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Research Article

ANALYSIS OF PRANLUKAST IN DOSAGE FORM BY A VALIDATED RP HPLC METHOD

Mamatha J[1]* and Devanna N[2]

[1]Faculty of Chemistry G. Pullaiah College of Engineering and Technology, Kurnool, A.P. State
[2]Department of Chemistry, JNTU College of Engineering, Anantapuramu, A.P. State

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ABSTRACT

A reverse phase high performance liquid chromatographic (RP-HPLC) method was developed and validated as per ICH guidelines for the analysis of Pranlukast in its capsule form. The analysis was performed on a C-18 column. Separation was completed isocratically by using a mobile phase of phosphate buffer and Ethylnitrile in 60:40 ratio at 30ºC and maintained at a flow rate of 1 millilitre per minute. Ultraviolet absorption was maximum at 238 nanometre wavelength. Linearity was satisfied in the range 28.125 ppm to 168.75 ppm, with correlation coefficient value of 0.999. The percent relative standard deviation for precision, accuracy and robustness were less than two. The limit of detection and limit of quantification were 0.07 ppm and 0.21 ppm respectively. All the validation results were within the acceptance limits

INTRODUCTION

Pranlukast (PLK) (Fig 1) is chemically N-[4-oxo-2-(1H-tetrazol-5yl)-4H-chromen-8yl]-4-(4-phenyl butoxy) benzamide.

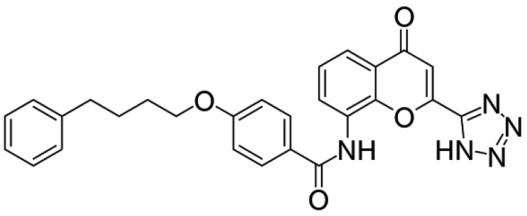

Figure 1

Its molecular formula is $C_{27}H_{23}N_5O_4$ and molecular weight is 481.512 gram per mole (g/mol). It is in the form of PLK hemihydrate in its dosage form Onon® capsules.

PLK is a cysteinyl leukotriene receptor –1 antagonist and work as an antiasthmatic. Its main function is the antagonism of bronchospasm seen in asthma cases caused due to allergic reactions. PLK is a perfect preventive treatment in adults and children with persistent asthma and allergic rhinitis of all severities. The earlier works related to PLK include development of a new powder design method to improve inhalation efficiency of PLK[1], Determination of PLK and its metabolites in human plasma by liquid chromatography mass spectrometry[2], Pharmacokinetics of PLK hydrate dry syrup[3], Enhancement of dissolution rate and gastrointestinal absorption of PLK[4], RP-HPLC method development and validation of Montelukast[5], a compound which works similar to PLK, study of PLK add on therapy in partial epilepsy[6], self microemulsifying drug delivery system for improved oral bioavailability of PLK[7], Physico-chemical crystal structure analysis of PLK Pseudo-polymorphs[8], and improving dissolution and oral bioavailability of PLK by particle surface modification[9]. The study explained in this research paper deals with RP-HPLC[10] method development for the identification and the analysis of PLK in its regular dosage form and validation of the developed method as per the International council for Harmonization of technical requirements for Pharmaceuticals for Human Use (1CH) Q2 (R1) guidelines.[11.] The present study acknowledges the application of the developed method in quality control study of PLK dosage form.

Experimental

Instrumentation

The RP-HPLC was worked with waters company made system fitted with 2695 pump, photo diode array detector and Empower 2 software.

Corresponding author:* **Mamatha J
Faculty of Chemistry G. Pullaiah College of Engineering and Technology, Kurnool, A.P. State

The column type was C-18, 100 millimetre (mm) length, 4.6 mm internal diameter and with particle size of 5 micrometer (µm).

Chemicals

A pure sample of PLK was received from spectrum labs. Onon® capsules were purchased from a pharmacy.
Ethylnitrile (EN), Orthophosphoric acid (OPA), methanol (Met) and water all of HPLC grade were purchased from Merck limited.
Diluent: A mixture of water and Met in the ratio of 50: 50 was used as a diluent.

Mobile Phase (MP): Phosphate buffer of pH 3 and EN in 60: 40 ratio was run as a MP.

Preparation of stock and working Standard (WS) solution

11.25 mg of PLK pure sample was taken into a 10ml volumetric flask. Diluent was added up to the mark to result in an HPLC grade stock solution of 1125 microgram per milliliter (µg/ml) or 1125 parts per million (ppm).

