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Method Development and Validation of Lorlatinib by RP-HPLC

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Abstract A simple, Accurate, precise method was developed for the estimation of the Lorlatinib in API form and Marketed pharmaceutical dosage form by RP-HPLC. Chromatogram was run through Hypersil C18 (4.6mm×150mm, 5µm) Particle size Column and Mobile phase containing Methanol and Water taken in the ratio of 25: 75% v/v was pumped through column at a flow rate of 1.0 ml/min. Temperature was maintained at 38ºC. Optimized wavelength selected was 310 nm. Retention times of Lorlatinib were found to be 3.513 minutes respectively. The %RSD for the Repeatability and Intermediate Precision of the Lorlatinib were found to be within limits. %Recovery was obtained 98.96% and it was found to be within the limits for Lorlatinib respectively. The LOD, LOQ values obtained from regression equations of Lorlatinib were 0.332µg/ml and 1.0078 µg/ml respectively. Regression equation of Lorlatinib was found to be y = 39948x + 16821 respectively. The Retention times was decreased and run time was decreased, so the method developed was simple and economical that can be adopted in regular Quality control test in Industries.

Keywords Lorlatinib, RP-HPLC, Method Development, Validation, Accuracy

INTRODUCTION

Lorlatinib is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC). Lorlatinib is available in markets as conventional tablets with a trade name of LORBRENA [1]. It has shown survival benefits in the treatment of lung cancer in phase III trials. Some high-performance liquid-chromatographic (HPLC) methods with ultraviolet (UV) have been developed. Some methods with tandem mass spectrometry (MS=MS) each with its own advantages and limitations has been reported for the assay of Lorlatinib or other ALK drugs in human plasma. The present article describes the quantitative determination and validation of Lorlatinib in bulk drug and in formulations by RP-HPLC method. The proposed method is simple and specific because it can determine Lorlatinib in the presence of its degradation products, excipients, and additives.

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•**IUPAC Name**:(10R)-7-Amino-12-fluoro-2,10,16-trimethyl-15-oxo-10,15,16,17-tetrahydro-2H-4,8-methenopyrazolo[4,3-h][2,5,11]benzoxadiazacyclotetradecine-3-carbonitrile

•**Molecular formula**: $C_{21}H_{19}FN_6O_2$

•**M.wt**: 406.42

•**Solubility**: It has high solubility in 0.1 M hydrochloric acid and very low solubility at a pH over 4.5.

•**Molecular structure**: (Fig:1)

Mechanism of action: Non-small cell lung cancer (NSCLC) accounts for up to 85% of lung cancer cases worldwide and remains a particularly difficult to treat condition. The gene rearrangement of anaplastic lymphoma kinase (ALK) is a genetic alteration that drives the development of NSCLC in a number of patients. Ordinarily, ALK is a natural endogenous tyrosine kinase receptor that plays an important role in the development of the brain and elicits activity on various specific neurons in the nervous system [2].

Subsequently, lorlatinib is a kinase inhibitor with in vitro activity against ALK and number of other tyrosine kinase receptor related targets including ROS1, TYK1, FER, FPS, TRKA, TRKB, TRKC, FAK, FAK2, and ACK. Lorlatinib demonstrated in vitro activity against multiple mutant forms of the ALK enzyme, including some mutations detected in tumors at the time of disease progression on crizotinib and other ALK inhibitors. Moreover, lorlatinib possesses the capability to cross the blood-brain barrier, allowing it to reach and treat progressive or worsening brain metastases as well. The overall antitumor activity of lorlatinib in in-vivo models appears to be dose-dependent and correlated with the inhibition of ALK phosphorylation [3].

Marketed Formulations: Lorbrena, Lorviqua, Lorbriqua, Lorlatini, Lorlacare 25.

AIM: The main aim of the present study is development of accurate, precise, sensitive, selective, reproducible and rapid analytical technique for estimation of Lorlatinib.

OBJECTIVES

Following are the objectives of present work:

To develop analytical method

- Selecting the HPLC separation mode.
- Selecting/ optimizing the mobile phase.
- Selecting column for analysis.
- Selecting the appropriate detector system.
- Selecting appropriate gradient/ isocratic medium.
- Selecting appropriate flow rate, Temperature.

To validate different parameters.

