EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Coden USA: EJBPBO
Volume: 13
Issue: 3
Year: 2026

RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR THE SIMULTANEOUS ESTIMATION OF SIMVASTATIN AND CARVEDILOL IN TABLET DOSAGE FORM

***Dhaval Kumar Patel**

Research Scholar, Pharmaceutical Sciences. C.U. Shah University, Wadhwan, Gujarat, India.

***Corresponding Author: Dhaval Kumar Patel**

Research Scholar, Pharmaceutical Sciences. C.U. Shah University, Wadhwan, Gujarat, India..

DOI: https://doi.org/10.5281/zenodo.18796403

How to cite this Article: *Dhaval Kumar Patel (2026). Rp-Hplc Method Development And Validation For The Simultaneous Estimation Of Simvastatin And Carvedilol In Tablet Dosage Form. European Journal of Biomedical and Pharmaceutical Sciences, 13(3), 164–171.

Article Received on 04/02/2026 **Article Revised on 24/02/2026** **Article Published on 01/03/2026**

ABSTRACT

For the simultaneous measurement of Simvastatin and Carvedilol in tablet dose form, a straightforward, accurate, precise, and reliable reverse phase high-performance liquid chromatographic (RP-HPLC) approach was created and validated. Using a mobile phase made up of 60:40 v/v of Phosphate buffer: Methanol (pH 4.0 adjusted with Orthophosphoric acid) at a flow rate of 1.0 mL/min, chromatographic separation was accomplished on a C18 column (250 × 4.6 mm, 5 µm). At 245 nm, detection was done. Simvastatin and Carvedilol were shown to have retention durations of 2.57 and 5.71 minutes, respectively. The ICH Q2(R1) guidelines were followed in the validation of the approach. With correlation values higher than 0.999, linearity was seen in the concentration range of 5–15 µg/mL for Simvastatin and 5-15 µg/mL for Carvedilol. The parameters of linearity, accuracy, precision, robustness, and system suitability were all within reasonable bounds. Simvastatin and Carvedilol in combination tablet dose form were routinely analyzed using the described approach with success.

KEYWORDS: Simvastatin, Carvedilol, RP-HPLC, Method Validation, ICH Guideline.

INTRODUCTION

Since cardiovascular diseases (CVDs) continue to be the world's leading cause of morbidity and mortality,[1] long-term pharmacotherapy involving antihypertensive medications and lipid-lowering medicines is required.[2] Because combination medication therapy can increase therapeutic efficacy, decrease pill load, and improve patient compliance, it has become increasingly important.[3] A member of the statin class, simvastatin lowers cholesterol by blocking the rate-limiting enzyme in the manufacture of cholesterol, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase.[4] It is widely recommended for the treatment of high cholesterol and the avoidance of cardiovascular problems caused by atherosclerosis.[5] Carvedilol, a non-selective β-adrenergic blocker with extra α1-blocking capabilities, is frequently used to treat ischemic heart disease, heart failure, and hypertension.[6] By concurrently controlling hypertension and dyslipidemia, the pharmaceutical combination of simvastatin plus Carvedilol reduces overall cardiovascular risk and offers synergistic cardiovascular protection.[7] The development of trustworthy analytical techniques for the simultaneous estimate of Simvastatin and Carvedilol is crucial for quality control and regulatory compliance due to the growing availability of fixed-dose combination formulations combining these drugs.[8] Because of its high sensitivity, accuracy, repeatability, and capacity to separate substances with a variety of physicochemical characteristics, Reverse Phase High Performance Liquid Chromatography (RP-HPLC) is one of the most popular analytical methods in pharmaceutical analysis.[9] Several analytical techniques, such as UV spectrophotometry and HPLC, have been described for the individual quantification of Simvastatin and Carvedilol, according to a study of the literature.[10-11] Nevertheless, there are very few techniques available for determining them simultaneously in combination tablet dosage forms.[12]

In order to guarantee accuracy, precision, linearity, robustness, and appropriateness for routine quality control analysis, the current study focuses on developing such a method with optimal chromatographic settings and validating it in accordance with ICH Q2(R1)

recommendations. With specific goals like creating an optimized RP-HPLC method that can effectively separate Simvastatin and Carvedilol with acceptable retention time and resolution, choosing the right chromatographic conditions, such as mobile phase composition, column type, flow rate, and detection wavelength, and validating the method, the research aims to develop and validate a straightforward, accurate, precise, and robust RP-HPLC method for the simultaneous estimation of Simvastatin and Carvedilol in tablet dosage form in accordance with ICH Q2(R1) guidelines. To use the approved technique for the quantitative assessment of Simvastatin and Carvedilol in pharmaceutical companies' marketed tablet formulations.

