WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Overview and Analytical Methods for Determination of Abiraterone

Jadhav Rajshri D*., Datar P.A*., Shete R.V*.

Department of Pharmaceutical Quality Assurance, Rajgad Dayanpeeth's College of Pharmacy, Bhor –Pune, Maharashtra, Pin - 412206. rajshrijadhav829@gmail.com

ABSTRACT :

A trustworthy, correct method for measuring Abiraterone using RP-HPLC became mounted. The separation method was finished on a desk bound segment chromatographic machine beneath optimized situations. Abiraterone acetate, a progesterone derivative, suggests capacity in treating cancer sufferers with resistance to different treatment plans. This study explores several screening methods to assess Abiraterone, consisting of fluorescence Spectrophotometry, liquid chromatography-Mass Spectrometry, and excessive-overall performance liquid chromatography for quantifying Abiraterone acetate in pharmaceutical products, pills, and biological samples. The take a look at additionally covers a method to monitor the stability of Abiraterone acetate, that is precious for its production, high-quality manage, and impurity detection in pharmaceutical formulations. it also includes the HPLC, HPTLC, UV, and LC MS.

Keywords – RP-HPLC Abiraterone, Method Development, Clinical applications,

Introduction :

Abiraterone, a derivative of steroidal progesterone, is utilized in treating hormone-refractory prostate cancer. Marketed under the brand name Zytiga, Abiraterone acetate was approved by the U.S. Food and Drug Administration (FDA) in April 2011 following an accelerated review process. Additionally, it has received approvals from various regulatory agencies, including the European Medicines Agency (EMA) on September 23, 2011, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) on September 5, 2011, and Australia's Therapeutic Goods Administration (TGA) on March 1, 2012. The active metabolite of Abiraterone functions as an irreversible inhibitor of the enzyme 17α-hydroxylase/lyase (CYP17), which is essential for androgen synthesis in the testes and adrenal glands. The progression of prostate cancer (PCa) is driven by activation of the androgen receptor, facilitated by potent androgens such as testosterone and dihydrotestosterone (DHT). Although androgen deprivation therapy (ADT), achieved through either medical or surgical castration, remains the standard treatment for advanced PCa, most patients eventually develop castration-resistant prostate cancer (CRPC), which accounts for the majority of PCa-related deaths. In the United States, approximately 180,000 new PCa diagnoses and 26,000 related deaths were estimated for 2016, establishing PCa as the most commonly diagnosed cancer and the second leading cause of cancer-related mortality in men. Abiraterone acetate, as an irreversible inhibitor of CYP17, was specifically approved by the FDA in April 2011 for the management of CRPC. Its molecular structure is defined by the chemical formula C26H33NO2.

Description :

Abiraterone is a potent, irreversible, and selective inhibitor of the enzyme 17α-hydroxylase/C17, 20-lyase (CYP17), which plays a key role in androgen biosynthesis. . Abiraterone was first approved for use by both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in 2011—on April 7 and September 14, respectively. Structurally, Abiraterone is a 3β-sterol, characterized as androsta-5, 16-dien-3β-ol, with a 3-pyridyl group attached at the 17th position. Administered as its O-acetate form, it is used to treat metastatic castrate-resistant prostate cancer. Abiraterone acts as an Antineoplastic agent and inhibits steroid 17α-monooxygenase (EC 1.14.99.9). It is classified as a 3β-hydroxy-Delta (5)-steroid and is derived from an Androstane hydride, with additional pyridine group characteristics

Mechanism of action :

17α-hydroxylase/C17,20-lyase (CYP17) is an essential enzyme involved in androgen biosynthesis. It is mainly found in the testes, adrenal glands, and prostate tumors. CYP17 facilitates two important biochemical steps: first, it adds a hydroxyl group at the 17α position of pregnenolone and progesterone, forming their 17α-hydroxylated forms; then, it removes the C20,21 side chain to generate dehydroepiandrosterone (DHEA) and androstenedione. These molecules serve as precursors to testosterone, a hormone closely linked to the growth and progression of prostate cancer. In cases of androgen-dependent prostate cancer, therapies aimed at lowering androgen levels have shown effectiveness..