EXPERIMENTAL WORK

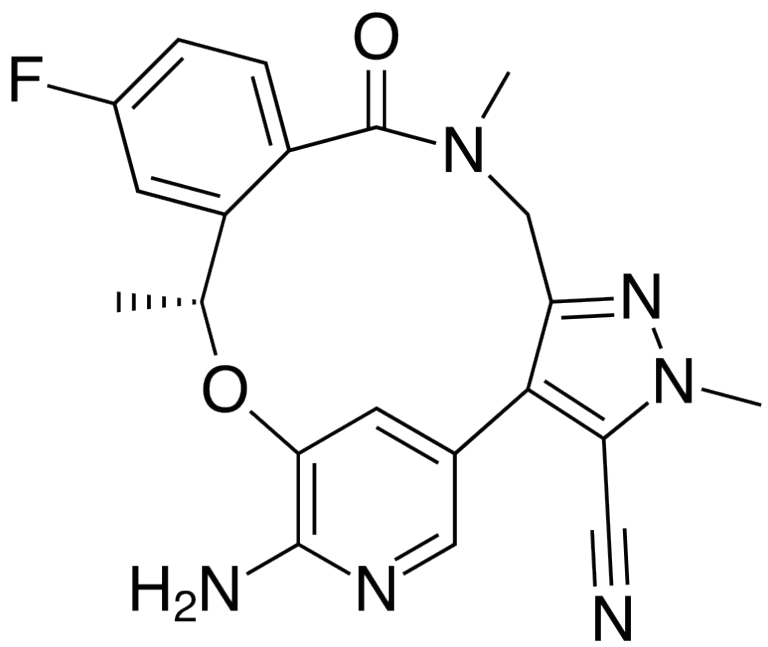

Figure 1: Structure of Lorlatinib

Table 1: Instruments used

S. No	Instruments And Glassware's	Model
1	HPLC	WATERS Alliance 2695 separation module, 996 PDA detector, Software: Empower 2.
2	pH meter	LabIndia
3	Weighing machine	Sartorius
4	Volumetric flasks	Borosil
5	Ultra sonicator	Labindia

Table 2: chemicals used

S. No	Chemical	Brand names
1	Lorlatinib	Hetero labs
2	Water and Methanol for HPLC	Loba Chem, Mumbai, India

(Table No:1 Instruments used)
(Table No:2 chemicals used)

HPLC METHOD DEVELOPMENT

Diluent Preparation:

Methanol : Water (50:50)

Preparation of standard solution:

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7ml of diluent and sonicate to dissolve and removal of air completely and make volume up to the mark with the same diluent.

Further pipette 1 ml of the above Lorlatinib stock solutions into a 10ml volumetric flask and dilute up to the mark with diluent.

Procedure:

Inject the samples by changing the chromatographic conditions and record the chromatograms, note the conditions of proper peak elution for performing validation parameters as per ICH guidelines.

Mobile Phase Optimization:

Initially the mobile phase tried was Water : Methanol, Water : Acetonitrile, Water with varying proportions. Finally, the mobile phase was optimized to Methanol, Water in proportion 25:75 v/v respectively.

Optimization of Column:

The method was performed with various C18 columns like Phenomenex column, Xterra, and Symmetry C18 column. Hypersil C18 (4.6 x 150mm, 5µm) was found to be ideal as it gave good peak shape and resolution at 1ml/min flow.

OPTIMIZED CHROMATOGRAPHIC CONDITIONS

Instrument used: Waters HPLC with auto sampler and PDA detector 996 model.
Temperature: 38ºC
Column: Hypersil C18 (4.6 x 150mm, 5µm)
Mobile phase: Methanol: Water (25:75 v/v)
Flow rate: 1ml/min
Wavelength: 310nm
Injection volume: 10µl
Run time: 6minutes

VALIDATION

Preparation of mobile phase:

Accurately measured 250 ml (25%) of HPLC Methanol and 750 ml of HPLC Water (75%) were mixed and degassed in a digital ultra sonicater for 10 minutes and then filtered through 0.45 µ filter under vacuum filtration.

VALIDATION PARAMETERS SYSTEM SUITABILITY

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 1 ml of the above Lorlatinib stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

Procedure:

The standard solution was injected for five times and measured the area for all five injections in HPLC. The %RSD for the area of five replicate injections was found to be within the specified limits.

