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Research Article

Estimation of Selpercatinib in Active Pharmaceutical Ingredient and Pharmaceutical Formulations by UV-Visible Spectroscopy

Jonnakuti Madhvilatha[1]*, Narendra Kumar Nyola[1], Niranjan Shishir Mahajan[2]

[1]School of Pharmacy, Shridhar University,Pilani, Rajasthan, India

[2]Adarsh College of Pharmacy, Sangli, Maharastra, India

*Corresponding Author: **Jonnakuti Madhvilatha**, School of Pharmacy, Shridhar University, Pilani Rajasthan, India

E-mail: narennyola2@gmail.com

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ABSTRACT

A simple, precise, accurate, and cost-effective UV-visible spectrophotometric method was developed and validated for the estimation of Selpercatinib in bulk and pharmaceutical formulations. The drug exhibited maximum absorbance at 240 nm 0.1 N hydrochloric acid. Beer's law was obeyed in the concentration range of 5–25 µg/mL with a correlation coefficient of 0.9994. The method was validated according to ICH Q2 (R1) guidelines for linearity, precision, accuracy, limit of detection (LOD), and limit of quantitation (LOQ). The LOD and LOQ values were found to be 0.72µg/mL and 2.2µg/mL, respectively. The proposed method was successfully applied to marketed formulations, yielding recovery values within acceptable limits (98–102%). The results confirm that the developed method is suitable for routine quality control analysis of Selpercatinib in bulk and dosage forms.

Introduction

Selpercatinib is a selective RET kinase inhibitor used in treatment of RET fusion-positive cancers. Lung cancer is among the most prevalent malignant tumors globally, representing a significant threat to human health and presenting a major challenge to public health. [3, 6], Among the various subtypes of lung cancer, non-small cell lung cancer (NSCLC) is the most prevalent, comprising approximately 85%–90% of all lung cancer cases ,[1,2] Surgical treatment is generally applicable to patients diagnosed at an early stage, while radiotherapy is primarily used to control the growth of localized tumors. Although chemotherapy is widely utilized in advanced cases, its detrimental effects on normal cells can lead to severe side effects, significantly reducing the patient's quality of life. [4, 5] Common targeted drugs currently include EGFR inhibitors, ALK inhibitors, KRAS inhibitors, and RET inhibitors. [7, 8,9,10] RET is a transmembrane glycoprotein receptor tyrosine kinase encoded by the RET proto-oncogene, which is located on chromosome 10. [11]

Currently, HPLC technology remains a commonly used method for detecting related substances in active pharmaceutical ingredients (API). [12, 13] Furthermore, researchers, focused on studying the impurities produced during forced degradation of selpercatinib and identifying their structures using liquid chromatography-mass spectrometry. The high-performance liquid chromatography method they established is only used for detecting degradation impurities with higher contents, while neglecting the separation of degradation products with unknown structures and process impurities.[14, 15] Accurate quantification of Selpercatinib in bulk and dosage forms is essential for quality control and therapeutic monitoring. RP-HPLC is a preferred analytical technique due to its sensitivity, specificity, and reproducibility. This study develops a validated, economical RP-HPLC method for Selpercatinib quantification in pure drugs and commercial formulations.

Materials and Methods

Materials

Pure Selpercatinib standard was obtained from a certified source. Commercial capsule and vial formulations were purchased from the local market. Dimethyl sulfoxide (DMSO) and 0.1 N HCl were used as analytical-grade solvents.

Instrumentation

A double-beam UV-visible spectrophotometer equipped with a 1 cm quartz cell was used for absorbance measurements. All readings were taken against a reagent blank.

Preparation of Standard Stock Solution

An accurately weighed quantity of 100 mg Selpercatinib was transferred to a 100 mL volumetric flask. The drug was dissolved in 25 mL DMSO and the solution was made up to the mark with 0.1 N HCl to obtain a concentration of 1000 µg/mL.

Preparation of Working Solutions

Aliquots of the standard stock solution were further diluted with 0.1 N HCl to prepare working standard solutions in the range of 2–10 µg/mL.

Selection of Detection Wavelength

The UV absorption spectrum of Selpercatinib (10 µg/mL) was recorded between 200 and 400 nm. The maximum absorbance (λmax) was observed at 240 nm, which was selected for all subsequent analyses.

Analysis of Marketed Formulation

Twenty capsules containing 40 mg Selpercatinib each were weighed, and an amount equivalent to 100 mg of the drug was transferred to a 100 mL volumetric flask. The sample was dissolved in 25 mL DMSO, diluted to volume with 0.1 N HCl, filtered, and suitably diluted to obtain a series of working concentrations for analysis at 240 nm.

