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A Comprehensive Novel Stability indicating Method Development and Validation for Simultaneous Assessment of Abiraterone and Niraparib in Bulk and Pharmaceutical Formulation by Ultra Performance Liquid Chromatography

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ABSTRACT

Background: This study aims to develop and validate an innovative, rapid and dependable reverse-phase Ultra Performance Liquid Chromatography method for the simultaneous quantification of the anticancer drugs Abiraterone and Niraparib in bulk and pharmaceutical formulations marketed under the brand name Akeega. By offering a precise and stability-indicating assay, this research addresses a critical need for efficient analytical methods to assess these two agents in combination, an area with limited prior exploration. This novel approach not only fills a significant gap in the quantification of these compounds but also enhances analytical reliability for combined anticancer therapies, supporting broader research and quality control efforts.

Method: The method was optimized for isocratic elution on a C18 HSS column (2.1 mm × 100 mm, 1.8 µm) using a mobile phase composed of methanol and buffer 60:40v/v at a flow rate of 0.3 mL/min providing stable performance at room temperature. Detection was carried out with a UV detector set to 259 nm using a 10 µL sample injection volume and a total run time of five minutes.

Results: The retention times for Abiraterone and Niraparib were observed at 1.0333 and 3.4833 minutes, respectively, demonstrating excellent peak separation and resolution. The method showed strong linearity within concentration ranges of 12.5–75 µg/mL for Abiraterone and 2.5–15 µg/mL for Niraparib with calibration curve regression equations of Y = 9668x - 3531 (R^2 = 0.999) for Abiraterone and Y = 9632x + 1803 (R^2 = 0.999) for Niraparib. The % RSD values indicating precision were below 2 at 0.239 and 0.265. The method yielded percentage mean recoveries of 99.4-99.7% for Abiraterone and 99.5-99.8% for Niraparib with % RSD values ranging from 0.1-0.2 and 0.1-0.3 respectively. Rigorous forced degradation tests, including acidic, alkaline, oxidative, photolytic, and thermal conditions, confirmed the method's effectiveness as a stability-indicating assay.

Conclusion: Following validation in alignment with International Council for Harmonization (ICH) guidelines the method was found to be linear, specific, accurate, robust, time-efficient and suitable for quality control and process monitoring in the bulk manufacturing of these drugs. This validated method offers a valuable tool for ensuring the quality and stability of Abiraterone and Niraparib supporting their development and regulatory compliance.

Keywords: Reverse phase UPLC, Abiraterone, Niraparib, Stability indicating method, Method development, Method validation, forced degradation studies

1. INTRODUCTION

The combination of anticancer drugs Abiraterone and Niraparib was approved by Food and Drug Administration in the year 2023 with brand name Akeega is used to treat prostate cancer and other types of cancers. Metastatic castration-resistant prostate cancer and metastatic high-risk castration-sensitive prostate cancer can be treated with an antiandrogen called abiraterone [1]. Abiraterone suppresses (CYP17), 17α-hydroxylase/C17,20-lyase a crucial enzyme

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in the production of androgen. It is predominantly seen in testicular, adrenal, and prostatic malignancies. Inhibiting CYP17 can also lead to enhanced mineralocorticoid synthesis by the adrenals. [2]. chemical name for abiraterone is "(3S,8R,9S,10R,13S,14S)-10,13-dimethyl-17-pyridin-3-yl2,3,4,7,8,9,11,12,14,15-decahydro-1Hcyclopenta[a]phenanthren-3-ol". Its molecular formula is $C_{24}H_{31}NO$ with a molecular weight of 349.509 g/mol. It appears as a white or off-white solid and is soluble in ethanol, DMSO, and dimethyl formamide [3]. Niraparib a poly-ADP ribose polymerase inhibitor is employed for the management of recurrent peritoneal carcinoma, fallopian tube, or persistent ovarian epithelial cancer which responds to chemotherapy with platinum [4]. Niraparib substantially and specifically blocks the polyADP-ribose polymerase (PARP) enzymes PARP-1 and 2[5,6]. PARPs play a crucial role in DNA repair by detecting and repairing intracellular DNA damage, including single-strand breaks (SSBs) and double-strand breaks. Its IUPAC name "2-[4-[(3S)-piperidin-3-yl] phenyl] indazole-7-carboxamide"[7]. Its chemical formula and weight is $C_{19}H_{20}N_4O$ and 320.396 gm/mole. It appears as an off-white to white crystalline solid, soluble in ethanol and DMSO but insoluble in water. Chemical structures of Abiraterone and Niraparib is displayed in (Figure 1[8] and 2[9]).

A comprehensive review of the literature revealed that there were not many analytical techniques described for the UHPLC, HPLC, or UPLC assay of abiraterone alone or in combination with other anti-tumor agents [10–17]. How ever, for the simultaneous estimation of abiraterone and niraparib, no stability indicating RP-UPLC technique was reported [18–25]. Therefore, a UPLC stability-indicating method must be created to be concurrent assessment of the two medicines in their formulation and bulk. A RP-UPLC stability-indicating approach for the concurrent assessment of abiraterone and niraparib was attempted to be developed in this work.