Clinical applications:

a. Abiraterone is a man-made steroidal inhibitor commonly used to treat prostate cancer, particularly in cases of metastatic castration-resistant prostate cancer (mCRPC).

b. Its mechanism of action involves blocking the androgen receptor (AR) signaling pathway, which is crucial for the proliferation and survival of prostate cancer cells.

c. Abiraterone suppresses the activity of the CYP17A1 enzyme, thereby reducing the production of androgens like testosterone. This prevents the stimulation of the androgen receptor, ultimately slowing down cancer cell growth.

d. Taken orally, Abiraterone is usually prescribed alongside prednisone to counter potential side effects from reduced testosterone, such as adrenal insufficiency.

Analytical Methods:

Various chromatographic techniques are employed to develop and validate Abiraterone in its pure form and dosage formulations using analytical approaches. Literature reviews indicate that several methods have been established for the quantitative analysis of Abiraterone, including UV spectroscopy, LC-UV, HPLC-UV, reverse-phase HPLC (RP-HPLC), and high-performance thin-layer chromatography (HPTLC).

Instrumentation and chromatography conditions :

Chromatographic separation was achieved using a Waters binary gradient HPLC system (Japan), equipped with an automated sample injector. Empower software was utilized for data collection and analysis. The separation was carried out on a Kromasil C18 column (250 mm × 4.6 mm, 4.0 µm) maintained at 40°C. The mobile phase consisted of acetonitrile (ACN) and a 10 mM ammonium acetate buffer, with the pH adjusted to 3.5 using acetic acid. Before use, the mobile phase was sonicated and filtered through a 0.45 µm nylon membrane filter (25 mm) to eliminate particulates. The flow rate was maintained at 0.6 mL/min, and 30 µL of each sample was injected. This method ensured efficient separation of the drug from its degradation products.

LC-MS:

The analysis was conducted using an Acquity H-Class UPLC system coupled with a Xevo TQ-S Micro Tandem Mass Spectrometer (Waters, Wilford, MA, USA). This setup provides high-resolution separation and enhanced sensitivity, making it well-suited for accurate quantification and detailed analysis of complex pharmaceutical mixtures and other analytical samples

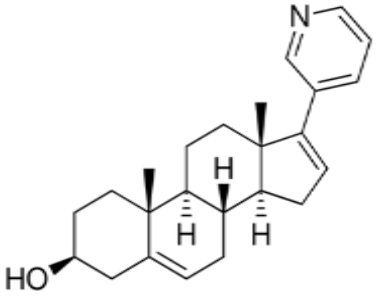

Figure: Structure of Abiraterone

Mixture Product:

Name	Ingredients	Route
Akeega	Abiraterone acetate(500mg) +Niraparib (100mg)	Oral
Akeega	Abiraterone acetate+Niraparib tosylayte monohydrate	Oral
Akeega	Abiraterone acetate + Niraparib tosylayte	Oral

1) Summary Of LC/MS,UPLC of Abiraterone :

Sr	**Method**	**Mobile phase**	**Column**	**Flow rate ml min−1**	**Wavelength nm**	**Linearity µg/mL**	**LOD&LOQ**	**Precision %**	**Ref.**
1	UPLC–MS/MS	acetonitrile:water:formic acid (90:10:0.1%, v/v/v)	BEH™ C18 column (50 × 2.1 mm, i.d. 1.7 µm,	0.3		0.1–50	0.1 ng mL−1	13.29	22
2	HPLC	Acetonitrile and glycine buffer 88.4mM (pH 9.0) (60:40, v/v).	C8 Xterra(®)	0.9	255 -373	1.75-50		3.5 - 7	23
3	LC–UV– ESI-MS						30 -80 pg/µL,	0.20, 0.30	24
4	spectrofluorimetric method					0.20 ~ 6.0	6.8 or 6.6 ng/mL,		25
5	HPLC	acetonitrile–water–10 mM potassium Dihydrogen phosphate (pH 3.0), 55:5:40, v/v/v		1.00	255	93.4–3251		0.56–4.98 and 3.03–7.18,	26
6	LC–MS/MS	2% propan-2-ol in Acetonitrile and 10 mM ammonium acetate	Luna C5 5 µm, 50 mm × 2.1 mm			5 to 500 nM		<13.9	27
7	LC-MS	(10 mM ammonium acetate: acetonitrile, 10:90 %v/v)	Atlantis dC(18)	0.70		0.20 to 201 ng/mL	LOQ 0.20 ng/mL	2.39to10.4 &4.84to9.53	28
8	Stability Indicating RP-HPLC	0.01N KH2PO4:Acetonitrile (60:40)	C18 150mm x 4.6 mm	1.1	235 nm	25 to150	0.953µg/ml and 2.888µg/ml	0.2	35

