A Novel QbD Approach to HPLC Estimation of Ticagrelor

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ABSTRACT

Ticagrelor is a potent oral antiplatelet agent widely used in the management of acute coronary syndrome and other cardiovascular disorders. Accurate and reliable analytical methods are essential for ensuring the quality, safety, and efficacy of pharmaceutical formulations containing ticagrelor. The present study aimed to develop, optimize, and validate a simple, sensitive, and cost-effective Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) method for the quantitative estimation of ticagrelor using a Quality by Design (QbD) approach. A Central Composite Design (CCD) was employed to systematically evaluate the effects of critical analytical parameters, including mobile phase composition and flow rate, on chromatographic responses such as retention time, peak area, theoretical plates, and peak symmetry. The optimized chromatographic conditions consisted of a Zorbax SB-C18 column with a mobile phase comprising methanol and 0.1 N citric acid solution in the ratio of 84.6:15.4 (v/v) at a flow rate of 0.97 mL/min. Under these conditions, ticagrelor exhibited a sharp and symmetrical peak with satisfactory retention time and resolution. The developed method demonstrated excellent linearity within the concentration range of 5–25 µg/mL, with a correlation coefficient of 0.9994. Validation studies performed according to ICH guidelines confirmed the method's accuracy, precision, specificity, repeatability, robustness, and ruggedness. Recovery studies showed an average recovery of 100.69%, indicating excellent accuracy and reliability of the method. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.115 µg and 0.349 µg, respectively. The QbD-based RP-HPLC method proved reliable, economical, and suitable for routine quality control and quantitative analysis of ticagrelor pharmaceutical formulations.

Keywords: Central composite design (CCD), P2Y12 receptor inhibitor, Quality-by-design (QbD), Ticagrelor, Validation.

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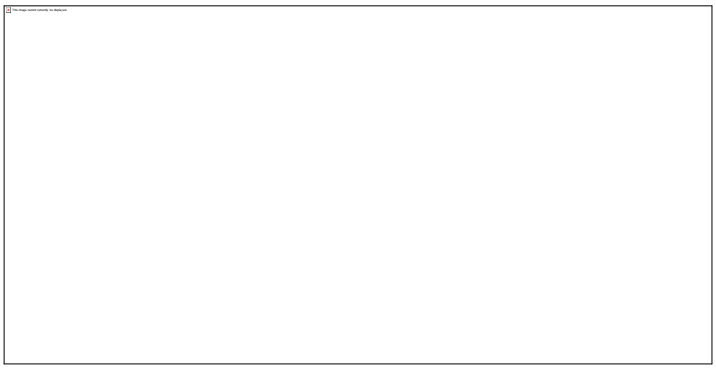
GRAPHICAL ABSTRACT



INTRODUCTION

The most common deadly and disabling health conditions throughout the world stem from cardiovascular diseases. The condition develops when a blood vessel forms a thrombus which blocks essential blood flow to organs including the heart and brain[1][2][3]. The initiation of these thrombotic events occurs because platelets in blood begin to activate and aggregate together to form clots [2] [3]. Antiplatelet therapy has become essential to both preventing and treating acute coronary syndromes (ACS) and myocardial infarction and ischemic stroke.[4][5][6] Among the various pathways involved in platelet activation, the adenosine diphosphate (ADP)–mediated signalling pathway through the P2Y12 receptor is particularly important in amplifying platelet aggregation[7]. Clinical practice evidence demonstrates that healthcare professionals use drugs which block this receptor to decrease thrombus formation risks [4] [6]. The thienopyridine class includes clopidogrel and prasugrel which function as irreversible P2Y12 receptor antagonists [8]. The agents require metabolic activation before they can produce their effects which lead to different results for patients [9]. Ticagrelor serves as a new oral antiplatelet drug which belongs to a different pharmacological category called cyclopentyl-triazolo-pyrimidines.[10][11][12]Ticagrelor directly inhibits the P2Y12 receptor through reversible binding without requiring metabolic activation in contrast to thienopyridines[14]. The drug's mechanism of action provides patients with faster relief from their symptoms while producing consistent results in preventing blood platelets from clumping together [15]. Ticagrelor not only prevents platelet aggregation but also affects extracellular adenosine level which contributes to its cardiovascular benefits. [16][17]

