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SIMPLIFIED UV SPECTROPHOTOMETRIC ANALYSIS OF ABIRATERONE ACETATE IN BULK AND FORMULATIONS

Ramakrishna.M, J.N.Suresh Kumar, Venkata Lakshmi Roshini.J, Sai Tejaswini.T, Jagadeesh.N, Jessie Snehita.K, Siva Reddy.A

Department of Pharmaceutical Analysis, Narasaraopeta Institute of Pharmaceutical Sciences, Kotappakonda road, Yallamanda, Narasaraopeta, Palnadu, Andhra Pradesh, India

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Abstract

Abiraterone acetate is an orally administered selective androgen biosynthesis inhibitor It is an irreversible inhibitor of cytochrome CYP17AThis enzyme is expressed in testicular, adrenal, and prostatic tumour tissues and is required for androgen biosynthesis. Abiraterone is used in combination with prednisone to treat a certain type of prostate cancer that has spread to other parts of the body.A Novel, simple, accurate, precise and reproducible UV spectrophotometric method has been developed and validated for estimation of Abiraterone acetate bulk and its formulations. After determining the solubility we had selected methanol as a solvent and Abiraterone acetate has absorbance at the wavelength of maximum λmax254nm.The drug was characterized by the melting point test. Proposed method was precise with RSD less than 2%.linearity test was approved within the range of 10-60µg/ml for with the correlation coefficient (R2) of 0.9991. Accuracy was 100.03%. LOD and LOQ were 0.006µg/ml and 0.018µg/ml respectively. The spike recovery of Abiraterone acetate in tablet was 99.88%.

Keywords: Abiraterone acetate, UV spectrophotometric method, solubility, λmax, linearity, LOD, LOQ, RSD.

***Corresponding Author**

Ramakrishna.M

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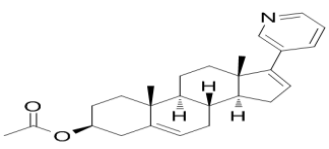
Introduction

Abiraterone is a derivative of steroidal progesterone and is an innovative drug that offers clinical benefit to patients with hormone refractory prostate cancer. Abiraterone is administered as an acetate salt prodrug because it has a higher bioavailability and less susceptible to hydrolysis than abiraterone itself [1-3]. FDA approved on April 28, 2011. Abiraterone acetate, sold under the brand name Zytiga among others, is an antiandrogen medication which is used in the treatment of prostate cancer. It is specifically indicated for use in conjunction with castration and prednisone for the treatment of metastaticcastration-resistaprostate cancer (mCRPC). Abiraterone-acetate chemical name is {[(3S,8R,9S,10R,13S,14S)-10,13-dimethyl-17pyridin-3-yl-2,3,4,7,8,9, 11,12,14,15 decahydro -1H-cyclopenta[a]phenanthren-3yl] acetate} - is an acetyl ester of Abiraterone. It is Soluble in organic solvents like ethanol di-methyl form amide sparingly soluble in buffers and practically in soluble in water. The metabolism of abiraterone is highly protein bounded >99%.

It is converted in vivo to abiraterone, an androgen biosynthesis inhibitor that inhibits 17α-hydroxylase/C17, 20-lyase (CYP17). This enzyme is expressed in testicular, adrenal, and prostatic tumour tissues and is required for androgen biosynthesis. Data for storage, Store it at room temperature (20° to 25°C), and in an air tight container and it shows melting point at 144°C -145°C.In vivo, abiraterone acetate is rapidly hydrolysed to abiraterone, which mediates its pharmacological actions. Abiraterone decreases serum testosterone and other androgens. A change in serum prostate-specific antigen (PSA) levels may be observed



Molecular formula: $C_{26}H_{33}NO_2$

Molecular weight: 391.5g/mol

The analytical process are generally validated following the general non-mandatory guidelines as this process varies so widely and there is no universal approach from regulatory bodies such as US FDA and EC.The most common reason for validation is to machinery in the pharmaceutical manufacturing process are being used in a way which will ensure safety, integrity, quality and strength of the product For use by general public.