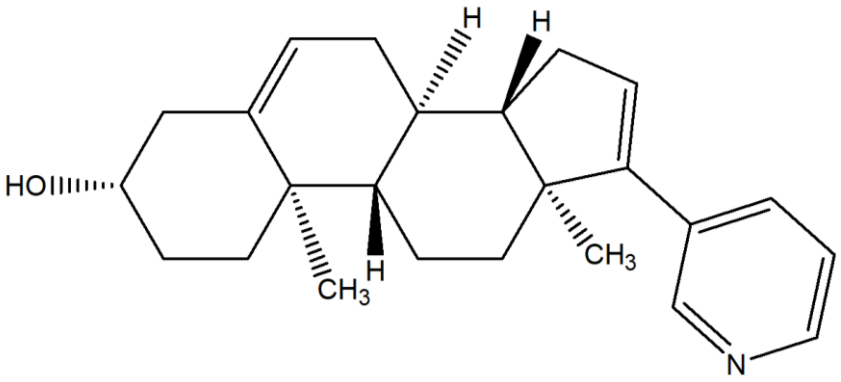

Figure 1: Chemical Structure of Abiraterone

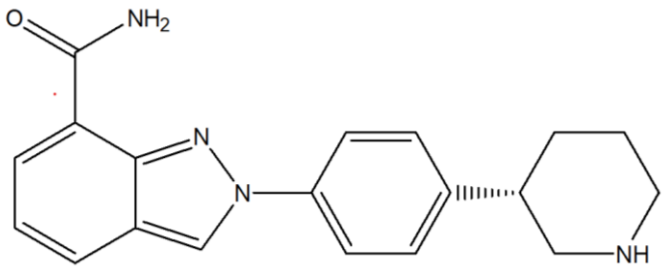

Figure 2: Chemical Structure of Niraparib

2. MATERIALS AND METHODS

Drug and dosage form

The drug samples of Abiraterone and Niraparib was obtained from Dr. Reddy's Laboratories, Hyderabad with 99.15% purity. Brand name akeega Tablets having 500 mg of Abiraterone and 100 mg Niraparib was purchased from local pharmacy. The chemicals utilized in the investigation such as glacial acetic acidand sodium acetate trihydrate were acquired from Merck chemicals in Mumbai. Merck Ltd. supplied HPLC-grade chemicals such as methanol and acetonitrile.

Instrumentation

Waters aquity UPLC System employed with Binary pump, autoinjector and UV detector. The data was acquired from Waters Empower software. Electronic weighing balance (Denver-SI-234 Bohemia) for weighing of all materials.pH meter (Systronics-Sr No S 1326 INDIA) was used to adjust pH of buffer solution. Ultrasonicator with (1.5L Capacity, GT Sonic INDIA) was used to sonicate the solutions. Vacuum Filtration (Borosilicate Vacuum Filtration Kit) was used to filter the solutions

Chromatographic conditions

The mobile phase consists of a accurately measured methanol and sodium acetate buffer 60:40 ratio. Mix the solvents completely using ultrasonic bath sonicator. Chromatographic separation was performed in isocratic elution using an HSS C18 (2.1 mm x 100 mm, 1.8 micron) column at room temperature at a flow rate of 0.3 mL/min. The sample injection volume was 10µL.

Preparation of solutions

Preparation of pH 4.8 sodium acetate buffer solution

13.608 g of sodium acetate trihydrate was dissolved in 800 mL of distilled water. Add approximately 3.2 mL of glacial acetic acid and mix the content for 2 min. pH of the solution was tune to 4.8 using glacial acetic acid and makes the solution up to the calibration mark in the flask.

Preparation of Mobile phase

Mix Methanol and buffer in the ratio of 60:40.

Diluent: Methanol is used as diluent.

Preparation of standard solution

Abiraterone and Niraparib, each weighing 50 mg, were separately dissolved in clean, dried 50 mL volumetric flasks. 50 mL of diluent was added to each flask and the mixtures were sonicated for two min to ensure complete dissolution of the analytes. The solutions were then filtered using a 0.2 µm membrane filter into separate clean, dry flasks, with the same solvent used to adjust the final volume. Separately, solutions of standard niraparib and abiraterone were composed at a concentration of 1000 µg/mL. From these solutions, 1 mL was shifted into a dry 10 mL volumetric flask and the volume was adjusted to 10 mL with diluent to achieve a concentration of 100 µg/mL for both abiraterone and niraparib. A 1 mL aliquot of this solution was further diluted in a 10 mL dry volumetric flask to obtain a final concentration of 10 µg/mL of niraparib which was used for the study.