Ticagrelor has become an essential treatment for acute manifestations of coronary artery syndromes and percutaneous coronary intervention patients because of its strong and continuous ability to prevent platelets from clumping together [4]. The therapeutic application of ticagrelor in cardiovascular disease treatment requires knowledge of its drug properties and its mechanism of action and medical value.[5]

PHARMACOLOGY OF TICAGRELOR

Ticagrelor, classified under cyclopentyl-triazolo-pyrimidines, functions as an oral antiplatelet medication by reversibly blocking the platelet P2Y12 receptor.[10][11]The drug introduces a new class of antiplatelet drugs which operates through different mechanisms than thienopyridines clopidogrel and prasugrel which permanently block the same target[6][8][12]. Ticagrelor operates as a direct-acting drug which does not need metabolic activation for its therapeutic effects. [18][19]

MECHANISM OF ACTION

Ticagrelor binds to the P2Y12 receptor at a site that does not overlap with the ADP binding site and thus inhibits platelet activation through its reversible non-competitive action. [7] [14] This binding blocks the activation of receptors through ADP because it hinders all downstream pathways which lead to platelet aggregation. The receptor stays in its inactive state which prevents platelet aggregation from happening. The P2Y12 receptor activation causes Gi-protein to inhibit adenylate cyclase activity which results in decreased cyclic adenosine monophosphate (cAMP) levels that lead to increased platelet aggregation. The receptor blocker ticagrelor prevents cAMP levels from decreasing which enables the body to maintain its intracellular signalling pathways that stop platelets from becoming active.[7] Ticagrelor and its active metabolite block the equilibrative nucleoside transporter-1 (ENT-1) which leads to higher levels of adenosine in the extracellular space[16][17]. The increased adenosine levels lead to two effects which include antiplatelet activity and vasodilation through A2A receptor activation. [16]

PHARMACODYNAMIC PROPERTIES

Ticagrelor produces potent, effective and consistent antiplatelet activity which outperforms earlier P2Y12 inhibitors. [15] The drug exhibits reduced inter-patient response differences because it does not need hepatic metabolic activation which prodrugs like clopidogrel require. The active metabolite of ticagrelor AR-C124910XX functions as an antiplatelet agent which shows P2Y12 receptor binding strength that matches the original drug. [10]

PHARMACOKINETIC PROPERTIES

Ticagrelor is an oral medication which begins to show its antiplatelet effects soon after patients take the drug. [18][22] .The drug undergoes primary metabolic processing within the liver which produces an active metabolite that leads to the total pharmacodynamic effects of the drug. The drug's reversible receptor binding causes its antiplatelet

effects to depend on drug levels in the bloodstream instead of how long platelets exist in the body. [19]

ADVERSE EFFECTS

1. Bleeding: The most important and frequently occurring adverse reaction with ticagrelor treatment is bleeding. This is due to the inhibition of platelet aggregation by the drug. Minor bleeding such as nosebleeds, bruising, and gastrointestinal bleeding may occur. [4][23]

2. Dyspnea: Shortness of breath is a frequently occurring adverse reaction with ticagrelor treatment. This usually occurs shortly after treatment with ticagrelor. It is usually a minor adverse reaction. In most patients, lung function is unaffected by ticagrelor treatment, and the symptoms disappear once the treatment is stopped. [17][24]

3. Bradyarrhythmia: Ticagrelor may cause slowing of the heart rate, including pauses in the heart's ventricles during early treatment with the drug. This usually does not cause symptoms and tends to improve with continued treatment. [24]

4. Hyperuricemia: Increased levels of serum uric acid may occur with ticagrelor treatment. This may pose a problem to patients with a history of gout. [25]

5. Gastrointestinal Disturbances: Some individuals may complain of gastrointestinal upsets such as nausea, diarrhoea, and abdominal discomfort during treatment with the drug. [26]

6. Headache and Dizziness: Occasional neurological effects such as headache, dizziness, and fatigue have been reported during treatment with the drug. [26]

7. Hypersensitivity Reactions: While rare, some individuals may exhibit hypersensitivity reactions such as rash, itching, and angioedema during treatment with the drug. [25]

