J Fluoresc (2013) 23:1279–1286
DOI 10.1007/s10895-013-1261-3

ORIGINAL PAPER

β-cyclodextrin Sensitized Spectrofluorimetry for the Determination of Abiraterone Acetate and Abiraterone

Aiqin Gong · Xiashi Zhu

Received: 19 April 2013 / Accepted: 25 June 2013 / Published online: 10 July 2013

Abstract A novel spectrofluorimetric method to determine abiraterone acetate and its active metabolite, abiraterone was developed, 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-CD and abiraterone acetate and the β-cyclodextrin sensitized spectrofluorimetry was examined. The various factors influencing fluorescence were discussed in details. The results showed that under the optimized conditions, the linear range of calibration curve for the determination of biraterone 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. No interference was observed from common co-existing substances or pharmaceutical excipient. The method was successfully applied to the analysis of abiraterone acetate in pharmaceutical formulation and abiraterone in human serum/urine.

Keywords Abiraterone acetate · Abiraterone · β-cyclodextrin · Sensitized spectrofluorimetry

Introduction

Abiraterone (Fig. 1a) is a CYP17 (17α-hydroxylase-C17, 20-lyase) inhibitor drug used in castration-resistant prostate cancer (formerly hormone-resistant or hormone-refractory prostate cancer)—i.e., prostate cancer not responding to androgen deprivation or treatment with antiandrogens. It is formulated as the prodrug abiraterone acetate (Fig. 1b) and marketed under the trade name Zytiga (approved by U.S. Food and Drug Administration in April 2011) [1].

Inactive ingredients in abiraterone acetate tablets are lactose monohydrate, microcrystalline cellulose, and so on. After oral administration, abiraterone acetate, the prodrug form present in the commercial preparation, is de-acetylated to abiraterone in vivo to inhibit CYP17 [2]. In clinical studies, abiraterone acetate is well tolerated and shows promising clinical activity in castration-resistant prostate cancer. The recommended dose of abiraterone acetate is 1,000 mg orally daily in combination with prednisone 5 mg twice daily [3]. Zytiga may cause serious side effects including high blood pressure (hypertension), low blood potassium levels (hypokalemia) and fluid retention (edema) [4]. In view of safe medication and investigating the pharmacokinetics of abiraterone acetate in patients, an analytical procedure is needed to determine abiraterone acetate in pharmaceutical formulation and abiraterone in human serum/urine.

Literature review reveals that the reported methods mainly focus on chromatographic techniques with MS detector for the determination of abiraterone acetate and abiraterone in human plasma [2] or abiraterone in rat and human plasma [5]. However, analytical techniques based on LC-MS involve a complex procedure and costly solvents and expensive instrumental set up which an ordinary laboratory cannot afford. Compared with chromatography, spectrofluorimetry attracts more and more interest with its high sensitivity and selectivity and simplicity, and thus has been used extensively in the analysis of drugs [6, 7].

The sensitivity of fluorescence analysis could be enhanced in suitable medium (such as fluorescence probe [7, 8], surfactant [7], room temperature ionic liquid [9]). β-cyclodextrin (β-CD) is a cyclic oligomer of seven linked D-glucopyranose units, which structure is that of a truncated cone with the hydrophilic outer surface and a hydrophobic internal cavity. Because of its peculiar

A. Gong · X. Zhu (✉)
College of Chemistry & Chemical Engineering,
Yangzhou University, Yangzhou, China
e-mail: xszhu@yzu.edu.cn

X. Zhu
e-mail: zhuxiashi@sina.com

A. Gong
Yangzhou Polytechnic Institute, Yangzhou 225002, China

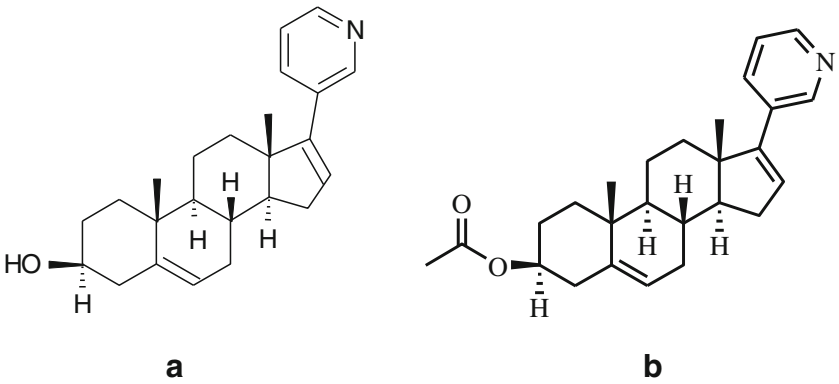

Fig. 1 Chemical structures of **a** abiraterone and **b** abiraterone acetate

molecular structure, β-CD could include guest molecules to form inclusion complexes. The formation of inclusion complex, in many cases, would alter the physical, chemical or biological properties of substrates, which could make up for the inadequate performance of the guest molecules application [10]. As analytical synergist, β-CD has been used in spectrophotometry [11, 12] or chromatography [13] for drug analysis.

