
H. Neelofar, Department of Pharmaceutical Analysis, Research Scholar, Sri Padmavathi School of Pharmacy, Tiruchanoor, JNTUA, Ananthapuram, Andhra Pradesh, India. E-mail: neelofar431@gmail.com

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low-density lipoprotein cholesterol (LDL-C) is a hallmark of dyslipidemia, a significant risk factor for atherosclerotic cardiovascular disease. The rate-limiting enzyme in cholesterol biosynthesis, 3-Hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, is inhibited by statins, like rosuvastatin, which are first-line treatments for LDL-C reduction. Nevertheless, a small percentage of patients either do not attain ideal lipid control or suffer from side effects linked to statins, which restricts their use.[4-6] An additional mechanism of action provided by the novel lipid-lowering agent Bempedoic acid is the inhibition of ATP citrate lyase, an enzyme upstream of HMG-CoA reductase in the cholesterol synthesis pathway. Interestingly, Bempedoic acid is a prodrug that acts on the liver but not the skeletal muscle, which lowers the possibility of statin-related muscle side effects.[7]

For patients who are statin-intolerant or who need extra lipid-lowering effectiveness, the combination of bempedoic acid and rosuvastatin has shown better LDL-C lowering than monotherapy, making it a promising therapeutic option.[8] Due to their complementary modes of action, this FDC is becoming more and more popular in the treatment of dyslipidemia. A thorough review of the literature was conducted to choose medications in various categories for which analytical method development and validation are required. A review of the literature was also conducted in order to choose the analytical techniques. As part of this, the first class of medications – antihyperlipidemic medications – was selected. Rosuvastatin and bempedoic acid together are a well-known FDC that has been selected for that.[9,10]

For this combination, two high-performance liquid chromatography (HPLC) methods were reported; it was found that the retention time was longer in these methods, and the reported ultra-performance liquid chromatography (UPLC) method, which has not yet been investigated, is based on the methods. Therefore, the purpose of this work is to develop a UPLC method.[11,12] The need for validated analytical techniques that can estimate multiple APIs in a single formulation at the same time has become crucial as the pharmaceutical industry continues to grow its FDC portfolio. Such techniques need to be robust, precise, sensitive, and specific to receive regulatory approval and be used for quality control. Furthermore, in accordance with ICH guidelines, stability studies are essential for evaluating the formulation's degradation profile under a variety of stress conditions (such as heat, light, acid/base hydrolysis, and oxidation).[13,14]

UPLC offers significant advantages over traditional HPLC in terms of resolution, speed, and sensitivity.[15] Therefore, developing a stability-indicating UPLC method for the simultaneous estimation of Rosuvastatin and Bempedoic acid in bulk and formulation is crucial. Such a method not only supports quality assurance during production but also ensures therapeutic consistency and regulatory compliance throughout the product's shelf life.[16-19]

MATERIALS AND METHODS

Chemicals and reagents

Rosuvastatin calcium and Bempedoic acid working standards were procured from Shree Icon Pharmaceutical Laboratories, Vijayawada. Commercially available fixed-dose combination tablets containing both drugs were used for analysis. HPLC-grade acetonitrile, Ammonium formate (Analytical Reagent), and water were purchased from Merck (India). Orthophosphoric acid (OPA, AR grade) was used for buffer preparation. All other chemicals used were of analytical grade. Rosuvastatin and bempodoic acid combination tablet containing ROS10 mg and BEM 180 mg was purchased from the local medical store.

Instrumentation and software

The chromatographic analysis was performed using an ACQUITY UPLC system (Waters) equipped with Empower 2.0 software and with a Photodiode Array (PDA) detector for data acquisition and processing. A pH meter (Model: pH700) from Eutech Instruments was used for pH adjustments of buffer solutions. Weighing of samples and reagents was carried out using an analytical balance (Model: BSA224S-CW) manufactured by Sartorius. All volumetric measurements, including those involving pipettes, beakers, and burettes, were performed using Class-A glassware supplied by Borosil. An ultrasonicator (Model: UCA 701) from Unichrome was employed for degassing of solvents and sample preparation. The mobile phase was delivered through an isocratic pump model from Waters to maintain a consistent flow throughout the analysis.[17]

Chromatographic conditions

The chromatographic analysis was performed using a Waters UPLC system equipped with a PDA detector. A sample injection volume of 5 µL was used for each run. The mobile phase consisted of Acetonitrile and Ammonium Formate buffer (pH adjusted to 3.0 with OPA) in a 20:80 v/v ratio, and the separation was carried out in isocratic mode. The analytical column used was an Acquity UPLC BEH Shield RP-18 column with dimensions 50 mm × 1.0 mm and a particle size of 1.7 µm. The flow rate of the mobile phase was set at 0.2 mL/min, and the total run time for the analysis was 3.0 min. Detection was carried out at a wavelength of 240 nm, and all chromatographic operations were conducted at ambient temperature (25°C).

Preparation of ammonium formate buffer

6.30 g of Ammonium formate was dissolved in 1 L of HPLC grade water and adjusted its pH-3.0 with OPA. Filtered through 0.22µ membrane filter paper.

Table 1: Results of the Bempedoic acid and Rosuvastatin trial-1

S.No	Name	Retention time	Area	USP resolution	USP tailing	USP plate count
1	Bempedoic acid	1.298	875607		0.98	1206
2	Rosuvastatin	1.818	85293	1.58	1.23	1653

Table 2: Results of the Bempedoic acid and Rosuvastatin trail-2

S.No	Name	Retention time	Area	USP resolution	USP tailing	USP plate count
1	Bempedoic acid	1.550	1562044		1.31	1025
2	Rosuvastatin	2.230	328197	6.14	1.17	2719

Table 3: Results of the Bempedoic acid and Rosuvastatin trail-3

S.No	Name	Retention time	Area	USP tailing	USP plate count	USP resolution
1	Bempedoic acid	1.661	5065806	1.05	1302	
2	Rosuvastatin	3.153	801330	1.06	2203	2.61

Table 4: Results of the Bempedoic acid and Rosuvastatin trail-4

S.No	Name	Retention time	Area	USP resolution	USP tailing	USP plate count
1	Bempedoic acid	0.573	1066766		1.17	2389
2	Rosuvastatin	0.746	190664	3.60	1.18	2986

Table 5: Results of the Bempedoic acid and Rosuvastatin trail-5

S.No	Name	Retention time	Area	USP resolution	USP tailing	USP plate count
1	Bempedoic acid	0.621	874187		1.03	4266
2	Rosuvastatin	1.089	195750	7.07	0.97	8008

Table 6: Chromatogram of Bempedoic acid and Rosuvastatin trail-6

S. No	Name	RT	Area	USP resolution	USP tailing	USP plate count
1	Bempedoic acid	0.627	3369565		1.07	8474
2	Rosuvastatin	1.254	754001	6.60	0.96	13810

Table 7: System suitability results

Parameter	Bempedoic acid	Rosuvastatin
Retention time (min)	0.627	1.254
Tailing factor	1.07	0.96
Theoretical plates	8474	13810
%RSD (Peak area)	0.60	0.36

Table 8: Results of the linearity study of the UPLC method

Drug	Linearity range (µg/mL)	Correlation coefficient (r^2)
Rosuvastatin	10–60	0.9998
Bempedoic acid	45–270	0.9997

UPLC: Ultra-performance liquid chromatography

Table 9: Results of the accuracy study of UPLC method

Level (%)	Rosuvastatin (% Recovery)	Bempedoic acid (% Recovery)
50	99.0	99.5
100	100.1	100.6
150	99.7	99.6

UPLC: Ultra-performance liquid chromatography

Preparation of mobile phase

Mobile phase was prepared by mixing Ammonium formate pH-3.0/OPA and ACN taken in the ratio 80:20. It was filtered through 0.22 µ membrane filter to remove the impurities that may interfere in the final chromatogram.

Table 10: Results of the precision study of UPLC method

Drug	Intra-day (%RSD)	Inter-day (%RSD)
Rosuvastatin	0.36	0.27
Bempedoic acid	0.66	0.71

UPLC: Ultra-performance liquid chromatography

Table 11: Results of the LOD and LOQ study of UPLC method

Drug	LOD (µg/mL)	LOQ (µg/mL)
Rosuvastatin	0.12	0.40
Bempedoic acid	0.54	1.80

UPLC: Ultra-performance liquid chromatography, LOD: Limit of detection, LOQ: Limit of quantitation

Preparation of stock and standard solutions

Standard stock solutions of Rosuvastatin and Bempedoic acid were prepared separately by dissolving 180 mg of Bempedoic acid, 40 mg of Rosuvastatin working standard into a 100 mL volumetric flask, adding 70 mL of diluent, and sonication was used to thoroughly dissolve the sample and bring the volume to the desired level (Stock solution).