2) Summary of Chromatographic methods of Abiraterone :

Sr. No.	Methods	Mobile Phase	Column	Wavelength nm	Retention time (Min)	Recovery	Linearity	LOD& LOQ	Ref.
1	RP-HPLC	0.01%KH2 PO4:Aceto nitrile 60:40	Azilent C18	235	_	_	25-150 %	1.629 and 4.937 µg/ml	**18**
2.	RP-HPLC QbD	Acetonitrile and phosphate buffer (10 mM KH2PO4) (20:80 %v/ v)	Princeton Merck-Hibar Purospher STAR	-	-	98% and 102%.	-	-	**19**
3.	RP-HPLC	methanol: Acetonitrile in the ratio 50:50 V/V	eclipse XDB C18 col	255 nm	7.453	-	-	-	**20**
4	Stability Indicating RP-HPLC	ammonium acetate buffer 10 mM, pH adjusted to 3.5 with acetic acid 10:90 % v/v as eluent	Kromasil C18	-	-	99.52 to 100.13 % .	5–30 µg/ml	-	**14**
6	RP-LC	Acetonitrile –water 50 to 70% (v/v).	X-Terra RP-18	255 nm	-	-	-	-	**21**
7.	RP-HPLC	buffer and Acetonitrile (50: 50 v/v) flow rate - 1.0 ml/ min	250 mm × 4.6 mm, 5m	235nm	4.372	-	-	-	**17**

3) Summary of UV Spectroscopic method of Abiraterone:

Sr.	Methods	Solvent	Wavelength	Correlation Coefficient	Linearity	Accuracy	LOD& LOQ	Recovery	Ref.
1.	UV	Methanol	254nm	0.9991	10-60µg/ml	100.03%	0.006µg/ml and 0.018µg/ml	99.88%.	33
2	Spectroscopic. (A)	Methanol	248 nm	0.9991	1-100 µg/m			99.70	34

	(B)		240 nm	0.9998	5-100 µg/mL			99.52	

Conclusion –

This review highlighted key analytical and bioanalytical techniques—including UV spectroscopy, HPTLC, HPLC, LC-MS/MS, and UPLC—used for the determination of Abiraterone. It provided an overview of recent developments in analytical method validation and the application of bioanalytical approaches for analyzing biological samples in pharmacokinetic studies in both animals and humans. Most of the current research emphasizes method development and stability testing of Abiraterone. Among these, the HPLC-UV method continues to be a valuable analytical tool due to its cost-effectiveness and reliability in bioanalytical applications. The insights presented here offer a strong foundation for future research in formulation, method development, and bioanalytical evaluation of Abiraterone.

References:

1. Attard G, Parker C, Eeles RA, Schroder F, Tomlins SA, Tannock I, Drake CG, de Bono JS. Prostate cancer, Lancet (London, England) 2016;387:70–82. doi: 10.1016/S0140-6736(14)61947-4.
2. Miyamoto D.T, Lee R.J, Stott S.L, Ting D.T, Wittner B.S, Ulman M, Smas M.E, Lord J.B, Brannigan B.W, Trautwein J, Bander N.H, Wu C.L, Sequist L.V, Smith M.R, Ramaswamy S,Toner M, Maheswaran S, Haber DA. Androgen receptor signaling in circulating tumor cells as a marker of hormonally responsive prostate cancer. Cancer Discov. 2012;2:995– 1003. doi: 10.1158/2159-8290.CD-12-0222
3. Guillemette E. Benoist1, Eric van der Meulen1, Floor J. E. Lubberman1, Winald R. Gerritsen Tineke J. Smilde, Jack A. Schalken , Jan H. Beumer , David M. Burger , and Nielka P. van Erp Analytical challenges in quantifying Abiraterone with LC-MS/MS in human plasma Biomed Chromatogr. 2017 November ; 31
4. .Deslypere J.P, Young M, Wilson J.D, McPhaul M.J. Testosterone and 5 alpha-dihydrotestosterone interact differently with the androgen receptor to enhance transcription of the MMTV-CAT reporter gene. Mol. Cell. Endocrinol. 1992;88:15–22. doi: 10.1016/0303-7207(92)90004
5. Montgomery R.B, Mostaghel E.A, Vessel R, et al. Maintenance of intratumoral androgens in metastatic prostate cancer: a mechanism for castration-resistant tumor growth. Cancer Res, 2008, 68(11):4447-4454.
6. Mostaghel E.A. Abiraterone in the treatment of metastatic castration-resistant prostate cancer. Cancer Manag Res, 2014, 6:39-51.
7. Desai K, Mc Manus J.M, Sharifi N. Hormonal Therapy for Prostate Cancer. Endocr Rev, 2021, 42(3):354-373.
8. O'Donnell A, Judson I, Dowsett M, Raynaud F, Dearnaley D, Mason M, Harland S, Robbins A, Halbert G, Nutley B, Jarman M: Hormonal impact of the 17alpha-hydroxylase/C(17,20)-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer. Br J Cancer. 2004 Jun 14;90(12):2317-25.
9. Ryan C.J, Cheng M.L Abiraterone acetate for the treatment of prostate cancer. Expert Opin Pharmacother. 2013 Jan;14(1):91-6.. Epub 2012 Nov 30.
10. Deepak Krishna Mhaske , Arjun Shankar Kumbhar The first RP-UHPLC method for Simultaneous Quantification of Abiraterone acetate, its four degradants, and six specified process impurities and correct identification of all analytes based on molecular weight Journal of Pharmaceutical and Biomedical Analysis Volume 234, 20 September 2023, 115568
11. H. Beckett and J. B. Stenlake. “Practical Pharmaceutical Chemistry”, Volume I and II, CBS Publishers & Distributors, New Delhi, India, 2000.
12. G. Ramana Rao, S. S. N. Murthy and P. Khadgapathi. Gas chromatography to pharmaceutical Analysis Eastern Pharmacist. 30(353): 35 (1987).
13. Jala Chandra Reddy, Development and validation of a novel RP-HPLC method for stability-indicating assay of Abiraterone acetate, Journal of Liquid Chromatography & Related Technologies, 2016,39(7): 354-363.
14. Gadhave R.V. stability indicating RP-HPLC-PDA method for determination of abiraterone acetate and characterization of its base catalyzed degradation product by LC-MS, International Journal of pharmacy and pharmaceutical sciences,2016
15. International conference on harmonization, ICH Q3A (R2) Impurities in New Drug Substances, **2006**
16. ICH guidelines for the stability of new drug substances and products. Q1A (R2) ICH, Geneva; 2005. p. 1-13.
17. P. Jitendra Kumar Syed.Rafiya, Tezenile .Magh, T.Venkata Lakshmi, T.Vakya Mani, D.Rama Brahma Reddy Development and Validation of RP-HPLC Method For Quantitative Analysis Of Abiraterone In Pure and Pharmaceutical Dosage FormAm. J. Pharm Health Res 2020;8(03) ISSN: 2321-3647

18. Bikash Ranjan Jena , Siva Prasad Panda, Umasankar kulandaivelu, Rajasekhar Reddy alavala G.S.N Koteswara RAO2, Suryakanta Swain, Gurudutta Pattnaik, Debashish Ghose A QbD Driven Development of an RP-HPLC Method for the Quantitation of Abiraterone Acetate for its Pharmaceutical Formulations in the Presence of Degradants Turk J Pharm Sci 2021;18(6):718-729