This work described a new spectrofluorimetric method for the determination of abiraterone acetate and abiraterone, based on the native fluorescence intensity of abiraterone acetate and abiraterone could be increased strongly in the medium of β-CD due to the formation of inclusion complex. The reaction conditions were optimized. The mechanism of β-cyclodextrin sensitized spectrofluorimetry was discussed with inclusion constant and quantum efficiency in different media. The method was successfully applied to the determination of abiraterone acetate in abiraterone acetate tablets and abiraterone in human serum/urine.

Experimental

Apparatus

A F-4500 spectrofluorimeter (Hitachi, Japan) was used for all the fluorescence measurement, with excitation and emission slits at 5.0 nm, λex=259 nm and 1-cm quartz cell. The pH was measured on a pH S-25 pH meter (Shanghai, China). All absorption spectral recordings and absorbance measurements were performed on a UV 2501 spectrophotometer (Shimadzu, Japan).

Chemicals

Abiraterone acetate standard, abiraterone standard and abiraterone acetate tablets (Batch number: 20130101, Labeled value: 125 mg/tablet) were kindly provided by Jiangsu Lianhuan pharmaceutical Co., Ltd. (Jiangsu, China). β-cyclodextrin and all other materials (analytical reagent grade) were purchased from reagent company of Guoyao (Shanghai, China).

Abiraterone acetate and abiraterone standard stock solutions of 2.0 mg/mL were prepared by dissolving 0.10 g of abiraterone acetate or abiraterone in 50 mL of anhydrous ethanol and kept in coolness and darkness. The stock solutions were further diluted with anhydrous ethanol to obtain a standard working solution of 0.20 mg/mL before using.

1.0 % β-CD solution was freshly prepared in distilled water. Series of HAc-NaAc buffer solution (pH 3.5–6.5), NH_4Ac buffer solution (pH 7.0) and NH_3-NH_4Cl buffer solution (pH 7.5–8.0) were prepared.

Sample Preparation

Abiraterone Acetate Tablets Treatment

Ten tablets of abiraterone acetate was weighed and crushed, and then sample powder of about one tablet was accurately weighed and placed in a 50 mL of beaker and dissolved with anhydrous ethanol. Insoluble excipient was removed by filtration through a 0.45 μm membrane filter. The filtered solution was diluted to 50 mL with anhydrous ethanol. The solution was further diluted 12.5-fold with anhydrous ethanol before using.

Serum/Urine Treatment

Firstly, serum and urine samples of healthy volunteer were collected from local hospitals and stored in polyethylene bottles. Then 1.0 mL of blank serum or urine sample was spiked with 1.0 mL of abiraterone stock solution. To the spiked serum or urine solution, 8.0 mL of acetonitrile was added. The mixture was vortex-mixed for 1 min and centrifuged for 15 min at 1,200 r/min [14]. Finally the supernatant was determined for abiraterone.

The concentration of abiraterone acetate in abiraterone acetate tablets and abiraterone in serum or urine was detected by working curve method with fluorescence system.

Fluorescence Measurements

In a 10 mL volumetric flask, 0.5 mL of 1.0 % β-CD solution, 1.5 mL of HAc-NaAc buffer solution (pH=5.5) and adequate

abiraterone acetate standard, abiraterone standard or sample solution were added; the solution was diluted to the mark with distilled water. Then fluorescence spectra were recorded in the range of 250–500 nm upon excitation at 259 nm.

Determination of Relative Fluorescence Quantum Yield

Fluorescence quantum yields of abiraterone acetate and abiraterone with or without β-CD were measured using 1.0×10^{-6} g/mL quinine sulfate as reference material.

Under the same apparatus conditions, according to the equation $\varphi_2=(\varphi_1A_1F_2)/(F_1A_2)$ [15] , the quantum yield of the analyte was calculated. In brief, φ_1 and φ_2 correspond to standard and unknown fluorescence quantum yield, F_1 and F_2 are the integral areas of two calibration fluorescence emission curves, and A_1 and A_2 are the absorbance ($\lambda_{absorbance}=\lambda_{excitation}$) of the standard and unknown, and$\varphi_1=0.55$ (25 °C) is known.

