

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF RIVAROXABAN IN
BULK DRUG AND PHARMACEUTICAL DOSAGE FORM BY RP-HPLC METHOD

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ABSTRACT

Rivaroxaban, an anticoagulant, plays a vital role in inhibiting blood clot formation. In this study, a reverse phase high-performance liquid chromatography (RP-HPLC) method was developed for the determination of rivaroxaban in tablets (Rivaban-10 mg). The method is simple, specific, accurate, and precise for the quantification of rivaroxaban in both bulk drug and pharmaceutical dosage forms. The analysis was conducted using an Agilent C18 column (4.6 mm × 100 mm) maintained at room temperature. The mobile phase was a mixture of methanol and 0.1% formic acid in a 65:35 (v/v) ratio, delivered at a flow rate of 1.0 mL/min. The effluent was monitored at 253 nm using a photodiode array (PDA) detector, and the total analysis time was 15 minutes. The method was validated according to ICH guidelines, with parameters such as linearity, accuracy, precision, specificity, limit of detection (LOD), limit of quantification (LOQ), and robustness assessed. The linearity range for rivaroxaban was found to be 5–30 µg/mL, with a correlation coefficient of 0.9992. The recovery rate for rivaroxaban ranged from 98% to 102%. The LOD and LOQ were determined to be 0.1242 µg/mL and 0.3776 µg/mL, respectively. This RP-HPLC method is reliable and has been successfully applied to the quantitative determination of rivaroxaban in tablet dosage forms, making it suitable for use in quality control testing laboratories.

KEYWORDS: RP-HPLC, Rivaroxaban, Analytical method development, Method validation, Anticoagulant, Tablet dosage form.

INTRODUCTION

Anticoagulants are used to prevent the formation of blood clots or to stop existing clots from growing larger. Blood clots can obstruct blood flow to vital organs like the heart or brain, potentially leading to heart attacks or strokes. Rivaroxaban, an oral anticoagulant based on oxazolidinone, is a potent and selective direct inhibitor of factor Xa. It is primarily used for preventing venous thromboembolism in adult patients following total hip or knee replacement surgeries.^[1] In addition to its anticoagulant properties, rivaroxaban has been implicated in the inhibition of the sodium-glucose co-transporter-2 (SGLT2), which is predominantly located in the proximal tubule of the nephron. SGLT2 is responsible for the reabsorption of approximately 90% of glucose in the kidneys. By inhibiting SGLT2, rivaroxaban facilitates the excretion of glucose through urine, which can aid in better glycemic control and potentially contribute to weight loss in patients with type 2 diabetes mellitus.^[1]

Rivaroxaban is a small molecule with low water solubility and a high degree of plasma protein binding (91–95%) in humans, primarily to serum albumin. Its elimination half-life is approximately 13.8 hours. The anticoagulant effect of rivaroxaban is largely due to its selective binding to the S1 and S4 pockets of factor Xa, a serine endopeptidase, which results in potent inhibition of its activity.^[2] By inhibiting factor Xa, rivaroxaban disrupts both the intrinsic and extrinsic pathways of the coagulation cascade, leading to a reduction in thrombin formation and the prevention of thrombus development. Importantly, rivaroxaban does not inhibit thrombin (activated Factor II) nor does it affect platelet function.^[3,4]

Chemically it is 5-chloro-N-[[[(5S)-2-oxo-3-[4-(3-oxomorpholin-4-yl) phenyl]-1, 3-oxazolidin-5-yl] methyl] thiophene- 2-carboxamide. Rivaroxaban has the empirical formula C₁₉H₁₈ClN₃O₅S and a molecular weight of 435.882 g/mol.^[5,6]

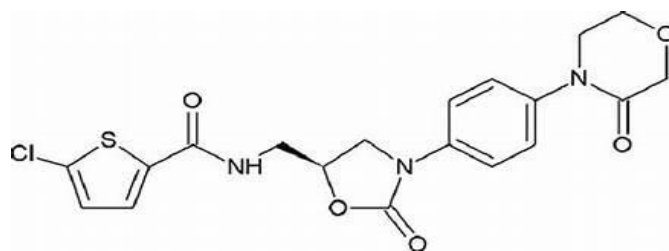


Figure 1: Chemical Structure of Rivaroxaban.

High-performance liquid chromatography (HPLC) is a separation technique where a solvent (Mobile phase) flows over a surface comprised of spherical particles or molecules (stationary phase). These particles coat the surface of the column. The separation is determined by the differing affinities of sample components for the stationary and mobile phases. HPLC is widely regarded as a reliable and cost-effective analytical method.^[7,8] The use of reverse-phase HPLC (RP-HPLC) often involves gradient elution, which can complicate the analysis. Therefore, the objective of this study is to develop an accurate, precise, robust, and consistent method for evaluating compounds in pharmaceuticals and drug products.^[9]

Rivaroxaban was approved for marketing by Health Canada and the European Commission in 2008. Although a method using HPLC-MS for determining rivaroxaban levels in human plasma for pharmacokinetic studies is documented in the literature, no method has been reported for its quantification in pharmaceutical dosage forms.^[10] Quality control is a critical aspect of the pharmaceutical industry, encompassing all procedures aimed at verifying the identity and purity of a pharmaceutical product.^[11] This includes stability testing of drug formulations, dissolution testing, and the analysis of raw materials and synthesized products. Given the need to analyze a large number of quality control samples, HPLC stands out as a versatile technique for examining a wide range of samples.^[12]

This study aimed to develop a straightforward, sensitive, rapid, and precise RP-HPLC method for the estimation of rivaroxaban. The analytical method was validated following the guidelines outlined by the International Council for Harmonisation (ICH) for method validation.

MATERIALS AND METHODS

Chemicals and Reagents

Rivaroxaban tablet formulation was obtained from a local pharmacy, specifically the marketed Rivaban-10 mg tablets (containing 10 mg of rivaroxaban per tablet) manufactured by Lupin Pharma Ltd., India. HPLC-grade methanol was sourced from Merck Ltd., India. Additionally, 0.1% orthophosphoric acid (OPA) of HPLC grade and HPLC-grade water were procured from Merck, Mumbai, India. The HPLC-grade water was prepared through double distillation and further purified using a Milli-Q water purification system.