8. Elevated Creatinine Levels: Some increases in serum creatinine levels have been reported in some individuals during treatment with the drug. [21][25]

OBJECTIVES

- To establish an easy, perceptive, accurate, and cost-effective approach based on reverse-phase high-performance liquid chromatography in evaluating ticagrelor's pharmaceutical preparations quantitatively.
- To optimize the HPLC conditions including the composition of the mobile phase, rate of its flow, analytical wavelength in addition to column characteristics for separating as well as detecting ticagrelor efficiently.
- To establish the validity of the optimized reverse phase high-performance liquid chromatography approach in compliance with ICH guidelines including evaluation of precision, accuracy, specificity, linearity, LOD together with LOQ.
- Application of the RP-HPLC analytical method validated as per guidelines, to perform ticagrelor's assay-based evaluation of raw materials in conjunction with commercial formulations.
- To ensure that the entire method is cost-effective, requires fewer solvents, has shorter run times, and is provided at reasonable costs without compromising quality.

METHODS

Chemicals: Ticagrelor (Standard drug), Methanol (HPLC grade), Distilled Water**,** 0.1 N Citric Acid (used in mobile phase)

REAGENTS

Methanol: 0.1 N Citric Acid (84.6: 15.4 v/v)

APPARATUS

Instrument:
Agilent 1100 Series High-Performance Liquid Chromatography System (HPLC) Software*: ChemStation*

Chromatographic Column: Zorbax SB-C18 Column

- Dimensions: **4.6 × 250 mm**
- Particle size: **5.0 µm**
- Stationary phase: **C18 (Agilent)**

STRUCUTRE

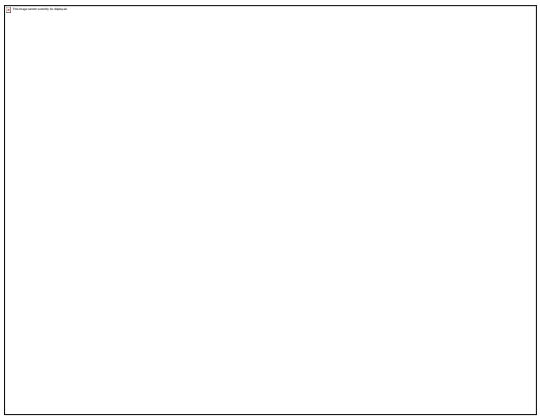


Figure 1: Structure of Ticagrelor

3-[7-[2-(3, 4-difluorophenyl) cyclopropyl] amino]-5-propylsulfanyltriazolo [5, 4-d] pyrimidin-3-yl]-5-(2-hydroxyethoxy) cyclopentane-1, 2-diol

CENTRAL COMPOSITE DESIGN

A central composite design (CCD) is a commonly employed experimental design within the Response Surface Methodology (RSM) framework. It accommodates full, fractional, or factorial layouts and is preferred due to its flexibility and ability to model curvature in the response surface. In this design, the experimental region is defined by a central point along with axial (or "star") points that extend beyond the factorial space. These axial points help in accurately estimating the quadratic effects of the studied factors. Because of its reliability in exploring and optimizing multivariable systems, CCD is frequently selected when precise interpretation of experimental responses is required.

In the present study, the effect of selected analytical parameters on method performance was evaluated. The independent variables investigated were the composition of the mobile phase (methanol-to-water ratio) and the flow rate. The responses assessed included retention time, peak area, number of theoretical plates, and peak symmetry.

A suitable column was chosen as per the requirements of the analytical procedure. Subsequently, different combinations of mobile phase ratios and flow rates were prepared and tested. The experimental runs generated through the CCD approach provided a structured dataset that facilitated method optimization and supported the later validation of the optimized chromatographic conditions.

Among the investigated conditions, the methanol–water ratio of 84.6: 15.4 (v/v) at a flow rate of 0.97 mL/min exhibited the most desirable chromatographic performance. This composition provided optimal retention time (~4.2 min), maximum peak area, high theoretical plate count, and excellent peak symmetry. The sharp and symmetrical peak obtained at this ratio indicates superior resolution and sensitivity.

