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AN ECO-FRIENDLY VALIDATED UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF ABIRATERONE ACETATE TABLETS BY HYDROTROPIC SOLUBILIZATION

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ABSTRACT

Background: Hydrotropic solubilization is an organic solvent-free approach for poorly water soluble drugs. Abiraterone acetate is a poorly water soluble anti-androgenic drug used to treat prostate cancer. Literature survey shows that various method such as HPLC, UPLC, LC-MS/MS and UV spectrophotometric method using methanol as solvent have been reported for the estimation of Abiraterone acetate. In this work, the selected hydrotropic agent sodium lauryl sulphate was employed to solubilize the drug, replacing harmful organic solvents. **Method:** The UV spectrophotometric analysis was carried out at 255 nm, the maximum absorption wavelength of Abiraterone acetate. Beer's law was found to be obeyed in the concentration range of 10-45µg/mL. The correlation co-efficient for Abiraterone acetate was found to be 0.99973.The results of analysis have been validated as per ICH guidelines. The molar absorptivity was calculated as 2.2244 X 10^4 l/mol.cm. Validation parameters such as accuracy, precision, and recovery were assessed, shows the recovery rates between 99.94 % to 99.96% and relative standard deviations below 2%. The proposed method was found to be accurate, eco-friendly and reproducible. The developed method can be applied to the routine quality control of Abiraterone acetate in tablet formulations.

KEYWORDS: Abiraterone acetate, Hydrotropy, Estimation, Solubility.

INTRODUCTION

Abiraterone acetate was described in 1995, and approved for medical use in the United States and the European Union in 2011.[1] It is also known as 17-(3-pyridinyl)androsta-5,16-dien-3β-ol acetate, is a synthetic androstane steroid and a derivative of androstadienol (androsta-5,16-dien-3β-ol), an endogenous androstane pheromone.[2] It is practically insoluble in water. Soluble to 20 mM in DMSO and to 100 mM in ethanol.It has poor oral bioavailability and is susceptible to hydrolysis by esterases, it was developed as an orally bioavailable prodrug with enhanced stability and absorption. In vivo, abiraterone acetate is rapidly hydrolysed to abiraterone, which mediates its pharmacological actions.[3] The drug works by suppressing the production of androgens, specifically it inhibits CYP17A1 and thereby decreases the production of testosterone.[4] In doing so, it prevents the effects of these hormones in prostate cancer. Since abiraterone is a selective inhibitor of CYP17, it is expected to have improved efficacy and minimized adverse events compared to other anti-androgens due to the reduced risk of non-specific enzyme inhibition affecting the synthesis of glucocorticoids and mineralocorticoids.[5]

Therapeutic effectiveness of a drug depends upon the bioavailability and ultimately the solubility of drug molecules. Currently only 8% of new drug candidates have both high solubility and permeability. Due to advanced research and development, there are varieties of new drugs and their derivatives are available. But more than 40% of lipophilic drug candidates fail to reach market due to poor bioavailability, even though these drugs might exhibit potential pharmacodynamic activities. The process of solubilization involves the breaking of inter-ionic or inter-molecular bonds in the solute, the separation of the molecules of the solvent to provide space in the solvent for the solute, interaction between the solvent and the solute molecule or ion. Hydrotropy is a unique and unprecedented solubilization technique in which certain chemical compounds termed as hydrotropes can be used to affect a several fold increase in the aqueous solubility of sparingly soluble solutes under normal conditions. This increase in solubility in water is probably due to the formation of organized assemblies of hydrotrope molecules at critical concentrations. Hydrotropes in general are water-soluble and surface-active compounds which can significantly enhance the solubility of organic solutes such as esters,

acids, alcohols, aldehydes, ketones, hydrocarbons and fats.[6-16]

The literature review reveals that the methods developed for Abiraterone acetate involve RP-HPLC, RP-UPLC. LC-MS/MS and a UV spectrophotometric method using methanol as solvent.[17-21] The primary goal of the present investigation is to establish a novel eco-friendly analytical method for the estimation of Abiraterone acetate in bulk material and tablet dosage forms. The validation of this newly developed method has been conducted by the ICH guidelines.[23]

MATERIALS AND METHODS

Instruments

1. Infra-red analysis was carried out by using Perkin Elmer Spectrum II FT-IR Spectrometer with attenuated total reflection (ATR) contact sampling method.
2. Spectrophotometric analysis was carried out by using a double beam UV-visible Spectrophotometer(Carry 100 UV) with 1cm matched quartz cells.