Determination of Inclusion Constant by Direct Fluorescence Technique

In a 10 mL volumetric flask, an aliquot of abiraterone acetate (2.0 μg/mL), 1.5 mL of HAc-NaAc buffer solution (pH=5.5)and various amounts of 8.81×10^{-4} mol/L β-CD (finally the $c_{\beta\text{-CD}}$ should be much more than $c_{\text{abiraterone acetate}}$) were added, and then diluted to the mark with deionized water and mixed thoroughly. After that, the fluorescence intensity of mixture was measured in a 1-cm quartz cell at 345 nm after excitation at 259 nm. The inclusion constant K was calculated according the modified Benesi–Hildebr and equation (double reciprocal plot) (Eq. 1) [16]

$$\frac{1}{F-F_0}=\frac{1}{K\cdot k\cdot Q\cdot C_0\cdot C_{CD}}+\frac{1}{K\cdot Q\cdot C_0} \quad (1)$$

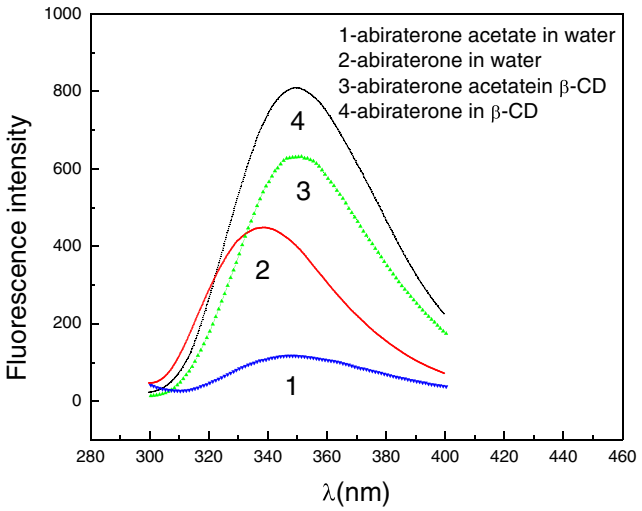

Fig. 2 Emission spectra of abiraterone acetate or abiraterone (abiraterone acetate or abiraterone: 2.0 μg/mL, β-CD: 0.05 %)

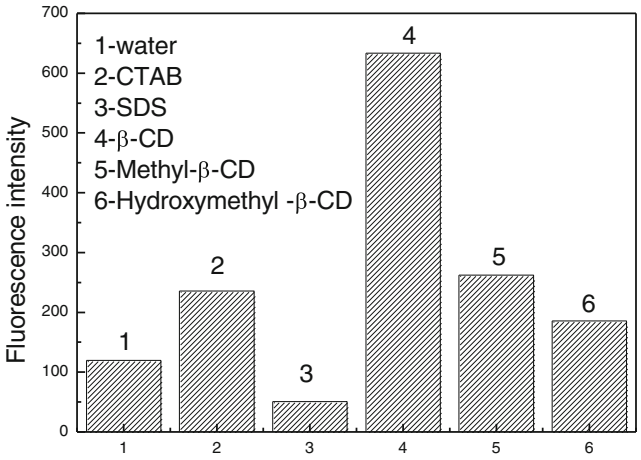

Fig. 3 Effect of different testing system on abiraterone acetate fluorescence intensity (abiraterone acetate: 2.0 μg/mL, all media:0.05 %)

Briefly, F and F_0 was the fluorescence intensity of abiraterone acetate with or without β-CD, k was the instrument constant, Q was fluorescence quantum yield, C_0 was the concentration of abiraterone acetate, C_{CD} represented the concentration of β-CD. K was the inclusion constant. The calibration graph was obtained by plotting $\frac{1}{F-F_0}$ versus $\frac{1}{C_{CD}}$. The intercept divided by the slope of calibration graph was K.

Results and Discussion

Fluorescence Spectra of Abiraterone Acetate and Abiraterone

The fluorescence spectra of abiraterone acetate and abiraterone in water (curve 1, 2) and β-CD (curve 3, 4) medium are shown in

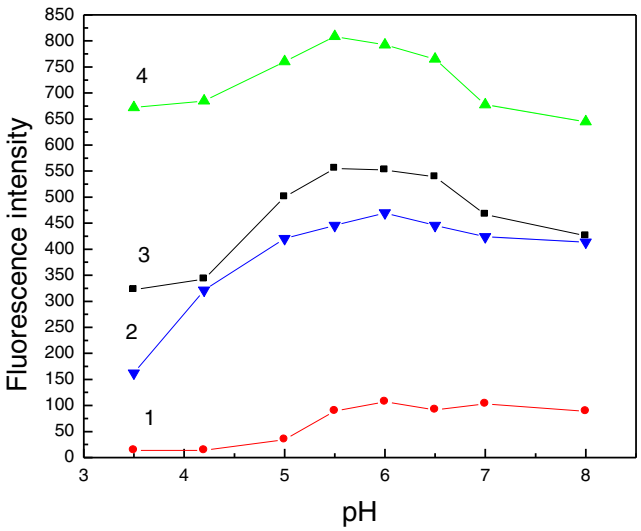

Fig. 4 Effect of pH on abiraterone acetate or abiraterone fluorescence intensity (abiraterone acetate or abiraterone: 2.0 μg/mL, β-CD: 0.05 %) 1- abiraterone acetate in water, 2- abiraterone in water, 3- abiraterone acetate in β-CD, 4- abiraterone in β-CD

Fig. 2. Comparing curve 1 and 3, 2 and 4, the fluorescence intensity of abiraterone acetate was enhanced about six times in 0.05 % β-CD system than that in water; while for abiraterone, the fluorescence intensity was increased two times.