Materials and methods

Reagents and chemicals

HPLC grade methanol (vizag chemicals), ethanol (biotexus energy private limited), sodium hydroxide (alpha chemika), hydrochloric acid (ideal chemicals), isopropanol (DFPCL) and abiraterone acetate (Dr.Reddy's, Hyderabad, India).

Instruments and equipment:

Weighing balance (IN-201L), ultrasonicator(Key Roy), UV visible double beam spectrophotometer(analytical- 2080)

Method development

Determination of solubility

Solubility

The ability of a solid, liquid or gaseous chemical substance (solute) to dissolve in solvent and to form a solution. The sample is slightly soluble in ethanol and sparingly soluble in methanol and practically insoluble in 0.1N HCL, 0.1N NAOH, distilled water. By considering the economical parameters we selected methanol as solvent

solubility	solvent
Sparingly soluble	methanol
Slightly soluble	ethanol
Practically insoluble	0.1N HCL, 0.1N NaOH, Isopropanol

Selection of detection wavelength

To determine the optimum λ_{max} of abiraterone acetate 100µg/ml of working standard solution was preferred and scanned in UV wavelength range of 200-400nm using methanol as a blank In the selected solvent drug show 254nmas λmax as shown in fig 1.

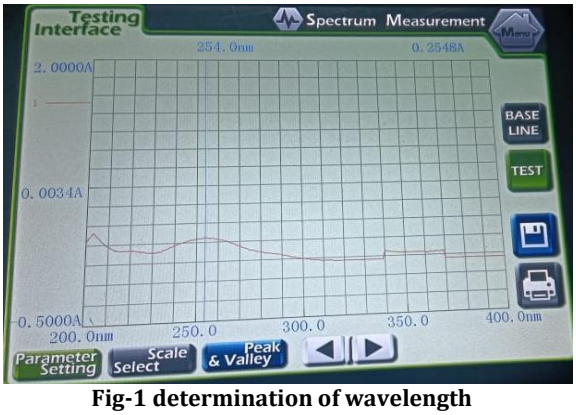


Fig-1 determination of wavelength

Standard preparation

Preparing for calibration curve

A calibration curve was plotted over a concentration range of 10-60µg/ml for abiraterone acetate by taking abiraterone acetate stock solution 1, 2,3,4,5 and 6 ml was shifted to a series of 10ml volumetric flask and make up the volume with distilled water up to the mark. Calibration curve was prepared by taking readings at λmax 254nm and plotted a graph by taking the abiraterone acetate concentration on x-axis and their representative absorbance on y axis calibration data shown in table 2 and fig 2.

Formulation linearity

20 tablets of Abiraterone acetate were weighed accurately and powdered by using mortar and pestle. The powder equivalent to100 mg of drug is taken into 100ml volumetric flask and add 3/4th volume of water. The solution is sonicated for 15 min and solution was made up to 100ml by using methanol (1000µg/ml) from the solution pipette out 10ml and make up to 100ml (working standard) and the solution from the filtrate pipette out 1,2,3,4,5,6 ml into a series of 10ml volumetric flask and make up the volume with methanol giving solution concentration 10,20,30,40,50,60µg/ml were prepared. The absorbance values of these were measured at 254nm. Given in the fig 9.

Standard preparation for recovery of abiraterone acetate

Preparation of standard stock solution:

Accurately weigh 100mg of abiraterone acetate transferred to 100ml volumetric flask and 3/4th of methanol was added and sonicated for 15min remaining volume is made up with methanol and labelled as standard stock solution

Preparation of sample stock solution:

20 tablets were weighed and the average weight of each tablet was calculated then the equivalent weight to 100mg was transferred into 100ml volumetric flask 3/4th of diluent were added and sonicated for 15min further the volume was made up with diluent and filtered by what man filter papers

Preparation of standard working solution:

10ml of abiraterone stock solution was pipetted out and taken in 100ml volumetric flask and remaining volume made up with diluent

Preparation of sample working solution:

10ml of filtered sample stock solution was transferred to 10ml volumetric flask and make up remaining amount with diluent

Method validation

Accuracy

To check the accuracy of the developed method and to study interference of formulation excipients, analytical recovery studies were conducted by taking 100µg/ml solution of formulation in each of three 10ml volumetric flask and then adding 10,20,30µg/ml of raw material the solution were prepared in triplicate the accuracy was indicated by percentage recovery as shown in table 4.

