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A REVIEW ON ANLYTICAL METHODS FOR ESTIMATION OF RIVAROXABAN IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

Rivaroxaban, an oral anticoagulant, requires accurate and reliable analytical methods for quality control and pharmacokinetic studies. This review explores various techniques used for Rivaroxaban analysis, including HPLC, TLC, and MS. HPLC is the preferred method due to its high sensitivity, specificity, and reproducibility. TLC is a simpler and cost-effective alternative for qualitative analysis. MS is valuable for characterizing degradation products and studying metabolism. Recent advancements in analytical techniques have improved sensitivity and robustness. Future research should focus on developing methods for complex matrices and standardizing analytical procedures for better comparability and reproducibility.

Keywords: Rivaroxaban, Anticoagulant, Analytical methods.

INTRODUCTION

Rivaroxaban - A Novel Oral Anticoagulant

Rivaroxaban (Fig.1) potent oral anticoagulant patented in 2007 and approved for medical use in the United States in 2011 and it has revolutionized the management of thromboembolic conditions. It is an anticoagulant medication (blood thinner) used to treat and prevent blood clots. Specifically it is used to treat deep vein thrombosis and pulmonary emboli and prevent blood clots in atrial fibrillation and following hip or knee surgery. It is taken by mouth. Its targeted inhibition of factor Xa, provides a more predictable and convenient approach compared to traditional anticoagulants like Warfarin. This review will dwell into the analytical methods & these are crucial for quality control, pharmacokinetic studies, and therapeutic drug monitoring of Rivaroxaban.

This introduction provides a foundation for a review article on analytical methods for Rivaroxaban. The subsequent sections can focus on specific analytical techniques, their applications, and recent advancements in the field.

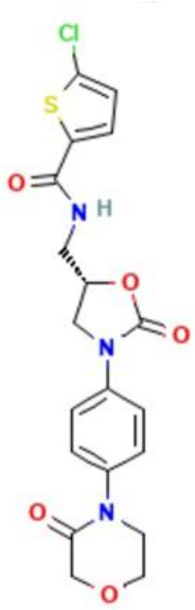

Figure-1: Structure of Rivaroxaban
Chemical name: 5-chloro-N-[[(5S)-2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]-1,3-oxazolidin-5-yl]methyl]thiophene-2-carboxamide.
Chemical formula: C19H18ClN3O5S
Molecular weight: 435.882 g/mol
Category: Factor Xa inhibitors

Table 1: Analytical methods described in the literature for the estimation of Rivaroxaban by UV Spectroscopy

S.No	Method	Solvents & Ratio	Detection Wavelength	Title	Year	Reference
1	UV method	dimethyl sulphoxide	270 nm	Development and validation of UV spectrophotometric method for the determination of rivaroxaban	2013	1
2	UV Spectrophotometric	Acetonitrile Buffer (pH 6.8) (40:60)	287 nm	"A Validated UV Spectrophotometric Method for the Determination of Rivaroxaban in Pharmaceutical Dosage Forms"	2016	2
3	UV Spectrophotometric	Methanol (50:50)	254 nm	"Development and Validation of a UV Spectrophotometric Method for Determination of Rivaroxaban in Bulk and Pharmaceutical Formulations"	2017	3
4	Spectrophotometric Analysis	Methanol Buffer (pH 6.8) (50:50)	250 nm	"Spectrophotometric Estimation of Rivaroxaban in Pharmaceutical Dosage Forms"	2017	4
5	First-Order Derivative Spectroscopy	Methanol Buffer (pH 6.8) (60:40)	245 nm	"First-Order Derivative Spectrophotometric Method for the Quantitative Analysis of Rivaroxaban in Tablet Dosage Form"	2018	5
6	UV Spectrophotometric Method	Acetonitrile:0.1 M HCl (60:40)	287 nm	"Validated UV Spectrophotometric Method for Rivaroxaban: Application to Quantitative Analysis in	2018	6