Reagents and Chemicals

1. Sodium lauryl sulphate (SLS) analytical grade was supplied from Astron Chemicals, Ahmedabad.
2. Water was purified by using glass distillation apparatus.
3. Abiraterone acetate was a gift sample from Cipla Labs. Ltd. Hyderabad, India.
4. Commercially available Pharmaceutical dosage form of Abiraterone acetate -(Xbira -250mg Batch no – PO230332B, Mfg. date 09/2023,Exp.date 08/2026.) manufactured by Cipla Laboratories Ltd. and marketed by R R T Pharma, Navi Mumbai, Maharashtra.

Methodology Adopted

1. Preliminary solubility study of Abiraterone acetate
2. Preparation of standard solution
3. Study of spectral characteristics of Abiraterone acetate in 10% SLS
4. Calibration curve of Abiraterone acetate R.S in 10% SLS
5. Statistical evaluation of calibration plot
6. Stability profile
7. Validation of the method
- Accuracy
- Precision
- Detection limit (LOD)
- Quantitation limit (LOQ)
- Linearity
- Range

8. Estimation of Abiraterone acetate in tablet dosage form
9. Recovery studies
10. Comparison of the prosed method with a reported method.

1. Preliminary solubility study of Abiraterone acetate

Solubility of Abiraterone acetate was determined at 28±1°C. An excess amount of the drug was added to screw capped glass vials of 40 ml capacity containing 10% SLS solutions, the vials were shaken mechanically for 1 hr at 28±1°C in a mechanical shaker and then centrifuged for 5 minutes at 2000 rpm. The supernatant of each vial was filtered through Whatmann filter paper. The filtrates were diluted suitably and analysed spectrophotometrically against corresponding solvent blank. A solution of 10 % SLS showed good solubility.

2. Preparation of standard solution

Prepared a solution of Abiraterone acetate R.S of concentration of 1mg/ml. From the above stock solution different dilutions of concentrations, 10 µg/ml to 45 µg/ml were prepared with distilled water.

3. Study of spectral characteristics of Abiraterone acetate in 10 % SLS

The diluted solution of Abiraterone acetate R.S was scanned in Carry UV 100 spectrophotometer in a wavelength range of 200-400 nm after enabling blank correction in the above region. An absorption band ranging from 200-400 nm was observed with maximum absorption at 255 nm.

4. Calibration curve of Abiraterone acetate in 10 % SLS

The absorbance of the drug solutions of concentrations ranging from 10-50µg/ml was measured at 255 nm with blank.

5. Statistical evaluation of calibration plot

The data in table (1) was used to derive a regression equation of the absorbance (Y) on the concentration (X) by the principle of least squares.

The equation is as follows

$Y = a x + b$

$Y = 0.02039X + 0.05431$

Correlation coefficient was found to be 0.9973

6. Stability Profile

The period over which absorbance value at 255 nm, of Abiraterone acetate remained stable was investigated using three different concentrations of 20, 30 and 50 µg/ml. The absorbance values were measured at 15 min intervals for a period of 1 hour.

7. Validation of the proposed Method

a. Accuracy

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted as reference value and the value found. Accuracy was evaluated by carrying out a recovery study and the method was found to be accurate.

b. Precision

Precision may be considered at three levels: repeatability, intermediate precision and reproducibility.

The repeatability of the method was studied using three different concentrations of Abiraterone acetate (10, 20 and 30µg/ml) which were prepared from stock solution. The absorbance was measured at 255 nm using distilled water as blank.

The intra-day and inter-day precision study of Abiraterone acetate was carried out by estimating the corresponding responses three times on the same day and on three different days (1^{st}, 2^{nd} and 5^{th} day) for three different concentrations of the drug (10, 20 and 30 µg/ml).

c. Detection limit (LOD)

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value.

d. Quantitation Limit (LOQ)

The quantitation limit of an individual analytical procedure is the lowest concentration of analyte in a sample, which can be quantitatively determined with a suitable level of precision and accuracy.

e. Linearity

The linearity of an analytical procedure is its ability, within a given range to obtain test results that are directly proportional to the concentration of analyte in the sample.

f. Range

The range of an analytical procedure is the interval between smallest and largest concentration that maintains a linear relationship between the concentration and the response of the method. The range of the proposed method was found to be 10-45µg/ml.