Selection of Media

The selection of media is very important in spectrofluorimetry. In this work, media such as Triton-X-100, SDS, CTAB, β-CD, methyl-β-CD, hydroxymethyl-β-CD were studied. The results indicated that there would be fluorescence emission of Triton-X-100 at 350 nm and interferes the determination of abiraterone acetate or abiraterone. Other media influence on the determination of abiraterone acetate is shown in Fig. 3. It could be seen from Fig. 3 that the influence of media on the fluorescence intensity of abiraterone acetate (F) could be divided two kinds. (1) F was quenched(such as SDS); (2) F was enhanced(such as CTAB, β-CD, methyl-β-CD, hydroxymethyl-β-CD). Maximum fluorescence intensity was observed in β-CD medium. Hence, β-CD was the medium of choice. As for abiraterone, the influence of media on fluorescence intensity was similar to that of abiraterone acetate.

Effect of pH

Effect of pH on F is shown in Fig. 4. It could be seen from Fig. 4 that (1) that the fluorescence intensity of abiraterone acetate or abiraterone in water was increased with pH increasing before pH 5.5, and reached a maximum value at pH 5.5. After pH 6.0, F was decreased (curve 1 and 2); (2) the variation tendency of F depending on pH in β-CD medium was similar to the situation in water, and the maximum sensitizing effect was found at pH 5.5 (curve 3and 4).

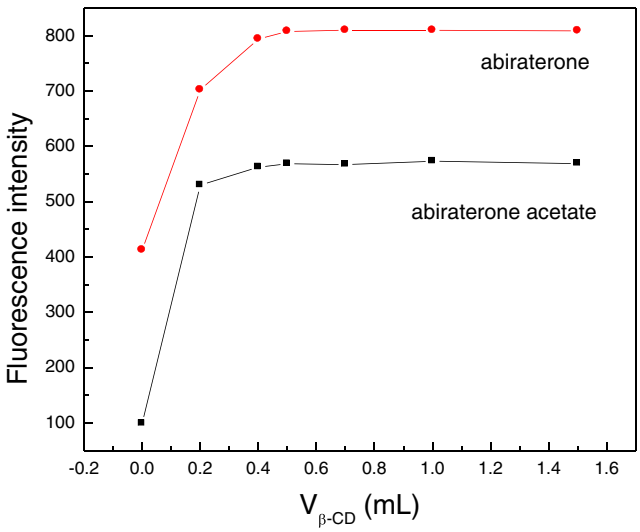

Fig. 5 Effect of β-CD amount on abiraterone acetate or abiraterone fluorescence intensity (abiraterone acetate or abiraterone:2.0 μg/mL)

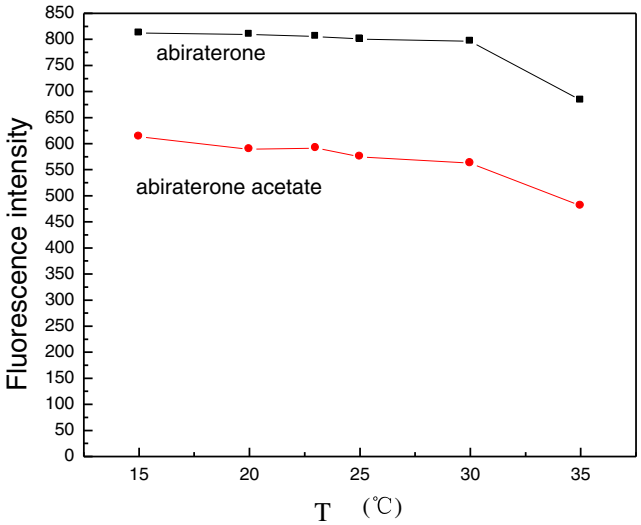

Fig. 6 The influence of temperature on determination (abiraterone acetate or abiraterone: 2.0 μg/mL, β-CD: 0.05 %)

Above examination indicated (1) because the pKa of abiraterone acetate is 5.19 [17], the fluorescence of abiraterone acetate probably came from its neutral form; (2) the inclusion action of β-CD and abiraterone acetate didn't change the structure of abiraterone acetate. Thus, a HAc-NaAc buffer solution of pH=5.5 was chosen for the determination.