MATERIALS AND METHODS

Chemicals and Reagents

Simvastatin and Carvedilol reference standards were obtained as gift samples - Carvedilol from West Coast Pharmaceuticals Works Limited, Ahmedabad Simvastatin from -Zydus Cadila, Ahmedabad. HPLC grade methanol, potassium dihydrogen phosphate, orthophosphoric acid, and distilled water were used.

Instrumentation

A High-Performance Liquid Chromatography (HPLC) - Agilent 1200 infinity-system with a quaternary gradient pump, online degasser, autosampler, and PDA detector was used to conduct the chromatographic analysis. Integrated chromatographic software was used for data collection and processing. A reverse phase C18 analytical column (250 mm × 4.6 mm, i.d., 5 µm particle size) was used to achieve separation, and it was kept at room temperature during the study. For every chromatographic run, the injection volume was set at 20 µL, and the mobile phase was supplied at a steady flow rate of 1.0 mL/min. A UV detector set at 245 nm was used to detect Simvastatin and Carvedilol. The detector was chosen based on the maximum absorbance (λmax) of both analytes to ensure optimal sensitivity. The mobile phase was degassed by ultrasonication and filtered through a 0.45 µm membrane filter before use in order to exclude particulate debris and dissolved gases. To guarantee full analyte dissolution, sample and reference solutions were produced using a calibrated analytical balance (sensitivity ±0.1 mg) and sonicated using an ultrasonic bath. Prior to injection into the HPLC system, solutions were filtered using 0.45 µm nylon syringe filters. For precise buffer pH adjustment, a digital pH meter was used, along with volumetric glassware for the class. To guarantee accuracy, a grade was applied to each solution preparation. Prior to sample analysis, system suitability tests were used to assess the overall performance of the HPLC system, making sure that parameters including theoretical plate count, tailing factor, resolution, and retention time repeatability were within acceptable bounds in accordance with ICH requirements.

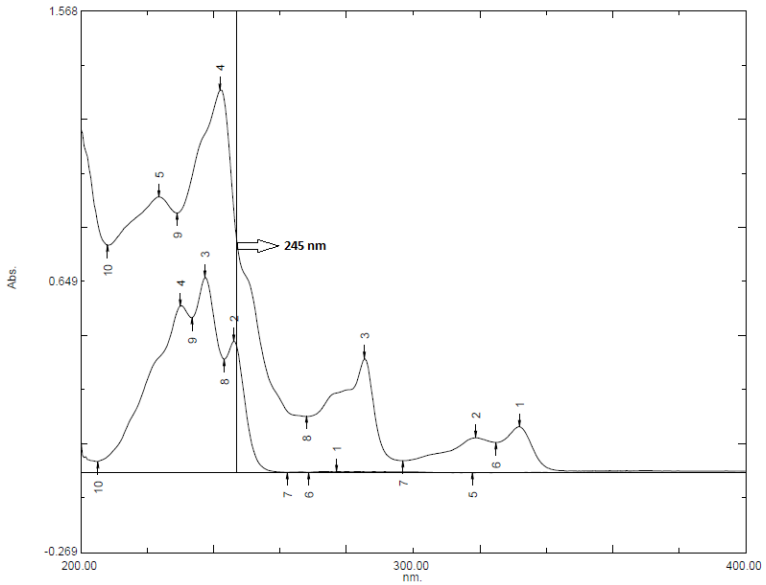

Figure 1. Overlay spectra in UV Visible spectra of Simvastatin and Carvedilol

Table 1: Optimized Chromatographic Conditions

Parameter	Condition
Column	C18 (250 × 4.6 mm, 5 µm)
Mobile Phase	60:40 v/v Phosphate buffer: Methanol (pH 4.0 adjusted with Orthophosphoric acid)
Flow Rate	1.0 mL/min
Detection Wavelength	245 nm
Injection Volume	20 µL
Run Time	10 min
Column Temperature	Ambient

Table 2: Composition of Simvastatin 20 mg + Carvedilol 20 mg per 350 mg tablet.