Preparation of Sample

After ten tablets were taken, they were finely powdered. 50 mL of solvent were added to a 50 mL flask containing a precisely weighed tablet powder equivalent to 50 mg of abiraterone. A 50 mL volumetric flask was thoroughly cleaned and dried before the solution was filtered through a 0.2µ membrane filter after being sonicated for two minutes using an ultrasonic bath sonicator. With the same diluent and the formulation stock solution containing 1000 µg/mL of abiraterone, the final volume was adjusted to the required level. To get 50 µg/mL of abiraterone, 1 ml of the aforementioned solution is diluted with 20 ml of solvent. 10 µg/mL of Niraparib is present in the formulation solution based on the dosage in the formulation of both medicines. Abiraterone and Niraparib in the formulation sample were quantified using this formulation solution.

Method Development

An attempt was made in the proposed work to create and evaluate a novel, quick stability indicating RP-UPLC method for the estimation of two drugs simultaneously in bulk and dosage form.

Selection of wavelength

A spectrophotometer was used to establish the maximum absorption wavelength for the detection of niraparib and abiraterone. Each standard solution of niraparib and abiraterone was scanned in the 200–400 nm range. The iso-absorption wavelength of Abiraterone and Niraparib was fixed at 259nm was shown in (Figure 3) as detection wavelength for further study.

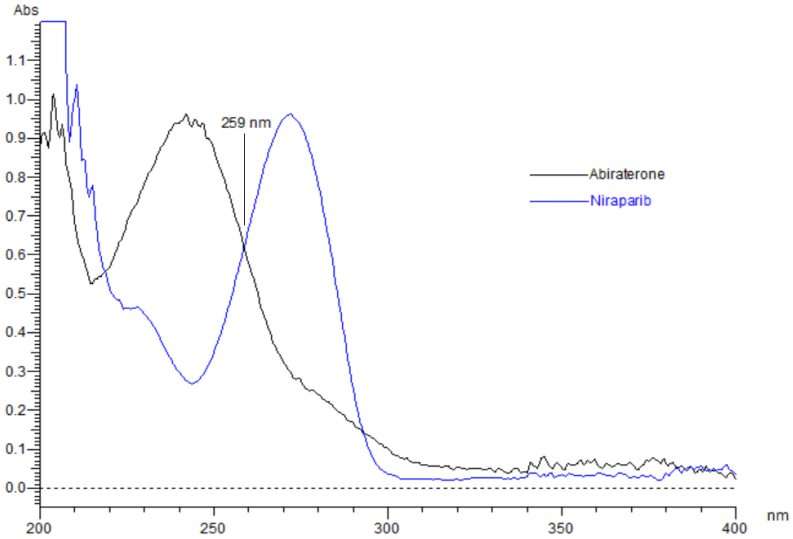

Figure 3: Overlay spectrum of Abiraterone and Niraparib

Optimization of chromatographic conditions

Attempts were made to develop an UPLC method for the selected combination on an isocratic mode; by using Methanol, acetonitrile and different buffers of different compositions were made to optimize the method. In conclusion, satisfactory separation of peaks with good resolution was attained on C18HSS (2.1mmx100 mm,1.8µm) column. Mobile phase consists of Methanol: buffer in 60:40 (v/v) with 0.3 mL/min flow rate at a wavelength of 259nm. The optimized chromatogram and conditions are shown in (Figure 4 and Table 1).

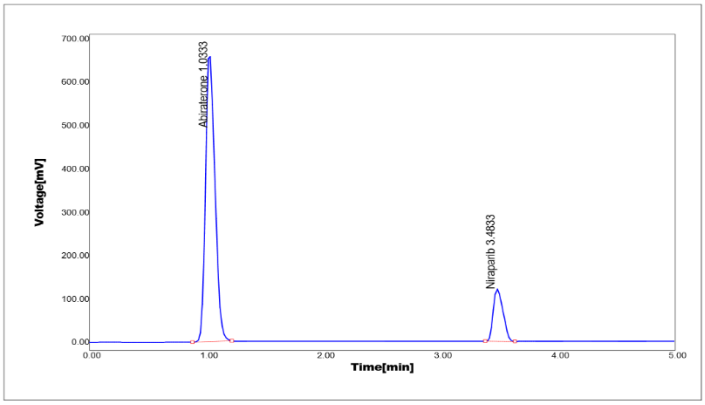

Figure 4: Optimized Chromatogram of Abiraterone and Niraparib

Table 1: Optimized Chromatographic conditions

Parameters	Condition
Column	C18HSS (2.1mm x100 mm, 1.8µm)
Mobile phase	Methanol: Buffer 60:40 (v/v)
Flow rate	0.3 mL/min
Temperature of Column	Ambient
Temperature of Sample	Ambient
Detection wavelength	259 nm
Volume of Injection	10 µL
Pump mode	Isocratic
Run Time	5 minutes
Retention time	Abiraterone -1.0333 minutes Niraparib-3.4833 minutes

Method Validation

The analytical method was validated for criteria such as system suitability, specificity, linearity, precision, accuracy, robustness, Limit of detection and Limit of Quantification forced degradation studies in accordance with ICH Q2 (R1).

