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New Spectrophotometric Techniques for the determination of Abiraterone acetate (A Steroidal Inhibitor) in Tablets

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ABSTRACT

Abiraterone acetate is specified for the treatment of prostate cancer. Two new simple spectrophotometric techniques have been established for the assay of Abiraterone acetate in pharmaceutical dosage forms. Abiraterone acetate shows linearity 1-100 µg/mL in methanol (λ_{max} 248 nm); y = 0.0251x + 0.0373 (Method A) and 5-100 µg/mL in HCl. (Method B) (λ_{max} 240 nm); y = 0.0276x - 0.0236 and the two methods are validated.

KEY WORDS: Abiraterone acetate, Spectrophotometry, validation, Methanol, Hydrochloric acid.

1. INTRODUCTION

Abiraterone (ABT) is a white to off-white, non-hygroscopic, crystalline powder with molecular weight 349.509 g/mol and pKa 5.19. It is chemically known as (3ß)-17-(pyridin-3-yl) androsta-5, 16-dien-3-ol (Sarker, 2011). It is an irreversible inhibitor of CYP17 which is an important enzyme in androgens production (Barrie, 1994) (Potter, 1995). Abiraterone was determined using different techniques - Spectrofluorimetry (Aiqin, 2013), HPLC-fluorescence detection (Belleville, 2015), liquid chromatography coupled to electrospray ionization mass spectrometry (Alaa, 2013), RP-HPLC/UV (Ramesh, 2013), LC-MS/MSESI (Sandip, 2012) and UPLC–tandem mass spectrometry (Tanveer, 2013) (Vanessa, 2006) in biological fluids. In the present study the authors have proposed two methods for Abiraterone in tablets.

2. EXPERIMENTAL

A UV-1800, Shimadzu double beam spectrophotometer was introduced. Analytical grade methanol (Merck), hydrochloric acid (Merck) were used. Abiraterone acetate gift samples were obtained from Glenmark Pharmaceuticals, India. The standard stock solution of ABT was prepared by dissolving ABT in methanol and diluted with methanol and HCl for A and B methods respectively.

Validation procedure (ICH guidelines, 2005) A series of drug solutions 1-100 µg/mL and 5-100 µg/mL were prepared in 0.1N hydrochloric acid and methanol and scanned in UV region against their blank for both methods and absorption spectrum was recorded. Calibration curves were drawn both the methods.

Precision and Accuracy: Precision study was performed by calculating the absorbance of 20 µg/mL solutions (n=6) for both method A and B followed by the %RSD determination. Accuracy was assessed from the recovery studies by spiking the marketed sample solutions with 80%, 100%, and 120% of pure drug solutions followed by RSD calculation.

Assay procedure for the marketed formulations (Tablets): ABT is available as tablets with brand names ZYTIGA (Label claim: 250 mg/tablet; Janssen-Cilag Ltd, India) and XIBRA (Label claim: 250 mg/tablet; Cipla Limited), ABIRAPRO (Label claim: 250 mg/tablet; Glenmark Pharmaceuticals, India. Twenty tablets of each brand were collected, powdered and extracted with methanol in a volumetric flask, sonicated and filtered. The resulting solution was diluted with HCl and methanol separately for method A and B.

3. RESULTS AND DISCUSSION

Two new spectrophotometric techniques were cultivated for ABT determination in hydrochloric acid and methanol. Abiraterone acetate has shown absorption maxima (λ_{max}) at 248 nm in methanol and at 240 nm in HCl for A and B methods respectively and the resulting absorption spectra was given in Figure.2 and Figure 3. Linearity was observed 1-100 µg/mL and 5-100 µg/mL with y = 0251x + 0.0373 and y = 0.0276x - 0.0236 with correlation coefficient 0.9991 and 0.9998 for A and B methods (Figure.4). Optical characteristics were given in Table.1.

Table.1. Optical characteristics of Abiraterone acetate

Parameters	Method	
	A	B
Linearity range (µg /mL)	1-100	5-100
λ_{max} (nm)	248	240
Molar extinction coefficient (Litre/mole/cm)	9.646448×10^3	9.091778×10^3
Sandell's sensitivity (µg/cm^2/0.001absorbance unit)	0.03623	0.03844
Slope	0.0251	0.0276
Intercept	0.0373	0.0236
Correlation coefficient	0.9991	0.9998

ABT was determined in marketed formulations (tablets) and recovery details were given in Table.2. The methods are said to be more precise (Table.3) and more accurate (Table.4), as their % RSD was not more than 2.0.