Instrumentation

The drug analysis was performed using an Agilent Technologies gradient system equipped with an auto-injector, a UV(DAD) (model G13148, serial number DE71365875), and a quaternary gradient pump (model G130A, serial number DE9180834). The system was fitted with a reverse-phase Agilent C18 column (4.6 mm x 100 mm; 2.5 μ m particle size), a 20 μ L injection loop, and a UV730D absorbance detector. The system was operated using ChemStation software version 10.1.

Chromatographic conditions

Accurately weigh 10 mg of rivaroxaban working standard and transfer it into a 10 mL volumetric flask. Dissolve the standard in methanol, sonicate for 15 minutes to ensure complete dissolution, and then dilute to the mark with the same solvent to prepare a 1000 μ g/mL stock solution. From this stock solution, transfer 0.1 mL into another 10 mL volumetric flask and dilute to the mark with a mobile phase consisting of methanol and water containing 0.1% formic acid. This results in a 10 μ g/mL solution, which is used for chromatographic analysis under the specified conditions.

Table 1: Optimized chromatographic conditions.

Parameters	Conditions
HPLC	Agilent Tech. Gradient System With Auto injector, UV Detector
Software	Chemstation 10.1
Column	(Agilent) C18 column (4.6mm x 100mm)
Particle size packing	2.5 μ m
Stationary phase	C-18 (Agilent)
Mobile Phase	Methanol : 0.1% Formic acid 65 : 35
Detection Wavelength	253 nm
Flow rate	1 ml/min
Temperature	Ambient
Sample size	20 μ l

Ph	2.7
Run Time	15 min

Preparation of stock standard solution

Accurately weigh 10 mg of rivaroxaban working standard and transfer it into a 10 mL volumetric flask. Add methanol as the diluent, sonicate for 15 minutes to ensure complete dissolution, and then dilute to the mark with methanol to prepare a 1000 µg/mL stock solution. From this stock solution, transfer 0.1 mL into another 10 mL volumetric flask and dilute to the mark using a mobile phase consisting of methanol and water with 0.1% formic acid, prepared in a 6:4 ratio (6.0 mL methanol: 4.0 mL 0.1% formic acid water, v/v).

Preparation of sample solution

Twenty tablets were individually weighed to calculate the average weight, then finely powdered. An amount of powder equivalent to 10 mg of rivaroxaban was transferred into a 10 mL volumetric flask. Five milliliters of diluent were added, and the mixture was sonicated for 5 minutes at a controlled temperature to ensure complete dissolution. The solution was then diluted to the mark with the same diluent and filtered through a 0.45 µm membrane filter. From this filtered solution, 1 mL was further diluted to 10 mL with the same diluent to obtain a final concentration of 100 µg/mL of rivaroxaban.

Analytical method validation

Analytical method validation was carried out as per ICH method validation guidelines Q2 (R1).

Linearity

Linearity in an analytical method refers to its capacity to produce test results that are directly proportional to the concentration of the analyte within a specified range, either directly or through a well-defined mathematical transformation.

The linearity of a method is assessed by plotting the response signals against the analyte concentrations and visually inspecting the resulting plot. The evaluation should be conducted using standard solutions at five different concentration levels, with each concentration measured at least three times. An r^2 value greater than 0.998 is generally considered indicative of a good fit between the data points and the regression line.^[13]

Preparation of standard stock solution for linearity

A precise amount of 10 mg of rivaroxaban was weighed and transferred into a 10 mL volumetric flask. The volume was brought up to the mark with diluent, and the mixture was sonicated for 10 minutes with occasional swirling to ensure complete dissolution. From this solution, 0.1 mL was taken and further diluted to 10 mL with the same diluent to prepare the final solution.

Accuracy (Recovery)

The accuracy of an analytical method refers to how closely the test results align with the true value. It is

often expressed as the percentage recovery of a known quantity of analyte added to the sample. To determine accuracy, the method is applied to samples with known amounts of analyte added, and the percentage of the analyte recovered is calculated from the test results.^[13]

Repeatability

The precision of the system was evaluated using the sample solution. Two replicate injections of a sample containing 20 µg/mL of rivaroxaban were performed, and the peak areas were measured. The percentage relative standard deviation (% RSD) was calculated, and the process was repeated twice to ensure consistency.^[14]

Precision

The precision of an analytical method refers to the consistency of individual test results when the method is repeatedly applied to multiple samples of a homogeneous material. It is typically expressed as the standard deviation or relative standard deviation (%RSD). Additionally, the results were analyzed using one-way ANOVA to compare within-day and between-day variations, with the mean squares from both assessed using the F-test.^[13]

Robustness

The robustness of an analytical method refers to its ability to remain consistent despite small, intentional variations in procedural parameters. This characteristic indicates the method's reliability under typical usage conditions.^[15]

Specificity

Specificity refers to the method's ability to accurately identify and measure the analyte in the presence of other components, such as impurities, degradation products, and matrix elements. The response of the analyte in the sample, including these potential interfering substances, is compared to the response of a solution containing only the pure analyte.^[14]

Limit of detection (LOD) and Limit of quantification (LOQ)

The Limit of Detection (LOD) is the lowest concentration of the analyte that can produce a detectable signal, while the Limit of Quantification (LOQ) is the lowest concentration that can be measured with acceptable accuracy and precision. In this study, six replicates of the analyte at the lowest concentration were analyzed and quantified.

The LOD and LOQ for the developed method were established by injecting progressively lower concentrations of the standard solution using the HPLC method.^[13]

Range

The range of an analytical method is the span between the highest and lowest concentrations of the analyte in the sample, within which the method has been shown to maintain acceptable precision, accuracy, and linearity.^[13]

Analysis of marketed formulation

To determine the rivaroxaban content in marketed tablets, 20 tablets were weighed, and the average weight was calculated. The tablets were ground into a fine powder, and an amount equivalent to 56.2 mg of rivaroxaban was accurately weighed. The drug was extracted from the powdered tablets using 10 mL of methanol, followed by sonication for 15 minutes to ensure complete extraction. After sonication, 0.2 mL of the supernatant was diluted to 10 mL with the mobile phase. This solution was injected into the HPLC system, and the drug's peak area was recorded.

A regression equation was generated from the peak areas of standard solutions. Using this regression equation and the peak area obtained from the sample, the rivaroxaban content in the sample was calculated. The amount of

rivaroxaban per tablet was determined based on the regression equation derived from the calibration curve, as detailed in the analysis of the tablet formulation in the results section.

RESULT AND DISCUSSION**1. Preliminary studies on Rivaroxaban****1.1. Melting point**

The procured reference standard of Rivaroxaban was found to reported melt in the range of 74-78°C respectively.