Precision

To check the precision of the proposed method the recovery studies performed three times in same day (intra-day) and recovery studies between days (inter-day) were analysed. The relative standard deviation of intra-day and inter-day values were calculated and given in table. The precision is expressed in the form of percent relative standard deviation as shown in table 5.

Determination of stability

The absorbance of 100µg/ml of abiraterone acetate was measured every15min for 2hrs the values are consistence throughout the experiment

Results and Discussion

Data for stability determination

Table-1 determination of stability

Sl.no	Time	Absorbance
1	0 min	0.2548
2	15min	0.2553
3	30min	0.2562
4	45min	0.2559
5	60min	0.2552
6	1hr15min	0.2549
7	1hr30min	0.2555
8	1hr45min	0.2557
9	2hrs	0.2554

Data for calibration curve

Table-2 determination of calibration curve

Sl.no	Concentration(µg/ml)	Absorbance
1	10	0.1717
2	20	0.3485
3	30	0.5354
4	40	0.7274
5	50	0.8669
6	60	1.0639
slope	0.1769	

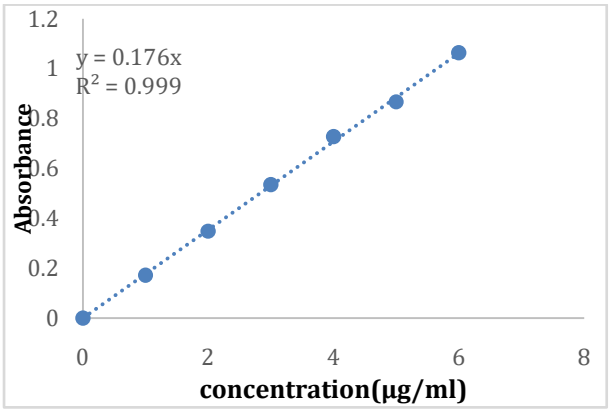


Fig- 2 Data of calibration curve in graphical representation

Data for determination of linearity

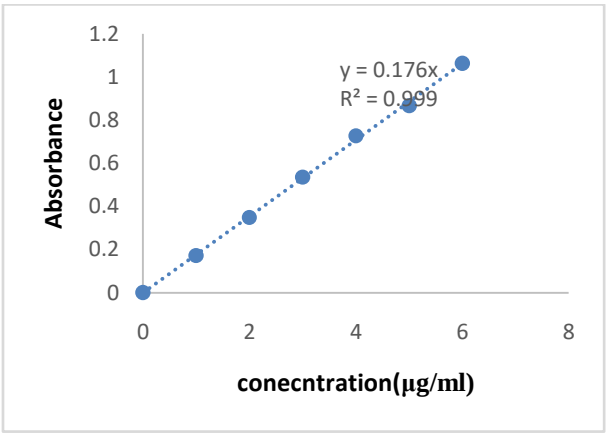


Fig-3 Linearity curve-1

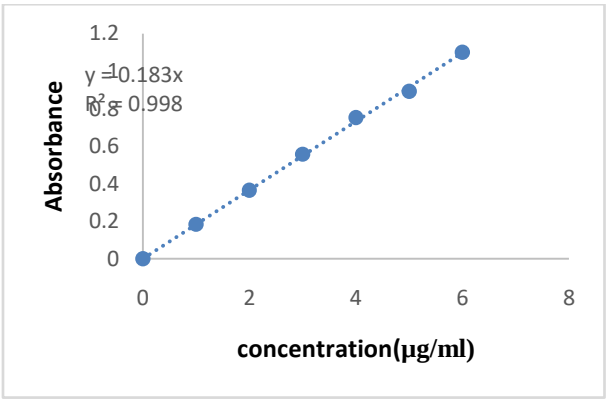


Fig-4 Linearity curve-2

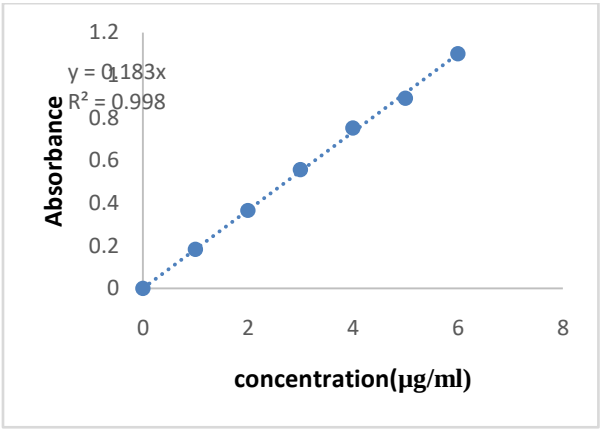


Fig-5 Linearity curve-3

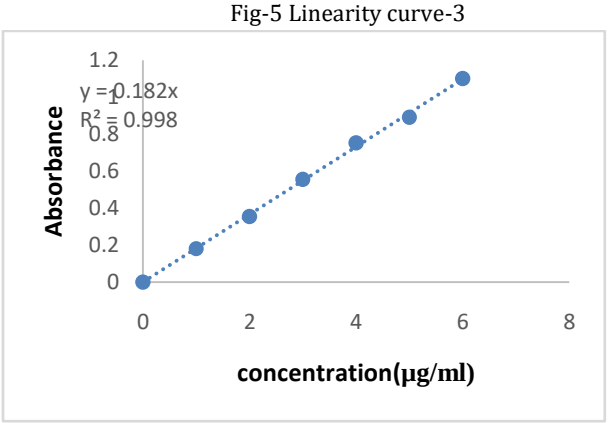


Fig-7 Linearity curve-5

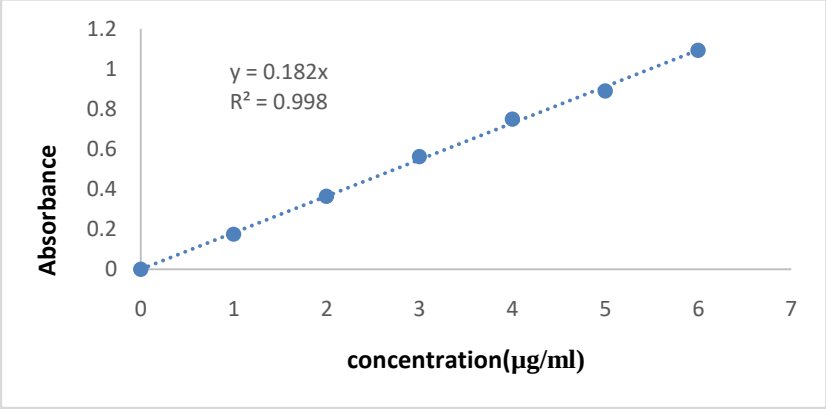


Fig-8 Linearity curve-6