Further pipette 5 mL of the aforesaid stock solutions into a 50 mL volumetric flask, dilute to the mark with diluent (180 ppm of Bempedoic acid and 40 ppm of Rosuvastatin).

Sample preparation

Twenty tablets were accurately weighed and powdered. A quantity equivalent to 28.4 mg of Bempedoic acid and Rosuvastatin sample into a 10 mL volumetric flask, add Diluent and sonicate it for up to 30 min to dissolve it completely and make the volume up to the mark with the same solvent (Stock solution).

Further pipette 1 mL of the above stock solutions into a 10 mL volumetric flask and dilute up to the mark with diluent. Then it is filtered through a 0.22-µm injection filter (180 ppm of Bempedoic acid, 40 ppm of Rosuvastatin).[9]

Analytical method validation

The developed method was validated as per the ICH Q2(R1) guidelines for the following parameters [Tables 1-13]:

System suitability

System suitability was evaluated by injecting six replicates (180 µg/mL and 40 µg/mL) of the respective Bempedoic acid and rosuvastatin standard solution and observing parameters such as retention time, theoretical plates, tailing factor, and % relative standard deviation (RSD). If the criteria were not specified, consider the values as follows, tailing factor for the

Table 12: Percentage purity for Bempedoic acid and Rosuvastatin

Brand	Drug	Area	Avg sample area (*n*=5)	Standard wt (mg)	Sample wt. (mg)	Label amount (mg)	Standard purity	Amount found (µg/mL)	% assay
Razel-BM 40	Bempedoic acid	3323541	3334065	180	28.4	180	99.9	17.95	99.7
		3344589							
	Rosuvastatin	754824	755675	40	28.4	40	99.8	4.012	100.3
		756525							

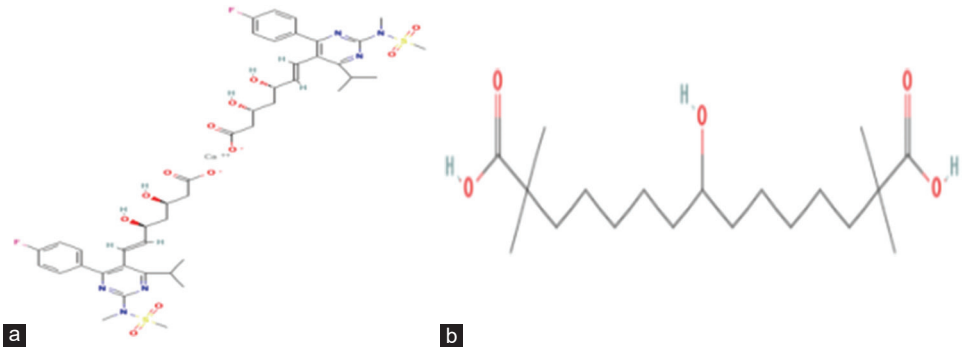

Figure 1: Chemical structures of analyte. (a) Rosuvastatin calcium, (b) Bempedoic acid

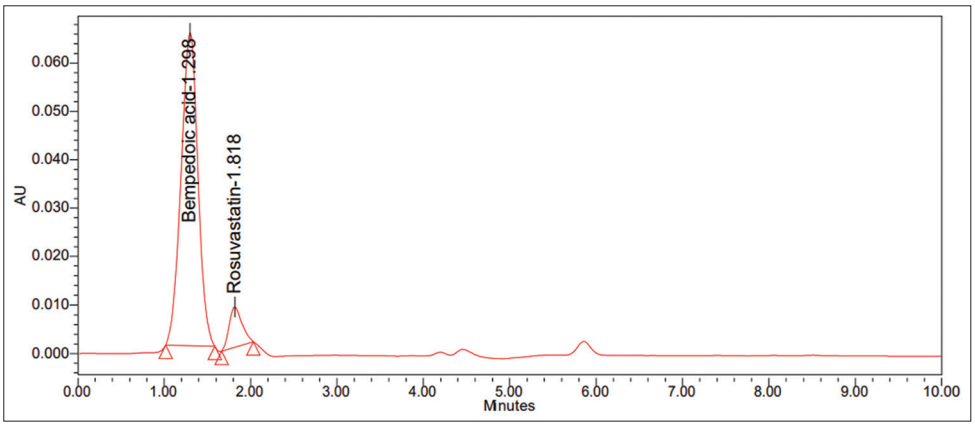

Figure 2: Chromatogram of Bempedoic acid and Rosuvastatin trail-1

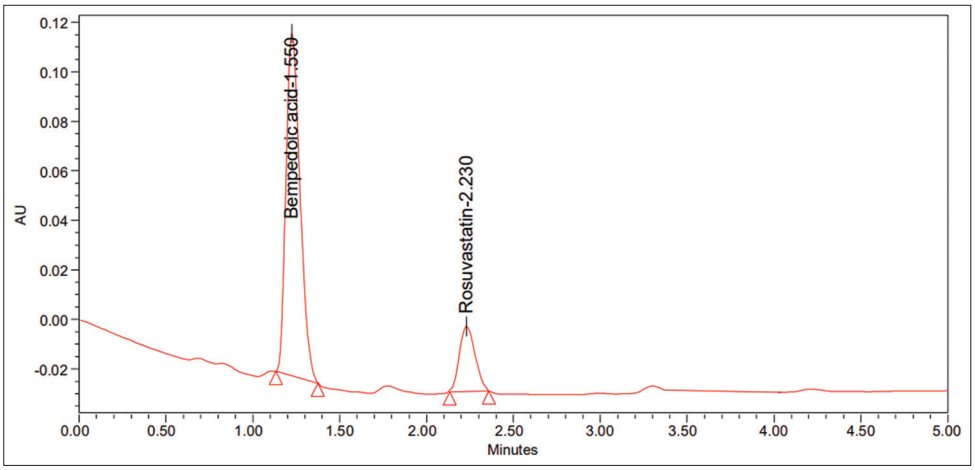

Figure 3: Chromatogram of Bempedoic acid and Rosuvastatin trail-2

peaks due to Bempedoic acid, Rosuvastatin in the standard solution should not be more than 2.0. Theoretical plates should not be <2000. Resolution should not be <2.[8]

Linearity and range

In a 100 mL clean, dry volumetric flask, accurately weigh and transfer 180 mg of Bempedoic acid, 40 mg of Rosuvastatin working standard. Diluent and sonication are used to thoroughly dissolve the standard and bring the volume to the desired level (Stock solution).

Calibration curves were constructed by plotting peak areas against concentration over a range of 45, 90, 135, 180, 225, 270 µg/mL for Bempodoic acid and 10, 20, 30, 40, 50, 60 µg/mL for Rosuvastatin. Linearity was assessed using regression analysis.

Accuracy

Accuracy was evaluated using the standard addition method at three levels: 50%, 100%, and 150% of the target concentration. Prepared and injected three sets of solutions in triplicate at each concentration. The percentage of recovery was derived.