Method Validation

Linearity

The method showed a linear response between 5-25 µg/mL. The regression equation was found to be $y = 0.0247x - 0.0002$ with a correlation coefficient (r) of 0.9994. The calibration curve indicated excellent linearity ($r^2 \approx 0.999$), verifying that absorbance was directly proportional to drug concentration. . (Fig. 2; Table 1 & 2)

Precision

Precision was evaluated through repeatability, intra-day, and inter-day studies.

- **Repeatability:** Analysis of five replicates at a fixed concentration showed a %RSD of 1.61%.
- **Intra-day precision:** Analysis at three concentration levels within the same day gave a %RSD of 1.08%.
- **Inter-day precision:** Evaluations over three consecutive days yielded a %RSD of 1.13%.
- All values were below 2%, demonstrating excellent precision. (Table 3,4,5, & 6)

Accuracy (Recovery Study)

Accuracy was determined by standard addition at three levels (80%, 100%, and 120%). The mean percentage recoveries were 100.05%, 101.05%, and

100.21%, respectively, with an overall average recovery of 100.44%. These results confirmed the reliability and unbiasedness of the method. (Table 7)

Sensitivity (LOD and LOQ)

LOD and LOQ were calculated using standard formulas based on the standard deviation of the response (σ) and slope (S): LOD = 3.3 × (σ/S), LOQ = 10 × (σ/S). The calculated LOD and LOQ values were 0.72 µg/mL and 2.2 µg/mL, respectively, signifying that the method is adequately sensitive. (Table 2)

Assay of Marketed Formulation

The validated method was used to determine Selpercatinib content in a marketed capsule formulation labeled to contain 120 mg of the drug. The average percentage assay was found to be 99.58%, which falls within the pharmacopeial acceptance criteria (98–102%). The low variability confirmed the method's applicability for routine assay of formulations. (Table 8)

Results and Discussion

The developed UV-visible spectrophotometric method showed excellent linearity, precision, and accuracy. The correlation coefficient value close to unity and low RSD values indicated minimal variability and strong reproducibility. Recovery results within the prescribed ICH limits demonstrated that common formulation excipients did not interfere with the analysis. The results also indicated the method's high sensitivity, as reflected in its low LOD and LOQ values. Overall, the procedure offers a reliable, reproducible, and economical alternative for the routine analysis of Selpercatinib in quality control laboratories.

Conclusion

A simple and reliable UV-visible spectrophotometric method for the estimation of Selpercatinib in active pharmaceutical ingredients and marketed formulations was successfully developed and validated. The method complies with ICH guidelines for analytical validation and can be applied for routine analysis due to its high accuracy, precision, and reproducibility.

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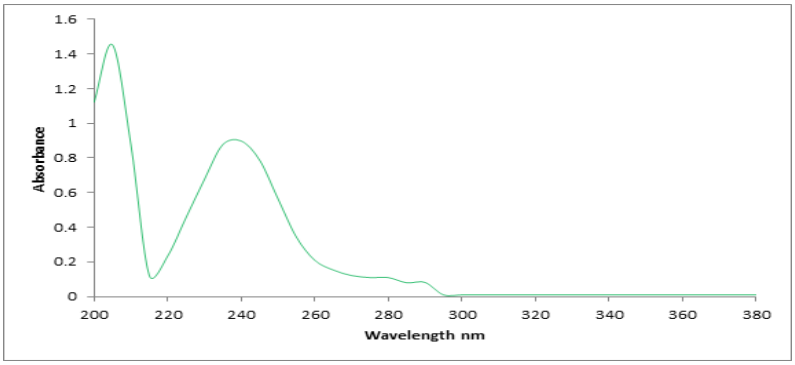