8. ESTIMATION OF ABIRATERONE ACETATE IN TABLETS

Extraction of Abiraterone acetate from Tablets

10 tablets were accurately weighed and finely powdered in a glass mortar. A weight equivalent to 25 mg was accurately weighed out and transferred to a 25ml stoppered tube. 5ml of 10% SLS was added and swirled gently for a period of 10 minutes. Allowed to settle, the clear supernatant solution was then transferred into a 25ml standard flask through a Whatmann filter paper. The residue was further extracted twice, with 10% SLS solution and passed through the same filter paper and the volume was finally made up to 25ml with 10% SLS to get a concentration of 1mg/ml. From the above sample, solutions of concentration of 20µg/ml and 30µg/ml were prepared. The absorbance of each solution was measured at 255nm using distilled water as blank.

9. Recovery studies

Accuracy of analysis was determined by performing recovery studies by spiking different concentrations of pure drug (Abiraterone acetate RS) in the pre analyzed tablet sample. This parameter was evaluated by the recovery studies at concentration levels of 50%, 100%, and 150% of the drug which consisted of adding known amounts of Abiraterone acetate reference materials to the samples.

10. Comparison of the proposed method with reported method[22]

The proposed method was compared with a reported UV spectrophotometric method using methanol as solvent. The results were compared statistically by student t-test and by the variance ratio F-test with those obtained by official method at 95% confidence level. The calculated t- and F- values did not exceed the theoretical values indicating that there were no significant differences between the precision of the proposed and official method.

RESULTS

The chemical structure and the Infrared spectrum of Abiraterone acetate is furnished in "Fig.1" and "Fig .2" respectively. The method development started with the solubility studies of abiraterone acetate using different hydrotropic agents such as urea, sodium acetate, sodium benzoate and sodium lauryl sulphate of different concentrations. Abiraterone acetate shows good solubility in 10% Sodium lauryl sulphate.

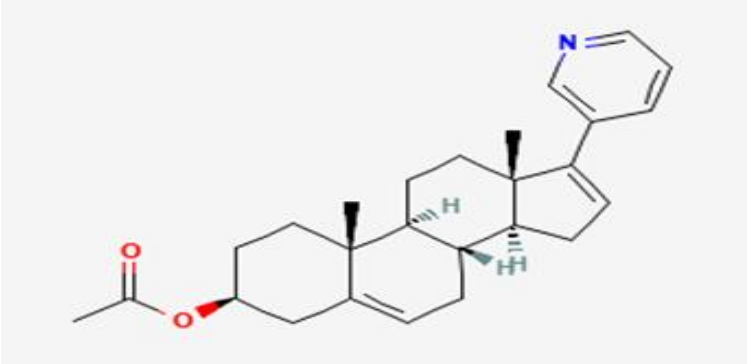

Fig.1: Chemical structure of Abiraterone acetate.

The spectral characteristics of Abiraterone acetate is furnished "Fig.3"**.** From the spectra it was found that the 10 % SLS used does not interfere with the sampling wavelength. Therefore 10% SLS is used for the solubilization of drug.

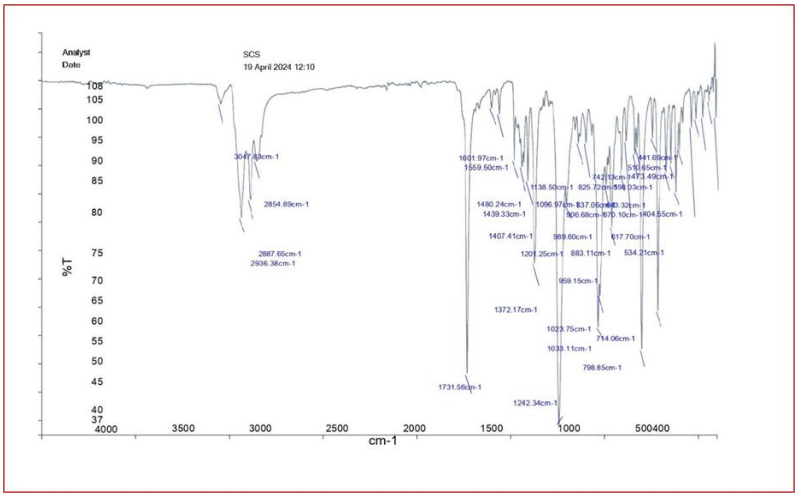

Fig. 2: FTIR spectrum of Abiraterone acetate.