1. System suitability

System performance was assessed using system suitability metrics. In order to ensure system appropriateness, 10µl of a standard solution containing Abiraterone (50 µg/mL) and Niraparib (10 µg/mL) was injected into the UPLC system six times.

2. Specificity

The ability to precisely measure an analyte of interest in the presence of additional components in a sample matrix is evaluated using the specificity parameter during technique validation.

3. Linearity

Preparation of sample solutions for Linearity

Standard calibration curve were prepared with the injection of working standard solutions at six concentration levels (Abiraterone 12.5, 25, 37.5, 50, 62.5, and 75µg/mL) and (Niraparib 2.5, 5, 7.5, 10,12.5 and 15µg/mL). The peak area responses at each concentration level for all the drugs were determined using the described chromatographic conditions.

4. Precision

The standard which contained Abiraterone(50µg/mL) and Niraparib(10µg/mL) was examined six times in a single day for intraday precision and three times over the

course of two days for interday precision.

5. Accuracy

A 50%, 100%, and 150% spiked version of the approach was used to test accuracy. The enhanced approach examined the augmented level solution of niraparib and abiraterone.

6. Robustness

The robustness investigation was carried out by slightly adjusting physical factors such as the detection wavelength of ±5 nm, pH of the mobile phase ±1, and the composition of the mobile phase ±5 ml.

7. Limit of Detection and Limit of Quantification

A study was carried out to determine the LOD and LOQ for abiraterone and niraparib. In accordance with the test protocol, a series of extremely diluted LOD and LOQ solutions were made and triple-injected into the UPLC system.

Forced Degradation Studies

The following stress conditions were used in stress research to show how well the sample's deterioration could be separated from its primary analyte peaks. All of the stressed samples were injected twice into the UPLC system under optimal chromatographic circumstances after being diluted to the necessary concentration using diluents. The chromatograms were then recorded and assessed for the assay and degradation percentages. Abiraterone and Niraparib's percentage degradation was computed.

Sample preparation for degradation: To 5 ml of stock solution of abiraterone and 10ml of stock solution of niraparib were mixed with 10 ml of 0.1N HCl,0.1N NaOH,3% Peroxide solution, oven at 60^0C, UV light 254 nm. The resultant solutions were diluted to obtain a concentration of (50 µg/mL & 10µg/mL) and 10µL were injected into UPLC system and the chromatogram were recorded to assess the stability of sample.

3. RESULTS

1. System suitability

The findings for both medications were listed in (Table 2) and the standard chromatogram is displayed in (Figure 5) indicating that the system suitability parameters were within the limit.

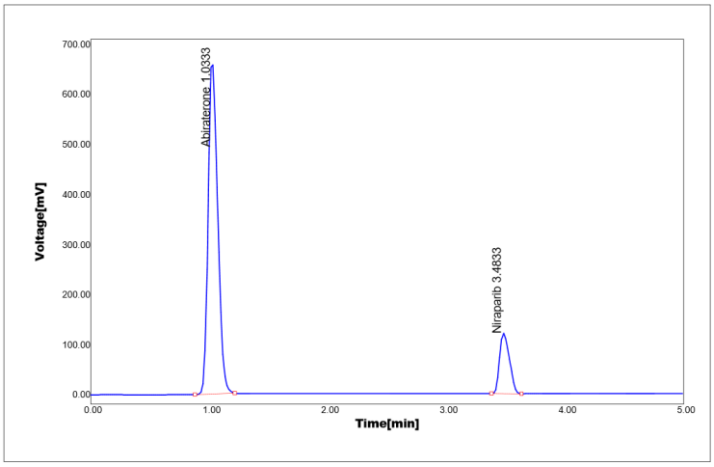

Figure 5: Chromatogram of Standard-Retention time of abiraterone at 50 µg/mL is 1.0333 and Retention time of niraparib at 10 µg/mL is 3.4833

Table 2: System suitability parameters

Parameter	Abiraterone	Niraparib
Theoretical plates	5237	9458
Tailing factor	0.98	1.03
Resolution	-	16.25
Retention Time	1.0333	3.4833

2. Specificity

It was performed by injecting blank (mobile phase only), Abiraterone, Niraparib individually and combined solutions. The chromatograms are displayed in (Figures 5,6,7,8).