SPECIFICITY STUDY OF DRUG

Preparation of Standard Solution:

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7ml of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 1 ml of the above Lorlatinib stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

Preparation of Sample Solution:

Take average weight of Tablet powder and crush in a mortar by using pestle and weight 10 mg equivalent weight of Lorlatinib sample into a 10mL clean dry volumetric flask and add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent.

Further pipette 1 ml of the above Lorlatinib stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

Procedure:

Inject the three replicate injections of standard and sample solutions and calculate the assay by using formula.

PREPARATION OF DRUG SOLUTIONS FOR LINEARITY

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7ml of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Preparation of Level – I (25µg/ml of Lorlatinib):

Pipette out 0.25ml of stock solution in to a 10ml volumetric flask and make up the volume up to mark by using diluent.

Preparation of Level – II (50µg/ml of Lorlatinib):

Pipette out 0.5ml of stock solution in to a 10ml volumetric flask and make up the volume up to mark by using diluent.

Preparation of Level – III (75µg/ml of Lorlatinib):

Pipette out 0.75ml of stock solution in to a 10ml volumetric flask and make up the volume up to mark by using diluent.

Preparation of Level – IV (100µg/ml of Lorlatinib):

Pipette out 1ml of stock solution in to a 10ml volumetric flask and make up the volume up to mark by using diluent.

Preparation of Level – V (125µg/ml of Lorlatinib):

Pipette out 1.25ml of stock solution in to a 10ml volumetric flask and make up the volume up to mark by using diluent.

Procedure:

Inject each level into the chromatographic system and measure the peak area.

Plot a graph of peak area versus concentration (on X-axis concentration and on Y-axis Peak area) and calculate the correlation coefficient.

PRECISION REPEATABILITY

Preparation of Lorlatinib Product Solution for Precision:

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7ml of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 1 ml of the above Lorlatinib stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

The standard solution was injected for five times and measured the area for all five injections in HPLC. The %RSD for the area of five replicate injections was found to be within the specified limits.

INTERMEDIATE PRECISION

To evaluate the intermediate precision (also known as Ruggedness) of the method, Precision was performed on different days by maintaining same conditions.

Procedure:

DAY 1:

The standard solution was injected for six times and measured the area for all six injections in HPLC. The %RSD for the area of six replicate injections was found to be within the specified limits.

DAY 2:

The standard solution was injected for six times and measured the area for all six injections in HPLC. The %RSD for the area of six replicate injections was found to be within the specified limits.

Accuracy:

For preparation of 50% Standard stock solution:

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.5 ml of the above Lorlatinib stock solution into a 10ml volumetric flask and dilute up to the mark with diluents.

For preparation of 100% Standard stock solution:

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 1 ml of the above Lorlatinib stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

For preparation of 150% Standard stock solution:

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 1.5 ml of the above Lorlatinib stock solution into a 10ml volumetric flask and dilute up to the mark with diluents.

Procedure:

Inject the Three replicate injections of individual concentrations (50%, 100%, 150%) were made under the optimized conditions. Recorded the chromatograms and measured the peak responses. Calculate the Amount found and Amount added for Lorlatinib and calculate the individual recovery and mean recovery values.

ROBUSTNESS

The analysis was performed in different conditions to find the variability of test results. The following conditions are checked for variation of results.

For preparation of Standard solution:

Accurately weigh and transfer 10 mg of Lorlatinib working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 1 ml of the above Lorlatinib stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

Effect of Variation of flow conditions:

The sample was analyzed at 0.9ml/min and 1.1ml/min instead of 1.0ml/min, remaining conditions are same. 10µl of the above sample was injected twice and chromatograms were recorded.

Effect of Variation of mobile phase organic composition:

The sample was analyzed by variation of mobile phase i.e. Methanol: Water was taken in the ratio and 20:80, 30:70 instead of 25:75, remaining conditions are same.10µl of the above sample was injected twice and chromatograms were recorded.

RESULTS AND DISCUSSION

(Fig :2 Optimized Chromatogram (Standard))

(Table:3 Optimized Chromatogram (Standard))

Observation: In this trail it shows well peak shape and proper plate count and tailing under limit in the chromatogram. So it's optimized chromatogram.