1.2. Solubility

The drug was found to be:

- Freely soluble in DMSO, Acetone, Ethanol, Methanol
- Insoluble in Water

1.3. UV Spectroscopy

UV absorption of 20 µg/mL solution of Rivaroxaban in methanol was generated and absorbance was taken in the range of 200-400 nm. 253 λ_{max}.

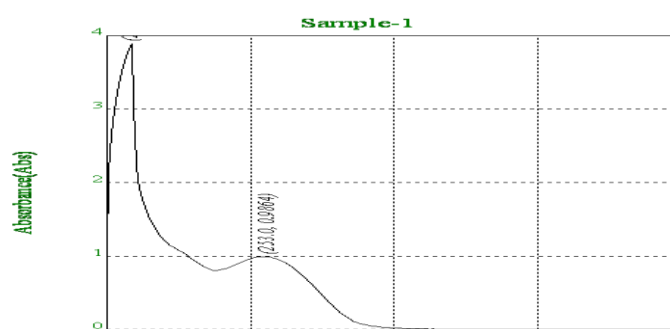


Figure 2: UV spectrum of Rivaroxaban.

Standard solutions were scanned within the wavelength range of 200-400 nm using a methanol solvent system as the reference. Rivaroxaban in methanol exhibited a maximum absorbance at 253 nm, which was chosen as the selected wavelength, as shown in Figure 2.

1.4. Chromatogram of rivaroxaban

After the selection of suitable mobile phase, it was then optimized for its reproducibility, sensitivity & accuracy. The optimized parameters for selected method are as below.

The results of optimized chromatographic conditions were shown in Table 1 and Figure 3.

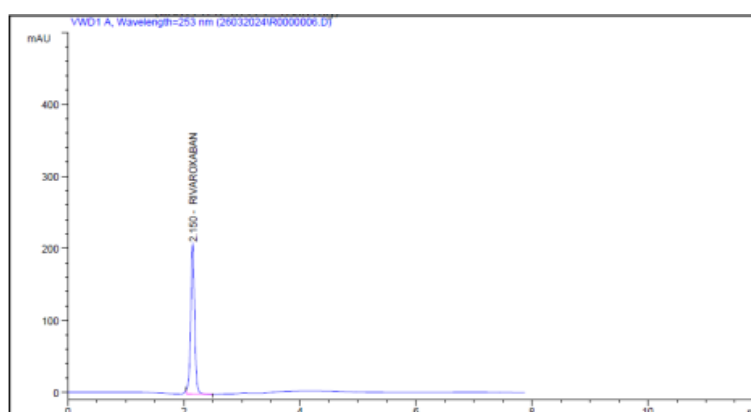


Figure 3: Chromatogram of standard rivaroxaban.

2. Analytical of method validation

1. Linearity

Working standard solutions of rivaroxaban, ranging from 10 to 50 µg/mL, were prepared from the standard stock solution using the mobile phase. A 20 µL aliquot of each sample solution was injected into the chromatographic

system using a mixed volume loop injector, and chromatograms were recorded. The peak areas corresponding to each concentration were documented (Table 2). The calibration curves are presented in Figure 4.

Table 2: Linearity of Rivaroxaban.

Sr. No.	Concentration µg/ml	Area Rivaroxaban
1	10	985.23
2	20	1989.82
3	30	3074.07
4	40	4085.68
5	50	4995.67

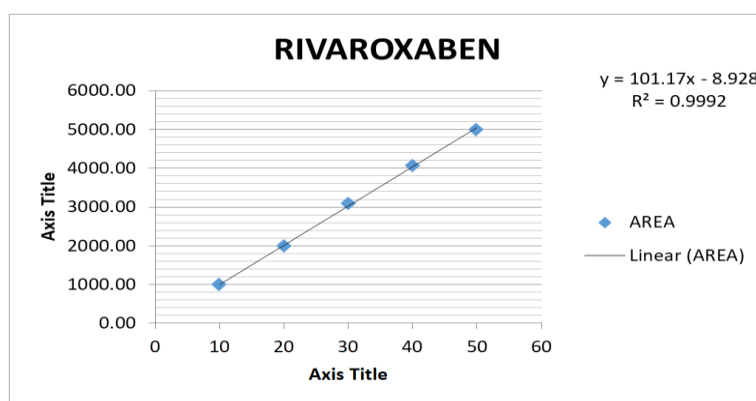


Figure 4: Calibration curve of Rivaroxaban.

Table 3: Regression equation data for Rivaroxaban.

Regression Equation Data Y=mx+c	
Slope(m)	101.1
Intercept(c)	8.928
Correlation Coefficient	0.999

- Linearity of Rivaroxaban was observed in the range of 5-30 µg/ml. Detection wavelength used was 253 nm.
- The calibration curve yielded correlation coefficient (r^2) 0.999 & 0.999 for Rivaroxaban respectively in table 3.

2. Accuracy

Recovery studies were performed to validate the accuracy of developed method. To pre analyzed Tablet solution, a definite concentration of standard drug (80%, 100%, and 120%) was added and then its recovery was analyzed (Table 4). Statistical validation of recovery studies shown in (Table 5).