Sr. No.	Ingredient	Function	Quantity (mg)
1	Simvastatin	Active ingredient (Lipid lowering agent)	20
2	Carvedilol	Active ingredient (Antihypertensive agent)	20
3	Microcrystalline Cellulose	Diluent & compressibility enhancer	170
4	Lactose Monohydrate	Diluent / Filler	100
5	Povidone K30	Binder	20
6	Starch	Conventional disintegrant	10
7	Colloidal Silicon Dioxide	Glidant	5
8	Magnesium Stearate	Lubricant	5
		Total	**350 mg**

Table 3: Summary of tablet evaluation parameters and observed results within acceptance limits as per standard guidelines.

Parameter	Result (All parameter under acceptance range)
Appearance	Uniform, Round shape, free from cracks
Average Weight	350 mg ± 5%
Hardness	5 – 8 kg/cm²
Friability	Not more than 1% weight loss
Disintegration Time	Not more than 30 minutes
Uniformity of Content	85 – 115%

Preparation of Standard Solutions

Methanol was used to create stock solutions of Simvastatin (100 µg/mL) and Carvedilol (100 µg/ mL). Working standards were created by diluting the mobile phase appropriately.

Sample Preparation

Weighed and powdered were twenty Tablet's. One tablet's equivalent weight was moved to a volumetric flask, dissolved in methanol, sonicated, filtered, and suitably diluted.

RESULTS AND DISCUSSION

Following ICH Q2 (R1) criteria, a systematic evaluation of the developed RP-HPLC technique for the simultaneous quantification of Simvastatin and Carvedilol was conducted. The findings for every validation parameter are examined point-by-point below.

Method Development and Optimization

In order to attain ideal separation, symmetric peak morphologies, and acceptable retention durations, a number of chromatographic settings were examined. We looked at various mobile phase combinations with Phosphate buffer at different pH levels and either methanol or. Broad peaks and insufficient resolution were the outcomes of early experiments employing mobile phases based on Acetonitrile. Phosphate buffer and Methanol were then used to produce sharper peaks and improved baseline stability. Acidic circumstances (pH 4.0) greatly enhanced peak symmetry and reduced tailing, according to pH optimization. The completed chromatographic settings included a C18 column with a flow rate of 1.0 mL/min of 60:40 v/v phosphate buffer: Methanol (pH 4.0 adjusted with Orthophosphoric acid) With retention lengths of roughly 2.57 and 5.71 minutes, respectively, Simvastatin and Carvedilol were well resolved under these circumstances, guaranteeing quick analysis with a 10-minute runtime.

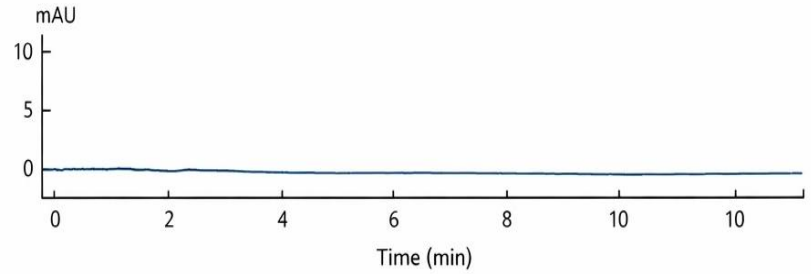

Figure 1: Blank chromatogram.