WS solutions of 112.5 ppm and other linearity range solutions were prepared from the stock solution by suitable dilution.

Preparation of Sample Solution (SS)

Five Onon®capsules contents were weighed to know the average content weight of single capsule. The weight equal to one capsule was diluted suitably, sonicated and filtered to prepare a SS of 112.5 ppm.

Optimized RP-HPLC Conditions: (Shown in Table-1) (Fig 2).

System Suitability (ST)

Table 1-RP-HPLC CONDITIONS

Detector Wavelength	238 nm
Diluent	Met : water (50:50) ratio
Mobile Phase	Phosphate buffer : EN (60 : 40) ratio
Buffer pH	3
Flow rate	1ml / min
Column	C-18
Temperature	30ºC
Injection Volume	10 Units
Runtime	5 Minutes

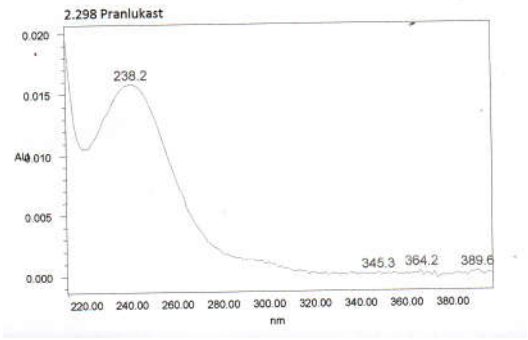

Figure – 2 – UV – VIS SPECTRUM OF PLK

To study the sensitiveness, resolution and reproducibility of the developed method ST study was performed.

PLK (WS) was injected into the HPLC system to facilitate the study of six different chromatograms. The accepetance criteria for Tailing factor (T), Theoretical plates (N), Standard deviation (SD), Percent relative standard deviation (%RSD) for Retention time (RT), and Peak area (PA) were checked.

Method validation

Validation was done systematically for linearity, Accuracy, Precision, Robustness, Limit of detection, (LOD) and limit of Quantification (LOQ).

RESULTS AND DISCUSSION

All the ST measurements met the criteria and are shown in table 2.

Table 2 System Suitability (ST)

ST Parameter	Reference Value	Results
RT	% RSD ≤ 2	0.26
PA (n = 6)	% RSD ≤ 2	1.4
T	$T \leq 2.0$	1.36
N	$N \geq 2000$	3792

Retention Time (RT): Blank sample or diluent showed no peaks in the developed method. The RT of the PLK pure sample was 2.298 minute (Fig 3).

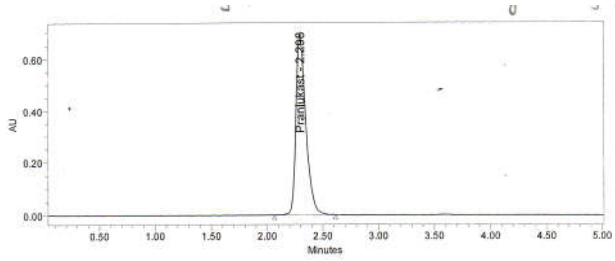

Figure 3 WS Chromatogram of Plk

The RT of the PLK (capsule content) was 2.299 minute. (Fig 4).

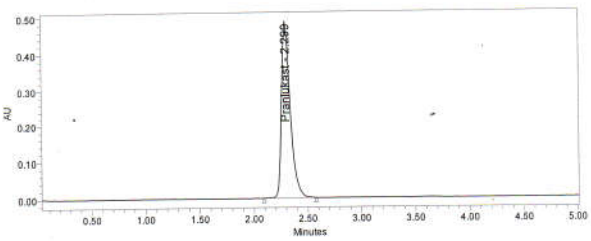

Figure 4 Sample Chromatogram of Plk

Linearity

Five different levels of PLK pure sample solutions ranging from 28.125 ppm to 168.75 ppm were prepared and each injected thrice into the HPLC system to study three chromatograms at each level.