Accuracy 80%

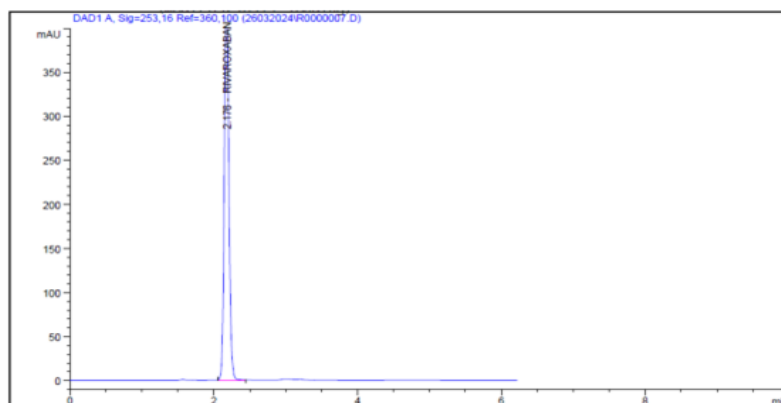
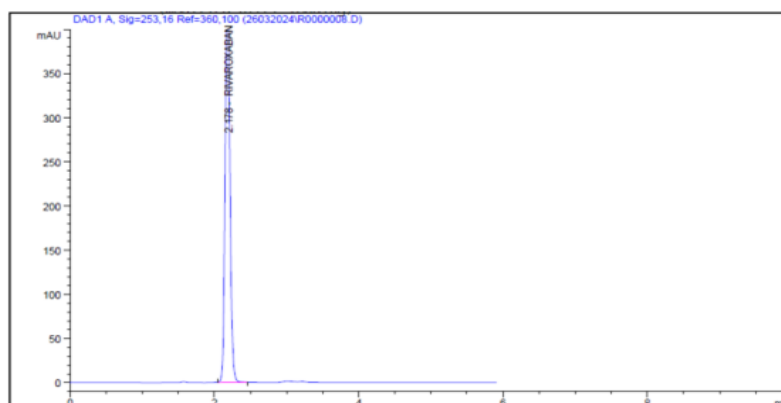
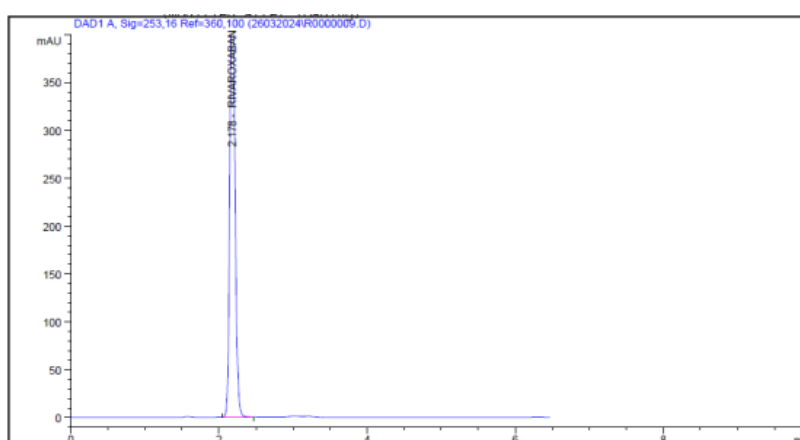


Figure 5: Chromatogram of Accuracy 80%-01.

Accuracy 100%**Figure 6: Chromatogram of Accuracy 100%-01.****Accuracy 120%****Figure 7: Chromatogram of Accuracy 120%-01.****Table 4: Result of recovery data for rivaroxaban.**

Drug	Sr No.	Level (%)	Amt. taken (µg/ml)	Amt. Added (µg/ml)	Area. Mean* ± S.D.	Amt. recovered Mean *±S.D.	%Recovery Mean *± S.D.
RVK	1	80%	10	8	17.9± 0.027	7.95± 0.027	99.36±0.34
	2	100%	10	10	20.1±10.18	10.18±0.098	101.82± 0.98
	3	120%	10	12	22.1±0.009	12.19±0.009	101.61 ±0.07

*mean of each 3 reading.

Table 5: Statistical Validation of Recovery Studies Rivaroxaban.

Level of Recovery (%)	Mean % Recovery	Standard Deviation*	% RSD
80%	99.36	0.34	0.35
100%	101.82	0.98	0.96
120%	101.61	0.07	0.07

*Denotes average of three determinations

Accuracy of method is ascertained by recovery studies performed at different levels of concentrations (80%, 100% and 120%). The % recovery was found to be within 98-102% (Table 4 & 5).

3. System suitability parameters (Repeatability)

To ascertain the resolution and reproducibility of the proposed chromatographic system for estimation of Rivaroxaban system suitability parameters were studied. The result shown in below (Table 6).

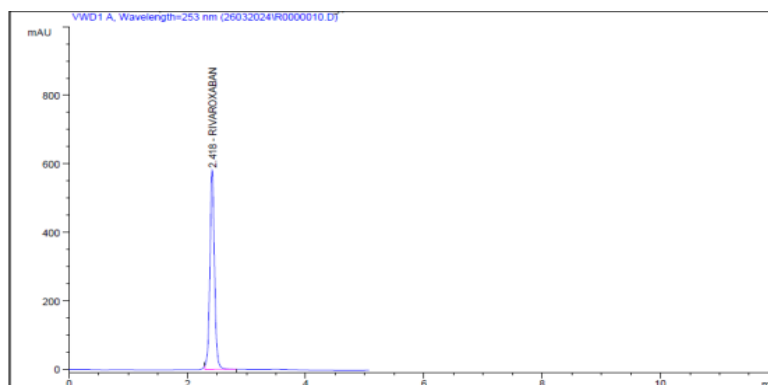


Figure 8: Chromatogram of System suitability No- 1 hr.

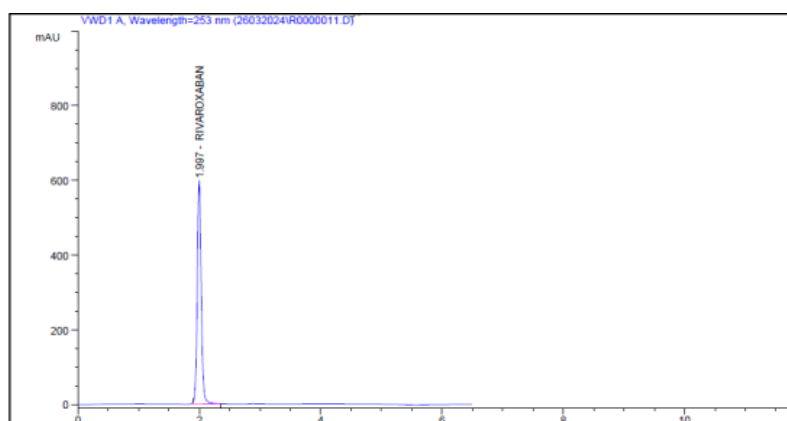


Figure 9: Chromatogram of System suitability No- 2 hr.

Result for Repeatability (SST)

Chromatogram System Suitability Results was found to be mean of five determination were also satisfactory,

hence the analytical method would be concluded that result shown in Table 6.

