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REVIEW ON RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR ESTIMATION OF RIVAROXABAN

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ABSTRACT

This review article was proposed to underline the method for development by RP-HPLC and validation of Rivaroxaban in individual and pharmaceutical dosage form. Rivaroxaban is an anti-clotting drug, acts on Factor Xa and stops the blood clot development. In this study, different types of RP-HPLC methods which are available at present for determination of rivaroxaban in tablets (Xarelto10 mg) were studied. There are different types of the methods described for estimation of this drug such as RP-HPLC, UPLC and U. But now a day's RP-HPLC plays the key role in quantitative determination of drug. The review was focused on different HPLC method development that werepreviously used for rivaroxaban. Literature study was carried out on RP-HPLC, HPTLC and UPLC methods of rivaroxaban. The center of the review was to develop as well as to validate a stable, economic and rapid method. The RP-HPLC method was preferred for assessment of rivaroxaban in its formulation and bulk. Here new aspects for method development and validation were studied which revealed high sensitivity and reproducibility.

INTRODUCTION

For the determination of the quantity of drug, a variety of analytical methods are used nowadays. There are various analytical methods like HPLC, UPLC and UV used for method development and validation of Rivaroxaban. HPLC is a separation technique based on the solid stationary phase and liquid mobile phase [1]. Chromatography is a mass transfer process involving adsorption. The working element of the column is adsorbent which is a granular material of solid particles (silica, polymers). The separation principle in reverse and normal phase is adsorption in which the mixture separates in accordance with relative affinities of substance towards the stationary phase. HPLC has a key role in the analytical validation methods [2]. HPLC is a separation method used for detection, separation and quantification the drug. For method optimization, number of chromatographic parameters was studied like pretreatment of sample, mobile phase selection, and column and detector selection. This article's aim is to review optimization of method, method development and validation. The HPLC method development depends on the polarity and solubility.

Table: Summary of HPLC method development and validation for Rivaroxaban

Method	Brief Introduction	References No.
RP-HPLC	Mobile phase: acetonitrile: 0.1% glacial acetic acid (70:30 v/v) Column: C18-G (4.6×250 mm, 5 µm) Flow rate: 1.0 ml/ min, Wavelength: 250 nm	9
RP-HPLC	Mobile phase: acetonitrile: water (55:45 v/v) Column: Phenomenex Luna 5 µm C18 100 A^0 Column (250x 4.6mm), Flow rate: 1.2 ml/ min, Wavelength: 249 nm.	10
RP-HPLC	Mobile phase: acetonitrile: KH_2PO_4 50 mm (pH 3.0)(40:60 v/v) Column: Nova-Pak C8,(4 µm,150 mm × 3.9 mm) Waters, Milford, USA, Flow rate: 1ml/ min, Wavelength: 270 nm	11
RP-HPLC	Mobile phase: methanol: acetonitrile (50:50 v/v). Column: Phenomenex C18 (250×4.6 mm,5 µm) 100A° particle size columns, Flow rate: 1 ml/min, Wavelength: 250 nm.	12
HPLC	Mobile phase: acetonitrile: water (55:45 v/v). Column: C18 column (phenomenex 250×4.6 mm, 5 µm) Flow rate: 1.2 ml/min, Wavelengt: 251 nm	13
HPLC	Mobile phase: methanol: 0.1M sodium acetate (40:60 v/v) Column: ACE-Ciano column (250 mm x 4.6 mm 5µm particle size). Flow rate:1 ml/min, Wavelength: 247 nm	14
UPLC	Mobile phase: 1 ml ortho phosphoric acid (H_3PO_4) and 10 ml sodium salt of octane 1-sulphonic acid ($C_8H_{18}O_3S$) as buffer: acetonitrile (90:10, 20:80) Column: Acquity UPLC BEH HSS T3 100 mm, 2.1 mm and 1.8 µm columns Flow rate: 0.45 ml/min Wavelength: 248 nm	15
HPTLC	Mobile phase: Methanol: toluene: triethanolamine (7:2.5:0.5 v/v/v). Stationary phase: Silica gel G F254 Wavelength: 249 nm	16
RP-HPLC	Mobile phase: (0.02M) mono basic potassium dihydrogen phosphate (KH_2PO_4): acetonitrile: methanol Column: Zorbax SB C-18 (250 mm × 4.6 mm, 3.5µ) Flow rate: 1 ml/min, Wavelength: 247 nm	17
UPLC-UV	Mobile phase: acetonitrile: water (90:10 v/v) Column: Agilent Poroshell 120 EC-C18-RP column Flow rate: 0.7 ml/min, Wavelength: 249 nm	18
RP-HPLC	Mobile phase: 10% ortho-phosphoric acid pH 4.0: acetonitrile (40:60%v/v), Column: Pearless C-18 column (4.6×250mm, 5µ particle size), Flow rate: 1ml/min, Wavelength: 249nm	19
RP-HPLC	Mobile phase: buffer (0.05M pH 4.0): methanol (30:70 v/v) Column: BDS hypersil C-18 (250 mm × 4.6 mm) 5µ, Thermo scientific, Flow rate: 1ml/min, Wavelength: 220nm	20
RP-UPLC	Mobile phase: acetonitrile:0.05 Mdiammonium hydrogen phosphate pH 3.0 (20:80 v/v) and acetonitrile: water (90:10, v/v) Column: BEH C8 column (100 mm× 2.1 mm,1.7 µm) Flow rate: 1 ml/min, Wavelength: 254 nm	21
RP-HPLC	Mobile phase: acetonitrile: KH_2PO_4buffer (pH 3.0 adjusted with	22