Table.2. Assay of Abiraterone acetate Tablets

Brand	Labeled Amount (mg)	*Amount obtained (mg)		% Recovery*	
		Method		Method	
		A	B	A	B
I	250.0	248.89	247.84	99.56	99.14
II	250.0	248.14	248.32	99.25	99.32
III	250.0	248.64	247.44	99.45	98.98

*Each value is average of three replicates

Table.3. Precision studies of Abiraterone acetate

Method	Conc. (µg/mL)	Intra-day precision	Inter-day precision
		*Mean Absorbance ± SD (% RSD)	*Mean Absorbance ± SD (% RSD)
A	5	0.1514 ± 0.0001 (0.04)	0.1515 ± 0.0016 (1.06)
	10	0.2765 ± 0.0001 (0.03)	0.2765 ± 0.0019 (0.70)
	20	0.5590 ± 0.0006 (0.11)	0.5593 ± 0.0050 (0.90)
B	5	0.0964 ± 0.0001 (0.10)	0.0970 ± 0.0006 (0.61)
	10	0.2601 ± 0.0002 (0.06)	0.2632 ± 0.0028 (1.05)
	20	0.5154 ± 0.0006 (0.11)	0.5182 ± 0.0054 (1.03)

*Mean of three replicates

Table.4. Accuracy studies of Abiraterone acetate

Method	Conc. (µg/mL)			*Mean Absorbance ± SD (% RSD)	Drug found (µg/mL)	% Recovery
	Formulation	Pure drug	Total			
A	12.5	7.5	20	0.5383 ± 0.0010 (0.19)	19.94	99.70
	12.5	12.5	25	0.6618 ± 0.0020 (0.30)	24.88	99.52
	12.5	17.5	30	0.7784 ± 0.0012 (0.15)	29.94	99.81
B	12.5	7.5	20	0.5258 ± 0.0008 (0.16)	19.90	99.52
	12.5	12.5	25	0.6661 ± 0.0002 (0.03)	24.99	99.96
	12.5	17.5	30	0.8014 ± 0.0006 (0.07)	29.89	99.64

*Mean of three replicates

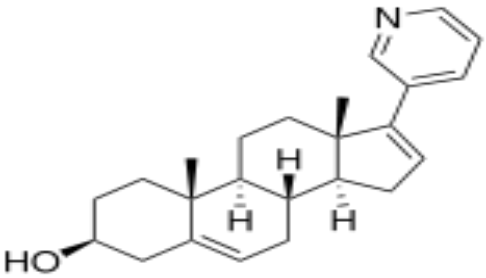


Figure.1. Chemical structure of Abiraterone (ABT)

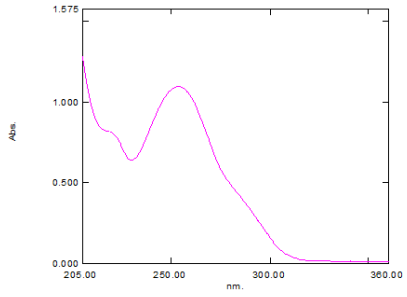


Figure. 2. Absorption spectrum of Abiraterone acetate (40 µg/mL) in methanol.

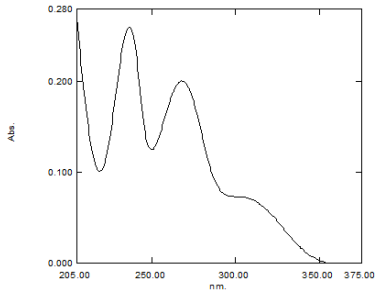
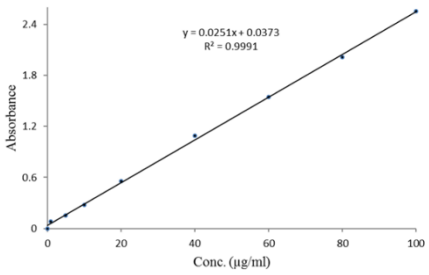
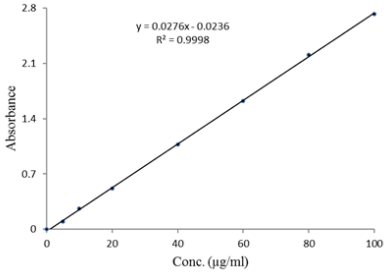


Figure. 3. Absorption spectrum of Abiraterone acetate (10 µg/mL) in Hydrochloric acid



(A)



(B)

Figure.4. Calibration curves of Abiraterone acetate in methanol (A) and hydrochloric acid (B)

4. CONCLUSION

The present reported methods can be employed for the determination of Abiraterone acetate in tablets successfully and there is no interference of excipients during the study.

5. ACKNOWLEDGMENT

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