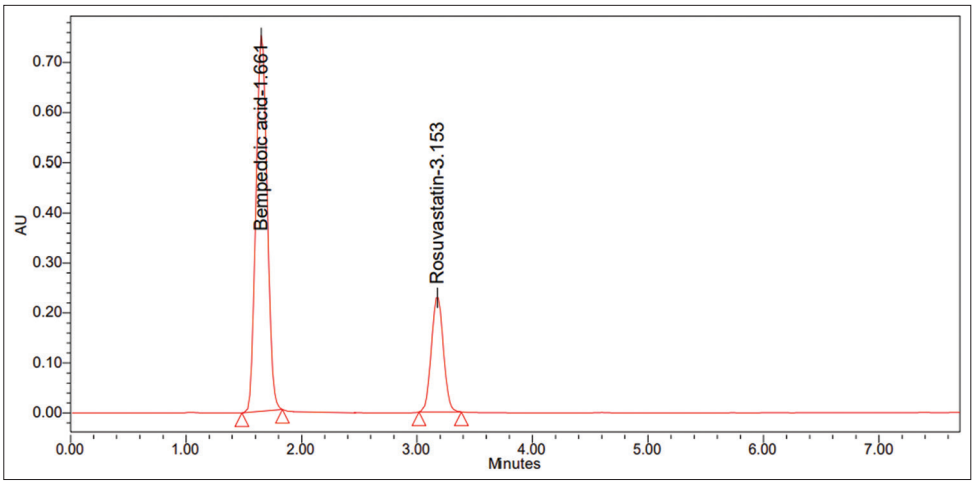

Figure 4: Chromatogram of Bempedoic acid and Rosuvastatin trail-3

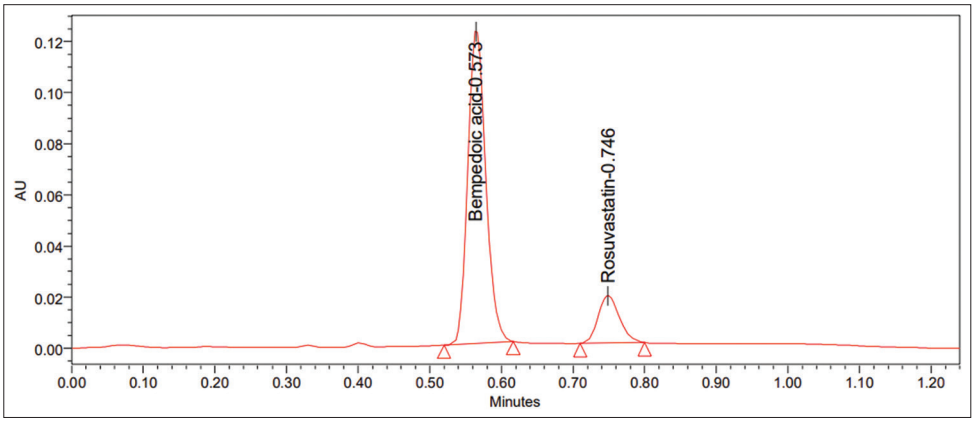

Figure 5: Chromatogram of Bempedoic acid and Rosuvastatin trail-4

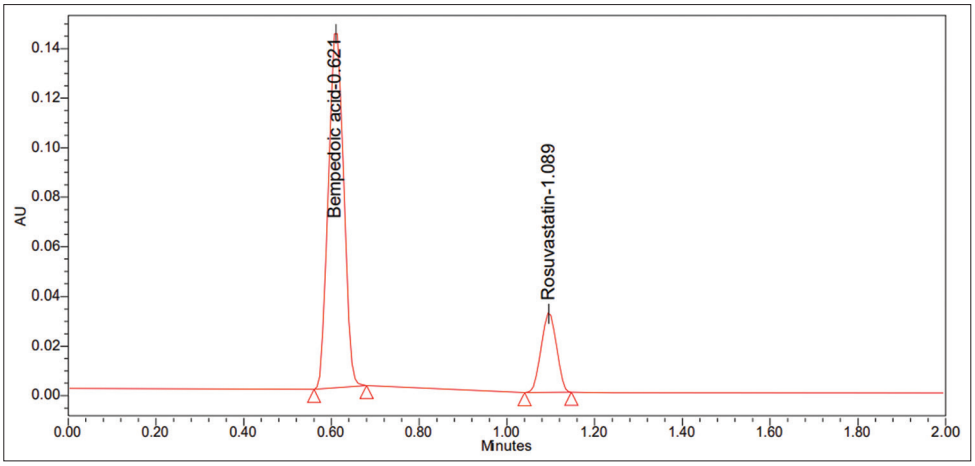

Figure 6: Chromatogram of Bempedoic acid and Rosuvastatin trail-5

Precision

For the developed reversed-phase HPLC method, both system precision and method precision were performed. System precision was carried out by injecting six replicate injections of the standard mixture at its target concentration. Various chromatographic parameters such as retention time, peak area, theoretical plates, and tailing factor, were assessed, and their % RSD was calculated. Method precision was carried out by injecting six replicate injections of the assay sample, and % RSD of the peak area and % assay values were calculated.

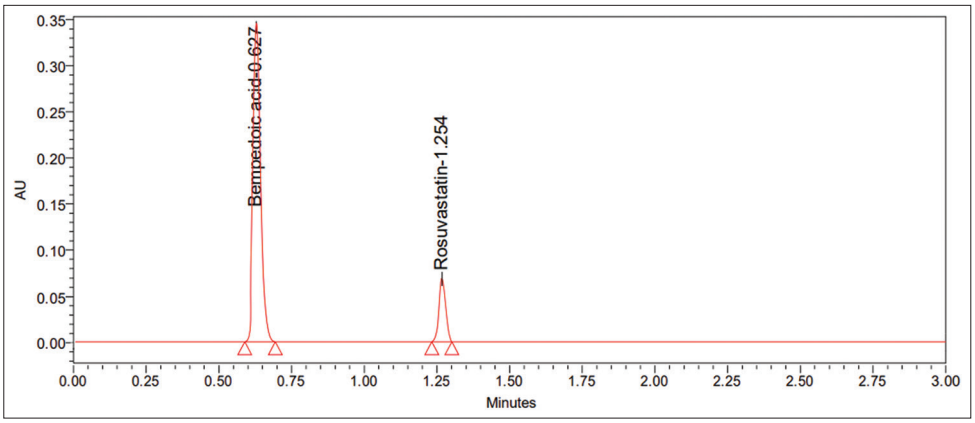

Figure 7: Chromatogram of Bempedoic acid and Rosuvastatin trail-6

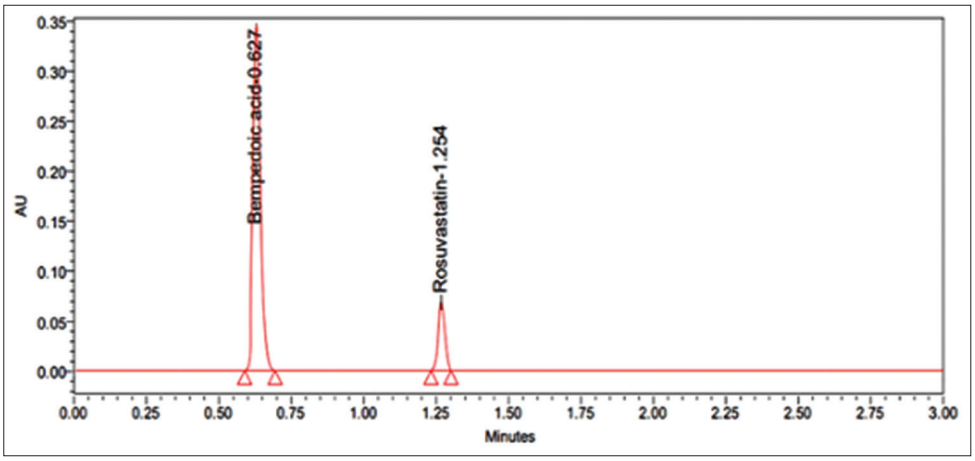

Figure 8: Chromatogram of Bempedoic acid and Rosuvastatin

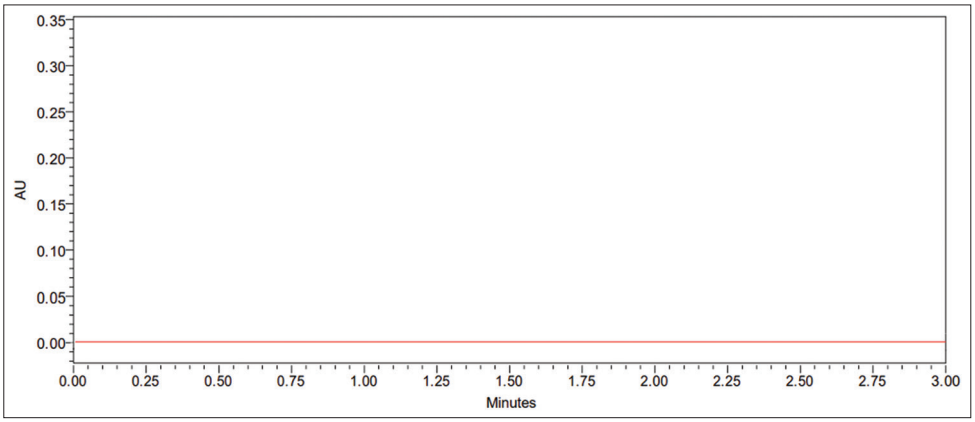

Figure 9: Chromatogram of blank

Limit of detection (LOD) and limit of quantitation (LOQ)

Standard solution 180 ppm of Bempedoic acid, 40 ppm of Rosuvastatin was prepared and analyzed using the varied flow rates along with the method flow rate.