Std	Run	FACTOR 1 MOBILE PHASE	FACTOR 2 FLOW RATE	R1 RT	R2 AREA	R3 TP	R4 TF
		%	mL/MIN	MIN	AUC	TP	TF
1	1	83	0.8	6.052	1269.485	6765	0.65
11	2	88	0.9	4.190	1131.926	6262	0.64
10	3	88	0.9	4.180	1136.544	6244	0.64
5	4	80.9289	0.9	6.170	1129.461	5942	0.67
4	5	93	1	3.185	1030.658	5059	0.70
2	6	93	0.8	3.936	1306.981	6008	0.68
7	7	88	0.758579	5.030	1367.732	7094	0.63
6	8	95.0711	0.9	3.334	1174.798	4699	1.06
12	9	88	0.9	4.206	1137.675	6242	0.65
8	10	88	1.04142	3.643	989.040	5602	0.65
3	11	83	1	4.912	1018.829	5688	0.67
9	12	88	0.9	4.205	1141.978	6255	0.64
13	13	88	0.9	4.172	1139.231	6248	0.64

Table 1: Experimental runs with independent variables are represented by the Central Composite Design (CCD) matrix, where **A** = Composition of mobile phase (%), **B** = Flow rate (mL/min), **RT** = Retention time (min), **AUC** = Area under curve, **TP** = Theoretical plates, **TF** = Tailing factor.

MOBILE PHASE PREPARATION

The mobile phase was created by combining 84.6 ml of methanol with 15.4 ml of water that contained 0.1N citric acid, achieving an 84.6:15.4 %v/v ratio. Subsequently, the mobile phase was vacuum filtered to eliminate impurities. Following this, it was sonicated for a duration of 10 minutes to ensure thorough mixing and the removal of any trapped air bubbles.

STOCK SOLUTION PREPARATION PROCEDURE

A 1000 µg/mL standard stock solution of Ticagrelor was made by dissolving 5 mg of the substance in 10 mL of methanol. To prepare samples of varying concentrations (10, 20, 30, 40, and 50 µg/mL), varying amounts of this standard solution were diluted to 10 mL with the mobile phase.

RESULT:

METHOD VALIDATION

The International Conference for Harmonization (ICH) proposed a complete validation procedure which researchers used to assess the performance of their HPLC method through testing its performance characteristics. The validation process involved testing the repeatability, specificity, precision, accuracy, and robustness of the proposed HPLC method. The researchers used the UV spectrophotometric method to analyse Ticagrelor standard and reference samples within the 200–400 nm wavelength range. Both samples exhibited characteristic absorption maxima at 220 nm and 294 nm. The overlay spectra showed excellent agreement, confirming the spectral similarity between standard and reference. The method

achieves validation for Ticagrelor identification through qualitative testing which also confirms the identity of the reference sample.

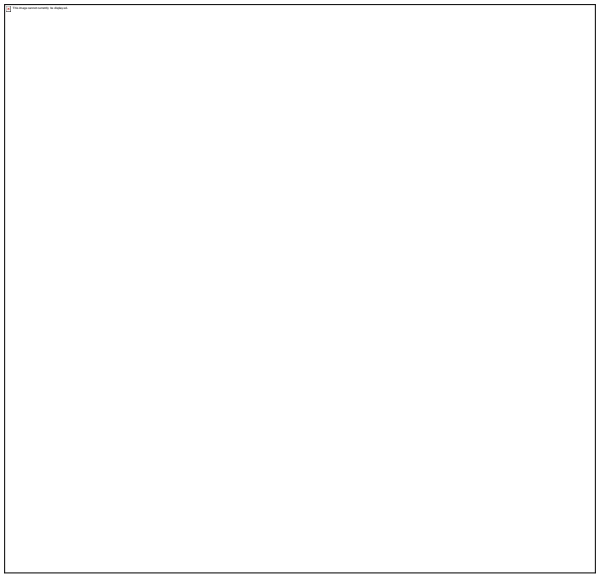


Figure 2: UV absorption spectrum of ticagrelor showing absorbance as a function of wavelength. Wavelength (nm) is represented along the X-axis, and absorbance (AU) along the Y-axis. The spectrum exhibits characteristic absorption peaks, with a prominent peak observed around 294 nm, indicating the λmax of ticagrelor used for analytical determination.