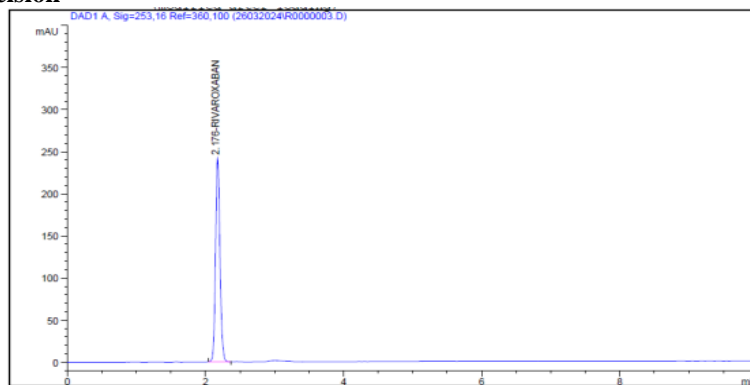
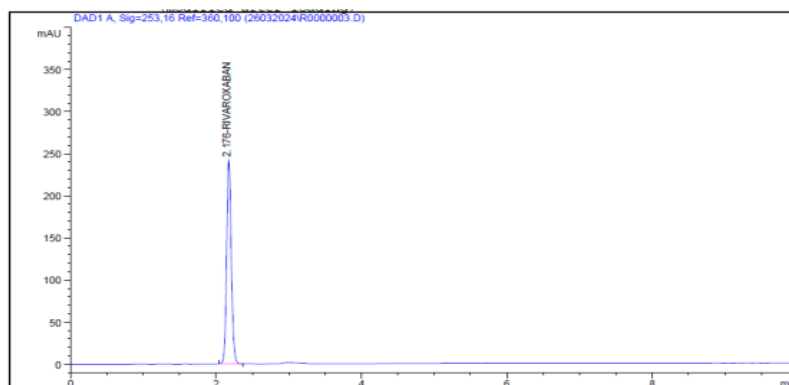
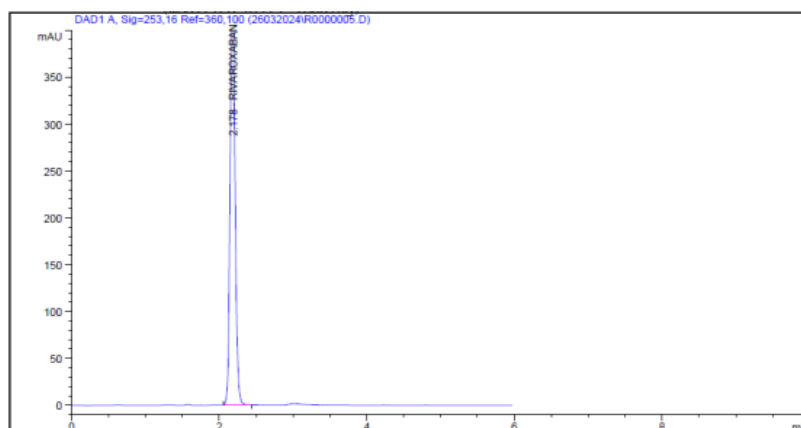
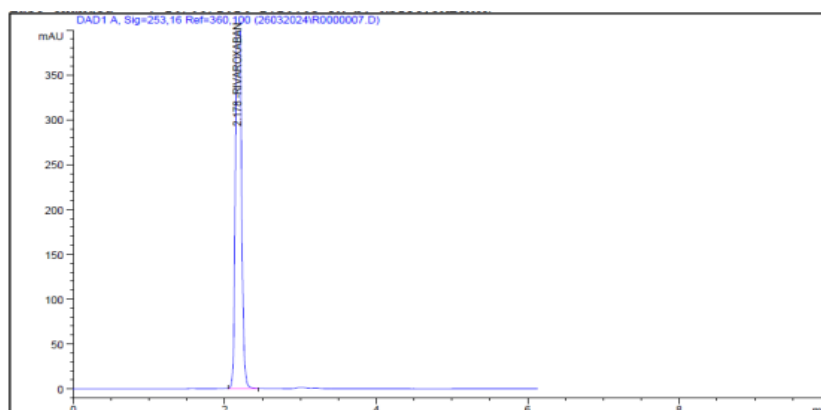
Table 6: Repeatability studies on Rivaroxaban.

Sr. no.	Concentration of Rivaroxaban (mcg/ml)	Peak area	Amount found (mg)	% Amount found
1	30.00	3012.556	29.69	98.98
2	30.00	3009.287		
	Mean	3010.92		
	SD	2.31		
	%RSD	0.08		

- Repeatability studies Rivaroxaban was found to be, The % RSD was less than 2, which shows high percentage amount found in between 98% to 102% indicates the analytical method that concluded (Table 6).

4. Precision

The method was established by analyzing various replicates standards of Rivaroxaban. All the solution was analyzed thrice in order to record any intra-day & inter-day variation in the result that concluded. The result obtained for intraday is shown in table 7 respectively.

Chromatogram of precision**Figure 10: Chromatogram of precision.****Figure 11: Chromatogram of Intraday precision (10 mcg).****Figure 12: Chromatogram Intra-day precision (20 mcg).****Figure 13: Chromatogram Intra-day precision (30 mcg).**

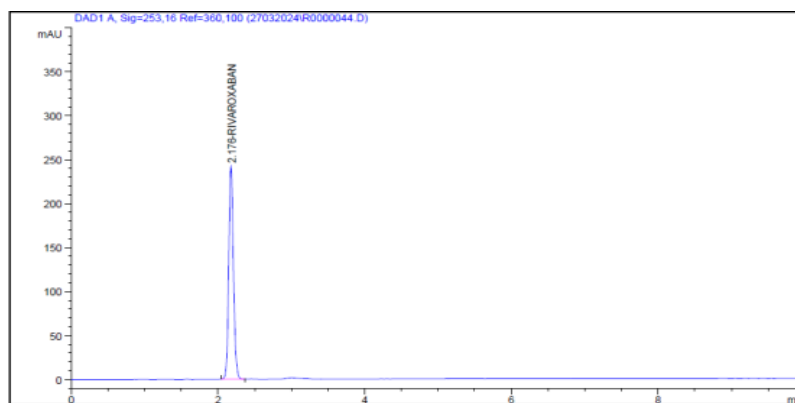


Figure 14: Chromatogram Inter-day precision (10 mcg).