19. P. Ravi Sankar, M.M. Eswarudu,P. Siva Krishna, A.Viswanath, P.Srinivasa Babu Optimized And Validated RP-HPLC Method For Quantification Of Abiraterone Acetate (An Antiprostate Cancer Drug) In pharmaceutical Dosage Form volume 27, Issue 7, 2021

20. Senem Sanli, Meryem Cansu ,Sahin Ayse Ozde Evaluation of the RP-LC method for determining the pK_a of abiraterone and its assay AK Journals

21. Kuna AK, Seru Ganapaty and Gadela V Radha Analytical Method Development and Validation for the Estimation of Abiraterone and its Impurity in Pharmaceutical Formulation By RP-HPLC Der Pharmacia Lettre, 2018, [9]: 19-31

22. Tanveer A Wani. Highly sensitive Ultra-Performance Liquid Chromatography–tandem mass spectrometry method for the determination of Abiraterone in human plasma. *Anal. Methods*, 2013; 5: 3693-3699.

23. Belleville Tiphaine, Noé Gaëlle, Huillard Olivier, Thomas-Schoemann Audrey, Vidal Michel. A HPLC-fluorescence method for the Quantification of Abiraterone in plasma from patients with metastatic castration-resistant prostate cancer. Journal of chromatography. B, 2015; 989.

24. Alaa Khedr, Ibrahim Darwish, Faida Bamane. Analysis of Abiraterone stress degradation behavior using liquid chromatography coupled to ultraviolet detection and Electrospray ionization mass spectrometry. Journal of Pharmaceutical and Biomedical Analysis, 2013; 74(23): 77-82.

25. Aiqin Gong and Xiashi Zhu. β-cyclodextrin Sensitized Spectrofluorimetry for the determination of Abiraterone Acetate and Abiraterone. Journal of Fluorescence, 2013; 23(6): 1279-1286

26. Ramesh Mullangi, Vijay Kumar S, Rudresha G, Sandip Gurav, Mohd Zainuddin, Purushottam Dewang, Raghava Reddy Kethiri, Sriram Rajagopal. Validated RP-HPLC/UV Method for the Quantitation of Abiraterone in rat plasma and its application to a pharmacokinetic study in rats. Biomedical Chromatography, 2013; 27(2): 203–207.

27. Vanessa Martins, Yasmin Asad, Nicola Wilsher, Florence Raynaud. A validated Liquid Chromatographic–tandem Mass Spectroscopy method for the Quantification of Abiraterone acetate and Abiraterone in human plasma. Journal of Chromatography B., 2006; 843(2): 262–267.

28. Sandip Dhondiram Gurav, Ravindra Punde, Junaid Farooqui, Mohd Zainudddin, Sriram Rajagopal, Ramesh Mullangi. Development and validation of a highly sensitive method for the determination of Abiraterone in rat and human plasma by LC-MS/MS-ESI: application to a pharmacokinetic study. Biomedical Chromatography, 2012; 26(6): 761-8.

29. Zytiga Abiraterone acetate tablets accessdata fda.gov.2011

30. G. Ramana Rao, S. S. N. Murthy and P. Khadgapathi. Gas chromatography to pharmaceutical analysis (Review). Eastern Pharmacist. 30(353): 35 (1987). S

31. Jala Chandra Reddy et al.., Development and validation of a novel RP-HPLC method for stability-indicating assay of Abiraterone acetate, Journal of Liquid Chromatography & Related Technologies,2016,39(7): 354-363.

32. Mukthinuthalapati Mathrusri Annapurna et al.., Stability Indicating RP-HPLC method for the determination of Abiraterone (An Anti-Cancer Drug), Research Journal (Placeholder1) of Pharmacy and Technology,2018,11(7): 3007-3012.