				Pharmaceutical Dosage Forms"		
7	Derivative Spectrophotometry	Methanol Solution (pH 7.4) (70:30)	250 nm	"Development and Validation of Derivative UV Spectrophotometric Method for Determination of Rivaroxaban"	2019	7
8	Area Under Curve (AUC) Method	Methanol (50:50)	254 nm	"A Simple and Validated UV Spectrophotometric Method for Quantification of Rivaroxaban in Human Plasma"	2020	8
9	UV Method	acetonitrile: water (60:40)	294 nm	Development and Validation of Ultra Violet-Visible Spectrophotometric Method for Estimation of Rivaroxaban in Spiked Human Plasma	2020	9
10	Double Beam UV Spectrophotometry	Methanol (50:50)	280 nm	"Development and Validation of a Simple UV Spectrophotometric Method for Estimation of Rivaroxaban in Tablets"	2021	10
11	UV-Spectrophotometric Method	Acetonitrile (50:50)	254 nm	"Development and Validation of UV-Spectrophotometric Method for Determination of Rivaroxaban in Tablets"	2021	11
12	UV-VIS Spectroscopy	Methanol Buffer (pH 7.4) (60:40)	254 nm	"Development of a Validated UV Method for Estimation of Rivaroxaban in Bulk and Formulations"	2022	12

Table 2: Analytical methods described in the literature for the estimation of Rivaroxaban by HPLC

S.No	Method	Stationary Phase	Mobile Phase	Detection wavelength	Title	Year	Reference
13	RP-HPLC	Phenomenex Luna 5 µm C18 100 Å LC Column (250 x 4.6 mm)	ACN:Water (55:45 v/v)	249 nm.	RP-HPLC method development and validation for estimation of Rivaroxaban in pharmaceutical dosage forms	2013	13
14	RP-HPLC	Phenomenex C18 (250×4. 6 mm, 5µm), 100°A particle size columns	Methanol: Acetonitrile (50:50 v/v).	PDA detector, 250 nm	Photolytic-Thermal Degradation study and method development of Rivaroxaban by RP-HPLC	2013	14
15	RP-HPLC	HPLC-Phenomenex C8 100A	HPLC - 0.1% OPA: ACN (60:40 V/V)	HPLC- 280 nm	Stress study and estimation of a potent anticoagulant drug Rivaroxaban by a validated HPLC method: Technology transfer to UPLC	2015	15
	UPLC	Particle Size -5 µmUPLC-Acquity UPLC BEH C8	UPLC- 0.1% OPA: ACN (55:45 V/V)	UPLC- 280 nm		2015	
16	RP-HPLC	C18 column (150 mm x 4.6 mm i.d.)	Acetonitrile: Water (70:30 v/v)	249 nm	Development and validation of a stability-indicating RP-HPLC method for the determination of Rivaroxaban in pharmaceutical	2015	16

					formulations		
17	RP-HPLC	Phenomenex Luna C18	Acetonitrile: Water (60:40 v/v)	248 nm	Development of validated RP-HPLC method for estimation of Rivaroxaban in pharmaceutical formulation	2015	17
18	RP-HPLC	Chiralcel OD-H (250 mm × 4.6 mm, 5 mm)	n-hexane – isopropanol (50: 50 v/v/)	UV Detector, 250 nm	Enantiomeric Separation Of Rivaroxaban By A Chiral Liquid Chromatographic Method	2015	18
19	RP-HPLC, TLC densitometric	Inertsil C18 (250 mm × 4.6 mm, 5 mm)	10 mM ammonium formate: Acetonitrile (30:70 v/v)	249 nm	Investigation of the profile and kinetics of degradation of Rivaroxaban using HPLC, TLC-densitometry and LC/MS/MS: Application to pre-formulation studies	1015	19
20	RP-HPLC	Nova-Pak C 8	mixture of Acetonitrile and KH 2 PO 4 50 mM (pH 3.0) (40:60, v / v)	270 nm	Development of a stability-indicating HPLC method and a dissolution test for Rivaroxaban dosage forms	2016	20
21	RP-HPLC	C18 column (Phenomenex 250 x 4.6 mm, 5 µm)	ACN: Water (55:45 v/v)	251 nm	Assay comparison of Rivaroxaban by new HPLC method with an existing method in tablet dosage form	2017	21
22	RP-HPLC	Purospher ® STAR Hibar ® C18	Acetonitrile and water in the ratio 80:20 v/v	240 nm	RP-HPLC Method Development and Validation for the Estimation of Rivaroxaban In Bulk And Tablet Dosage Form	2017	22
23	RP-HPLC	ZorbaxSB C18 (250 mm X 4.6 mm, 3.5 µ)	HPLC column using buffer (0.02M mono basic potassium di hydrogen phosphate) and solvent mixture (Acetonitrile:	240 nm	Development and Validation of Stability Indicating RP-HPLC Method for Rivaroxaban and Its Impurities	2018	23