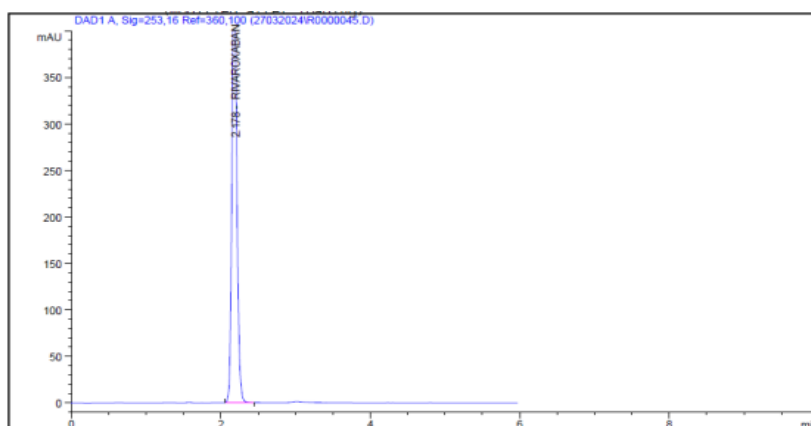


Figure 15: Chromatogram Inter-day precision (20 mcg).

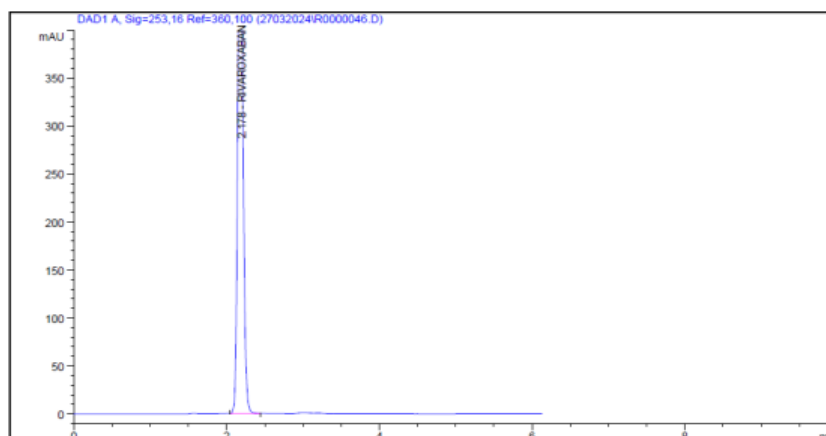


Figure 16: Chromatogram Inter-day precision (30 mcg).

Table 7: Result of Intraday and Inter day Precision for Rivaroxaban.

Concn (µg/ml)	Intraday Precision			Interday Precision		
	Mean± SD	%Amt Found	%RSD	Mean± SD	%Amt Found	%RSD
10	1028.49±0.10	102.61	0.48	1030.5±3.01	101.05	0.29
20	2050.48±2.15	101.85	0.46	2054.19±9.01	101.15	9.01
30	3015.65±1.74	99.72	0.21	3016.83±1.98	99.17	0.07

*Mean of each 3 reading

- Intraday and Inter day Precision for Rivaroxaban which shows the high precision %amount in between 98% to 102% indicates to analytical method that concluded.

5. Robustness

The robustness of a method refers to its ability to remain consistent despite small, intentional variations in its parameters. To assess the robustness of the proposed method, deliberate minor changes were made to the

optimized method parameters. The effects of variations in mobile phase composition, flow rate, and wavelength on the retention time and tailing factor of the drug peak were examined.

The mobile phase composition was adjusted by ± 1 mL/min, and the flow rate was varied within the

optimized chromatographic conditions. The results of the robustness evaluation are presented in Table 8. The robustness parameters were found to be satisfactory, indicating that the analytical method is reliable under varying conditions.

Flow Rate Change 0.9 ml

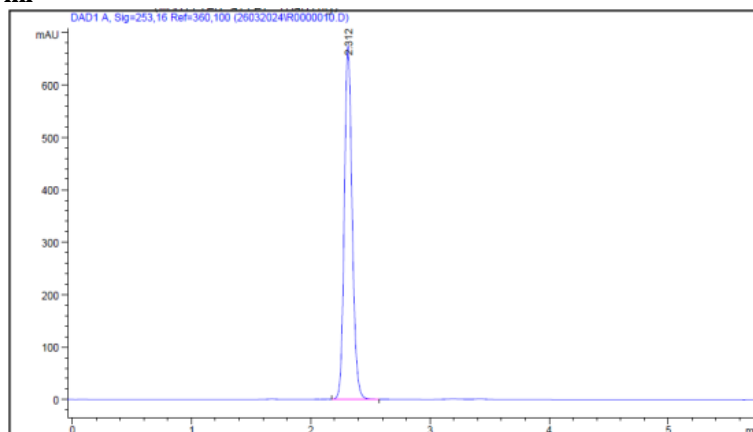


Figure 17: Chromatogram of Flow rate change 0.9ml-01.

Flow Rate Change 1.1 ml

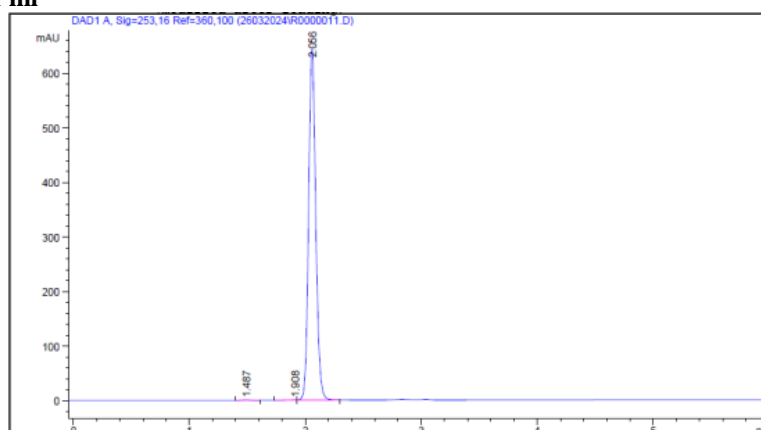


Figure 18: Chromatogram of Flow rate change 1.1 ml-01.

Mobile phase composition Change: 64 ml Meoh + 0.1% buffer)36ml Water.