Effect of Ionic Strength

The effect of ionic strength was studied by adding KCl solution to abiraterone acetate or abiraterone solutions. The results showed that F was significant decreased when the concentration of KCl was over 0.50 mol/L. In this study, 1.5 mL of HAc-NaAc buffer solution (1.0 mol/L) can satisfy the requirement of ionic strength.

Effect of β-CD Amount

The effect of 1.0 % β-CD amount on F was studied in the range of 0.2–1.5 mL (Fig. 5). The maximum fluorescence intensity was obtained with 0.4 mL of the reagent. After that, F was almost not affected with enhancing amount of 1.0 % β-CD up to 1.5 mL. Thus, 0.5 mL of 1.0 % β-CD was chosen as an optimum amount for all measurements.

Effect of Reaction Time

The effect of reaction time on the formation of inclusion complex was studied at room temperature. It was observed that the inclusion complex (β-CD-abiraterone acetate and β-CD-abiraterone) got stabilized immediately after mixing the drug and reagent and remained stable at least for about 2 h.

Table 1 Tolerance limits of interfering substances

Tested substances	Tested substances to analyte ratio (w/w)
Glucose	50000
SO_4^{2-}	9600
K^+	8000
Cl^-, Na^+	4500
Tartaric acid	2500
Cane sugar, citric acid	1250
Lactose	625
Ni^{2+}	500
Zn^{2+}	350
Mg^{2+}	100
Ca^{2+}	80
Al^{3+}	50
Pb^{2+}	7.5
Cu^{2+}	1

Effect of Temperature

Temperature is an important factor in spectrofluorimetry. The effect of temperature on F is shown in Fig. 6. As can be seen, F was almost unchanged in the range of 15~30 °C, but dramatically decreased when T >30 °C. So, 20 °C (room temperature) was chosen for this work.

Effect of Potential Interferences

The potential interference of the proposed method was evaluated by analyzing the standard solution of abiraterone acetate in the presence of tablet excipients such as lactose, microcrystalline cellulose, croscarmellose sodium, sucrose, magnesium stearate, colloidal silicon dioxide and other possible coexisting substances. It was found that the solubility of microcrystalline cellulose, croscarmellose sodium, magnesium stearate or colloidal silicon dioxide was very small under the examination condition and could be eliminated as sediment from solution.

The effects of other substances were discussed in the determination of 2.0 μg/mL abiraterone acetate. The level of tolerated concentrations of foreign substances was considered as the maximum concentration found to cause a change in signal, less than ±5 %, compared with the signal without foreign substances. The tolerance limits are listed in Table 1. As indicated in Table 1, there was little interference from the excipients in abiraterone acetate tablets and other possible existing substances.

Table 2 The performance characteristic of the proposed method

Parameters	Abiraterone acetate	Abiraterone
Linear range (μg/mL)	0.20~6.0	
Limit of detection (LOD)(ng/mL)	6.8	6.6
Limit of quantitiation(LOQ)(ng/mL)	22.4	21.8
Slope (b)	301.9	316.4
S.D. of slope	1.3	2.0
Intercept (a)	43.19	82.49
S.D. of intercept	0.98	1.2
Correlation (r, n=8)	0.997	0.996
S.D. of reagent blank (n=11)	0.688	

Table 3 Test of precision of the proposed method

Proposed method	Added (μg/mL)	Found[a] (μg/mL)		RSD (%)	
		Abiraterone acetate	Abiraterone	Abiraterone acetate	Abiraterone
Interday	1.00	1.02	0.98	0.15	0.20
	2.00	1.98	2.02	0.22	0.18
	3.00	3.05	3.04	0.18	0.23
Intraday	1.00	1.03	1.04	0.24	0.25
	2.00	2.05	2.02	0.30	0.28
	3.00	2.96	2.95	0.21	0.26

[a] Mean for five independent determinations

Analytical Application

Linearity and Limits of Detection

The calibration graphs for determining abiraterone acetate and abiraterone were obtained under the experimental conditions described above by plotting fluorescence intensity versus concentration. The analytical parameters obtained are given in Table 2. The results showed that a good linear relationship was observed over the range 0.20~6.0 μg/mL.

Precision and Repeatability

To evaluate intra-day and inter-day precisions, analysis of abiraterone acetate and abiraterone at three concentration levels (1.00, 2.00, 3.00 μg/mL) was carried out by performing five experiments on the same day using the same analyte standard solution and over five consecutive days using different solutions. The results are summarized in Table 3. The intra-day and inter-day RSD values for the determination of biraterone acetate and abiraterone ranged from 0.15 % to 0.30 %, from 0.18 % to 0.28 %, respectively, reflecting the usefulness of the method in routine use.

