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Review Article

A Review on Analytical Techniques for the assay of Apixaban

Maanikonda Bala Krishna* and Mukthinuthalapati Mathrusri Annapurna

GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, India

***Corresponding Author:** Maanikonda Bala Krishna, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, India.

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Abstract

Apixaban is an anticoagulant, or blood thinner. It makes your blood flow through your veins more easily. This means your blood will be less likely to make a dangerous blood clot. Apixaban is a selective, reversible, direct inhibitor of factor Xa indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. The present review article summarises the analytical methods so far developed for the estimation of Apixaban.

Keywords: Apixaban; Analytical Methods; Factor Xa

Introduction

Apixaban is chemically 1-(4-methoxyphenyl)–7–oxo–6–[4–(2–oxopi-peridinin-1-yl) phenyl]–4, 5,6, 7–tetrahydropyrrole[3,4–c] pyridine-3-carboxamide with molecular formula $C_{25}H_{25}N_5O_4$ and molecular weight 459.497 g/mol and is a white to pale yellow coloured powder. It is an inhibitor of coagulation factor Xa and acts by interfering with the conversion of prothrombin to thrombin and preventing the formation of cross-linked fibrin clots. Apixaban is indicated for the prophylaxis of deep vein thrombosis. The present review article summarises the analytical methods so far developed for the estimation of Apixaban in pharmaceutical formulations as well as biological fluids. Apixaban is a highly potent, selective, and efficacious and it is an orally bioavailable inhibitor of blood coagulation factor [1]. Apixaban (BMS-562247, Eliquis TM) was developed by Bristol Myers Squibb and Pfizer to use it as an antithrombotic/anticoagulant agent [2,3]. Apixaban is approved for the prevention of stroke and systemic embolism in patients with non valvular atrial fibrillation, the prophylaxis of deep vein thrombosis which may lead to pulmonary embolism in patients who have undergone hip or knee replacement surgery [4].

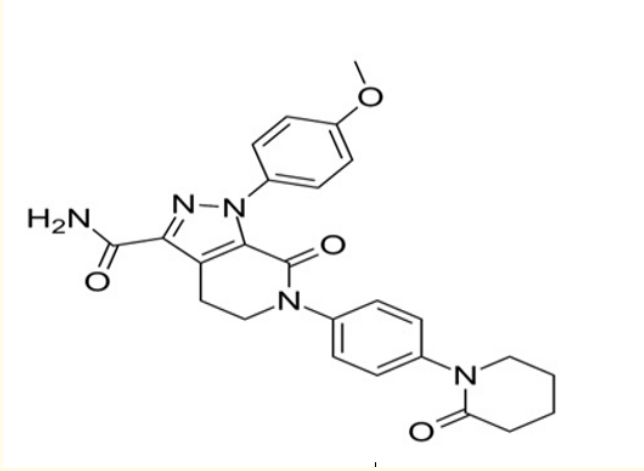

Figure 1: Chemical structure of apixaban.

The present review article summarises the analytical techniques so far developed such as spectrophotometry [5-9], high performance liquid chromatography [10-13] including QbD [14] and impurity profiling [15] studies as well as liquid chromatography-mass spectrometric methods [16-18] for the determination of Apixaban (Table 1).

Reagent/ Mobile phase (v/v)	λ_{max} (nm)	Linearity (µg/ml)	Comment	Ref
Spectrophotometric methods				
Methanol	280	2-10	-	5
Methanol	269 -289	5-25	-	6
Water, Sodium Hydroxide Methanol Ethanol	278	10-80		7
Dimethyl Sulfoxide	282	5-20		8
Methanol	269-289 and 266.21-304.62		Area under curve and First order derivative spectrophotometric method	9
Liquid chromatographic methods				
[Buffer: Methanol (90:10)]: [Buffer: Acetonitrile: Methanol (20:20:60)] (Buffer: 10 mM phosphate buffer (pH 5.0) adjusted with Triethyl amine	235	0-40	Gradient mode	10
Sodium acetate: Acetonitrile (50:50)	-	10 - 50	-	11
Phosphate buffer (pH 4.5): Methanol (60:40)	220	0.01 - 0.22	-	12
Methanol: Water (50.2: 49.8)	220	1 - 35	-	13
{Buffer: Acetonitrile (90:10)}: {Water: Acetonitrile (10:90)}	280	-	QbD Impurities Stability indicating (Gradient mode)	14
Phosphate buffer: Acetonitrile	225	-	Stability indicating & Process related 9 Impurities	15
Liquid chromatography-Mass spectrophotometric methods				
Acetonitrile: Ammonium formate buffer (pH 4.2) (70:30)		0.001 - 0.301	LC-MS/MS	16
2.5 mM Ammonium formate (pH 3.0): 0.1% formic acid in Methanol		1.01 0.5	UPLC-MS/MS (Gradient mode)	17
0.1% aqueous formic acid: 0.1% formic acid in Acetonitrile		0.0005 - 0.5	UHPLC-MS/MS Dried blood spots (Liquid -Liquid extraction)	18

Table 1: Review of spectrophotometric methods for the determination of apixaban.