33. Ramakrishna .M J.N.Suresh Kumar Lakshmi Roshini.J Sai Tejaswini.T Jagadeesh.N Jessie Snehita.K Simplified uv spectrophotometric analysis of abiraterone acetate in bulk and formulations Int J. Pharm. Drug. Anal, Vol: 12, Issue: 1, 2024; 37-42

34. Debi Prasad Pradhan and Routhu Krishna Chaitanya New Spectrophotometric Techniques for the determination of Abiraterone acetate (A Steroidal Inhibitor) in Tablets JCPS Volume 10 Issue 2 April - June 2017 ISSN: 0974-2115

35. Anusha Jeripothula1, Pavani Digigam2 and K. Abbulu3 Stability Indicating Method Development and Validation for Determination of Abiraterone in Bulk and Pharmaceutical Dosage Form by RP-HPLC World J Pharm Sci 2020; 8(8): 119-125

36. Guillemette E Benoist , Eric vander Meulen , J.E.Lubberman , Winald R Gerritsen , Tineke J Smilde , Jack A Schalken , Jan H Beumer , David M Burger , Nielka P van Erp Analytical challenges in quantifying Abiraterone with LC-MS/MS in human plasma Biomed Chromatography. Author manuscript; available in PMC 2018 November 01.

37. Pushpa Latha E, Syeda Bushra Yunus, Navya Sree O, Juveriya Naz, Anusha M, Mani Sagar G, Sameul Shine S. Da Review On Analytical Methods For Estimation Of Abiraterone Acetate P wjpmr, 2016, 2(2), 23-25

38. Mohammad Alyamania,e, Zhenfei Lia, Sunil K. Upadhyayd, David J. Andersone, Richard J. Auchusd, and Nima Sharif Development and validation of a novel LC–MS/MS method for simultaneous determination of Abiraterone and its seven steroidal metabolites in human serum: Innovation in separation of Diastereoisomers without use of a chiral column J Steroid Biochem Mol Biol. Author manuscript; available in PMC 2018 September 01.

39. Adhave R. V., Tamnar A. B. ,Bansode A. S., Choudhari V. P. Stability Indicating RP-HPLC-PDA Method For Determination Of Abiraterone Acetate And Characterization of Its Base Catalyzed Degradation Product By LC-MS

40. Alaa Khedr , Ibrahim Darwish [b], Faida Bamane Analysis of Abiraterone stress degradation behavior using liquid chromatography coupled to Ultraviolet detection and Electrospray ionization mass spectrometry Journal of Pharmaceutical and Biomedical AnalysismVolume 74, 23 February 2013, Pages 77-82

41. Deepak Krishna Mhaske , Arjun Shankar Kumbhar The first RP-UHPLC method for Simultaneous Quantification of Abiraterone acetate, its four degradants, and six specified process impurities and correct identification of all analytes based on molecular weight Journal of Pharmaceutical and Biomedical Analysis Volume 234, 20 September 2023, 115568

42. S. Vijay Kumar, G. Rudresha, Sandip Gurav, Mohd Zainuddin, Purushottam Dewang, Raghava Reddy Kethiri, Sriram Rajagopal, Ramesh Mullangi Validated RP-HPLC/UV method for the Quantitation of Abiraterone in rat plasma and its application to a pharmacokinetic study in rats Biomedical chromatography,

43. DasameswaraRao Kavitapu , Arthanareeswari Maruthapillai ,Sudarshan Mahapatra , J. Arockia Selvi New Stability indicating RP-HPLC method for the determination of Abiraterone acetate, its related substances and degradation products in bulk and dosage form Volume 34, Part 2, 2021, Pages 469-478 j.matpr.2020.02.665

44. V. Bukkapatnam, Mathrusri Annapurna Mukthinuthalapati And K. C. Routhu Study on Stress Degradation Behaviour of Abiraterone Acetate in Film Coated Tablets and Identification of Major Stress Degradation Product by Liquid Chromatography-Ultraviolet-Electrospray IonizationMass Spectrometry Indian Journal of Pharmaceutical Sciences March-April 2022

45. P.Sharifi N, Gulley J.L, Dahut WL. Androgen deprivation therapy for prostate cancer. JAMA. 2005;294:238–244. doi: 10.1001/jama.294.2.238. Computed by PubChem 2.2 (Pub Chem release 2021.10.14)