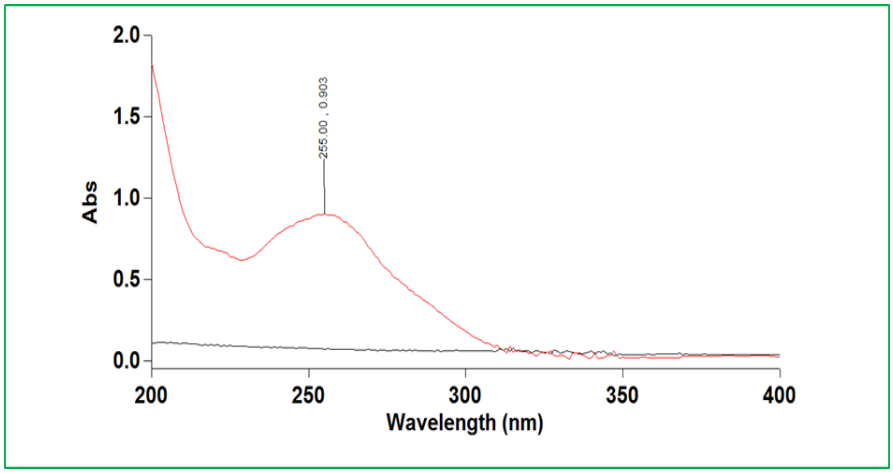

Fig. 3. UV absorption spectrum of Abiraterone acetate.

The calibration curve was constructed by plotting absorbance versus concentration and the regression equations and absorptivity coefficients were calculated. Good linearity was observed in the concentration range of 10-45 µg/ml, The data is furnished in Table.1 and Fig: 4.

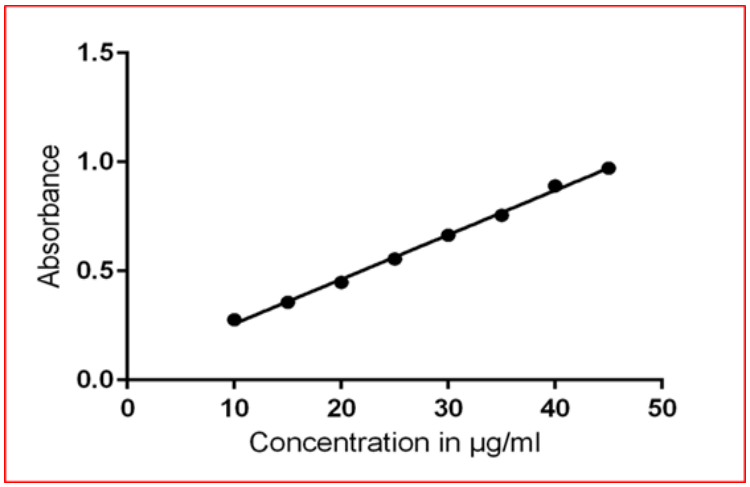

Fig.4. calibration plot of Abiraterone acetate.

Table 1: Calibration data of Abiraterone acetate RS.			
S.No	**Volume of ABA stock solution (ml)**	**Concentration of ABA in final solution (µg/ml)**	**Absorbance at 255nm**
1	10	10	0.2768
2	15	15	0.3574
3	20	20	0.4476
4	25	25	0.5561
5	30	30	0.6642
6	35	35	0.7685
7	40	40	0.8902
8	45	45	0.9720
Inference: The data reveals that Beer's law is obeyed from 10-45 µg/ml.			

The optical characteristics of Abiraterone acetate for the developed method is furnished in table.2.

Table 2: Optical Characteristics of Abiraterone acetate.		
No	**Parameters**	
1	Beers law limit	10-45µg/ml
2	Correlation coefficient	0.9973
3	Y= ax + b	Y = 0.02039X + 0.05431
4	Molar absorptivity	2.2244X 10^4 L/mol.cm.

Table 3: Data of stability study of Abiraterone acetate.						
Sl: No	**Concentration in (µg/ml)**	**Absorbance at 255 nm in 15minutes intervals**				
		0	15	30	45	60
1	10	0.278	0.278	0.276	0.274	0.277
2	20	0.448	0.447	0.447	0.446	0.448
3	30	0.664	0.663	0.664	0.662	0.660

Data of stability study is obtained and is furnished in table.3 and graph is shown in "Fig.5".