Conclusion

The present review article helps the readers to do research in a new field apart from the presenting existing analytical techniques for the anti-viral drug Apixaban.

Bibliography

1. Pinto DJ., *et al*. "Discovery of 1-(4-methoxyphenyl)-7-oxo-6-(4-(2-oxopiperidin1-yl) phenyl)-4,5,6,7-tetrahydro-1H -pyrazolo[3,4-c]pyridine-3-carboxamide (Apixaban, BMS-562247), a highly potent, selective, efficacious, and orally bioavailable inhibitor of blood coagulation factor". *Xa Journal of Medicinal Chemistry* 50 (2007): 5339-5356.

2. Eliquis (Package Insert), Bristol-Myers Squibb Company, Princeton, NJ (2012).

3. Agrawal R., *et al*. "Apixaban: A new player in the anticoagulant class". *Current Cancer Drug Targets* 13 (2012): 863-875.

4. Luettgen JM., *et al*. "Apixaban inhibition of factor Xa: microscopic rate constants and inhibition mechanism in purified protein systems and in human plasma". *Journal of Enzyme Inhibition and Medicinal Chemistry* 26 (2011): 514-526.

5. Malode PA., *et al*. "Development and validation of simple UV Spectrophotometric method for the determination of Apixaban in API and its bulk dosage form". *Indo American Journal of Pharmaceutical Research* 7.4 (2017): 8150-8158.

6. Akiful Haque M., *et al*. "Method development and validations of Apixaban in bulk and its formulations by UV-Spectroscopy (area under curve)". *International Journal of Pharmaceutical Sciences and Research* 10.3 (2019): 1387-1391.

7. Mahendra B., *et al*. "Method developed for the determination of Apixaban by using U.V. Spectrophotometric". *International Journal of Research in Pharmaceutical Chemistry and Analysis* 1.2 (2019): 83-87.

8. Pravalika Reddy P and G Tulja Rani. "Development and validation of UV Spectrophotometric method for the determination of Apixaban in bulk and pharmaceutical dosage forms". *Indo American Journal of Pharmaceutical Sciences* 4.8 (2017): 2425-2429.

9. Dudhe PB., *et al*. "Determination of Apixaban from bulk and tablet dosage form by area under curve and first order derivative spectrophotometric methods". *International Journal of Chem Tech Research* 10.5 (2017): 703-711.

10. Sonal Shinde., *et al*. "Assay and organic impurity profiling of Apixaban using an ascentis express C18 column and UV detection".

11. Kashid AM., *et al*. "Analytical method development and validation for estimation of Apixaban by RP-HPLC". *Indian Drugs* 54.4 (2017): 76-79.

12. Swarup Suresh Prabhune., *et al*. "Stability-indicating high-performance liquid chromatographic determination of Apixaban in the presence of degradation products". *Scientia Pharmaceutica* 82 (2014): 777-785.

13. Jéssica BE., *et al*. "Analytical quality by design approach for a stability-indicating method to determine Apixaban and its related impurities". *Chromatographia* 83 (2020): 65-75.

14. Mirza Layeeq Ahmed Baig and Syed Ayaz Ali. "A validated LC-MS/MS method for the estimation of Apixaban in human plasma". *Journal of Applied Pharmaceutical Science* 7.4 (2017): 044-052.

15. Hyeon-Cheol Jeong., *et al*. "Quantification of Apixaban in human plasma using ultra performance liquid chromatography coupled with tandem mass spectrometry". *Translational and Clinical Pharmacology* 27.1 (2019): 33-41.

16. Naiyu Zheng., *et al*. "Center punch and whole spot bioanalysis of Apixaban in human dried blood spot samples by UHPLC-MS/MS". *Journal of Chromatography B* 988 (2015): 66-74.

17. Subramanian VB., *et al*. "Stability-indicating RP-HPLC method development and validation for determination of nine impurities in Apixaban tablet dosage forms. Robustness study by quality by design approach". *Biomed Chromatogr* 34.1 (2020).

18. Shashikant BL., *et al*. "Development and validation of stability indicating RP-HPLC method on core shell column for determination of degradation and process related impurities of Apixaban-An anticoagulant drug". *American Journal of Analytical Chemistry* 6.6 (2015): 56264.