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Review Article

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A REVIEW ON ANALYTICAL METHODS FOR ESTIMATION OF ABIRATERONE ACETATE

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ABSTRACT

Abiraterone acetate is a derivative of steroidal progesterone that offers clinical benefit to patients with hormone refractory prostate cancer. Few analytical methods used for the estimation of Abiraterone has been reviewed in this paper. These include High performance liquid chromatography, Liguid Chromatography – Mass spectroscopy, Spectrofluorimetry to determine the amount of Abiraterone acetate in bulk drugs, pharmaceutical formulations and biological fluids. Stability indicating method for Abiraterone acetate is also described. These analytical methods can be used for qualitative and quantitative estimation of Abiraterone acetate, its related impurities or degradants in bulk, formulation and biological fluids.

KEYWORDS: Abiraterone acetate, analytical methods, biological fluids.

INTRODUCTION

Abiraterone acetate belongs to the class of known as androgens and derivatives and are 3-hydroxylated C19 steroid hormones[1], chemically known as (3β)17-(3-pyridinyl) androsta-5,16-dien-3-yl acetate.[2] Abiraterone acetate is indicated for the treatment of prostate cancer.[1] Abiraterone is an orally active inhibitor of the steroidal enzyme CYP17A1 (17 alpha-hydroxylase/C17,20 lyase) that inhibits CYP17A1 in a selective and irreversible manner via covalent binding mechanism. CYP17A1 is an enzyme which catalyzes the androgen biosynthesis and is expressed at higher amount in testicular, adrenal, and prostatic tumor tissue. More specifically, Abiraterone at a dose of 250mg/day acts by inhibiting the conversion of 17-hydroxyprognenolone to dehydroepiandrosterone (DHEA) by the enzyme CYP17A1 to lower serum levels of testosterone and other androgens.[1] Abiraterone is poorly absorbed but Abiraterone acetate is well and rapidly absorbed orally. Abiraterone acetate is widely distributed throughout the body with apparent volume of distribution. It is 99% bound to alpha-1-acid glycoprotein and albumin. It is excreted in faeces (88%) and urine (5%).[3] The main side effects of Abiraterone acetate Hypertension, Hypokalemia, and Fluid Retention due to Mineralocorticoid Excess, Adrenocortical Insufficiency, Hepatotoxicity.[4] Recent studies suggest the combination of Abiraterone acetate with prednisone for the treatment of metastatic, castration-resistant prostate cancer.[1]

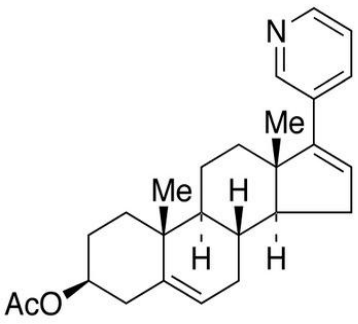

Fig. 1 Structure of Abiraterone acetate.

Analytical Methods for Abiraterone acetate

Many different analytical methods have been reported for the estimation of Abiraterone acetate in bulk and dosage form as well as in biological fluids.

Tanveer A. Wani developed a highly sensitive ultra-performance liquid chromatography–tandem mass spectrometry method for the determination of Abiraterone in human plasma. After a simple protein precipitation using methanol, Abiraterone acetate and Carbamazepine (internal standard; IS) were separated on an Acquity UPLC BEH™ C_{18} column (50 × 2.1 mm, i.d. 1.7 µm, Waters, USA) using a mobile phase

of acetonitrile : water : formic acid (90 : 10 : 0.1%, v/v/v) pumped at a flow rate of 0.3 mL min^{-1}. The elution of Abiraterone acetate and Internal Standard were found at 0.61 and 0.48 min, respectively. The mass spectrometric determination was carried out using an electrospray interface operated in the positive mode with multiple reaction monitoring (MRM) mode. The precursors to product ion transitions of *m/z* 350.1 > 156.0, and *m/z* 237.0 > 179.0 were used to quantify Abiraterone acetate and IS, respectively and *m/z* 350.1 > 170.0 transition was used as the qualifying ion for Abiraterone acetate. Linearity was found in the concentration range of 0.1–50 ng mL^{-1} with correlation coefficient of (0.995) and with a limit of quantitation found to be 0.1 ng mL^{-1}. The precisions (intra- and inter-assay) were found to be satisfactory; the %RSD did not exceed 13.29%. The accuracy of the method was proved; recoveries of Abiraterone acetate from spiked human plasma were 75.83–78.33%. The UPLC–MS/MS proposed method is found to be simple, rapid and highly sensitive, and hence it could be applied reliably for pharmacokinetic and toxicokinetic studies in both animals and humans.[5]

Alaa Khedr et al. developed a validated stability-indicating LC–UV–ESI-MS analytical method was established to analyze Abiraterone (ABR) and its potential degradation products (DPs) and was performed according to ICH guidelines. Determination of trace amounts of DPs that might be released was done under different environmental conditions .Various Stress conditions such as thermal effect, acid-base hydrolysis, oxidation and UV-light were investigated. For UV light and oxidation ABR was found to be sensitive. Upon exposure to UV-irradiation five potential mono-oxygenated ABR products were generated. Detection of compounds like Di-, tri-, and tetra-oxygenated Abiraterone was done and on long exposure to UV light they were progressively increased in quantity. The limit of detection (LOD) and limit of quantification (LOQ) of Abiraterone by ESI-MS method were 30 and 80 pg/µL, respectively. The intra-day and inter-day RSD was found to be 0.20%, 0.30% respectively.[6]