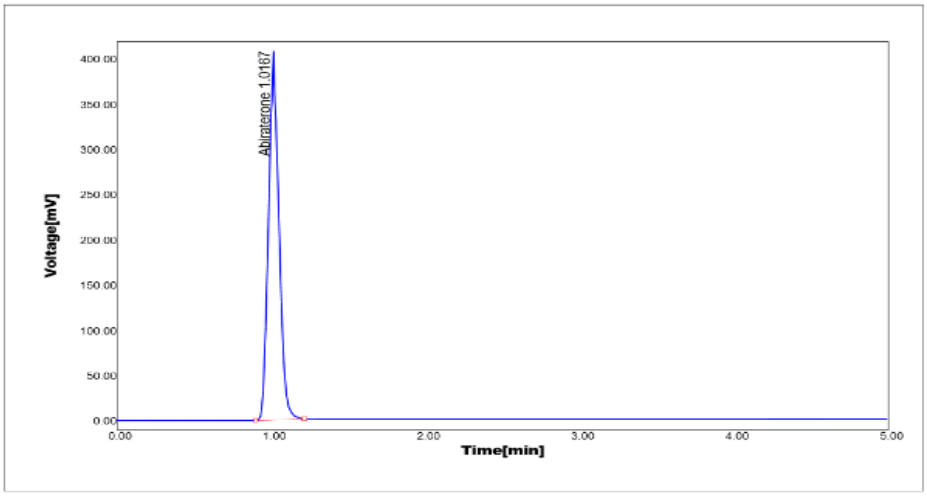

Figure 6: Chromatogram of individual abiraterone-showing a well-defined peak at 1.0167 minutes corresponding to abiraterone's retention time under optimized chromatographic conditions

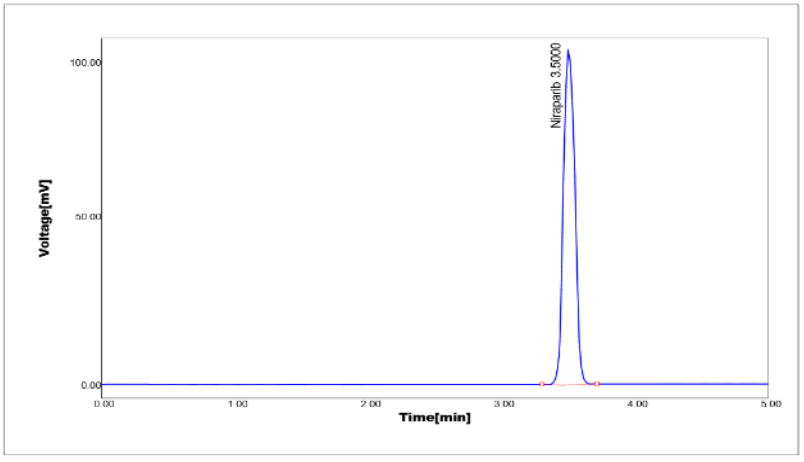

Figure 7: Chromatogram of Individual Niraparib-Retention time at 3.5000

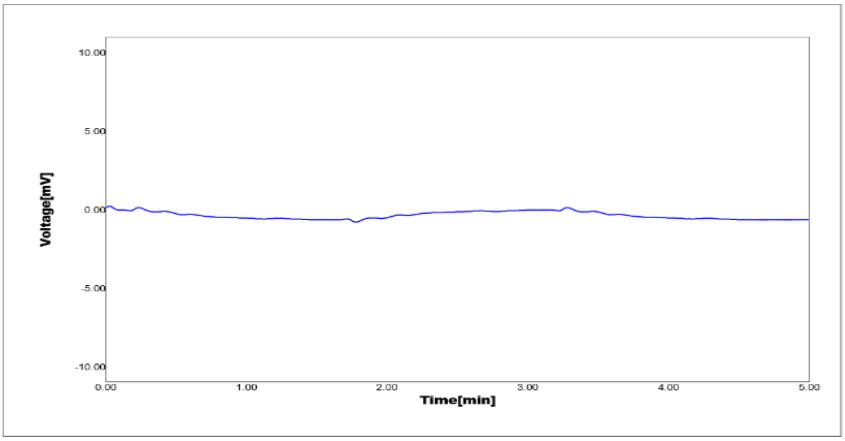

Figure 8: Chromatogram of Blank – Run with only mobile phase Methanol and buffer in the ratio of 60:40v/v.

3. Linearity

The calibration curve for Abiraterone (12.5-75 µg/mL) and Niraparib (2.5-15 µg/mL) were found to be linear. The regression equations for Abiraterone and Niraparib were Y=9668x-3531 (R2-0.999) and Y=9632.x+1803 (R2-0.999) respectively which were shown in the (Table 3).

Table 3: Linearity results for Abiraterone and Niraparib

S.No.	Abiraterone		Niraparib	
	Concentration (µg/mL)	Peak Area	Concentration (µg/mL)	Peak Area
1	12.5	117384.3	2.5	25417.8
2	25	239172.3	5	50882.3
3	37.5	356702.1	7.5	73934.2
4	50	486243.4	10	98812.7
5	62.5	590889.6	12.5	119847.3
6	75	726459.4	15	147632.2
Slope	9668.7		9632.5	
Intercept	3531.7		1803.2	
Correlation Coefficient	0.999		0.999	

4. Precision

The response of peak area and the percentage RSD of Abiraterone and Niraparib was tabulated. The %RSD is less than 2 in both the precision studies for Abiraterone and Niraparib were regarded satisfactory and is shown in (Tables 4 and 5).