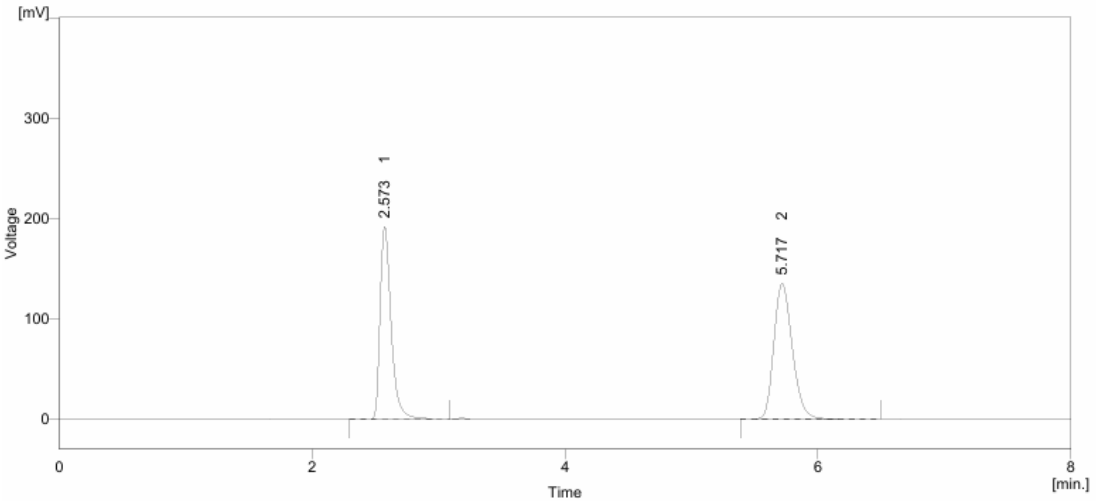

Figure 2: Standard chromatogram showing Simvastatin (RT = 2.573 min) and Carvedilol (RT = 5.717 min)

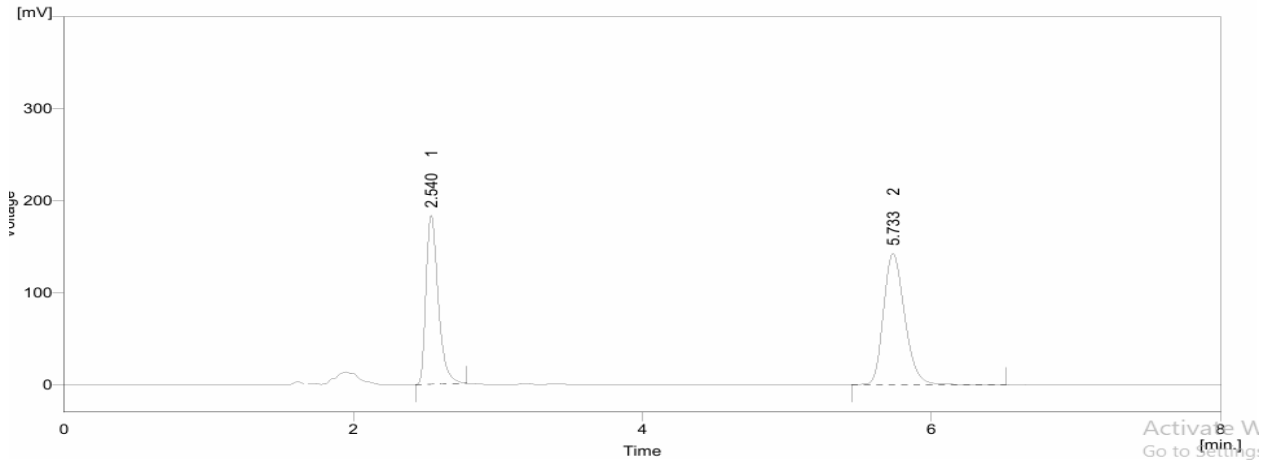

Figure 3: Sample chromatogram showing Simvastatin (RT = 2.540 min) and Carvedilol (RT = 5.733 min).

Method Validation

Linearity

For Simvastatin and Carvedilol, linearity was assessed throughout concentration ranges of 5–15 µg/mL and 5-15 µg/mL, respectively. Peak area was plotted versus concentration to create calibration curves. With correlation values (R2) of 0.9995 for Simvastatin and 0.9989 for Carvedilol, both medications demonstrated exceptional linearity. Reliability for quantitative analysis was confirmed by the regression equations, which showed a direct proportional link between analyte concentration and detector response.