Ramesh Mullangi et al developed and validated a novel high-performance liquid chromatography (HPLC) assay method for the estimation of Abiraterone (ABR) in rat plasma. The simple liquid–liquid extraction process was performed for the extraction of ABR and diclofenac (internal standard, IS) from rat plasma. a Waters Alliance system with a Betasil C_{18} column maintained at ambient room temperature by using isocratic mobile phase [acetonitrile–water–10 mM potassium dihydrogen phosphate (pH 3.0), 55:5:40, v/v/v] at a flow rate of 1.00 mL/min with a total run time of 10 min. The eluate was detected at 255 nm using an UV detector. As per FDA guidelines method validation was performed and the results were accordingly to the acceptance criteria. The linearity was maintained over a concentration range of 93.4–3251 ng/mL ($r^2 = 0.997$). The intra-day and inter-day precision results were found to be 0.56–4.98 and 3.03–7.18, respectively, in rat plasma. The developed & validated HPLC method was successfully applied to a pharmacokinetic study of ABR in rats.[7]

Belleville Tiphaine et al developed a simple and sensitive liquid chromatographic method with fluorescence detection for estimation of Abiraterone in plasma. Protein precipitation performed with acetonitrile followed by liquid-liquid extraction using diethyl ether. The chromatographic analysis was performed on C8 Xterra(®) MS column where Abiraterone and hydroxy-itraconazole (internal standard) were separated using a mobile phase of acetonitrile and glycine buffer 88.4mM (pH 9.0) (60:40, v/v). Isocratic elution of samples was done at a flow rate of 0.9 mL/min with a run time of 11-min. The excitation and emission wavelengths in fluorimetry were 255 and 373nm, respectively. The Linear calibration curve was found in the range of 1.75-50ng/ml. Inter- and intraday precision were found to be less than 3.5 and 7%, respectively. This method can be used in routine clinical practice to monitor plasma Abiraterone concentrations in mCRPC patients.[8]

Aiqin Gong and Xiashi Zhu developed a novel spectrofluorimetric method to determine Abiraterone acetate and its active metabolite, based on the fact that fluorescence intensity of Abiraterone acetate and Abiraterone could be enhanced in β-cyclodextrin (β-CD) due to the formation of the inclusion complex. The inclusion interaction of β-cyclodextrin and Abiraterone acetate and the β-cyclodextrin sensitized spectrofluorimetry were examined. The results showed that under the optimized conditions, the linear range of calibration curve for the determination of Abiraterone acetate and Abiraterone was 0.20 ~ 6.0 µg/mL, and the detection limit (LOD) was 6.8 ($r = 0.997$) or 6.6 ng/mL ($r = 0.996$), respectively. Common co-existing substances or pharmaceutical excipient did not show any interference. The method was successfully applied to the analysis of Abiraterone acetate in pharmaceutical formulation and Abiraterone in human serum/urine.[9]

Vanessa Martins et al developed and validated a sensitive and selective LC–MS/MS method for the quantification of Abiraterone acetate and its metabolite, Abiraterone (an androgen biosynthesis inhibitor) in human plasma. Extraction of analytes by SPE with cation mixed-mode polymer cartridges was performed. Chromatographic analysis was performed on a Luna C5 5 µm, 50 mm × 2.1 mm i.d. column, using a mobile phase of 2% propan-2-ol in acetonitrile and 10 mM ammonium acetate. The assay was found to be linear over a concentration range of 5 to 500 nM ($r^2 = 0.998$). The intra- and inter-day coefficients of variation were <13.9% for both analytes. This method will be applied to a clinical trial investigating the pharmacokinetics of Abiraterone acetate and Abiraterone in patients with prostate cancer.[10]

Sandip Dhondiram Gaurav et al developed and validated liquid chromatography coupled to tandem mass spectrometry with and electrospray ionization which was highly sensitive, rapid assay method for the estimation of Abiraterone (ART) in rat and human plasma. The assay procedure involves simple protein precipitation extraction of ART and Phenacetin (internal standard, IS) from rat and human plasma. Chromatographic separation was achieved with an Atlantis dC(18) column maintained at 40°C using an isocratic mobile phase (10 mM ammonium acetate:acetonitrile, 10:90 %v/v) at a flow-rate of 0.70 mL/min with a total run time of 3.5 min. The MS/MS ion transitions monitored were 350.3 → 156.0 for ART and 180.2 → 110.1 for IS. Method validation was performed as per FDA guidelines and the results met the acceptance criteria. The lower limit of quantitation achieved was 0.20 ng/mL and the linearity range extended from 0.20 to 201 ng/mL. The intra- and inter-day precisions were in the ranges 2.39-10.4 and 4.84-9.53% in rat plasma and 3.82-10.8 and 6.97-8.94% in human plasma.[11]

CONCLUSION

Few analytical methods have been reported for the estimation of Abiraterone acetate in pharmaceutical formulations and biological matrices. It can be concluded that only spectrofluorimetry, HPLC-UV, HPLC-Fluorimetry and LC/MS/MS can be widely used for Abiraterone acetate estimation in biological fluids like plasma, urine and serum. It was also found that HPLC-UV method was used for impurity profiling of Abiraterone acetate. Thus, this current review gives complete detail of the analytical methods available on Abiraterone acetate which can be helpful for further research work studies on it.

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