VALIDATION

Blank: (Fig:3 chromatogram showing blank)

System suitability: (Fig:4 Chromatogram showing injection -1)

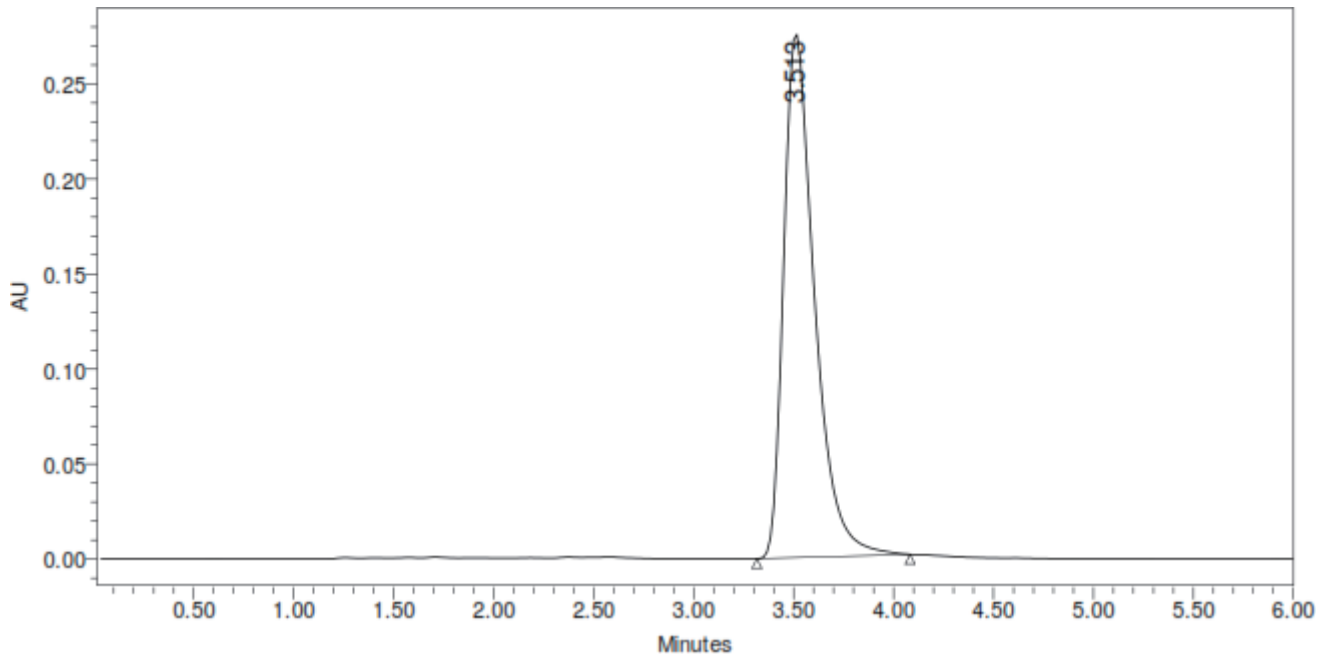

Figure 2: Optimized Chromatogram (Standard)