Accuracy and Recovery

The accuracy of the proposed method was examined by performing recovery experiments through standard addition

Table 4 Results of sample determination and recovery

Sample	Added (μg/mL)	Found (μg/mL)	RSD (%)	Recovery(%)
Abiraterone acetate tablet	0.0	2.09	0.8	/
	1.0	3.10	1.3	101.0
	2.0	4.05	1.5	98.0
	3.0	4.96	1.2	95.7
Serum	0.0	1.56	2.1	/
	1.0	2.62	1.0	106.2
	2.0	3.60	1.9	101.9
	3.0	4.64	2.3	102.6
Urine	0.0	1.87	0.8	/
	1.0	2.86	1.6	99.0
	2.0	3.84	2.3	98.4
	3.0	4.67	1.7	93.2

Average value of three determination

technique. In examination known quantities of pure abiraterone acetate were mixed with definite amounts of preanalyzed abiraterone acetate tablet, or abiraterone were mixed with definite amounts of preanalyzed human urine/serum. After that mixtures were analyzed following the proposed method. The data are listed in Table 4. Obtained mean values of the recoveries ranged from 95.7 % to 101.0 %, from 101.9 % to 106.2 % and from 93.2 % to 99.0 % for abiraterone acetate tablets and human serum/urine; the RSD was from 0.8 % to 1.5 %, from 1.0 % to 2.3 % and from 0.8 % to 2.3 %, respectively, which indicating both good accuracy and precision.

Comparison of Different Methods

The results obtained in this article were compared with those by other methods for the determination of abiraterone acetate and abiraterone (Table 5). It can be seen from Table 5 the LOD of HPLC-MS is lower than that of proposed method, but the recovery is poorer than the recovery of this work. Moreover HPLC-MS generally requires complex and expensive equipment. In words, the present study had the rapidity, simple, cheap advantage over HPLC-MS and lower LOD over HPLC-UV.

Sample Determination

The method was applied to determine abiraterone acetate in abiraterone acetate tablets and abiraterone in spiked human urine and serum. The data are listed in Table 4. The result of abiraterone acetate tablets obtained by the proposed method (130.6 mg/tablet) was in good agreement with the label value (125 mg/tablet).

Discussion of Sensitizing Effect Mechanism

Because the property of abiraterone acetate is similar to that of abiraterone, the interaction of abiraterone acetate and β-CD is discussed in this paper.

Inclusion Interaction of Abiraterone Acetate and β-CD

The photochemical and photophysical properties of guest molecules could be altered due to the formation of a host-guest inclusion complex. The change of fluorescence intensities of the abiraterone acetate in the presence of β-CD might be due to the following two reasons: (1) the formation of a host-guest inclusion complex. In this situation abiraterone acetate molecules would enter the hydrophobic cavity of β-CD and the hydrophobic cavity of β-CD provided the different microenvironment for abiraterone acetate; (2) it may be a solvent effect caused by a higher concentration of β-CD.

To demonstrate the formation of host-guest complex (β-CD - abiraterone acetate), several experimental techniques were used:

(1) β-CD is the cyclic oligosaccharides consisting of seven d-(+)-glucopyranose units. If the change of fluorescence intensities of abiraterone acetate is caused by β-CD solvent effect, the same influence could also be caused by glucose [19].

The effect of glucose on the spectra of abiraterone acetate was tested. When the addition of glucose (in an equivalent mass of 4.4×10^{-4} mol/L β-CD) to a 2.0-μg/mL of abiraterone acetate solution, the fluorescence spectra of abiraterone acetate were neither spectral shifts nor intensity changed, which contrasted with those found when β-CD was added. It indicated that the fluorescence spectra changes of abiraterone acetate induced by β-CD

Table 5 Comparison of methods for the determination of abiraterone acetate and abiraterone

Technique	Sample	Linearity range	LOD	Recovery	Reference
LC-MS/MS+SPE	Abiraterone acetate Abiraterone	5~500 nM	5 nM	73~80 % 71~77 %	[2]
LC-MS/MS-ESI	Abiraterone	0.2~201 ng/mL	0.20 ng/mL		[5]
LC–UV	Abiraterone	10–200 μg/mL	4 μg/mL	95~105 %	[18]
Fluorescence	Abiraterone acetate Abiraterone	0.2~6.0 μg/mL	6.8 ng/mL 6.6 ng/mL	91.5~101.0 % 93.2~106.2 %	This work

Table 6 Chemical shifts δ of protons in β-CD and abiraterone acetate -β-CD (D_2O as solvent)

	β-CD					
	H_1	H_2	H_3	H_4	H_5	H_6
$\delta_{\beta\text{-CD}}$	4.994	3.593	3.904	3.509	3.792	3.817
$\delta_{\text{abiraterone acetate -}\beta\text{-CD}}$	4.986	3.606	3.871	3.527	3.681	3.789
$\Delta\delta^a$	−0.008	0.013	−0.033	0.018	−0.111	−0.028

[a] $\Delta\delta=\delta_{\text{abiraterone acetate -}\beta\text{-CD}}-\delta_{\beta\text{-CD}}$

might be due to the formation of inclusion complexes (β-CD- abiraterone acetate), namely there was the conclusion interaction between β-CD and abiraterone acetate.