The calibration curve of PA versus ppm was plotted. The linear regression equation and the correlation coefficient (r) value depicted linear relationship between PA and the concentration of the solution. (Table-3). (Fig-5)

Table 3 Linearity

Linearity Level in Percetage	Concentration (ppm)	PA (n = 3)	% RSD
25	28.125	461344	1.0
50	56.25	949280	0.7
75	84.35	1383862	0.25
100	112.5	1894378	0.5
125	140.625	2332840	0.38
150	168.75	2800573	0.11
Regression line Equation y = 16622x + 702.8			
r = 0.999			
Slope = 16622			
Y-intercept = 702.8			
R^2 = 0.999			

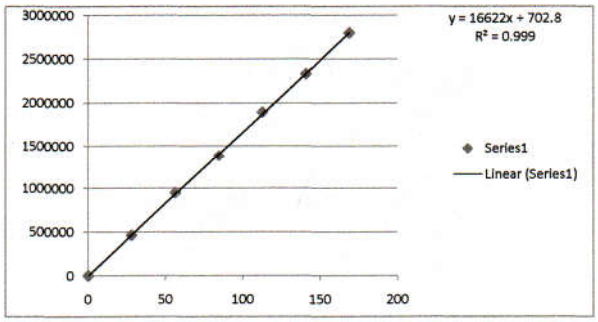

Figure 5 Linearity

at 50%, 100% and 150%. Chromatograms were studied for triplicate samples at each concentration.

The percent recovery, RSD, % RSD for each level were within the accepetance limits and are depicted in (Table-4).

Precision

All the precision studies were done with 112.5 ppm sample solution.

Six replicate chromatograms were taken on the same day to study Intraday precision and on two different days to study Interday precision.

To acknowledge the method precision assay calculations were done for six HPLC runs of the sample solution. The average percent assay was calculated as 100.28 for Onon capsules (112.5mg).

For all the precision experiments the RSD, % RSD calculated were within the acceptance limits as shown in Table-5.

Robustness

Small variation in the experimental conditions (Table 6) showed little or no effect on the average PA, RT, % RSD values and hence the method developed was Robust. (Table-7)

Table 4 ACCURACY (Recoverty calculation of PLK)

Recovery Level %	Sample (ppm)	Std. Added ppm	Total amount (ppm)	Y PA (n = 3)	x ppm (n = 3)	x-112.5 Amount Recovered. (ppm)	% Recovery	% RSD
50	56.25	112.5	168.75	2804982	168.70	56.20	99.92	0.80
100	112.5	112.5	225	3735872	224.71	112.21	99.74	0.45
150	168.75	112.5	281.25	4679898	281.5	169	100.15	0.73

Table 5 Precision

Sample	Intraday Precision	Interday Precision	Method Precision	% Assay
1	1884751	1827743	1856116	99.07
2	1885774	1844286	1892904	101.03
3	1852456	1851203	1857167	99.13
4	1864868	1853112	1875309	100.09
5	1834366	1787152	1908523	101.87
6	1907732	1832027	1882752	100.49
Average	1871658	1832587	1878795	100.28
S.D	263725.5	24465.5	20458.4	1.09
% RSD	1.40	1.3	1.1	1.08

Table 6 Experimental Conditions

Value	I	II	III
Buffer pH	2.8	3.0	3.2
Column temperature (ºC)	28	30	32
Flow rate (ml/min)	0.98	1.0	1.02

LOD: The lowest concentration of the sample that can be detected under the developed conditions was calculated from the regression line as 0.0701 ppm.

LOQ: The lowest concentration of the sample that can be detected with adequate precision and accuracy was calculated from the regression line as 0.2126 ppm.

CONCLUSION

The RP-HPLC method developed for the analysis of PLK showed less retention time and was linear, sensitive, simple, precise, accurate and robust. The diluent and mobile phase solutions required low cost for preparation. In the developed method the pure sample and the dosage form showed similar retention time and showed no interference with the excipients

Table 7 Robustness Results

Value	pH			Temp			Flow rate (ml/min)		
	2.8	3.0	3.2	2.8	30	32	0.8	1.0	1.2
Mean PA (n = 3)	1911772	1878795	2009769	1977979	1878795	2010340	2044141	1878795	1832481
SD	17520	20458.4	38698	19746.5	20458.4	29622	35473	20458.4	31474.7
% RSD	0.9	1.1	1.9	1.0	1.1	1.5	1.7	1.1	1.7

Accuracy

Accuracy was studied by adding a known fixed amount of the PLK standard to a sample with predetermined content of PLK and hence the method can be used for the quality control tests of PLK.

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