LINEARITY

The 5–25 µg/ml series was created from the 500 µg/ml stock through proper dilution with mobile phase to establish linearity testing. The standards were run under the fixed HPLC conditions which resulted in a clear peak area increase that occurred in direct proportion to the standards. The calibration curve demonstrated excellent linear behaviour through its slope of 23.491m and intercept of 2.203 c.

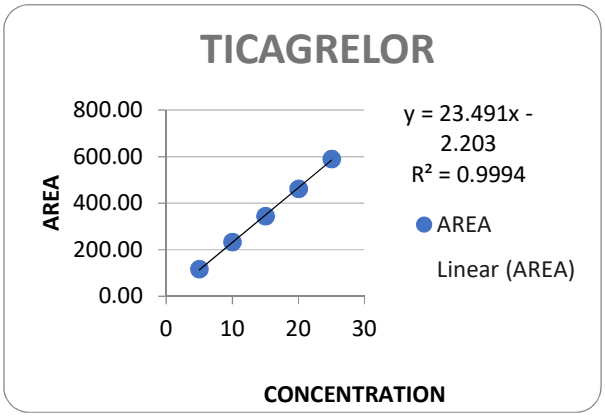


Figure 3: Linearity curve of ticagrelor showing the relationship between concentration and peak area. The X-axis represents concentration (µg/mL), while the Y-axis represents peak area obtained from the analytical method. A strong linear relationship was observed with regression equation y = 23.491x − 2.203 and correlation coefficient (R^2 = 0.9994), indicating excellent linearity over the studied concentration range.

PARAMETERS	HPLC METHOD
Range	**5-25** µg /ml
Slope	**23.491 m**
Intercept	**2.203 c**
Correlation coefficient	**0.999**

Table 2: Linearity parameters

REPEATABILITY

Repeatability was confirmed through testing multiple times with a single solution prepared according to standard stock procedures. All measurements used identical instrument settings together with the consistent mobile phase over the

course of the testing process. The results showed peak area measurements had small variation which demonstrated the method could produce consistent results during short testing periods and would deliver identical outcomes throughout one complete analysis.

SPECIFICITY

The assessment of specificity involved testing both the standard solution and the tablet sample under identical chromatographic conditions to confirm that no peaks interfered with the detection of Ticagrelor. Constant mobile phase was maintained and column and wavelength settings while they tested both blank samples and placebo solutions. The chromatograms demonstrated a distinct peak which represented the drug without any interference from excipients or background noise. The method demonstrates selective measurement of Ticagrelor because it remains unaffected by other formulation components.

PRECISION

Precision was examined through multiple tests of the prepared standard which maintained identical chromatographic conditions throughout testing. The peak areas showed stable measurement results through multiple injections because %RSD values stayed under 1%. The method demonstrates stable performance because it produces identical measurement results during repeated testing with consistent system operations.

ACCURACY

The assessment of accuracy involved testing tablet solutions which contained specific quantities of standard stock. The measured values through the established calibration equation produced results which matched the theoretical amounts with high accuracy. The method shows a strong capacity to measure actual drug content in the formulation because it achieved near 100% recovery results together with low standard deviation and percent relative standard deviation values.

ROBUSTNESS

Robustness was examined by performing experiments that used controlled wavelength tests which included 293NM and 295NM wavelength variations while all other test parameters remained constant. The peak responses showed almost no change while the %RSD values maintained their acceptable range. The method demonstrates suitability for everyday laboratory operations because its performance remains stable under different testing conditions.

RUGGEDNESS

Ruggedness studies were conducted by testing the same sample at different times with different operators. The solutions prepared from identical stock materials produced measurements which showed high consistency because their %RSD values remained under 1% and their results approached the expected measurement. The method shows its dependable performance because different analysts and standard daily work conditions do not affect its results.