			Methanol mixture)				
24	RP-HPLC	Macherey-Nagel Nucleodur C18	Acetonitrile and water in gradient program	254nm	Development and Validation of a Liquid Chromatography Method for the Analysis of Rivaroxaban and Determination of Its Production Related Impurities	2018	24
25	RP-HPLC	Inertsil C8	Potassium phosphate buffer (pH 3.0) and Acetonitrile	250 nm	Development and validation of stability indicating assay by HPLC method for estimation of Rivaroxaban	2019	25
26	RP-HPLC	Nucleosil C18 (250 mm x 4.6 mm; 5 µmparticle size)	Acetonitrile: Water (50:50 v/v)	251 nm	Novel Validated RP-HPLC Method for Determination of Rivaroxaban in Bulk and its Pharmaceutical Dosage Form	2020	26
27	RP-HPLC	Phenomen ex Luna C18 column (4.6 x 250mm, 5µm particle size)	Water: Acetonitrile (45:55 v/v)	249 nm	Devolpement and validation of stability-indicating RP-HPLC method for Rivaroxaban in tablet dosage form	2022	27
28	RP-HPLC	Chiralpak IC (250×4.6 mm, 5 µm)	Mobile Phase A-Acetonitrile: Ethanol:n-butyl amine (95:5:0.5 v/v/v) Mobile Phase B-Milli-Q water:Methanol:n-butyl amine (50:50:0.5 v/v/v)	254 nm	Stability Indicating HPLC Method Development and Validation of Rivaroxaban Impurities and Identification Forced Degradation Products by LC- MS/MS	2022	28

29	RP-HPLC	Sun Q C18 HPLC column	Acetonitrile : Buffer(sodium acetate buffer) 80:20 v/v	UV Detector, 249 nm	Analytical method development and validation of rivaroxaban in bulk and pharmaceutical dosage form by using RP-HPLC	2022	29
30	HPTLC	Pre-coated silica gel 60	Toluene: Ethyl Acetate: Methanol: Ammonia (3:5.5:1.5:0.1 v/v)	284 nm	Validated Stability Indicating HPTLC Method Development for Rivaroxaban in Tablets	2024	30
31	RP-HPLC	Exsil 100 ODS C18 column (250×4.6 mm, 5 µm)	Acetonitrile: Water: Methanol at a ratio of 60:30:10 (v/v/v)	DAD detector	A bio analytically validated RP-HPLC method for simultaneous quantification of Rivaroxaban, Paracetamol, and Ceftriaxone in human plasma: a combination used for COVID-19 management	2024	V 31

CONCLUSION

The reviewed HPLC methods demonstrate their effectiveness in the analysis of Rivaroxaban. These methods offer high sensitivity, selectivity, and accuracy for the quantification of Rivaroxaban in various matrices, including bulk drug substances, pharmaceutical formulations, and biological fluids. The development of stability-indicating HPLC methods further enhances the utility of these techniques in assessing drug stability and degradation pathways.

However, it's important to note that the suitability of a specific HPLC method depends on the analytical goal, the complexity of the sample matrix, and the required sensitivity and specificity. Continuous optimization and validation of HPLC methods are crucial to ensure reliable and accurate results.

UV Spectrophotometry offers a simple, rapid, and cost-effective method for the analysis of Rivaroxaban. While it may not provide the same level of sensitivity and selectivity as HPLC, it can be a valuable tool for routine quality control and stability studies.

However, the application of UV Spectrophotometry to complex matrices or in the presence of interfering substances may be limited. In such cases, more sophisticated analytical techniques like HPLC may be necessary.

Overall, UV Spectrophotometry can be a useful tool for the analysis of Rivaroxaban, particularly when combined with appropriate sample preparation techniques and careful method development.

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