On evaluation of the above results, it can be concluded that the variation in flow rate affected the method significantly. Hence, it indicates that the method is robust even with a change in the flow rate ±10%.

- The variation of the Organic Phase ratio

Standard solution of 180 ppm of Bempedoic acid, 40 ppm of Rosuvastatin was prepared and analyzed using the varied mobile phase ratio.

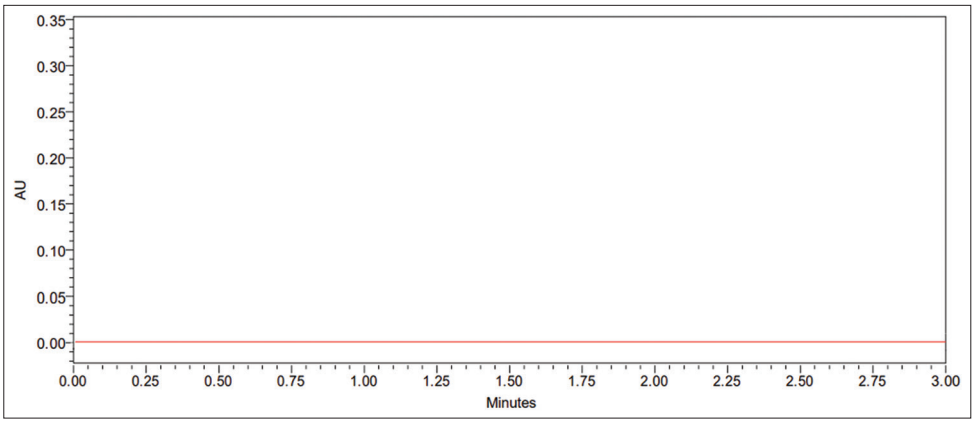

Figure 10: Chromatogram of placebo

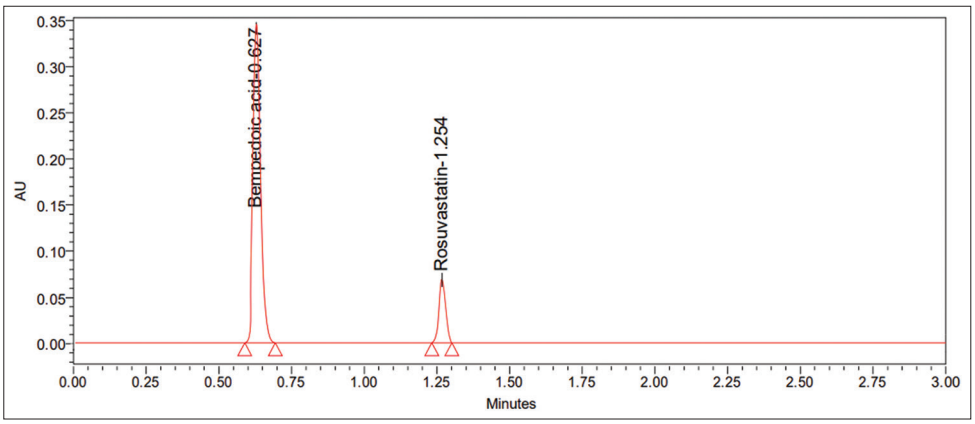

Figure 11: Optimized chromatogram

Table 13: Results of the forced degradation study of UPLC method

Stress condition	% Degradation (Rosuvastatin)	% Degradation (Bempedoic acid)	Peak purity
Acidic (0.1N HCl)	0.3	11.4	Pure
Basic (0.1N NaOH)	13.1	13.8	Pure
Peroxide	15.3	15.6	Pure
Thermal (60°C)	1.6	3.0	Pure
Photolytic (UV light)	2.3	0.9	Pure
Hydrolysis	3.9	3.1	Pure

UPLC: Ultra-performance liquid chromatography, UV: Ultraviolet

Acceptance criteria

The % RSD for the area of three standard injections and 3 sample preparation results should not be more than 2%.

The % Assay for each level should be between 98.0% and 102.0%.

LOD and LOQ were determined based on the signal-to-noise ratio of 3:1 and 10:1, respectively.

Specificity

Specificity of an analytical method is ability to measure specifically the analyte of interest without interference from blank and known impurities. For this purpose, blank chromatogram, standard chromatogram and sample chromatogram were recorded. The chromatogram of blank shows no response at the retention times of drugs which confirms the response of drugs was specific.

Robustness

As part of the Robustness, deliberate changes in the Flow rate, Mobile Phase composition, Temperature Variation was made to evaluate the impact on the method.

- The flow rate was varied at 0.18–0.22 mL/min

Standard solution 180 ppm of Bempedoic acid, 40 ppm of Rosuvastatin was prepared and analyzed using the varied flow rates along with the method flow rate.

On evaluation of the above results, it can be concluded that the variation in flow rate affected the method significantly. Hence, it indicates that the method is robust even by change in the flow rate ±10%.