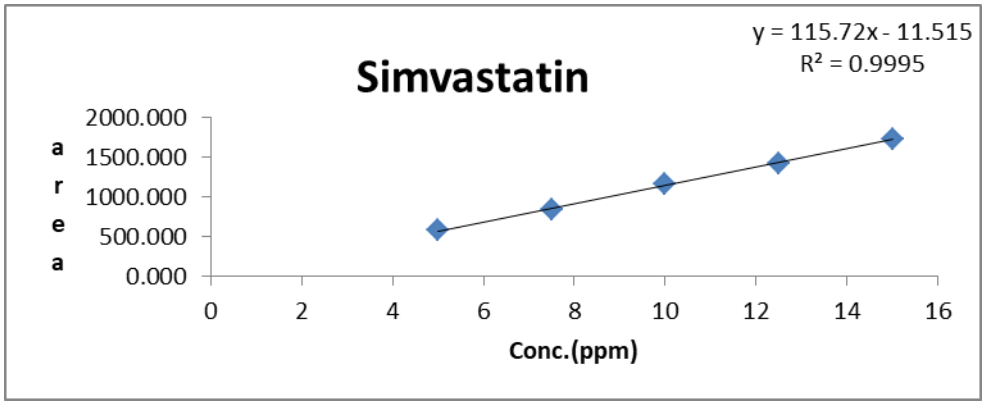

Figure 4: Calibration curve of simvastatin.

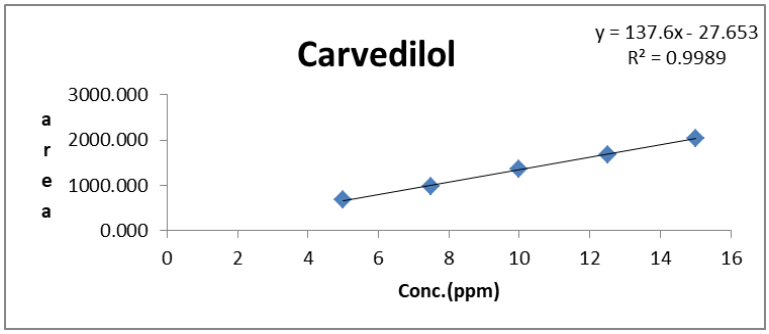

Figure 5: Calibration curve of Carvedilol.

Table 4: Results of Linearity.

Drug	Range (µg/mL)	Regression Equation	R^2
Simvastatin	5-15	y = 115.72x - 11.515	0.9995
Carvedilol		y = 137.6x - 27.653	0.9989

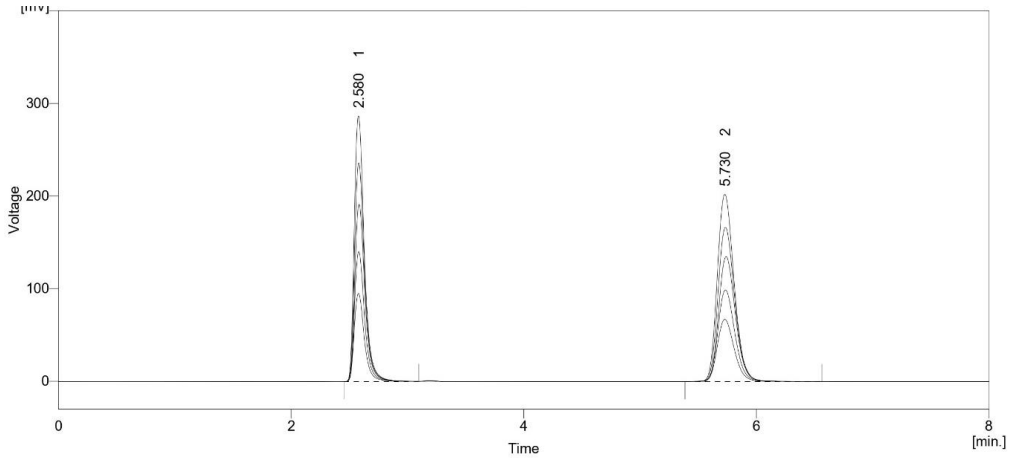

Figure 6: Linearity chromatogram of Simvastatin Carvedilol.