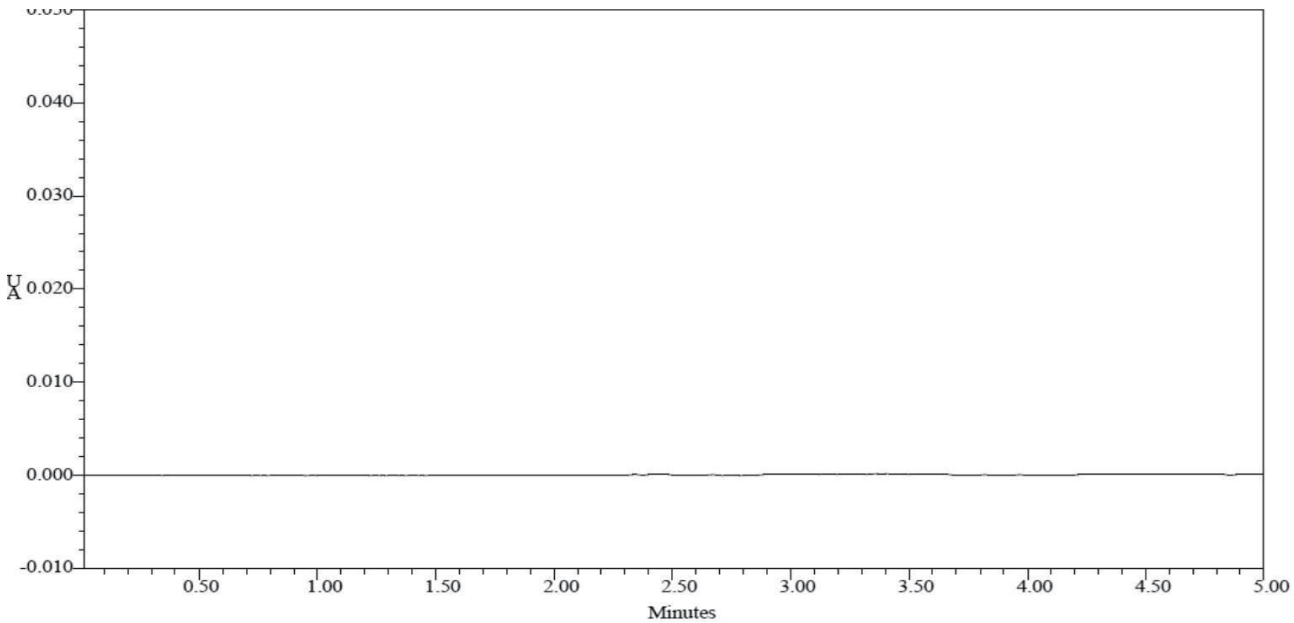

Figure 3: Chromatogram showing blank (mobile phase preparation)

Table 3: Optimized Chromatogram (Standard)

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lorlatinib	3.513	2955864	275463	1.1	7483

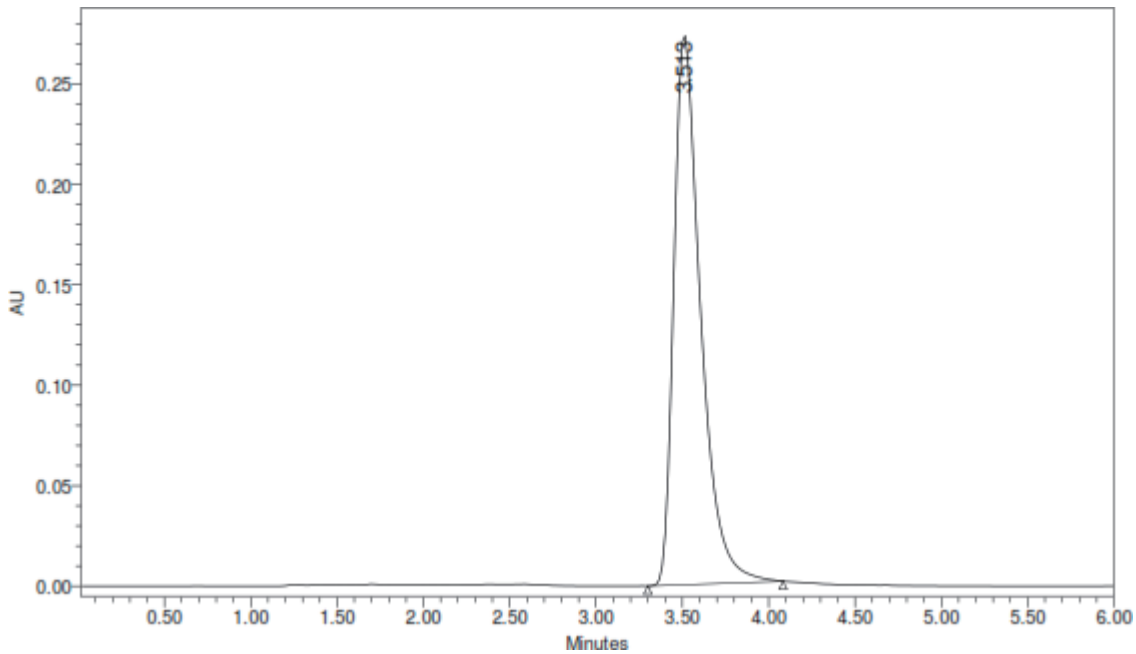

Figure 4: Chromatogram showing injection -1

Table 4: Results of system suitability for Lorlatinib

S.No	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate Count	USP Tailing
1	Lorlatinib	3.513	2947512	275468	7482	1.1
2	Lorlatinib	3.516	2958476	275366	7471	1.1
3	Lorlatinib	3.515	2965848	275175	7387	1.1
4	Lorlatinib	3.517	2952644	275916	7286	1.1
5	Lorlatinib	3.512	2951652	275949	7465	1.1
Mean			2955226			
Std. Dev.			7112.232			
% RSD			0.240666			