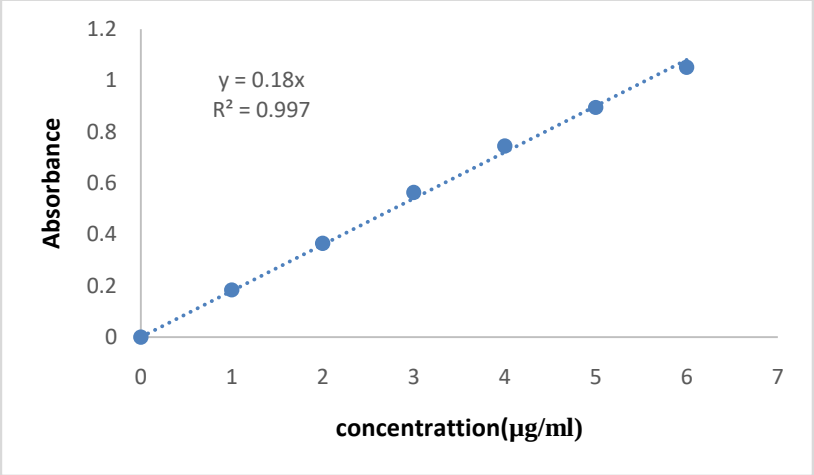


Fig-9 Data for formulation linearity

Table-3: Data for determination of LOD and LOQ

Sl.no	slope	LOD(µg/ml)	LOQ(µg/ml)	SD
1	0.1769	0.006	0.018	0.002
2	0.1831			
3	0.1826			
4	0.1828			
5	0.1823			
6	0.18			

Table 4 data for accuracy of abiraterone acetate

Sl.no	**Amount of drug present in (µg/ml)**	**Amount added (µg/ml)**	**absorbance**	**Amount recovery(µg/ml)**	**Percentage (%)**	**SD**	**RSD**
1	20	10	0.5238	9.9	99		
1	20	10	0.5237	10	100		

1	20	10	0.5235	10.1	100.1	0.42	0.420
2	20	20	0.6990	19.9	99.5		
2	20	20	0.7006	20	100		
2	20	20	0.7008	20.01	100.5		
3	20	30	0.8775	29.99	99.9		
3	20	30	0.8777	30	100		
3	20	30	0.8779	30.01	100.03		

Table 5: recovery of abiraterone acetate

Sl.no	Amount of drug present in (µg/ml)	Amount added (µg/ml)	absorbance	Amount recovery(µg/ml)	Percentage (%)	SD	RSD
1	20	10	0.5067	10.01	100.1	0.399	0.3996
1	20	10	0.5080	10	100		
1	20	10	0.6837	9.9	99		
2	20	20	0.6840	20.01	100.05		
2	20	20	0.6830	20	100		
2	20	20	0.6837	19.9	99.5		
3	20	30	0.8607	30.01	100.3		
3	20	30	0.8610	30	100		
3	20	30	0.8600	29.9	99.6		

Results of validation parameters

A UV spectrophotometric method has been developed and validated for determination of abiraterone acetate in pure form and its pharmaceutical dosage forms. The process was done by using distilled water as a solvent with the detection wavelength set at 264nm. Abiraterone acetate was checked for its stability in the chosen solvent and found to be stable. The method was linear