(2) The polarity of the hydrophobic cavity of β-CD is similar to that of alcohols (R–OH). The effect of different alcohols on the fluorescence spectra of abiraterone acetate was investigated, which could reflect the inclusion interaction between β-CD and abiraterone acetate [10].

Ethanol/water and 2-propanol/water were used as media to obtain the fluorescence spectra of abiraterone acetate at different alcohol/water ratios. It was found that the emission wavelength of abiraterone acetate was red-shifted, and its fluorescence intensity was gradually enhanced as the percentage of the 2-propanol increased but decreased as the percentage of the ethanol increased. The facts suggested that the microenvironment around abiraterone acetate molecules in the presence of β-CD was similar to that in alcohols/water, thus it indicated the formation of inclusion complexes (β-CD-abiraterone acetate).

(3) The protons chemical shifts of β-CD in different system are measured by ^{1}H NMR spectroscopy, which could illustrate whether guest molecules enter the cavity of β-CD.

According to the ^{1}H NMR spectra of β-CD and β-CD-abiraterone acetate, apparent changes in chemical shifts of different protons in β-CD could be observed (Table 6). From Table 6 it could be seen in β-CD-abiraterone acetate system dramatic upfield shifts of β-CD's interior H-3, H-5 and H-6 protons were occurred, but the shifts of β-CD's outside H-1, H-2 and H-4 protons could be neglected. Because H-3 and H-5 are interior H of β-CD, the apparent shift changes of H-3 and H-5 indicate that the guest molecules (abiraterone acetate) enter the cavity along β-CD's wide rim, and the apparent chemical shifts possibly resulted from the shielding effect exerted by the inclusion of the guest molecule into β-CD's cavity.

All the above facts indicated obviously that a steady inclusion complex was formed between β-CD and abiraterone acetate. Figure 7 showed the formation progress of inclusion complexes (β-CD- abiraterone acetate).

The inclusion constant K is an important parameter for characterizing the inclusion interactions of β-CD with guest molecules. K would show the intensity of binding force of β-CD with guest molecules. So far, the methods, including spectrum (UV–vis and fluorescence), HPLC, surface tension, electrochemistry, calorimetry, dynamics and competition method [20], were used to determine inclusion constants. In this paper, the inclusion constant of β-CD and abiraterone acetate was determined by direct fluorescence technique. The K was 2.5×10^3 L/mol at 20 °C.

Fluorescence Quantum Yield

The fluorescence quantum yield is one of the mostly basic and significant parameters in all the characters of fluorescence substance. It represents the ability of translating absorption energy to fluorescence [21]. The fluorescence quantum yield of abiraterone acetate (2.0 μg/mL) with or without 0.05 % β-CD was 0.015 and 0.21 respectively. It was found that the quantum yield Φ_f was approximately 14 times higher in the presence of β-CD than in the absence of β-CD.

The Φ_f value is closely related to chemical structure and microenvironment of the system. The sensitization of β-CD

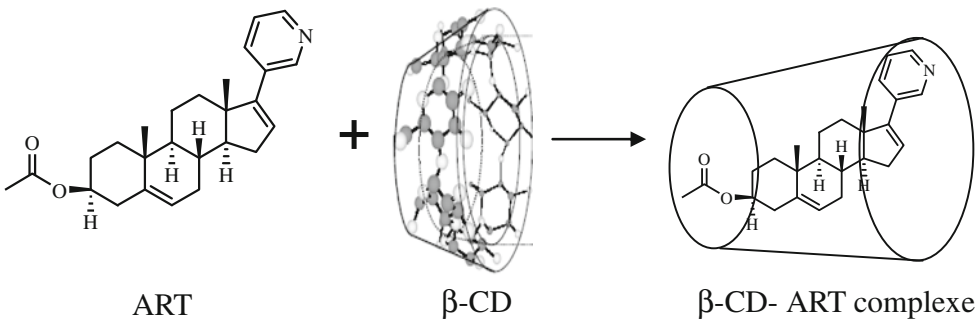

Fig. 7 The formation progress of β-CD- abiraterone acetate inclusion complexes

on abiraterone acetate fluorescence intensity was possibly because that the measured fluorescence substance singlet state was protected by β-CD owing to the inclusion of β-CD. The inclusion interaction could make a more suitable microenvironment for phosphor, which prevented collision inactivation.