- The variation of the Organic Phase ratio

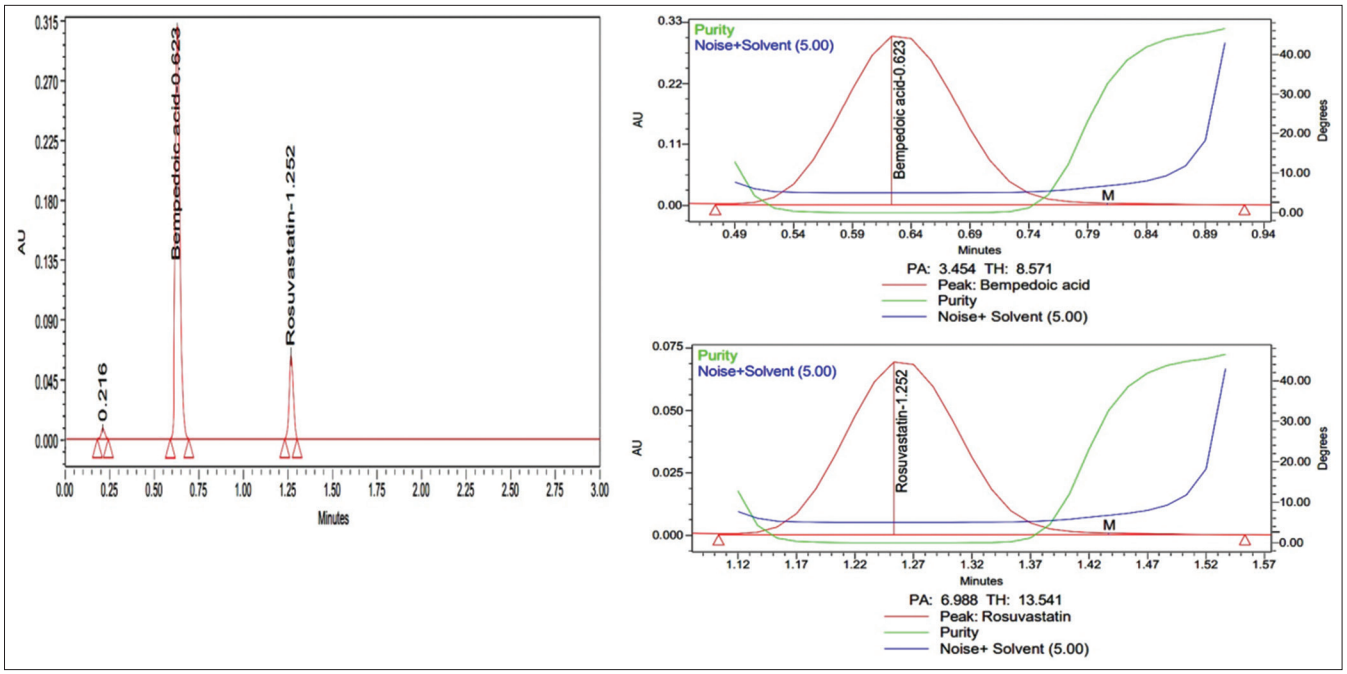

Figure 12: Chromatogram of acid degradation

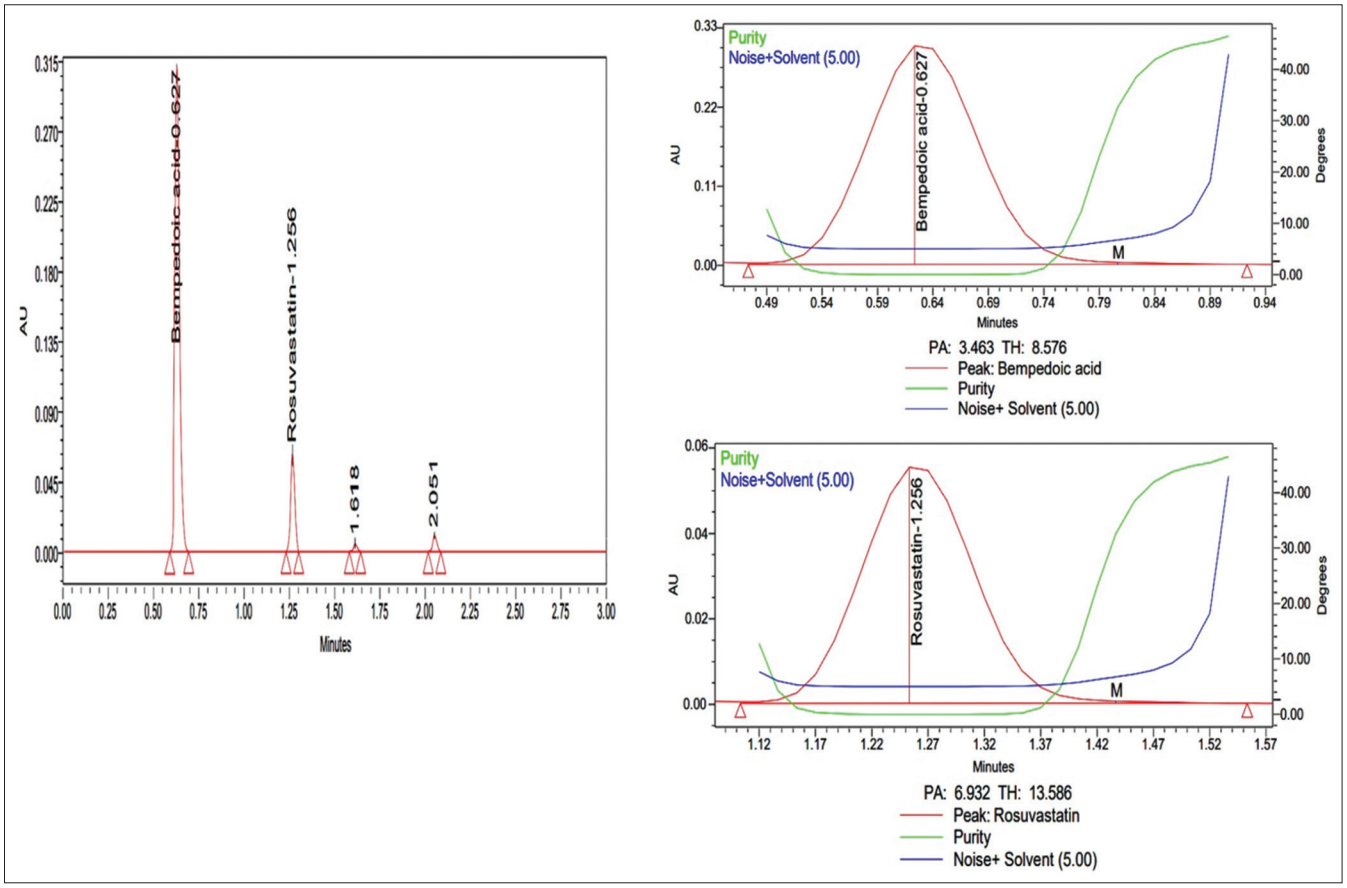

Figure 13: Chromatogram of alkali degradation

Standard solution of 180 ppm of Bempedoic acid, 40 ppm of Rosuvastatin was prepared and analyzed using the varied mobile phase ratio.

Acceptance criteria

The % RSD for the area of three standard injections and 3 sample preparation results should not be more than 2%.

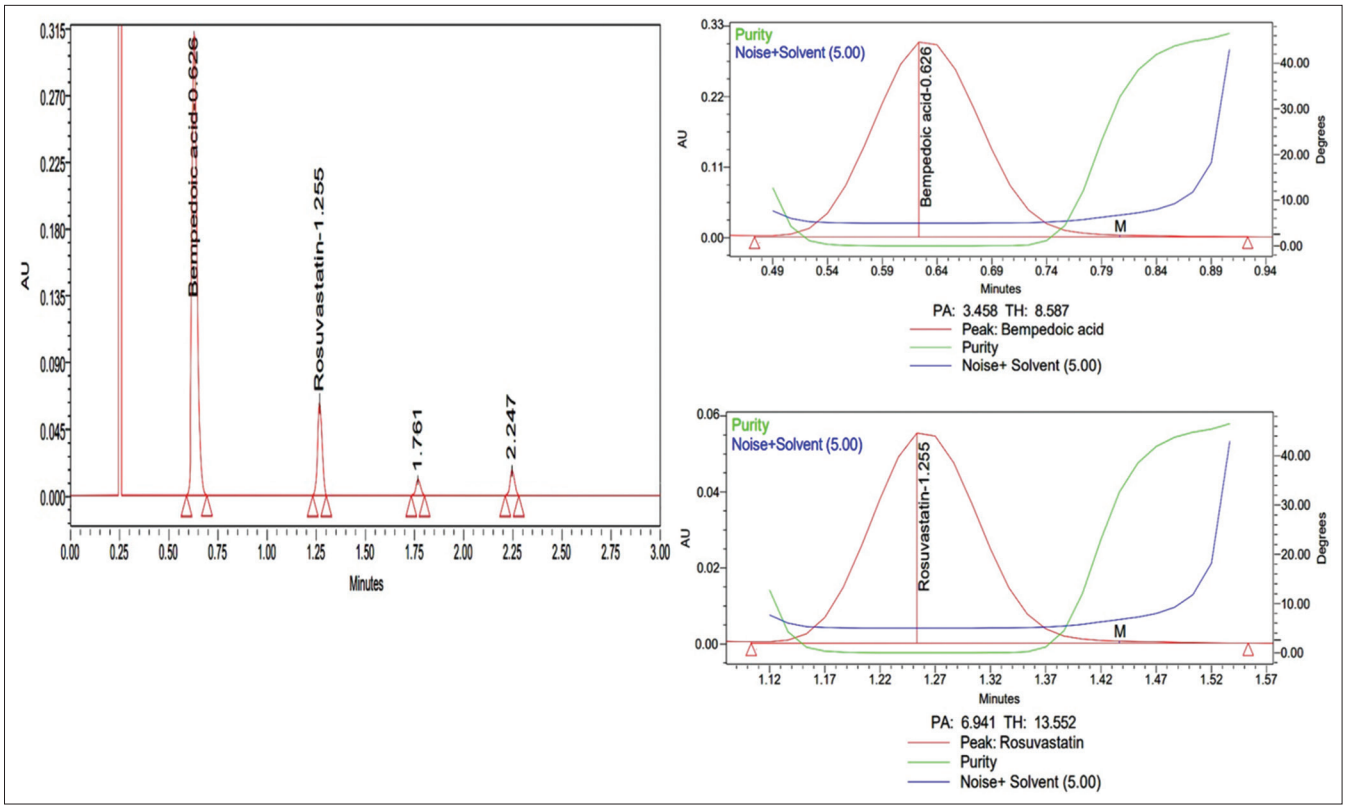

Figure 14: Chromatogram of peroxide degradation

The % Assay for each level should be between 98.0% and 102.0%.

Forced degradation and stability studies

Forced degradation studies were conducted under the following conditions to evaluate the stability-indicating nature of the method [Figures 1-19]:

Acidic hydrolysis

Accurately weigh and transfer 28.4 mg of Bempedoic acid and Rosuvastatin sample into a 10 mL volumetric flask, add 1 mL of 1N HCl, and leave it for 15 min. After 15 min, add 1 mL of 1N NaOH to neutralize the solution and diluted to volume with diluent and mixed. Sonicate this solution for 20 min to dissolve the contents. Further dilute 1–10 mL with diluent. This solution was filtered and transferred to vials.