LABEL CLAIM ANALYSIS

The label claim was verified by preparing tablet solution equivalent to 5 mg of Ticagrelor using Stock-II solution of 500 µg/ml, diluting it to 20 µg/ml, and then analysing it using the calibration equation. The quantity obtained was found to be around 100-101% of the claim, which is verified by low SD and %RSD values, indicating that the formulation is correct in terms of quantity of drug present in it, and the method is accurate for assessing its quantity.

Result of linearity and range

CONCENTRATION	AREA OF PEAK	SD	%RSD
5	115.94	1.18	1.009
10	233.17	0.11	0.05
15	344.52	0.4	0.12

20	462.81	0.3	0.07		
25	592.58	2.11	0.36		
	Average SD	0.82			
Result of Repeatability					
CONCENTRATION	AREA 1	AREA 2	MEAN	SD	%RSD
25 µg /ml	594.6	593.37	594	0.87	0.15
Result of Intraday Precision					
CONCENTRATION	AREA 1	AREA 2	MEAN	SD	%RSD
10	235.03	233.89	234	0.81	0.34
15	346.79	347.59	347	0.57	0.16
20	468.43	467.45	468	0.69	0.15
Result of Interday Precision					
CONCENTRATION	AREA 1	AREA 2	MEAN	SD	%RSD
10	235.58	235.2	235	0.27	0.11
15	349.48	349.27	349	0.15	0.04
20	461.1	460.23	461	0.62	0.13

Result of 80 % extra Ticagrelor Standard				
ACCURACY	g/ml	AMT FOUND	AMT RECOVERED	% RECOVERY
80%	5	9.07	4.07	101.83
	5	9.05	4.05	101.19
			MEAN	101.245

Result of 100 % extra Ticagrelor Standard				
ACCURACY	g/ml	AMT FOUND	AMT RECOVERED	% RECOVERY
100%	5	10.0773	5.08	101.55
	5	9.97816	4.98	99.56
			MEAN	100.555

Result of 120% extra Ticagrelor Standard				
ACCURACY	g/ml	AMT FOUND	AMT RECOVERED	% RECOVERY
120%	5	11.01	6.01	100.17
	5	11.0215	6.02	100.36
			MEAN	100.265

Result of Robustness for Wavelength 293nm				
CONCENTRATION	AREA	MEAN	SD	%RSD

5	118.83	118.655	0.2	0.17
5	118.48			
Result of Robustness for Wavelength 295nm				
CONCENTRATION	AREA	MEAN	SD	%RSD
5	118.49	118.61	0.16	0.14
5	118.72			
Result of Robustness for Melting point (83.6 + 16.4)				
CONCENTRATION	AREA	MEAN	SD	%RSD
5	119.55	120.3	1.01	0.84
5	120.98			
Result of Robustness for Melting point (85.6+14.4)				
CONCENTRATION	AREA	MEAN	SD	%RSD
5	119.89	120.29	0.56	0.46
5	120.68			

Result of Ruggedness			
CONCENTRATION	AMT FOUND	LABEL CLAIM	% ASSAY
10	10.08867	1.008867	101
10	10.06185	1.006185	101

Result of Label Claim		
AMT FOUND	LABEL CLAIM	% ASSAY
19.78	0.9888085	98.88

Table 3: The table presents comprehensive results of method validation including linearity and range, repeatability, intraday and interday precision, accuracy (recovery studies at 80%, 100%, and 120% levels), robustness (evaluated by deliberate variations in wavelength and experimental conditions), ruggedness, and assay of Ticagrelor. Linearity was assessed within the interval of concentration 5-25 µg/ml. Precision was expressed as %RSD of replicate measurements, and accuracy was determined as percentage recovery. Ruggedness was evaluated under different conditions, while assay results include determination of Ticagrelor content expressed as percentage assay, along with label claim analysis of the marketed formulation.

LOD AND LOQ

LOD: The limit of detection is defined as the minimum concentration of an analyte that can be identified without the requirement for exact quantification.