Accuracy (% Recovery)

Three levels of accuracy were assessed using the usual addition method: 80%, 100%, and 120%. For Simvastatin and Carvedilol, the mean percentage recoveries varied from 99.70 % to 100.00 % and 99.85 % to 100.18%, respectively. These outcomes show that the approach is precise and matrix interference-free.

Table 5: Accuracy (% Recovery).

Level	Simvastatin (%)	Carvedilol (%)
80 %	100.005	100.187
100 %	99.704	99.859
120 %	99.726	99.862

Precision

Intraday Precision

Three concentrations of each drug were analyzed on the same day in order to evaluate intraday precision. Simvastatin's percentage relative standard deviation (%RSD) was 1.43%, while Carvedilol was 0.86 % for 50%, 100 %, 150 % conc. Excellent repeatability and precision are indicated by low percentage RSD values (<2%).

Table 6: Results of Intraday Precision.

Drug	Conc.	%RSD
Simvastatin	50	1.86
	100	1.30
	150	1.13
Carvedilol	50	0.98
	100	0.91
	150	0.69

Interday Precision

Three days in a row were used to assess interday precision. Simvastatin's percentage RSD was 1.01%, while Carvedilol's 0.74% for 50%, 100 % , 150 % conc. Excellent repeatability and precision are indicated by low percentage RSD values (<2%).

Table 7: Results of Interday Precision.

Drug	Conc.	%RSD
Simvastatin	50	0.86
	100	1.33
	150	0.86
Carvedilol	50	1.01
	100	0.73
	150	0.48

LOD and LOQ

The slope of the calibration curve and the response standard deviation were used to compute LOD and LOQ. Simvastatin and carvedilol had LOD values of 1.64 µg/mL and 0.78 µg/mL, respectively, while their LOQ values were 4.98 µg/mL and 2.38 µg/mL. These outcomes show how sensitive the approach is.

Table 8: Results of LOD and LOQ.

Drug	LOD (µg/mL)	LOQ (µg/mL)
Simvastatin	1.64	4.98
Carvedilol	0.78	2.38

Repeatability

Six replicate injections were performed for both analytes at 100 % concentration (10µg/mL). The chromatographic peak areas obtained were statistically evaluated. The method demonstrates excellent system precision and repeatability at 10µg/mL for both compounds. Since %RSD < 2 %, the chromatographic system is suitable for quantitative analysis, and the method can be considered reliable for routine quality control analysis.

Table 9: Results of Repeatability.

Std	Simvastatin Area	Carvedilol Area
1	1152.641	1360.443
2	1130.157	1360.437
3	1156.096	1364.549
4	1158.440	1329.654
5	1156.093	1364.530
6	1153.795	1361.806
Average	1151.204	1356.903
SD	10.507	13.477
%RSD	0.913	0.993

System Suitability

Six replicate standard solutions were injected in order to evaluate the system's applicability. Retention time, theoretical plates, tailing factor, and resolution were among the parameters that were assessed. Theoretical plate counts of Approx. 5000 for Simvastatin and Carvedilol demonstrated significant column efficiency. For both analytes, tailing factors were less than 1.6, indicating symmetric peak morphologies. Excellent chromatographic separation was demonstrated by the resolution between the two peaks exceeding 14.0. The HPLC system's sufficiency was confirmed when all system suitability metrics satisfied acceptance criteria.

Table 10: Results of System Suitability.

Parameter	Simvastatin	Carvedilol
Retention Time (min)	2.57	5.71
Theoretical Plates	4146	7188
Tailing Factor	1.65	1.37
Resolution	—	14.91

Robustness

In order to assess robustness, intentional changes were made to the flow rate (±0.2 mL/min), pH ±0.2. With % RSD values staying below 2%, these modifications had no discernible impact on peak areas or retention

durations. This attests to the method's resilience to small operational adjustments.