Basic hydrolysis

Accurately weigh and transfer 28.4 mg of Bempedoic acid and Rosuvastatin sample into a 10 mL volumetric flask, add 1 mL of 1N NaOH, and leave it for 15 min. After 15 min add 1 mL of 1N HCl to neutralize the solution and dilute to volume with diluent and mix. Sonicate this solution for 20 min to dissolve the contents. Further dilute 1–10 mL with diluent. This solution was filtered and transferred to vials.

Peroxide degradation

Accurately weigh and transfer 28.4 mg of Bempedoic acid and Rosuvastatin sample into a 10 mL volumetric flask, add 1 mL of 10% H_2O_2, leave it for 15 min, after 15 min diluted to volume with diluent. Sonicate this solution for 20 min to dissolve the contents. Further dilute 1–10 mL with diluent. This solution was filtered and transferred to vials.

Reduction degradation

Accurately weigh and transfer 28.4 mg of Bempedoic acid and Rosuvastatin sample into a 10 mL volumetric flask, add 1 mL of 10% Sodium bisulfite, leave it for 15 min, after 15 min diluted to volume with diluent. Sonicate this solution for 20 min to dissolve the contents. Further dilute 1–10 mL with diluent. This solution was filtered and transferred to vials.

Thermal degradation

250 mg of Bempedoic acid and 100 mg of Rosuvastatin standard drug was exposed at 105°C for 6 h, and the exposed standard was analyzed. From this exposed standard, accurately weigh and transfer 180 mg of Bempedoic acid and 40 mg of Rosuvastatin exposed standard transferred into a 100 mL volumetric flask, add 70 mL of diluents, and sonicate for 20 min, and diluted to volume with diluent. Further pipette 5 mL of the above solution into a 50 mL volumetric flask and make up to the mark with diluents.

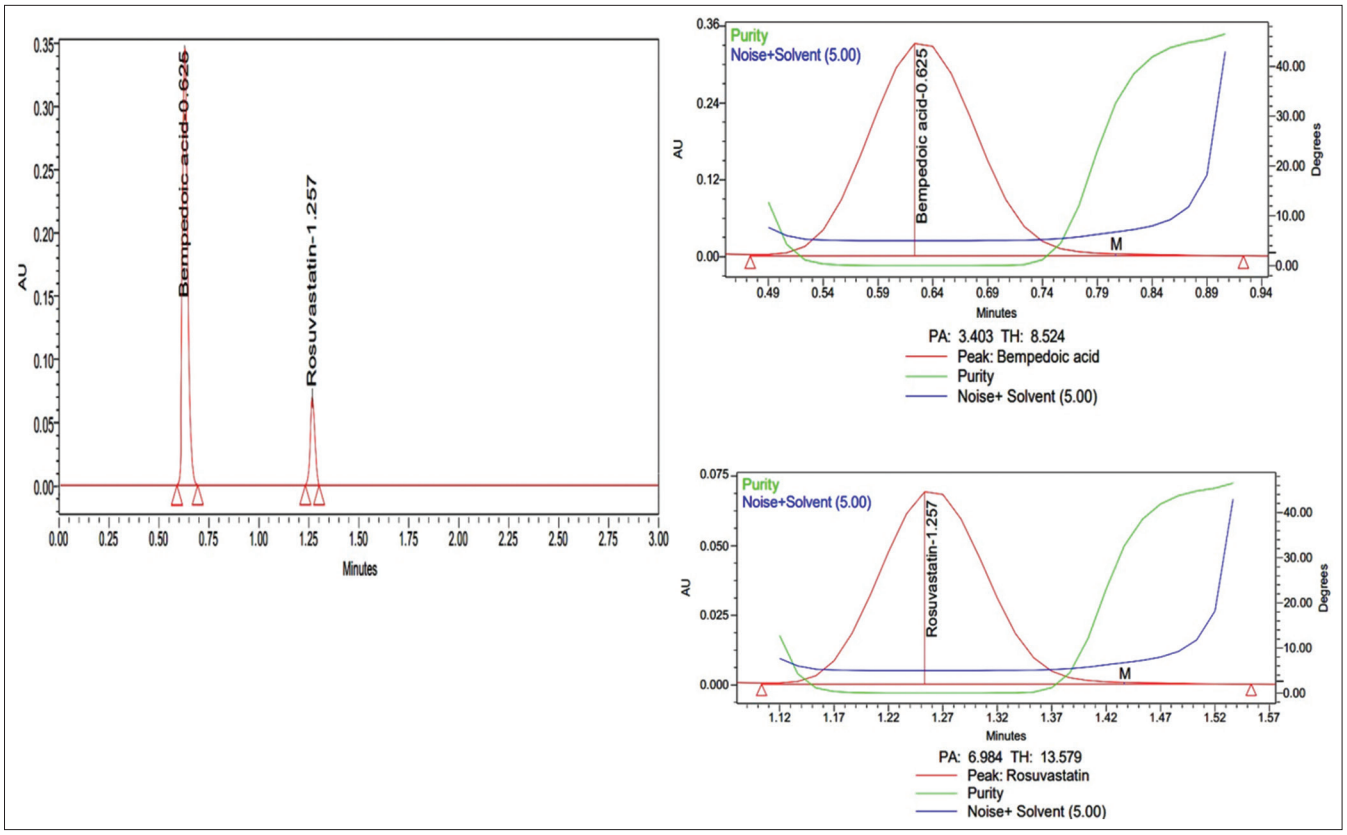

Figure 15: Chromatogram of reduction degradation

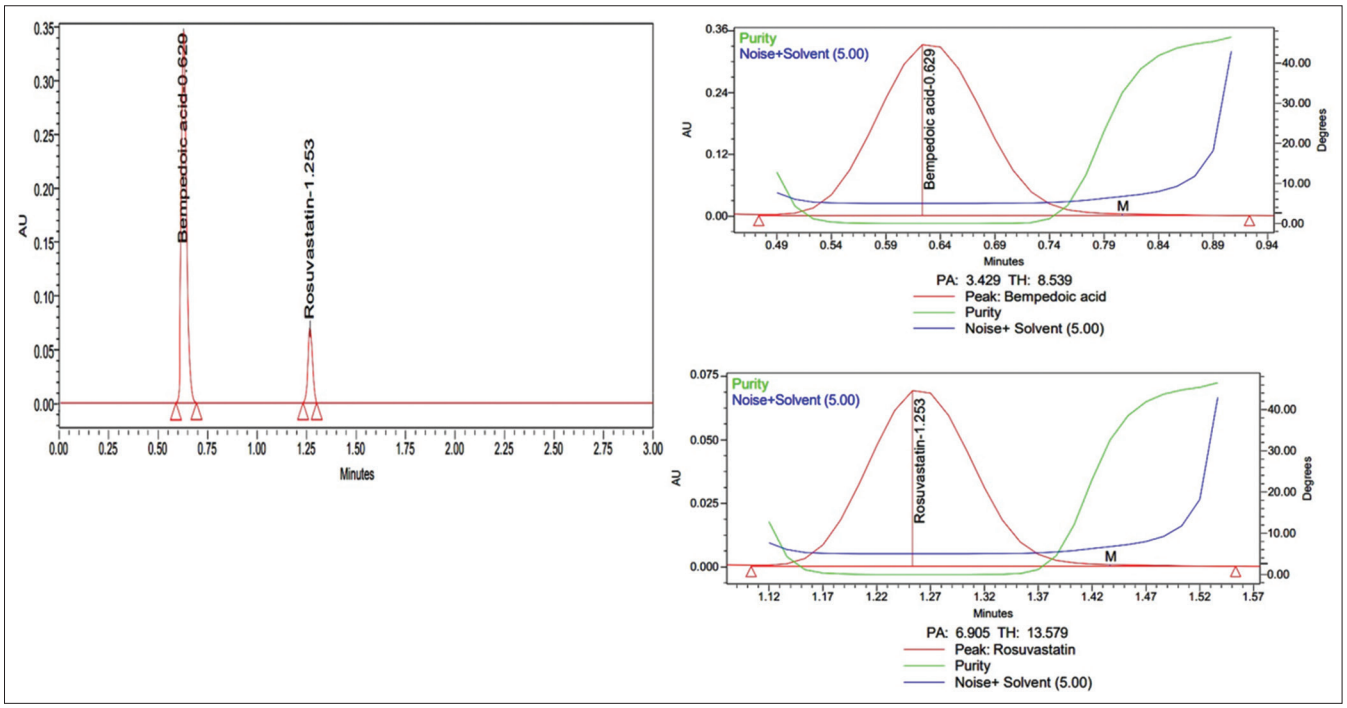

Figure 16: Chromatogram of thermal degradation

Photolytic degradation

50 mg of Bempedoic acid and Rosuvastatin sample was placed in a photo stability chamber for 6 h and the exposed sample was analyzed. From this exposed sample, accurately weigh and transfer 28.4 mg of Bempedoic acid, and Rosuvastatin exposed sample transferred into 10 mL volumetric flask, add 7 mL of diluents, and sonicate for 20 min and diluted to volume with diluent. Further pipette 1 mL of the above solution into a