Table 4: Results of Intraday Precision

S.No.	Abiraterone		Niraparib	
	Concentration (µg/mL)	**Average Area(n)**	**Concentration (µg/mL)**	**Average Area(n)**
1	50	485659.9	10	98986.6
2	50	485076.4	10	98783.1
3	50	483034.2	10	98239.6
4	50	486000.3	10	98476.7
5	50	484736.1	10	98753.4
6	50	486194.8	10	98625.3
Mean	485117		98644.12	
Std dev	1159.431		260.9867	
% RSD	0.239		0.265	

Table 5: Results of Interday Precison

S.No.	Abiraterone		Niraparib	
	Day 1	**Day 2**	**Day 1**	**Day 2**
1	487556.3	485125.4	98747.5	98466.9
2	482499.3	484541.5	98684.2	98407.6
3	483569.1	482936.9	98575.5	98249.5
Mean	**484541.6**	**484201.3**	**98669.07**	**98374.67**
Std dev	**2665.067**	**1133.226**	**86.99289**	**112.3795**
% RSD	**0.550**	**0.234**	**0.088**	**0.114**

5. Accuracy

The percentage recovery range of 98-102 was deemed satisfactory. (Tables 6 and 7) summaries the accuracy results.

Table 6: Accuracy results of Abiraterone

S.No	Recovery Level	Concentration (µg/mL)			Average Area(n)	Amount found (µg/mL)	% Recovery	% Mean Recovery &% RSD
		Target	**Spiked**	**Final**				
1	50 %	25	12.5	37.5	356595.1	37.49	99.97	99.68 0.277
2		25	12.5	37.5	354633.2	37.28	99.42	
3		25	12.5	37.5	355489.3	37.37	99.66	
4	100 %	25	25	50	485611.3	49.94	99.87	99.76 0.110
5		25	25	50	485076.4	49.88	99.76	
6		25	25	50	484541.5	49.82	99.65	
7	150 %	25	37.5	62.5	586339.8	62.02	99.23	99.48 0.273
8		25	37.5	62.5	587639.7	62.16	99.45	
9		25	37.5	62.5	589530.6	62.36	99.77	

Table 7: Accuracy Results of Niraparib

S.No	Recovery Level	Concentration (µg/mL)			Average Area (n)	Amount Found µg/mL	% Recovery	% Mean Recovery & % RSD
		Target	Spiked	Final				
1	50 %	5	2.5	7.5	73675.4	7.474	99.65	99.55 0.114
2		5	2.5	7.5	73631.1	7.469	99.59	
3		5	2.5	7.5	73512.8	7.457	99.43	
4	100 %	5	5	10	98427.3	9.961	99.61	99.76 0.142
5		5	5	10	98605.2	9.979	99.79	
6		5	5	10	98704	9.989	99.89	
7	150 %	5	7.5	12.5	119883.3	12.504	100.03	99.82 0.325
8		5	7.5	12.5	119188.1	12.431	99.45	
9		5	7.5	12.5	119835.3	12.499	99.99	

6. Robustness

The solution of standard produced according to the test protocol was put into the UPLC instrument. (Tables 8 and 9) show the results of the robust study.

Table 8: Robustness results of Abiraterone

Parameter	Optimized conditions	Used condition	Peak area	Retention time	Tailing factor	Theoretical plates
Mobile phase Composition	Methanol: buffer (60:40 v/v)	Methanol: buffer (65:35 v/v)	484590.2	1.0167	0.99	5264
		Methanol: buffer (55:45 v/v)	485951.7	1.0333	0.98	5301
pH of mobile phase	4.8	pH changed as 4.7	485319.5	1.0000	0.99	5142
		pH changed as 4.9	484541.5	1.0500	0.98	5091
Detector wavelength	259	Detector wavelength 264nm	484249.8	1.0000	0.99	5145
		Detector wavelength 254nm	483471.8	1.0333	0.99	5388

Table 9: Robustness results of Niraparib

Parameter	Optimized conditions	Used condition	Peak area	Retention time	Tailing factor	Theoretical plates
Mobile phase Composition	Methanol: buffer (60:40 v/v)	Methanol: buffer (65:35 v/v)	98763.3	3.6833	1.06	9571
		Methanol: buffer (55:45 v/v)	98506.4	3.4333	1.04	9385
pH of mobile phase	4.8	pH changed as 4.7	98802.8	3.4667	1.07	9507
		pH changed as 4.9	98585.4	3.5000	1.05	9324
Detector wavelength	259	Detector wavelength 264nm	98466.9	3.4833	1.03	9313
		Detector wavelength 254nm	98140.8	3.7167	1.05	9519

7. Limit of Detection and Limit of Quantification

Signal to noise ratio was used to determine the limit of detection and limit of quantification. The sensitivity results are presented in (Table 10).