Conclusions

In this paper, a new fluorimetric method was developed for the determination of abiraterone acetate and abiraterone, which based on the fact that fluorescence intensity of abiraterone acetate and abiraterone could be enhanced dramatically by β-CD. Compared with the reported two methods (LS-MS), the fluorimetric method possessed such merits as simple operation and cheaper apparatus. The examination results showed no interferences from the common excipients and additives. The statistical parameters and recovery data revealed good accuracy and precision of the proposed method. Therefore, it is concluded that the proposed method is simple, sensitive and rapid for the determination of abiraterone acetate and abiraterone.

Acknowledgments The authors acknowledge the financial support from the National Natural Science Foundation of China (20875082, 21155001) and a project funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions and the Foundation of the Excellence Science and Technology Invention Team in Yangzhou University

References

1. Qi BH (2011) Abiraterone acetate. Chin J Med Chem 21(5):407–410
2. Vanessa M, Yasmin A, Nicola W (2006) A validated liquid chromatographic—tandem mass spectroscopy method for the quantification of abiraterone acetate and abiraterone in human plasma. J Chromatogr B 843(2):262–267
3. Zytiga (abiraterone acetate) general information. http://www.medilexicon.com/drugs/zytiga.php
4. Zytiga (abiraterone acetate tablets) drug information. http://www.rxlist.com/zytiga-drug.htm
5. Sandip GG, Ravindra P, Junaid F (2012) 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. Biomed Chromatogr 26(6):761–768
6. Wang F, Huang W (2007) Determination of curcumin by its quenching effect on the fluorescence of Eu^{3+}–tryptophan complex. J Pharm Biomed Anal 43:393–398
7. Wang L, Guo CC, Chu ZJ (2009) Luminescence enhancement effect for the determination of balofloxacin with balofloxacin–europium (III)-sodium dodecylbenzene sulfonate system. J Lumin 129:90–94
8. Zhu XS, Gong AQ, Yu SH (2008) Fluorescence probe enhanced spectrofluorimetric method for the determination of gatifloxacin in pharmaceutical formulations and biological fluids. Spectrochim Acta A 69:478–482
9. Zhu XS, Jiang RR (2011) Determination of iron(III) by room temperature ionic liquids/ surfactant sensitized fluorescence quenching method. J Fluoresc 21:385–391
10. Zhu XS, Sun J, Wu J (2007) Study on the inclusion interactions of β-cyclodextrin and its derivative with dyes by spectrofluorimetry and its analytical application. Talanta 72:237–242
11. Yanez C, Salazar R, Nunez-Vegrar LJ (2004) Spectrophotometric and electrochemical study of the inclusion complex between β-cyclodextrin and furnidipine. J Pharm Biomed Anal 35:51–56
12. Martin L, Leon A, Olives AI (2003) Spectrofluorimetric determination of stoichiometry and association constants of the complexes of harmane and harmine with β-cyclodextrin and chemically modified β-cyclodextrins. Talanta 60:493–503
13. Lu Z, Feng YL (2005) Simultaneous determination of trace ofloxacin, pefloxacin and sparfloxacin by β-Cyclodextrin inclusion thin layer chromatography- fluorescence detection. Chin J Anal Chem 33(7):106–109
14. Chen WY, Li H, Luo WH et al (2007) Rapid determination of schisandr in B by liquid chromatography mass spectrometry and analysis of plasma pharmacokinetics in rat. Chin J Modern Med 17:1665–1673
15. Chen GZ, Huang XZ, Xu JG (1990) Spectrofluorimetric analytical method, 2nd. Science publishing house, Beijing, 16
16. Catena GC, Bright FV (1989) Thermodynamic study on the effects of beta-cyclodextrin inclusion with anilinonaphthalenesulfonates. Anal Chem 61(8):905–909
17. ZYTIGA(abiraterone acetate). http://www.rxlist.com/zytiga-drug.htm
18. Khedr A, Darwish I, Bamane F (2013) Analysis of abiraterone stress degradation behavior using liquid chromatography coupled to ultraviolet detection and electrospray ionization mass spectrometry. J Pharm Biomed Anal 74:77–82
19. Liu XP, Yang Y, Zhang GM (2003) Study on the inclusion interaction of vitamin B_6 and β-Cyclodextrin and its derivatives by competitive fluorescence inclusion method. Chin J Anal Chem 31(8):996–999
20. Xu H, Chen L, Li H (2002) Determination of formation constant on cyclodextrins inclusion complexes. Anal Test Tech Inst 8(2):9–17
21. Zhu XS, Bao L, Guo R, Jun W (2004) Determination of aluminium(III) in water samples in microemulsion system by spectrofluorimetry. Anal Chim Acta 523:43–48