with correlation coefficient 0.9997 in the concentration range of 100µg/ml. The limit detection and limit quantification were 0.018 µg/ml and 0.006 µg/ml, respectively. The intra and inter-day precisions were satisfactory; the relative standard deviations did not exceed 2%.The accuracy of the method is high as can be seen from the mean recovery values of abiraterone acetate which were in the range of 10-60µg/ml the method met the ICH regulatory requirements

Sl.no	parameter	Result
1	Detection of wavelength	254nm
2	Beer- Lambert law (µg/ml)	10-60(µg/ml)
3	Regression equation(y=mx+c)	0.1769
4	Slope	0.1769
5	Accuracy(%mean recovery)	100.03%
6	LOD	0.006
7	LOQ	0.018
8	Standard deviation	0.42
9	Relative standard deviation	0.420

Conclusion

A simple, novel, economical, rapid, precise, and accurate UV spectrophotometric method was developed for the estimation of abiraterone acetate in bulk and pharmaceutical formulations. The method was developed by using distilled water as solvent. The developed method was validated for parameters via accuracy, precision, and linearity, limit of detection and limit of quantification as per ICH guidelines. All the parameters were found to be within the acceptance limits. The results indicated that the proposed method for the estimation of abiraterone acetate is very accurate and cost effective and can be employed in routine sample analysis of abiraterone acetate in bulk and pharmaceutical formulation.

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