Table 10: Results of LOD and LOQ

S No	Analyte	Sensitivity	
		LOD	LOQ
1	Abiraterone	0.25 µg/mL	0.825 µg/mL
2	Niraparib	0.05µg/mL	0.165 µg/mL

Forced Degradation Studies

(Tables 11 and 12) provide the degradation data for abiraterone and niraparib.

Table 11: Degradation studies of Abiraterone

Stress condition	Area value	% Degradation	% Assay
Acid	485708.5	0.110	99.89
Base	486194.8	0.010	99.99
Peroxide	484006.7	0.460	99.54
Thermal	482936.9	0.680	99.32
UV light	485659.9	0.120	99.88

Table 12: Degradation studies of Niraparib

Stress condition	Area value	% Degradation	% Assay
Acid	98536.3	0.280	99.72
Base	98160.5	0.660	99.34
Peroxide	98140.8	0.680	99.32
Thermal	98802.8	0.010	99.99
UV light	98377.9	0.440	99.56

Assay

The commercial tablet (AKEEGA) was examined individually by introducing 10µL of solutions of standard and sample into the UPLC machine and then recording chromatograms. By comparing standard and sample peak areas, the quantity of the medication included in marketed tablets was determined. (Table 13) displays the assay results whereas (Figure 11) depicts the chromatogram.

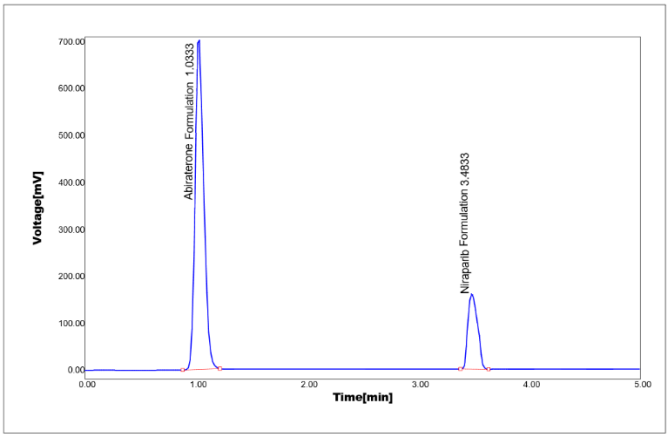

Figure 11: Chromatogram of Marketed Formulation

Table 13 : Results of Assay

S.No	Drug	Brand Name	Dosage	Area value	Concentration prepared(µg/ml)	Concentration found (µg/ml)	% Assay
1	Abiraterone	AKEEGA	500 mg	485453.4	50	49.919	99.84
2	Niraparib		100 mg	98445.1	10	9.96	99.63

4. DISCUSSION

The ultra-performance liquid chromatography (UPLC) method was optimized and validated as a stability-indicating approach for the simultaneous estimation of abiraterone and niraparib in bulk and dosage forms. The analysis was performed using isocratic elution on a C18 HSS column (2.1 mm × 100 mm, 1.8 µm) with a flow rate of 0.3 mL/min at ambient temperature and an injection volume of 10 µL over a 5-minute run time. The mobile phase consisted of methanol and buffer (60:40), and detection was carried out using a UV detector at 259 nm. The retention times were 1.0333 min for abiraterone and

3.4833 min for niraparib. The results of the optimized chromatographic conditions are presented in Table 1.

System suitability parameters, including tailing factor and theoretical plates, were within acceptable limits when standard solutions of both drugs were injected six times. Typical chromatograms for sample formulations, individual drug solutions, and blanks showed no interfering peaks, demonstrating the method's specificity. Calibration curves were linear in the ranges of 12.5–75 µg/mL for abiraterone and 2.5–15 µg/mL for niraparib, with regression equations of $Y = 9668x - 3531$ ($R^2 = 0.999$) and $Y = 9632x + 1803$ ($R^2 = 0.999$), respectively, indicating excellent correlation between peak area and concentration.

Precision was confirmed by six injections of 50 µg/mL abiraterone and 10 µg/mL niraparib, with %RSD values of 0.239 and 0.265, respectively, demonstrating high reproducibility. Accuracy was validated through recovery studies, with mean recoveries and %RSD of 99.4–99.7% (0.1–0.2) for abiraterone and 99.5–99.8% (0.1–0.3) for niraparib. Robustness was assessed by varying mobile phase composition (±5 mL), pH (±1), and wavelength (±5 nm), with no significant effect on results.

The limits of detection (LOD) and quantification (LOQ) were 0.25 and 0.825 µg/mL for abiraterone and 0.05 and 0.165 µg/mL for niraparib, indicating high method sensitivity. Stress studies under acidic, alkaline, oxidative, thermal, and photolytic conditions confirmed the method's stability-indicating capability, with degradation clearly distinguishable from the principal analyte peaks. Stressed samples were appropriately diluted and injected twice, with percentage degradation and assay values within acceptable limits.