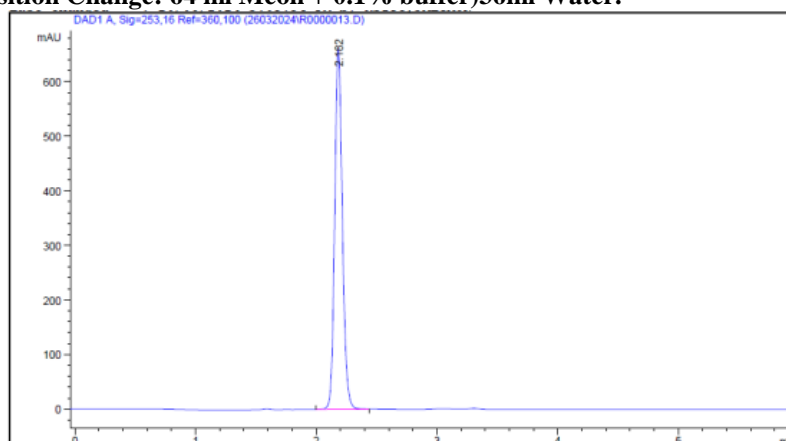
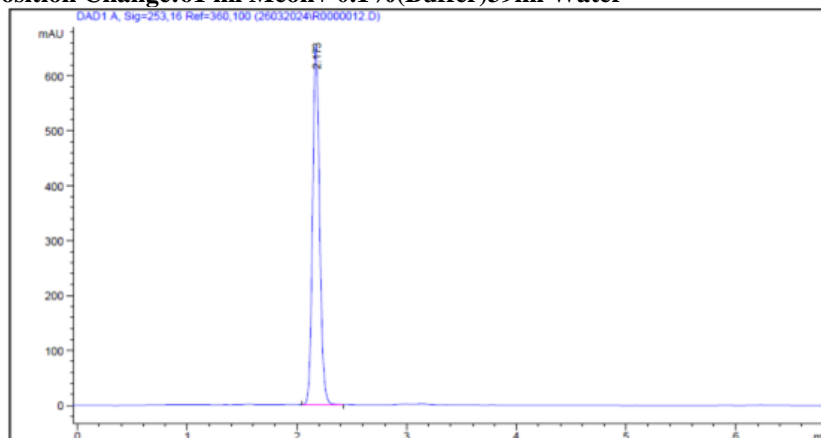
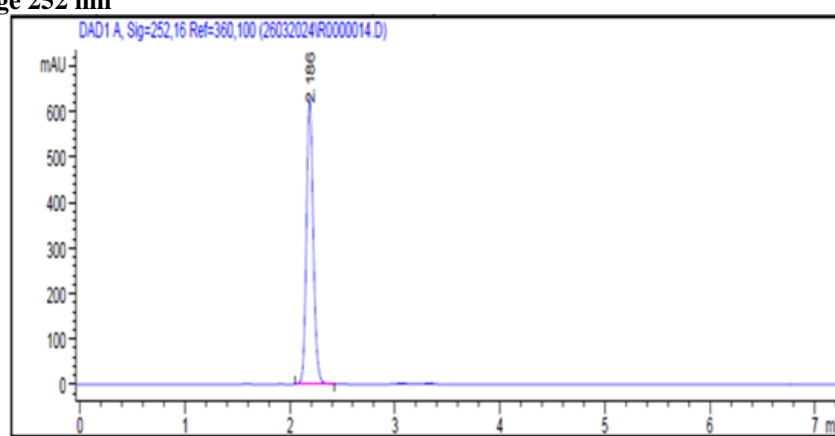
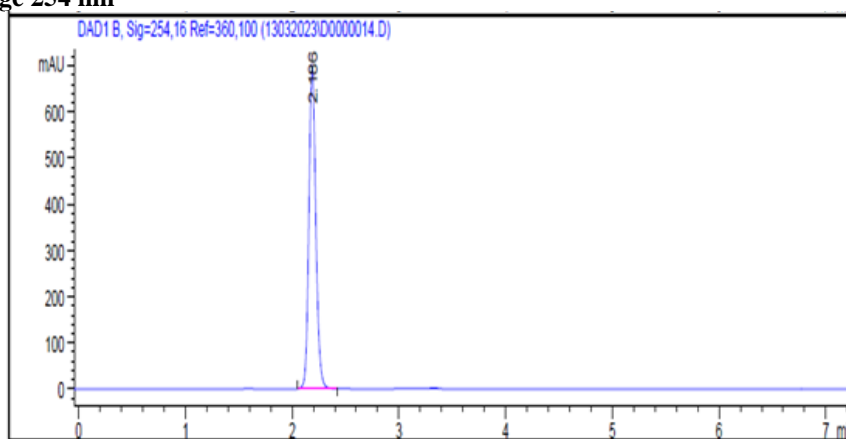


Figure 19: Chromatogram of Mobile phase composition change 64ml Meoh + 0.1 % (buffer)36ml Water.

Mobile phase composition Change: 61 ml Meoh+ 0.1%(Buffer)39ml Water**Figure 20: Chromatogram of Mobile phase composition change 66ml Meoh +0.1 % (Buffer) 34ml Water.****Wavelength Change 252 nm****Figure 21: Chromatogram of wavelength change 252 nm.****Wavelength Change 254 nm****Figure 22: Chromatogram of wavelength change 254 nm.****Table 8: Result of Robustness Study of Rivaroxaban**

Parameters	Conc. (µg/ml)	Amount of detected (mean ±SD)	%RSD
Mob-phase composition 64 + 36 ml) Methanol + 0.1% (Buffer) water	30	2925.3±14.27	0.49
Mob-phase composition (66 ml + 34 ml) Methanol + 0.1% (Buffer) water	30	2928.40±6.85	0.23
Wavelength change 252 nm	30	2866.4±27.56	0.96

Wavelength Change 254 nm	30	1224.41±4.24	0.35
Flow rate change (0.9 ml)	30	3097.1±2.12	0.07
Flow rate change (1.1 ml)	30	2953.20±7.02	0.24

Robustness study of rivaroxaban

Changes were made to the flow rate (± 1 mL/min), the pH of the mobile phase, and the wavelength to assess the method's robustness. The %RSD for the peak area was calculated and should be less than 2%. The results, as presented in Table 8, demonstrate that the analytical method remained consistent and reliable under these variations.

6. Limit detection

The LOD is the lowest limit that can be detected. Based on the S.D. deviation of the response and the slope the limit of detection (LOD) may be expressed as:

$$\text{LOD} = 3.3 (\text{SD})/S = 3.3 \times 3.82 / 101.1 = \mathbf{0.1242}$$

Where, SD = Standard deviation of Y intercept

S = Slope

The LOD of Rivaroxaban was found to be 0.1242 ($\mu\text{g/mL}$) analytical methods that concluded.

7. Limit quantification

The LOQ is the lowest concentration that can be quantitatively measured. Based on the S.D. deviation of the response and the slope,

The quantitation limit (LOQ) may be expressed as:

$$\text{LOQ} = 10 (\text{SD})/S = 10 \times 3.82 / 101.1 = \mathbf{0.3776}$$

Where, SD = Standard deviation Y intercept

S = Slope

The LOQ of Rivaroxaban was found to be 0.3776 ($\mu\text{g/mL}$) analytical methods that concluded.

