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R E S E A R C H A R T I C L E

Analytical Method Development and Validation of Palbociclib in Its Pure Dosage Forms

K. Nithiyananthan[1*], K.V.S Prasadarao[2]

[1]*Research Scholar, Acharya Nagarjuna University, Guntur.*
[2]*Principal, Rahul institute of Pharmaceutical sciences and Research, Chirala.*

A B S T R A C T

A simple, rapid, and robust RP-HPLC method have been developed and validated to measure Palbociclib at single wavelength (320nm). A isocratic elution of samples performed on YMC C18 column (4.6×150mm) 5µ, flow rate was 0.6 ml/min, mobile phase ratio was Water: meoH (20:80%v/v).The instrument used was WATERS HPLC Auto Sampler, Separation module 2695, photo diode array detector 996, Empower-software version-2. The retention times were found to be 2.497 mins. The % purity of Palbociclib was found to be 99.94%.The system suitability parameters for Palbociclib such as theoretical plates and tailing factor were found to be 4187, 1.5. The analytical method was validated according to ICH guidelines (ICH, Q2 (R1)). The linearity study of Palbociclib was found in concentration range of 20µg-100µg and correlation coefficient (r^2) was found to be 0.999, % recovery was found to be 99.95%, %RSD for repeatability was 0.24, % RSD for intermediate precision was 0.15. The precision study was precision, robustness and repeatabilty.LOD value was 3.04 and LOQ value was 10.14.

Keywords: YMC C18 column, Palbociclib, RP-HPLC.

A R T I C L E I N F O

Corresponding Author
K. Nithiyananthan
Research scholar,
Acharya Nagarjuna University, Guntur.
MS-ID: JPBMAL4176

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1. Introduction

Palbociclib (codenamed PD-0332991, trade name Ibrance) is a drug for the treatment of HR-positive and HER2-negative breast cancer developed by Pfizer. It is a selective inhibitor of the cyclin-dependent kinases CDK4 and

CDK6. Palbociclib was the first CDK4/6 inhibitor to be approved as a cancer therapy.

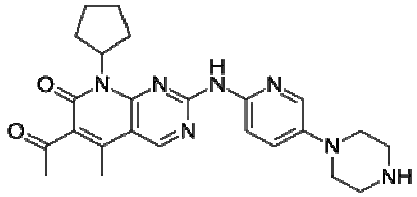

Fig 1: Chemical structure of Palbociclib

2. Materials and Methods

Materials: Palbociclib, KH_2PO_4, Water and Methanol for HPLC, Acetonitrile for HPLC, Ortho phosphoric Acid.

Instrumentation:

HPLC-auto sampler –UV detector, Separation module2695, UV.detector2487, Empower-software version-2 Waters. U.V double beam spectrophotometer LABINDIA, UV 3000^{+}pH meter, Weighing machine.

Chromatographic conditions

Column : YMC C18 (4.6×150mm)5µ
Mobile phase ratio : Methanol :Water (80:20 v/v)
Detection wavelength : 320 nm
Flow rate : 0.6 ml/min
Injection volume : 20µl
Column temperature : Ambient
Auto sampler temperature : Ambient
Run time : 6.0min
Retention time : 2.497min

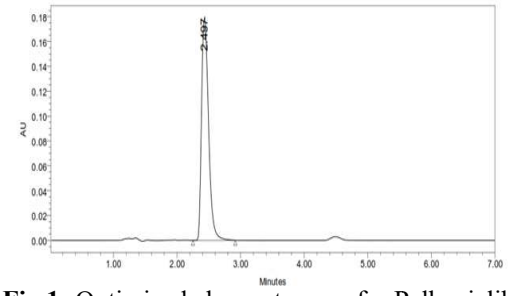

Fig 1: Optimized chromatogram for Palbociclib

Observation:

The separation was good, peak shape was good, so we conclude that there is no required for increse the retention times of peak, so it is taken as final method.

Sample solution preparation:

10 mg of Palbociclib tablet powder was accurately weighed and transferred into a 10 ml clean dry volumetric flask, add about 2ml of diluent and sonicate to dissolve it completely and making volume up to the mark with the same solvent(Stock solution). Further pipette 10ml of the above stock solution into a 100ml volumetric flask and was diluted up to the mark with diluent.

Standard solution preparation:

10 mg Palbociclib working standard was accurately weighed and transferred into a 10ml clean dry volumetric flask and add about 2ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution).Further pipette out 1ml of the above stock solution into a 10ml volumetric flask and was diluted up to the mark with diluent.

Method Validation

Specificity:

The system suitability for specificity was carried out to determine whether there is any interference of any impurities in retention time of analytical peak. The specificity was performed by injecting blank.