Table 11: Results of Robustness study.

#	parameter	Parameter Variation	Simvastatin (%RSD)	Carvedilol (%RSD)
1	Flow rate	0.8 mL/min	1.71	0.66
		1.2 mL/min	1.59	1.96
2	pH	3.8	1.51	1.48
		4.2	1.60	0.75

Assay of Tablet

Tablet formulations comprising Simvastatin (20 mg) and Carvedilol (20 mg) were subjected to the validated procedure. Simvastatin and carvedilol have medication contents of 94.32% and 105.54%, respectively, according to assay results, which are within pharmacopeial acceptability standards (90 % to 110%). This attests to the method's suitability for regular quality control analysis.

Table 12: Results of Assay of Tablet.

Drug	Label Claim (mg)	Amount Found (mg)	% Assay	% RSD
Simvastatin	20	19.92	94.32	1.33
Carvedilol	20	21.11	105.54	0.79

DISCUSSION

The goal of the current work was to create a quick, accurate, and validated RP-HPLC method for the simultaneous measurement of carvedilol and simvastatin in tablet dose form. Achieving symmetric peak morphologies, appropriate retention times, sufficient resolution between analytes, and repeatable results with low solvent consumption were the main goals of method optimization. Several combinations of buffer systems and organic solvents were used in the first chromatographic experiments.

Longer retention periods and poor peak symmetry were the outcomes of Acetonitrile based mobile phases. Methanol and phosphate buffer were then used to increase baseline stability and peak resolution. With retention periods of roughly 2.57 minutes for Simvastatin and 5.71 minutes for Carvedilol, the optimized mobile phase, which was composed of 60:40 v/v Phosphate buffer: Methanol (pH 4.0 adjusted with Orthophosphoric acid), provided distinct, well-resolved peaks. The method is appropriate for routine quality control since these retention periods show effective separation within a brief analytical runtime.

With correlation values more than 0.999 for both medications, the devised technique showed excellent linearity over the concentration ranges of 5–15 µg/mL for Simvastatin and 5-15 µg/mL for Carvedilol. The method's high analytical sensitivity is demonstrated by the linear regression equations derived from calibration curves, which verify a direct proportionality between concentration and peak area. These results demonstrate the method's suitability for quantitative analysis and are in line with ICH acceptance standards.

Recovery trials at three concentration levels (80%, 100%, and 120%) were used to assess the method's accuracy. Excellent concordance between added and recovered amounts was shown by the percentage recoveries for Simvastatin and Carvedilol, which ranged from 99.70 % to 100.00 % and 99.85 % to 100.18%, respectively. These findings corroborate the established method's specificity and show that excipients in the tablet formulation do not affect drug quantification. For both intra-day and inter-day analyses, precision studies showed %RSD values less than 2%, indicating high repeatability and intermediate precision.

Reliability of the analytical process and consistent system performance are demonstrated by low variability in peak areas. The method's suitability for regular laboratory use is supported by this reproducibility. By determining the limits of detection and quantification, the method's sensitivity was further validated. The method's capacity to detect and quantify low quantities of both medications with acceptable accuracy is demonstrated by the LOD values of 1.64 µg/mL for Simvastatin and 0.78 µg/mL for Carvedilol, as well as the LOQ values of 4.98 µg/mL and 2.38 µg/mL, respectively.

System suitability parameters such as theoretical plates, tailing factor, resolution, and retention time repeatability were found to be within acceptable limits. Theoretical plate counts Approx. 5000 for both analytes, reflecting good column efficiency, while tailing factors were close to unity, indicating symmetric peak shapes. Adequate chromatographic separation was confirmed by a resolution of more than 14 between the Simvastatin and Carvedilol peaks. By purposefully altering chromatographic parameters including flow rate and pH, robustness tests were carried out. With % RSD values staying below 2%, these little adjustments had no discernible impact on peak regions or retention durations. This proves that even with minor operational changes, the approach is stable and dependable. Assay results of 94.32 % for Simvastatin and 105.54 % for Carvedilol, which are within pharmacopeial acceptability

limits (90-110 %), were obtained when the validated method was applied to commercial tablet formulations.