(Table:4 Results of system suitability for Lorlatinib)

Acceptance criteria: %RSD of five different sample solutions should not more than 2

•The %RSD obtained is within the limit, hence the method is suitable.

SPECIFICITY

(Table:5 Peak results for assay standard)

Assay (Sample):

(Table:6 Peak results for Assay sample)

%ASSAY = (Sample area/Standard area) × (Weight of standard/Dilution of standard) × (Dilution of sample/Weight of sample) × (Purity/100) × (Weight of Tablet/Label claim) × 100

=2966460/2965058 × 10/100 × 100/0.0145 × 99.8/100 × 0.0361/25 × 100

=99.28

The % purity of Lorlatinib in pharmaceutical dosage form was found to be 99.28%.

LINEARITY

CHROMATOGRAPHIC DATA FOR LINEARITY STUDY

(Table 7: Linearity)

Table 5: Peak results for assay standard

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lorlatinib	3.518	2967593	275837	1.1	6583
2	Lorlatinib	3.517	2967399	275922	1.1	5938
3	Lorlatinib	3.515	2960183	271844	1.1	5883

Table 6: Peak results for Assay sample

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lorlatinib	3.511	2983744	275833	1.1	7584
2	Lorlatinib	3.511	2958374	275984	1.1	6294
3	Lorlatinib	3.514	2957262	275481	1.1	8194

Table 7: Linearity

Concentration (µg/ml)	Average Peak Area
25	1083048
50	1973321
75	2955166
100	4063921
125	5006038

LINEARITY PLOT

The plot of Concentration (x) versus the Average Peak Area (y) data of Lorlatinib is a straight line.

Y = mx + c

Slope (m) = 39948

Intercept(c)=16821

Correlation Coefficient (r) = 0.999

VALIDATION CRITERIA

The response linearity is verified if the Correlation Coefficient is 0.99 or greater.

CONCLUSION

Correlation Coefficient (r) is 0.99, and the intercept is 16821. These values meet the validation criteria.

Precision:

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions.

REPEATABILITY

(Table:8 Results of repeatability for Lorlatinib)

Acceptance criteria:

%RSD for sample should be NMT 2

•The %RSD for the standard solution is below 1, which is within the limits hence method is precise.

Intermediate precision:

(Table:9 Results of Intermediate precision for Lorlatinib)

Acceptance criteria:

%RSD of Six different sample solutions should not more than 2

Day 2:

(Table:10 Results of Intermediate precision Day 2 for Lorlatinib)

Acceptance criteria:

•%RSD of Six different sample solutions should not more than 2

ACCURACY

Accuracy at different concentrations (50%, 100%, and 150%) were prepared and the % recovery was calculated.

Table 8: Results of repeatability for Lorlatinib

S. No	Peak name	Retention time	Area(µV*sec)	Height (µV)	USP Plate Count	USP Tailing
1	Lorlatinib	3.528	2958412	275994	7586	1.1
2	Lorlatinib	3.516	2951161	275932	7595	1.1
3	Lorlatinib	3.514	2959393	275961	8692	1.1
4	Lorlatinib	3.519	2953485	275942	7971	1.1
5	Lorlatinib	3.512	2950821	275276	9746	1.1
Mean			2954654			
Std.dev			4026.17			
%RSD			0.136265			

Table 9: Results of Intermediate precision for Lorlatinib

S.No	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate count	USPTailing
1	Lorlatinib	3.517	2957451	275842	7198	1.1
2	Lorlatinib	3.514	2951866	275631	8581	1.1
3	Lorlatinib	3.517	2950912	276946	7658	1.1
4	Lorlatinib	3.517	2957198	275639	792	1.1
5	Lorlatinib	3.512	2950273	275194	7569	1.1
6	Lorlatinib	3.518	2951784	275189	7592	1.1
Mean			2953247			
Std. Dev.			3213.361			
% RSD			0.108808			