LOQ: The limit of quantitation refers to the minimum concentration of an analyte that can be quantitatively determined with suitable precision and accuracy. The LOD is a key parameter in quantitative analysis for measuring trace levels of compounds in sample matrices, especially in determining the impurities and degradation products. [27]

Calculation for LOD: 3.3* Avg SD/ Slope

Calculation for LOQ: 10* Avg SD/ Slope

LOD	0.11516771 µg
LOQ	0.34899306 µg

Table 4: Result of LOD & LOQ

DISCUSSION

The current study shows the successful development of a strong RP-HPLC method for quantifying ticagrelor using an AQbD-based approach. The use of central composite design allowed for a systematic evaluation of important analytical factors, especially composition of mobile phase and flow rate. This helped clarify their effects on chromatographic responses. The optimized conditions yielded a distinct, symmetrical peak with a relatively short retention time. This indicates efficient separation and makes it suitable for regular analysis.

The validation results confirm that the method is dependable. Excellent linearity across the chosen concentration range shows a strong link between concentration and detector response. Low %RSD values in precision and repeatability tests indicate high consistency. Recovery values near 100% confirm the method's accuracy. The lack of interfering peaks shows good specificity, ensuring selective estimation when excipients are present.

Compared to several traditional HPLC methods for ticagrelor, which often require longer run times and more solvent, this method offers better efficiency and resource use. The inclusion of AQbD principles further improves the method's strength by reducing variability and boosting reproducibility. A significant feature of this method is its fit with eco-friendly analytical practices. The shorter run time and reduced solvent use lead to less chemical waste and lower operating costs, supporting sustainable lab practices. However, the study is limited to specific parameters, and further investigation into factors like pH and temperature could deepen understanding of the method. Overall, the method is reliable, efficient, and suitable for regular quality control applications.

CONCLUSION

The present work was successful in developing a reliable RP-HPLC method for the quantification of ticagrelor in pharmaceutical preparations. The optimization strategy adopted was found to make the analytical procedure more efficient.

The results of the validation experiments indicated that the analytical procedure was accurate, precise, and sensitive enough to be employed in the routine analysis of the compound. It can therefore be concluded that the proposed method is reliable and can be employed as an efficient tool in the estimation of ticagrelor in pharmaceutical formulations.

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ABBREVIATIONS

ADP - Adenosine diphosphate, RP-HPLC - Reverse Phase High-Performance Liquid Chromatography, AQbD - Analytical Quality by Design, ICH - International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use , DoE – Design Of Experiment,CCD- Central composite design, ACS- Acute Coronary Syndromes, cAMP- Cyclic Adenosine Monophosphate,ENT-1 - equilibrative nucleoside transporter-1 , RSM - Response Surface Methodology, RT – Retention Time ,AUC – Area Under Curve ,TP – Theoretical Plates ,TF – Tailing Factor, SD – Standard Deviation, RSD- Relative Standard Deviation , LOD- Limit Of Detection, LOQ – Limit Of Quantitation.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest related to this study.

FINANCIAL SUPPORT AND SPONSORSHIP

This study was carried out without any sponsorship or financial assistance.

AUTHOR CONTRIBUTIONS

Dr. Deepak Pokharkar provided academic guidance, contributed to the conceptualization of the study, and reviewed the manuscript critically for intellectual content. The co-authors were primarily responsible for data compilation, literature review, analysis, and creating the finished manuscript. The manuscript was prepared with contributions from all authors in reviewing and approving the final version.

SUMMARY

The aim of current study was to develop and validate a simple and reliable RP-HPLC method for the quantitative estimation of ticagrelor in pharmaceutical formulations. Ticagrelor, inhibitor of P2Y12 receptor, is used as a therapeutic option for cardiovascular diseases such as acute coronary syndrome. To ensure the efficacy, safety, and quality of such drugs, precise analytical techniques are necessary. The method was developed using a Zorbax SB-C18 column with a mobile phase of methanol and 0.1 N citric acid in the ratio of 84.6:15.4 (v/v). The analytical quality by design approach with central composite design was utilized as a tool for optimizing the analytical method to evaluate the impact of mobile phase composition and flow rate on the analytical performance. The analytical method was validated as per ICH guidelines for various parameters such as linearity, precision, accuracy, specificity, robustness, and limits of detection. The analytical method was found to be highly linear within a concentration range of 5–25 µg/mL with a correlation coefficient of 0.999. The precision and accuracy studies showed consistent results with low %RSD values and accuracy close to 100%, indicating that the analytical method is reliable and can be used for the analysis of ticagrelor.

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