This demonstrates that the approach is appropriate for quantitatively estimating both medications in combined dosage forms. The suggested RP-HPLC approach has a number of benefits over previously published techniques, such as a faster runtime, a simpler mobile phase composition, better resolution, and thorough validation in accordance with ICH requirements. Additionally, the technique necessitates less sample preparation, which cuts down on analysis time and solvent usage and increases cost-effectiveness. All things considered, the developed RP-HPLC technique exhibits outstanding performance features in terms of robustness, specificity, linearity, sensitivity, accuracy, and precision. These characteristics make the approach a trustworthy analytical tool for estimating Simvastatin and Carvedilol in pharmaceutical formulations at the same time.

CONCLUSION

In compliance with ICH Q2(R1) criteria, a straightforward, quick, accurate, and reliable RP-HPLC technique was successfully developed and validated for the simultaneous measurement of Simvastatin and Carvedilol in tablet dose form. Effective analysis was made possible by the well-optimized chromatographic conditions, which offered acceptable resolution and brief retention periods. Excellent linearity, accuracy, precision, sensitivity, robustness, and specificity were shown in the validation results. The technique produced assay values within acceptable pharmacopeial limits and was successfully applied to commercial tablet formulations. The suggested approach is appropriate for routine quality control and regulatory analysis of Simvastatin and Carvedilol in combined pharmaceutical preparations due to its simplicity, dependability, and affordability.

REFERENCES

1. Velidakis N, Stachteas P, Gkougkoudi E, Papadopoulos C, Kadoglou NPE. Classical and novel lipid-lowering therapies for diabetic patients with established coronary artery disease or high risk of coronary artery disease—a narrative clinical review. Pharmaceuticals (Basel)., 2024; 17(5): 568.
2. Popat A, Yadav S. Comparative effectiveness of novel combination therapies for simultaneous management of hypertension and hypercholesterolemia: a systematic review and meta-analysis. Cureus, 2024; 16(10): e71876.
3. Alvarado-Tapias E, Brujats A, Puente A, et al. Hemodynamic effects of carvedilol plus simvastatin in cirrhosis with severe portal hypertension and suboptimal response to β-blockers: a randomized trial. Hepatology, 2025; 82(1): 140-154.
4. Islam MS, Sultan MZ, Islam MS, Simol HA, Salam MA. Development and validation of a new RP-HPLC method for simultaneous estimation of ramipril and carvedilol. Bangladesh Pharm J., 2023; 26(1): 15-19.
5. Mourad SS, Barary MA, El-Yazbi AF. Simple simultaneous analysis of various cardiovascular drug mixtures with vincamine: comparative eco-friendly assessment. BMC Chemistry 2024; 18: 197.
6. Yuan L, Liu W, Zhang S, et al. Optimization and validation of an HPLC method for the analysis of carvedilol and impurities. ACS Omega, 2025; 10(34): 39212-39224.
7. Jayavarapu KR, Dassari PK, Hussian MA, Reshma J. Method development and validation of Sitagliptin and Simvastatin in tablet dosage form by RP-HPLC. Int J Allied Med Sci Clin Res., 2024; 12(4): 480-487.
8. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Pharmaceutical development of fixed dose combination products. Geneva: ICH, 2009.
9. Snyder LR, Kirkland JJ, Dolan JW. Introduction to modern liquid chromatography. 3rd ed. Hoboken: Wiley, 2010.
10. Patel J, Patel A. Development and validation of RP-HPLC method for estimation of Simvastatin in tablet dosage form. J Pharm Sci Res., 2011; 3(3): 1028–31.
11. Kumar R, Rao K. Validated RP-HPLC method for determination of Carvedilol in pharmaceutical dosage forms. Int J Pharm Sci Rev Res., 2012; 14(2): 45–49.
12. Singh S, Sharma N. Simultaneous estimation of combined drug formulations by RP-HPLC: A review. Int J Pharm Pharm Sci., 2014; 6(4): 1–7.