Table 10: Results of Intermediate precision Day 2 for Lorlatinib

S.No	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate count	USPTailing
1	Lorlatinib	3.513	2951856	275936	7941	1.1
2	Lorlatinib	3.511	2958281	275243	7289	1.1
3	Lorlatinib	3.516	2950188	275861	7692	1.1
4	Lorlatinib	3.518	2957476	275179	7923	1.1
5	Lorlatinib	3.511	2957552	275177	7588	1.1
6	Lorlatinib	3.519	2951173	275167	7384	1.1
Mean			2954421			
Std. Dev.			3717.063			
% RSD			0.125814			

Accuracy50%: (Table:11 Results of Accuracy for concentration-50%)

Accuracy100%: (Table:12 Results of Accuracy for concentration-100%)

Accuracy150%: (Table :13 Results of Accuracy for concentration-150%)

(Table : 14 Accuracy results for Lorlatinib)

Table 11: Results of Accuracy for concentration-50%

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lorlatinib	3.519	1493974	275846	1.1	6576
2	Lorlatinib	3.520	1493884	275823	1.1	7591
3	Lorlatinib	3.519	1492763	275095	1.1	6793

Table 12: Results of Accuracy for concentration-100%

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lorlatinib	3.516	2983879	275832	1.1	7489
2	Lorlatinib	3.518	2984742	275149	1.1	6946
3	Lorlatinib	3.519	2967465	275151	1.1	6288

Table 13: Results of Accuracy for concentration-150%

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lorlatinib	3.517	4462182	275647	1.1	7488
2	Lorlatinib	3.519	4469564	275976	1.1	7276
3	Lorlatinib	3.520	4489636	276448	1.1	7198

Table 14: Accuracy results for Lorlatinib

%Concentration (at specification Level)	Area	Amount Added (ppm)	Amount Found (ppm)	% Recovery	Mean Recovery
50%	1493540	50	49.13	98.26%	
100%	2978695	100	99.36	99.36%	98.96%
150%	4473794	150	148.91	99.27%	

Acceptance Criteria:

The percentage recovery was found to be within the limit (98-102%).

The results obtained for recovery at 50%, 100%, 150% are within the limits. Hence method is accurate.

LIMIT OF DETECTION FOR LORLATINIB

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value.

LOD= 3.3 × σ / s = 0.332µg/ml

Quantitation limit

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined.

LOQ= 10×σ/S = 1.0078 µg/ml

Robustness

(Table:15 Results for Robustness)

Acceptance criteria

The tailing factor should be less than 2.0 and the number of theoretical plates (N) should be more than 2000.

SUMMARY

Table 15: Results for Robustness

Parameter used for sample analysis	Peak Area	Retention Time	Theoretical plates	Tailing factor
Actual Flow rate of 1.0 mL/min	2955782	3.513	7487	1.1
Less Flow rate of 0.9 mL/min	2958396	3.897	6178	1.1
More Flow rate of 1.1 mL/min	2956434	3.218	6933	1.2
Less organic phase	2950682	3.707	6738	1.2
More organic phase	2957268	3.350	6294	1.1