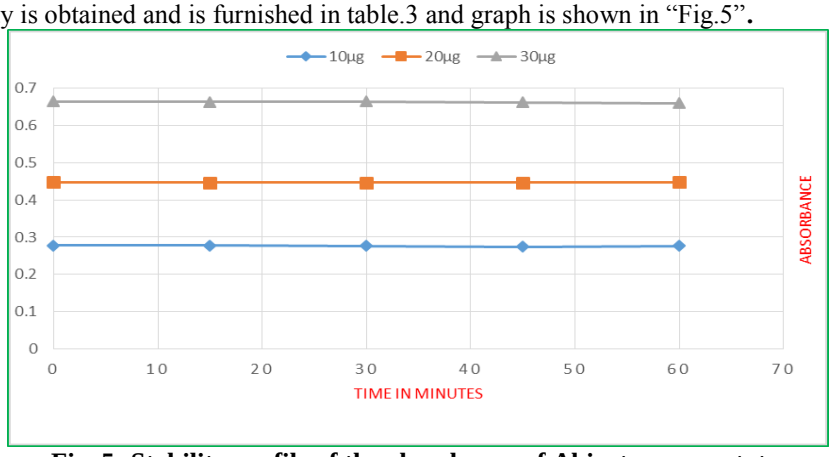

Fig. 5: Stability profile of the absorbance of Abiraterone acetate.

The results of repeatability studies, intra-day precision and inter-day precision is furnished in table.4, 5 &6 respectively. The LOD of Abiraterone acetate by the proposed method was found to be 5µg/ml. The LOQ of Abiraterone acetate by the proposed method was found to be 10 µg/ml.

Table 4: Result of repeatability study.				
SI: No	**Concentration (µg/ml)**	**Absorbance at 255nm**	**Mean value**	**Standard deviation**
1	10	0.278 0.279 0.276	0.277	0.00141
2	20	0.448 0.446	0.447	0.00094

		0.447		
3	30	0.664 0.665 0.666	0.665	0.00082

Table 5: Results of intra-day precision study.

SI No.	Concentration (µg/ml)	Absorbance at 255 nm			RSD,%
		0 hr	1.5 hr	3hr	
1	10	0.278	0.275	0.279	0.48
2	20	0.447	0.445	0.447	0.55
3	30	0.665	0.664	0.665	0.20

Table 6: Results of inter-day precision study.

SI No.	Concentration (µg/ml)	Absorbance at 255 nm			RSD,%
		1st day	2nd day	5th day	
1	10	0.275	0.274	0.274	0.48
2	20	0.446	0.448	0.450	0.21
3	30	0.665	0.670	0.663	0.36

The result of estimation of Abiraterone acetate tablets are furnished in table .7.

Table 7: Results of estimation of Abiraterone acetate tablets.

Sl. No	Conc. of ABA (µg/ml)	Standard Absorbance at 255nm	Sample Absorbance at 255nm	Label claim	Active content per tablet (mg)	Average content per tablet (mg)
1	20	0.447	0.440	99.51	248.00	248.53
2	30	0.666	0.662	99.62	249.05	

Table 8: Results of recovery studies.

Brand name	ABA R.S added /spiked	Total concentration found	% recovery of pure drug * (Mean±S.D) (n=3)	%RSD
Xbira (Cipla) 250 mg	125mg	374.99	99.99 ±0.429	0.48
	250 mg	500.08	100.02 ± 0.126	0.36
	375mg	625.02	100.00 ± 0.305	0.28

The result of recovery study and the result of comparison of proposed method with reported method is given in table.8 & table.9 respectively.

Table. 9: Comparison of the results by Proposed (Method A) and reported spectrophotometric method (Method B).

Parameters	Method A	Method B
Solvent	10% SLS and further dilution with distilled water	Methanol
Detection wavelength	255nm	244nm
Correlation coefficient	0.9973	0.9964
Linearity	10-45 µg/ml	40-80 µg/ml
Abiraterone content in mg	248.56	248.70
Recovery (%)	99.99-100.00	97.80 -99.85
[b]Tabulated t-value is 2.77 and tabulated F-value is 6.39		

DISCUSSION

The method showed good repeatability and recovery with relative standard deviation less than 2. The method was validated in accordance with the requirements of ICH guidelines and statistically proved by 't' test and corresponding 'F' values. The developed method shows significant concern regarding accuracy due to less volatility of SLS & distilled water.

CONCLUSION

The UV spectrometric technique discussed in the current work has the following advantage: it is consistent,

reliable, accurate, economical and applicable technique for analysing Abiraterone acetate tablets.

CONFLICTS OF INTEREST

The authors have no conflict of interest regarding this investigation.

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