Fig. 1 :UV spectra of Selpercatinib

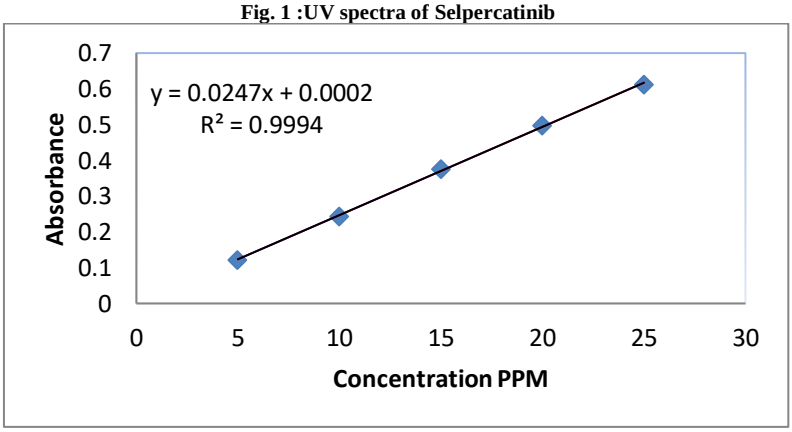

Fig. 2 :Calibration curve for Selpercatinib

Table 1: Linearity data of Selpercatinib

S. No.	Actual Concentration PPM	Absorbance	Concentration Found PPM
1	5	0.122	4.93
2	10	0.244	9.87
	15	0.376	15.21
4	20	0.498	20.15
5	25	0.612	24.77

Table 2: Analytical performance parameters of Selpercatinib

Parameters	Zero order
Wavelength Maxima	240
Regression Equation	0.0247x - 0.0002
Correlation coefficient	0.9994
LOL(µg/ml)	05-25
LOD(µg/ml)	0.72
LOQ(µg/ml)	2.2

Table 3: Intraday Precision Study on single concentration level

S. No	Actual Concentration µg/ml	Absorbance	Concentration found µg/ml
1	15	0.376	15.23
2	15	0.37	14.98
3	15	0.372	15.06
4	15	0.372	15.06
5	15	0.371	15.02
		Mean	**15.073**
		STDV	**0.092**
		%RSD	**0.613**

Table 4 :Repeatability study: Intra-day studies with three concentration levels

S. No.	5µg/ml	10µg/ml	15µg/ml
1	0.123	0.239	0.375
2	0.127	0.243	0.368
3	0.128	0.248	0.365
4	0.127	0.243	0.361
5	0.124	0.248	0.362
SD	0.0022	0.0038	0.0056
MEAN	0.13	0.2442	0.3662
%RSD	1.723	1.570	1.537
Mean % RSD	1.610		

Table 5 :Repeatability study: with different analyst

S. No.	Analyst I			Analyst II		
	5µg/ml	10µg/ml	15µg/ml	5µg/ml	10µg/ml	15µg/ml
1	0.123	0.239	0.375	0.127	0.245	0.378
2	0.127	0.243	0.368	0.129	0.242	0.38
3	0.128	0.248	0.365	0.127	0.239	0.372
4	0.127	0.243	0.361	0.125	0.239	0.378
5	0.124	0.248	0.362	0.128	0.24	0.379
SD	0.0022	0.0038	0.0056	0.0015	0.0025	0.0031
MEAN	0.13	0.2442	0.3662	0.13	0.241	0.3774
%RSD	1.723	1.570	1.537	1.166	1.058	0.829
Mean % RSD	1.610			1.018		

Table 6 :Inter-day studies with three concentration levels

	Con	1	2	3	4	5	SD	Mean	%RSD
Day 1	**5**	0.132	0.13	0.129	0.128	0.132	0.0018	0.1302	1.374
	10	0.241	0.24	0.238	0.243	0.245	0.0027	0.2414	1.119
	15	0.378	0.376	0.378	0.38	0.371	0.0034	0.3766	0.912
Day 2	**5**	0.129	0.13	0.127	0.128	0.129	0.0011	0.1286	0.887
	10	0.234	0.235	0.23	0.239	0.236	0.0033	0.2348	1.393
	15	0.376	0.37	0.369	0.372	0.378	0.0039	0.373	1.038
Day 3	**5**	0.128	0.127	0.13	0.124	0.127	0.0031	0.2352	1.324
	10	0.238	0.233	0.234	0.239	0.232	0.0041	0.373	1.089
	15	0.369	0.37	0.372	0.375	0.379	0.0041	0.3730	1.0890
Mean %RSD				1.136					

Table 7: Recovery data of Selpercatinib

Concentration taken 18 ppm (80%)		Concentration taken 20 ppm (100%)		Concentration taken 22 ppm (120%)	
Absorbance	**Conc. found ppm**	**Absorbance**	**Conc. found ppm**	**Absorbance**	**Conc. found ppm**
0.443	17.94	0.498	20.17	0.543	21.99
0.454	18.39	0.489	19.81	0.542	21.95
0.437	17.70	0.51	20.66	0.548	22.20
Mean Con	18.01		20.21		22.05
SD of Con.	0.349		0.426		0.13
% Recovery	100.05		101.05		100.21
MEAN RECOVERY		**100.440**			

Table 8 :Assay of Selpercatinib (Tablet)

Parameters	Amount present
Label Claim 120 mg	120
Assay Result	119.5
% Assay	99.58

*****Mean of three reading

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