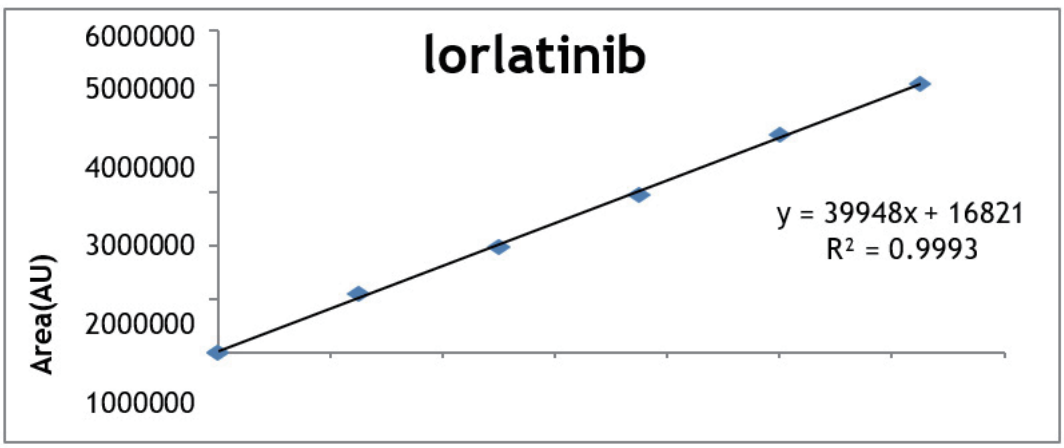

Figure 5: Calibration curve of lorlatinib

The analytical method was developed by studying different parameters. First of all, maximum absorbance was found to be at 310nm and the peak purity was excellent. Injection volume was selected to be 10µl which gave a good peak area. The column used for study was Hypersil C18 (4.6 x 150mm, 5µm) because it was giving good peak. 38º C temperature was found to be suitable for the nature of drug solution. The flow rate was fixed at 1.0ml/min because of good peak area and satisfactory retention time. Mobile phase is Methanol: water was fixed due to good symmetrical peak. So this mobile phase was used for the proposed study.

Methanol: water was selected because of maximum extraction sonication time was fixed to be 10min at which all the drug particles were completely soluble and showed good recovery.Run time was selected to be 6min because analyze gave peak around 3.5 and also to reduce the total run time. The percent recovery was found to be 98.0-102 was linear and precise over the same range. Both system and method precision was found to be accurate and well within range. The analytical method was found linearity over the range of 25-125µg/ml of the target concentration. The analytical passed both robustness and ruggedness tests. On both cases, relative standard deviation was well satisfactory.

CONCLUSION

In the present investigation, a simple, sensitive, precise and accurate RP-HPLC method was developed for the quantitative estimation of Lorlatinib in bulk drug and pharmaceutical dosage forms. This method was simple, since diluted samples are directly used without any preliminary chemical derivatisation or purification steps. Lorlatinib was freely soluble in ethanol, methanol and sparingly soluble in water. Methanol: water was chosen as the mobile phase. The solvent system used in this method was economical. The %RSD values were within 2 and the method was found to be precise. The results expressed in Tables for RP-HPLC method was promising. The RP-HPLC method is more sensitive, accurate and precise.

This method can be used for the routine determination of Lorlatinib in bulk drug and in Pharmaceutical dosage forms.

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Conflict of interest

None to declare for all authors.

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References

1 https://go.drugbank.com/drugs/DB12130
2 https://pubchem.ncbi.nlm.nih.gov/compound/lorlatinib#section=Computed-Properties/
3 https://en.m.wikipedia.org/wiki/Lorlatinib
4 Chromatography, (online). URL:http://en.wikipedia.org/wiki/Chromatography.
5 ICH Q2A, "validation of analytical methods, definitions and terminology", ICH Harmonized tripartite guideline, (1999).
6 K.Kalyan Chakravarthi and K. Himabindu. RP-HPLC Method Development and Validation for the Determination of lorlatinib in Bulk and Its Pharmaceutical Formulation. International Journal of Research Publication and Reviews.2021;2(9): (958-63).
7 Anuradha N. D. and Syed Azhar Nizami. RP-HPLC method development and validation for the determination of lorlatinib in bulk and its pharmaceutical formulation. world journal of pharmacy and pharmaceutical sciences.8(6):((1142-50).
8 Claudia Spataria,b , Wenlong Lic , Alfred H. Schinkelc, Gaetano Ragnob , Jan H.M. Schellensa,d , Jos H. Beijnena,d,e , Rolf W. Sparidansa. Bioanalytical assay for the quantification of the ALK inhibitor lorlatinib in mouse plasma using liquid chromatography-tandem mass spectrometry.J Chromatogr B Analyt Technol Biomed Life Sci. 2018;1083: (204-08).
9 Santhosh Illendula, Naveen Kumar Singhal; A Review: Novel analytical method development and validation for the determination of selected anti cancer & anti viral drugs, World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS) 2022; 11(07): (533-66).
10 Santhosh Illendula, Shailesh Sharma; UPLC method development and validation of acalbritinib in bulk and pharmaceutical dosage form, International Journal of Chemical and Biochemical Sciences (IJCBS) 2024; 25(14): (397-11).