Linearity:

10 mg of Palbociclib working standard was accurately weighed and was transferred into a 10ml clean dry volumetric flask, add about 2ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent.

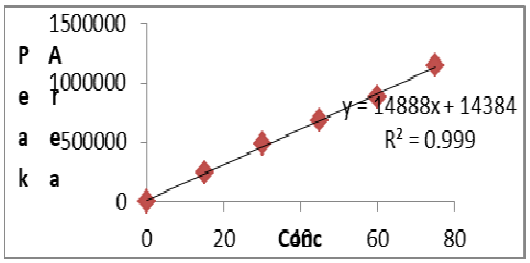

Fig 3: Calibration graph for Palbociclib

Range:

Based on precision, linearity and accuracy data it can be concluded that the assay method is precise, linear and accurate in the range of 20µg/ml-100µg/ml of Palbociclib.

Accuracy:

10mg of Palbociclib working standard was accurately weighed and transferred into a 10ml clean dry volumetric flask add about 2ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution).

Precision: 10 mg of Palbociclib working standard was accurately weighed and transferred into a 10ml clean dry volumetric flask add about 2ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent.

Intermediate Precision/Ruggedness:

To evaluate the intermediate precision (also known as ruggedness) of the method, precision was performed on different days by using different make column of same dimensions.

Limit of detection (LOD): LOD's can be calculated based on the standard deviation of the response (SD) and the slope of the calibration curve (S) at levels approximating the LOD according to the formula. The standard deviation of the response can be determined based on the standard deviation of y-intercepts of regression lines.

Limit of quantification:

LOQ's can be calculated based on the standard deviation of the response (SD) and the slope of the calibration curve (S) according to the formula. Again, the standard deviation of the response can be determined based on the standard deviation of y-intercepts of regression lines.

Robustness: As part of the robustness, deliberate change in the flow rate, mobile phase composition was made to evaluate the impact on the method.

System suitability: 10 mg of Palbociclib working standard was accurately weighed and transferred into a 10ml clean dry volumetric flask and add about 2ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution).

3. Results and Discussion

Table 1: Linearity Results for Palbociclib

S.No	Linearity Level	Concentration	Area
1	I	20 ppm	264840
2	II	40 ppm	491451
3	III	60 ppm	677620
4	IV	80 ppm	873311
5	V	100 ppm	1048958
Correlation Coefficient			0.999

Table 2: Accuracy results for Palbociclib

%Concentration (at specification level)	Average Area	Amount added (mg)	Amount found (mg)	% Recovery	Mean recovery
50%	728287	5	4.96	99.91%	99.95%
100%	1378202	10	9.98	99.18%	
150%	2115480	15	15.02	99.60%	

Table 3:% RSD results for Palbociclib

	Name	RT	Area	Height(µV)
1	Palbociclib	2.423	693877	117760
2	Palbociclib	2.424	696531	117366
3	Palbociclib	2.424	693977	117612
4	Palbociclib	2.424	695278	117573
5	Palbociclib	2.423	697676	117829
Mean			695468	
Std.Dev.			1642.7	
%RSD			0.24	

Table 4: Intermediate precision results of Palbociclib

	Name	RT	Area	Height(µV)
1	Palbociclib	2.423	693078	117646
2	Palbociclib	2.424	693338	117177
3	Palbociclib	2.424	695080	117534
4	Palbociclib	2.424	694843	117535
5	Palbociclib	2.423	695336	117665
Mean			694335	
Std.Dev.			1047.5	
%RSD			0.15	

Table 5: Results for Limit of Detection

Drug name	Standard deviation(σ)	Slope(s)	LOD(µg/ml)
Palbociclib	1642	14888	3.04

Table 6: Results for Limit of Quantification

Drug name	Standard deviation(σ)	Slope(s)	LOQ(µg/ml)
Palbociclib	1642	14888	10.14

Table 7: Robustness results for Palbociclib (Change the flow rate)

S. No	Flow rate (ml/min)	System suitability results	
		USP Plate Count	USP Tailing
1	0.8	4187	1.5

2	**1**	**4512**	**1.4**
3	1.2	4084	1.4

Table 8: Robustness results for Palbociclib (Change the mobile phase composition)

S. No	**Change in organic composition in the mobile phase**	**System suitability results**	
		USP Plate Count	**USP Tailing**
1	5 % less	4194	1.5
2	*Actual	4524	1.5
3	5 % more	3097	1.4

4. Conclusion

A fast, accurate, and a simple an isocratic RP-HPLC method with PDA detector for the estimation and analysis of Lenvatinib pure dosage form in the pharmaceuticals was developed and validated as per ICH guidelines. Hence the suggested RP-HPLC method can be used for routine analysis of Palbociclib in API and Pharmaceutical dosage form.

5. References

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