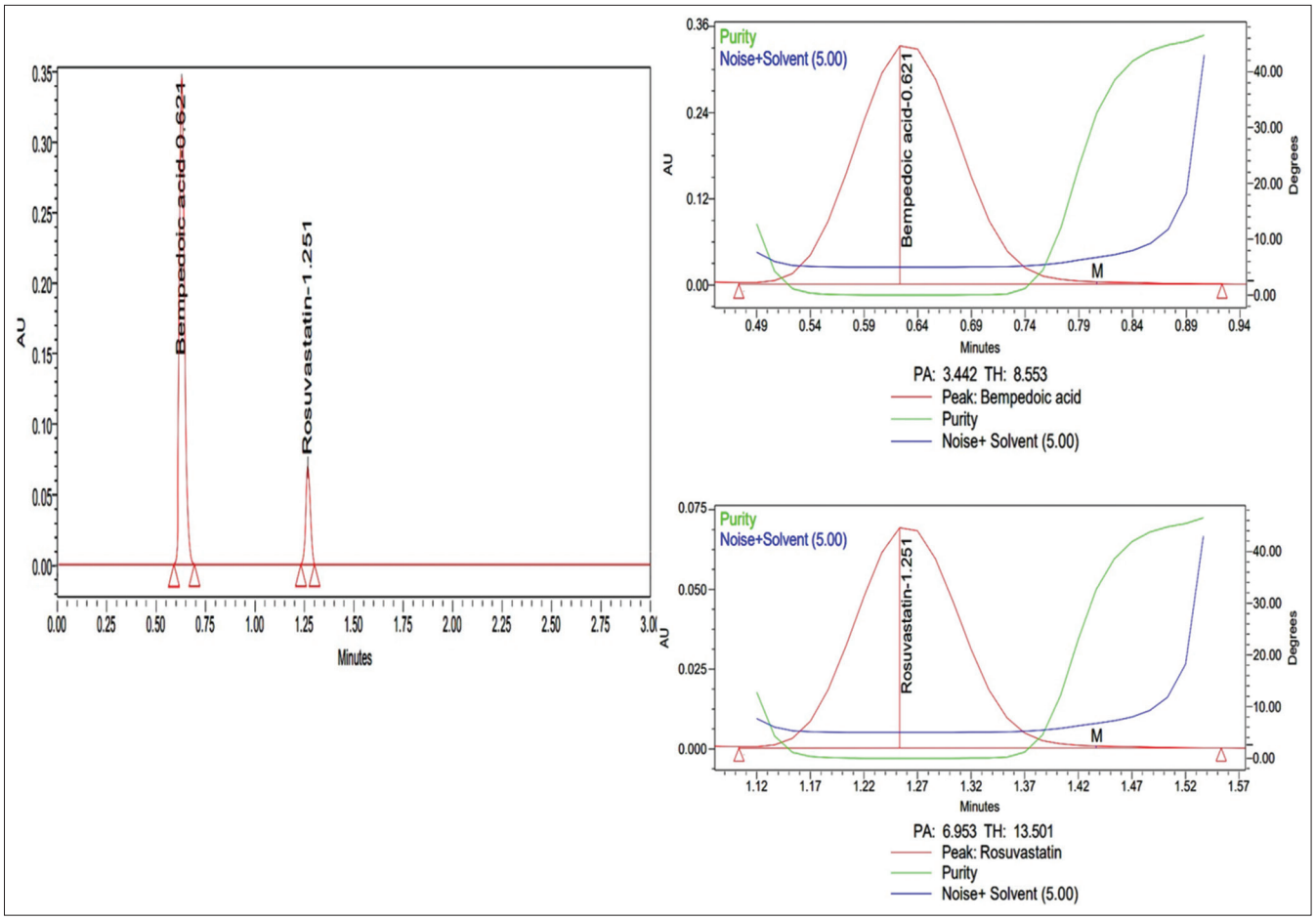

Figure 17: Chromatogram of photolytic degradation

10 mL volumetric flask and make up to the mark with diluents. This solution was filtered and transferred to vials.

Hydrolysis degradation

Accurately weigh and transfer 28.4 mg of Bempedoic acid and Rosuvastatin sample into a 10 mL volumetric flask, add 1 mL of HPLC water and leave it for 15 min. After15 min, diluted to volume with diluent. Further pipette 1 mL of the above solution into a 10 mL volumetric flask and make up to the mark with diluents. This solution was filtered and transfer to vials.

Acceptance criteria

Purity threshold is always more than the purity angle.

After each stress condition, samples were neutralized (if necessary), diluted, and analyzed by the developed UPLC method. Degradation products, if any, were evaluated by PDA detection and peak purity analysis.

RESULTS AND DISCUSSION

Method development and optimization

The main aim of this study is to develop a new accurate, reproducible, robust, linear method for the determination of Rosuvastatin and Bempedoic acid by using RP-UPLC, which helps for quality control laboratories' routine use and to develop the method both qualitatively and quantitatively.

A number of trials were performed using different mobile phases and columns to achieve optimal resolution, peak shape, and runtime. The best separation was achieved using an Acquity UPLC BEH C18 column (50 × 2.1 mm, 1.7 µm) with a mobile phase of 0.1% Ammonium formate (pH 3.0) and acetonitrile in an 80:20 v/v ratio. Rosuvastatin and Bempedoic acid showed sharp, symmetrical peaks with retention times of approximately 0.627 and 1.254 min, respectively, and good resolution (Rs > 2.0).

Trail_1

- Mobile Phase: Acetonitrile: 0.1% Formic acid (70:30)
- Column: Phenomenex C18(50×2.1 mm, 1.6 µ)
- Flow Rate: 0.2 mL/min
- Injection Volume: 5 µL
- Run Time: 10 min

Observation

System suitability conditions are not within the limit.