	orthophosphoric acid) (40:60 % v/v) Column: HIBAR-5µ C_{18} column (250×4.6 mm) Flow rate: 1 ml /min, Wavelength: 248 nm	

Validation of a drug by the guidelines of ICH for HPLC method gives accuracy, specificity, linearity, limit of quantification (LOQ) and limit of detection (LOD). [3,4]

HPLC Method Development: When no official methods are available for new products then novel methods are developed. The time and cost are reduced using alternate methods for existing products which is producing better precision and ruggedness. When the existing procedure is replaced by a more specific alternative method, it is possible to compare the laboratory records with merit and demerits of both methods. The HPLC-method's objective is to separate, quantify the active pharmaceutical ingredients, intermediates, degradants and reaction impurities. [5]

Steps for HPLC method development [5,6]

1. Information on sample
2. Define separation goals
3. A special procedure requirement, sample pretreatment, if any.
4. Detector selection and setting
5. Separation conditions optimization
6. Check for problems or special procedural requirements
7. Recovery of purified material
8. Quantitative calibration / Qualitative method
9. Method validation for release to laboratories

Drug Profile: Rivaraxoban is 5-chloro n-{[(5S)-2-oxo-3-[4-(3-xomorpholin-4-yl) phenyl]-1, 3-oxozolidin-5-yl] methyl} thiophene-2-corboxamide [7]. It belongs to the class of direct factor Xa inhibitor accepted for the avoidance of venous thromboembolic actions in patients undergone in whole hip or whole knee replacement surgery. The drug blocks the enlargement of the pathway of the coagulation cascade by binding directly to the factor Xa thus prevent the development of thrombus [8]. Molecular formula of rivaroxaban is $C_{19}H_{18}CIN_3O_5S$. Molecular weight of drug is 435.881 g/mol.

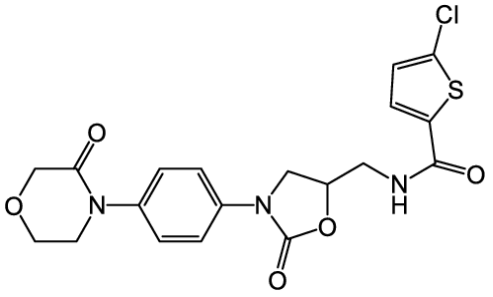

Figure: **Chemical Structure of Rivaroxaban**

CONCLUSION: This review describes the general technique of HPLC method development and validation of Rivaroxaban. The general approach for the method development for the separation of Rivaroxaban was discussed. The selection of buffer and mobile phase composition plays a dramatic role on the separation selectivity. Final method optimization can be performed by changing the concentration of mobile phase modifiers, gradient slope, temperature, flow rate. The optimized method needs to be validated with various parameters as per ICH guidelines.

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