The validated method was successfully applied to commercial tablet formulations, yielding assay results of 99.84% for abiraterone and 99.63% for niraparib.

5. CONCLUSION

The present study describes a novel UPLC stability-indicating method for the determination of abiraterone and niraparib in bulk and tablet formulations. The developed method offers several advantages: it eliminates the need for time-consuming extraction steps, simplifies solution preparation, and allows chromatogram recording within five minutes. Consequently, the method is fast, simple, sensitive, accurate, and reliable. It has been successfully applied in research laboratories, industrial quality control departments, and accredited testing facilities for routine analysis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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تطوير واعتماد طريقة جديدة شاملة لتحريض الاستقرار لتقييم أبيراتيرون ونيرباريب في تركيبة صيدلانية وتجميلية باستخدام تقنية كروماتوغرافيا السائل فائقة الأداء (UPLC)

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ملخص

الخلفية :تهدف هذه الدراسة إلى تطوير واعتماد طريقة مبتكرة وسريعة وموثوقة للكروماتوغرافيا السائلة فائقة الأداء في الطور العكسي، وذلك للتقدير الكمي المتزامن لعقاري أبيراتيرون ونيراباريب المضادين للسرطان، في تركيبات سائبة وصيدلانية تُسوّق تحت العلامة التجارية "أكيغا ."ومن خلال تقديم تحليل دقيق ومُؤشر على الثبات، يُلبي هذا البحث حاجةً ماسةً إلى أساليب تحليلية فعّالة لتقييم هذين العاملين معًا، وهو مجالٌ لم يُستكشف سابقًا إلا بشكل محدود .ولا يقتصر هذا النهج المبتكر على سد فجوة كبيرة في تقدير كميات هذه المركبات، بل يُعزز أيضًا موثوقية التحليلات لعلاجات السرطان المُركّبة، مما يدعم جهودًا بحثيةً أوسع نطاقًا ومراقبة جودة.

الطريقة :تم تحسين الطريقة لإجراء عملية إفلات متساوي الكثافة على عمود من الفولاذ عالي السرعة 2.1) C18 مم 100 × مم، 1.8 ميكرومتر (باستخدام طور متحرك مكون من الميثانول ومحلول منظم 60:40 فولت/فولت بمعدل تدفق 0.3 مل/دقيقة، مما يوفر أداءً مستقرًا في درجة حرارة الغرفة .تم الكشف باستخدام كاشف للأشعة فوق البنفسجية مضبوط على 259 نانومتر ، باستخدام حجم حقن عينة 10ميكرولتر ، ومدة تشغيل إجمالية خمس دقائق.

النتائج :لوحظت أزمنة بقاء أبيراتيرون ونيراباريب عند 1.0333 و 3.4833دقيقة على التوالي، مما يدل على فصلٍ ودقةٍ ممتازين للذروة . أظهرت الطريقة خطيةً قويةً ضمن نطاقات تركيز تتراوح بين 12.5 و 75ميكروغرام/مل لأبيراتيرون و 2.5و 15ميكروغرام/مل لنيراباريب، مع معادلات انحدار منحنى المعايرة ($Y = 9668x - 3531$ ($R^2 = 0.999$ لأبيراتيرون و ($Y = 9632x + 1803$ ($R^2 = 0.999$لنيراباريب . كانت قيم الانحراف المعياري النسبي (%RSD) التي تشير إلى الدقة أقل من 2 عند 0.239 و .0.265حققت الطريقة متوسط نسبة استرداد تراوحت بين 99.4% و 99.7%لأبيراتيرون و 99.5%و 99.8%لنيراباريب، مع قيم انحراف معياري نسبي (RSD) تراوحت بين 0.1% و 0.2%و 0.1%و 0.3%على التوالي .وقد أكدت اختبارات التحلل القسري الصارمة، التي شملت الظروف الحمضية والقلوية والأكسدة والتحلل الضوئي والحراري، فعالية الطريقة كاختبار مؤشر على الثبات.

الاستنتاج :بعد التحقق من صحة هذه الطريقة، بما يتماشى مع إرشادات المجلس الدولي للتنسيق (ICH)، وُجد أنها خطية، ومحددة، ودقيقة، ومتينة، وموفرة للوقت، ومناسبة لمراقبة الجودة ومراقبة العمليات في التصنيع بالجملة لهذه الأدوية .تُقدم هذه الطريقة المُعتمدة أداةً قيّمة لضمان جودة واستقرار أبيراتيرون ونيراباريب، مما يدعم تطويرهما وامتثالهما للأنظمة.

الكلمات الدالة: مرحلة عكسية من UPLC، أبيراتيرون، نيراباريب، طريقة الإشارة إلى الاستقرار، تطوير الطريقة، التحقق من صحة الطريقة، دراسات التحلل القسري.

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