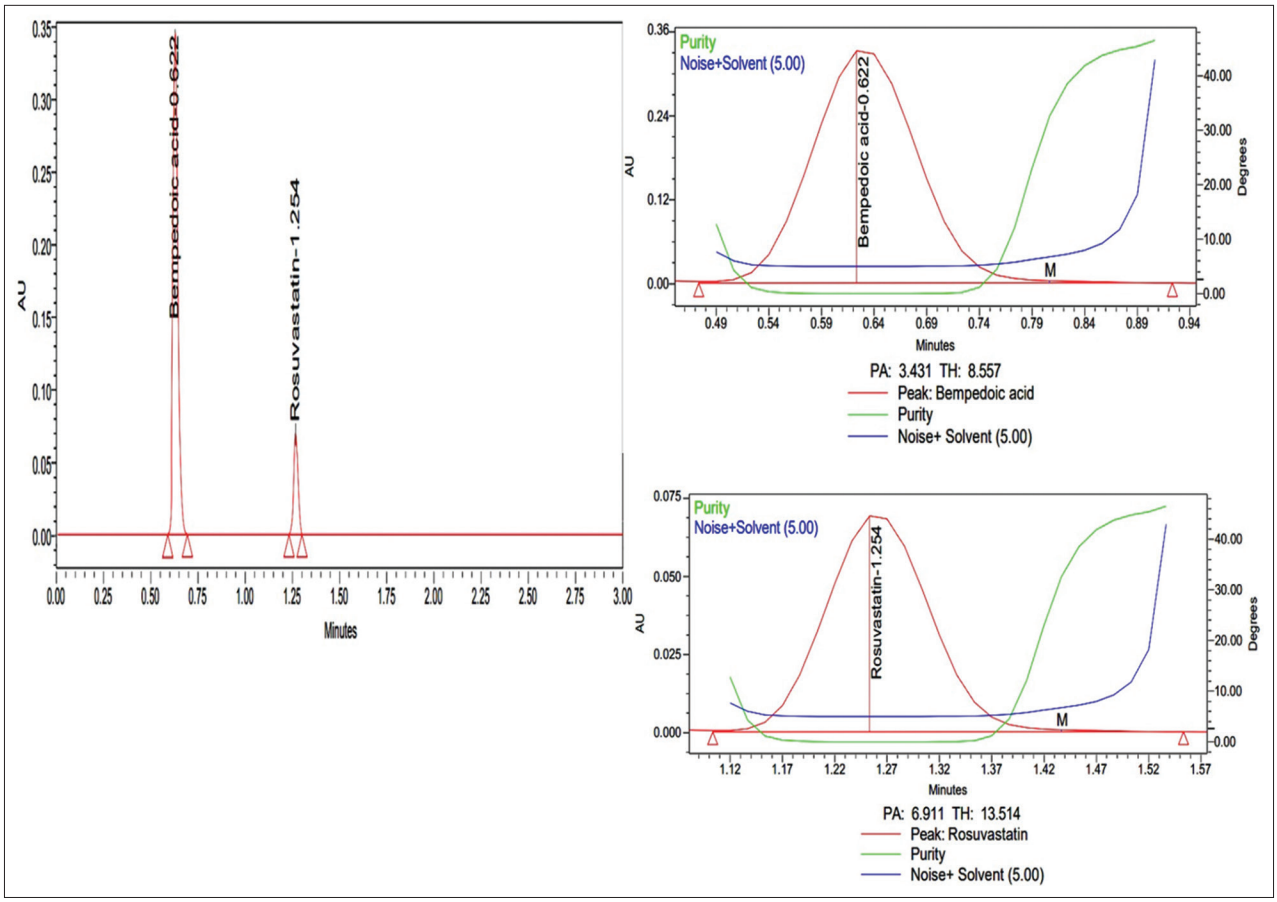

Figure 18: Chromatogram of hydrolysis degradation

Trail_2

- Mobile Phase: Acetonitrile: 0.1% Formic acid (60:40)
- Column: Phenomenex C18(50×2.1 mm, 1.6 µ)
- Flow Rate: 0.2 mL/min
- Injection Volume: 5 µL
- Run Time: 5.0 min

Observation

Base line is not sufficient.

Trail_3

- Mobile Phase: Acetonitrile: 0.1% Formic acid (50:50)
- Column: Phenomenex C18 (50×2.1 mm, 1.6 µ)
- Flow Rate: 0.2 mL/min
- Injection Volume: 5 µL
- Run Time: 8 min

Observation

Plate count is not within the limit.

Trail_4

- Mobile Phase: Acetonitrile: Ammonium formate pH-3.0/ OPA (30+70)
- Column: Acquity UPLC BEH shield RP-18 (50 mm×1.0 mm, 1.7 µm)
- Flow Rate: 0.2 mL/min
- Injection Volume: 5 µL
- Run Time: 1.30 min

Observation

Unknown peaks are observed.

Trail_5

- Mobile Phase: Acetonitrile: Ammonium formate pH-3.0/ OPA (25+75)
- Column: Acquity UPLC BEH shield RP-18 (50 mm×1.0 mm, 1.7 µm)
- Flow Rate: 0.2 mL/min
- Injection Volume: 5 µL
- Run Time: 2 min

Observation

Response of the peaks are very low.

Trail_6 (Optimized method)

- Mobile Phase: Acetonitrile: Ammonium formate pH-3.0/ OPA (20+80)

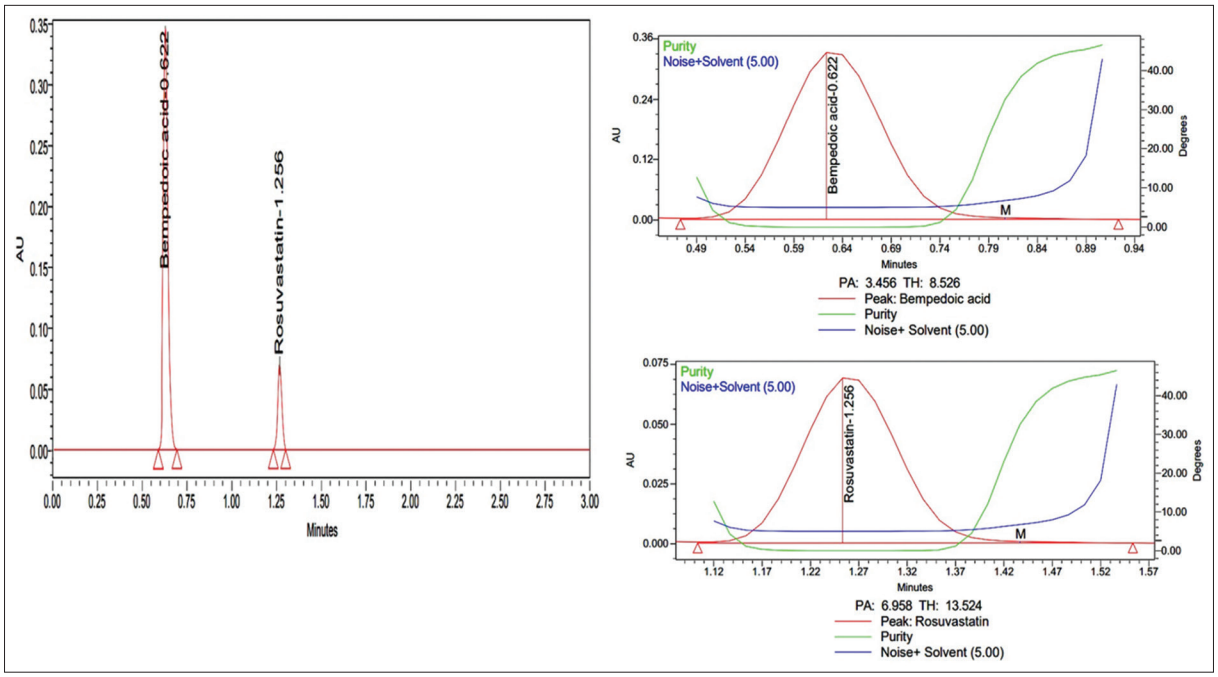

Figure 19: Chromatogram of control degradation

- Column: Acquity UPLC BEH shield RP-18 (50 mm×1.0 mm, 1.7 µm)
- Flow Rate: 0.2 mL/min
- Injection Volume: 5 µL
- Run Time: 3 min

Observation

This method is suitable for validation.

System suitability

System suitability parameters were within acceptable limits (n = 6).

Linearity and range

The method showed excellent linearity in the range of 45–270 µg/mL for Bempedoic acid and 10–60 µg/mL for Rosuvastatin.

Regression equations:

- Rosuvastatin: y = 18675.28x + 436.11
- Bempedoic acid: y =18558.01x + 8379.93.

Accuracy (Recovery studies)

Accuracy was evaluated using standard addition at 50%, 100%, and 150% levels.

Precision

Precision results indicated that the method is reproducible.

LOD and LOQ

The limit of detection (LOD) and limit of quantification (LOQ) for rosuvastatin were found to be 0.12 µg/mL and 0.40 µg/mL, respectively.

For bempedoic acid, the LOD and LOQ were 0.54 µg/mL and 1.80 µg/mL, respectively.

Robustness

Minor variations in flow rate, pH, and mobile phase ratio did not significantly affect the method, confirming its robustness (%RSD < 2% in all cases).

Specificity

No interference was observed at the retention times of Rosuvastatin and Bempedoic acid from blank or excipients, confirming the specificity of the method.

Assay

Assay of Razel-BM 40 tablets showed 99.7% for bempedoic acid and 100.3% for rosuvastatin. The amounts found were 17.95 µg/mL and 4.012 µg/mL, respectively, close to label claims. Results confirm the suitability of the method for routine tablet analysis.

Forced degradation and stability studies

All major degradant peaks were well separated from the drug

peaks, demonstrating the stability-indicating capability of the method.

CONCLUSION

A rapid, precise, and accurate UPLC method was successfully developed and validated for the simultaneous estimation of Rosuvastatin and Bempedoic acid in bulk and pharmaceutical dosage form. The method demonstrated excellent linearity, specificity, and sensitivity, along with robustness under small variations in chromatographic conditions. Forced degradation studies confirmed the stability-indicating nature of the method, with effective separation of degradation products. Due to its simplicity and short runtime, the method is suitable for routine quality control and stability analysis in pharmaceutical industries.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

I hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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