3. Analysis of tablet formulation

Procedure

Weigh 20 rivaroxaban tablets and calculate the average weight. Accurately weigh and transfer an amount equivalent to 56.2 mg of rivaroxaban into a 10 mL volumetric flask. Add approximately 10 mL of diluent, sonicate until completely dissolved, and then dilute to the mark with diluent. Mix thoroughly and filter the solution through a 0.45 μm filter. Transfer 0.2 mL of the filtered stock solution into a 10 mL volumetric flask and dilute to the mark with diluent to obtain a concentration of 20 $\mu\text{g/mL}$. Chromatograms of the test samples are shown in Figures 23 and 24. The amount of rivaroxaban per tablet was determined by extrapolating the area value from the calibration curve. The analysis was repeated five times for the tablet formulation. The assay results, including the % label claim and % RSD, are presented in Tables 27 and 28.

Brand name: Rivaban-10 (10 mg) (Cipla Pvt)

Total weight of 20 Tablet Powder wt.	11.24gms
Avg Powder Weight	56.2 gms./Tab
Eq. Wt for 5 mg	10 x 56.2 / 10 = 56.2 mg
Take 56.2 mgs in 10 water i.e	1000 $\mu\text{g/mL}$ Rivaroxaban

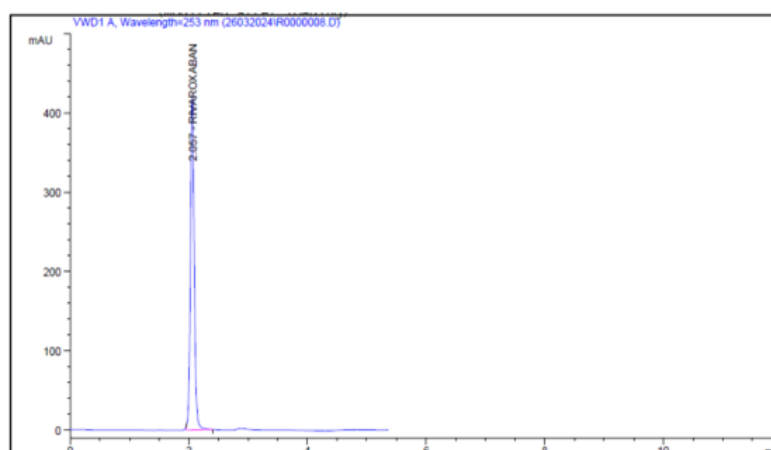


Figure 23: Chromatogram for marketed formulation.

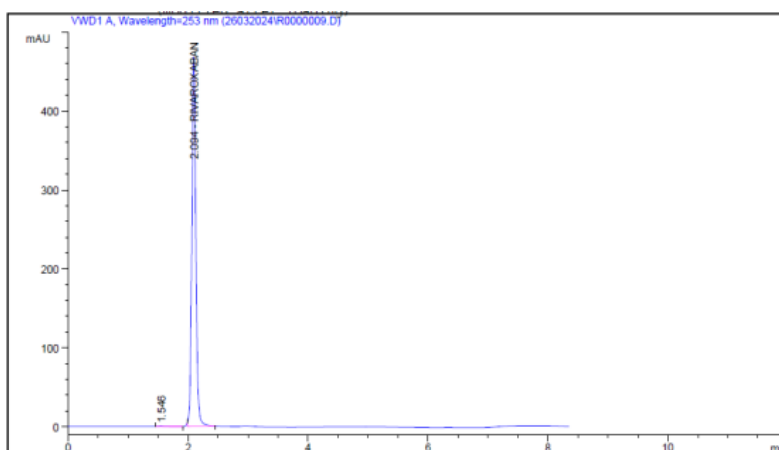


Figure 24: Chromatogram for marketed formulation.

Table 9: Analysis of marketed formulation.

Sr.no	Amount present in mg	Area(I)	Amount found in mg	% Label claim
	RVK	RVK	RVK	RVK
1	20	1998.366	19.67792	98.39
2	20	2000.113	19.6952	98.48
Mean	-	1999.24	19.69	98.43
SD	-	1.236	0.012	0.061
%RSD	-	0.062	0.062	0.062

- Analysis of marketed formulation were also % Label Claim was found to be 98-102% Satisfactory are concluded (Table 9).
- Tablet Assay for % Label Claim

Table 10: Tablet for % Label claim.

Sample	Label claimed	% Label claimed \pm SD	% RSD
Rivaban	10mg	98.43 \pm 0.061	0.062

Tablet Assay for % Label claim for was also was found to be 100.99% and %RSD are less than 2 satisfactory results that concluded (Table 10).

SUMMARY AND CONCLUSION

Rivaroxaban is an anticoagulant. This study focuses on the "Analytical Method Development and Validation of Rivaroxaban in Bulk Drug and Pharmaceutical Dosage Form by RP-HPLC." The objective was to develop an RP-HPLC method for the simultaneous estimation of rivaroxaban in tablet formulations.

The method utilized an Agilent Tech Gradient System equipped with an auto-injector, UV (DAD) and gradient detector, a Reverse Phase Agilent C18 column (4.6 mm x 100 mm; 2.5 μ m), a 20 μ L injection loop, and a UV730D absorbance detector, with ChemStation 10.1 software for analysis. The mobile phase consisted of methanol and water with 0.1% formic acid (65:35, v/v) at pH 3, with a detection wavelength of 253 nm and a flow rate of 1 mL/min. The retention time for rivaroxaban was 2.150 minutes.

The developed method was validated according to ICH guidelines, demonstrating linearity, precision, range, and

robustness within the specified limits. The method proved to be simple, accurate, precise, cost-effective, and reproducible. Therefore, it is suitable for routine quality control analysis of rivaroxaban in both bulk drug substances and pharmaceutical formulations.

Conclusions for HPLC method

- The developed RP-HPLC method provides selective and reliable quantification of rivaroxaban. It has demonstrated accuracy, precision, robustness, and specificity.
- This method offers advantages over previously reported methods due to its shorter retention time, isocratic mode, and the use of a cost-effective, readily available mobile phase and column. Additionally, it utilizes UV detection and achieves better peak resolution.
- The results obtained using the proposed method were consistent with the label claim of the formulation. The low standard deviation and coefficient of variation values confirm the method's suitability for the routine analysis of rivaroxaban in tablet dosage forms.

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