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Research Article

An Advanced Stability-Indicating RP-UPLC Method for Rapid Quantification of Vimseltinib in Bulk and Pharmaceutical Formulations

B. Pavani[1]*, R. Krishna Kalyani[1], C. Hari kumar[2], M. Pradeep Kumar[3]

1 Department of Pharmaceutical Analysis, 2 Department of Pharmacology, 3 Department of Pharmaceutics, Vasavi Institute of Pharmaceutical Sciences, Kadapa 516247

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ABSTRACT:

A simple, Accurate, precise method was developed for the estimation of the Vimseltinib in bulk and pharmaceutical dosage form RP-UPLC technique. Chromatographic conditions used are stationary phase CHS 50mm x 2.1 mm, 1.8m ,Mobile containing Buffer 0.1% OPA: Acetonitrile taken in the ratio 70:30 was pumped through column at a flow rate of 0.3 ml/min. Buffer used in this method was 0.1% OPA buffer. Temperature was maintained at 30°C. Optimized wavelength selected was 264.0 nm. Retention time of Vimseltinib was found to be 0.848 min. %RSD of the Vimseltinib was and found to be 0.4%. %Recovery was obtained as 99.52% for Vimseltinib. LOD and LOQ are 0.01 µg/ml and 0.04 µg/ml. %Assay was obtained as 99.50% for Vimseltinib. Regression equation of Vimseltinib is y = 7260.5x + 329. Retention times were decreased and that run time was decreased, so the method developed was simple and economical that can be adopted in regular Quality control test in Industries.

Key Words: Vimseltinib, UPLC, validation, Method Development.

Introduction:

Vimseltinib (DCC-3014) is a novel, orally bioavailable and highly selective colony-stimulating factor-1 receptor (CSF1R) inhibitor developed for the treatment of macrophage-mediated disorders, particularly tenosynovial giant cell tumor (TGCT). TGCT is a rare, locally aggressive neoplasm affecting synovial joints, bursae, and tendon sheaths, characterized by overexpression of colony-stimulating factor-1 (CSF1), which recruits inflammatory macrophages expressing CSF1R into the tumor microenvironment. These macrophages constitute a major portion of the tumor mass and contribute significantly to disease progression and joint destruction.[1]

CSF1R is a receptor tyrosine kinase that regulates macrophage survival, proliferation, differentiation, and activation. Abnormal activation of the CSF1/CSF1R signaling pathway has been implicated in several inflammatory and neoplastic disorders. Therefore, selective inhibition of CSF1R has emerged as an important therapeutic strategy in oncology and inflammatory disease management.[2] Vimseltinib was rationally designed using switch-control kinase inhibitor technology to selectively inhibit CSF1R while minimizing off-target inhibition of related kinases such as KIT, FLT3, and PDGFR.[3] This enhanced selectivity differentiates vimseltinib from earlier CSF1R inhibitors and may reduce adverse effects associated with nonspecific kinase inhibition.

Mechanistically, vimseltinib binds to the switch pocket region of CSF1R and stabilizes the receptor in its inactive conformation, thereby blocking downstream signaling pathways involved in macrophage recruitment and activation.[4] Preclinical studies demonstrated that vimseltinib effectively suppresses CSF1R-dependent signaling, reduces inflammatory cytokine production, decreases tumor-associated macrophage populations, and inhibits osteoclast-mediated bone destruction.[3] These findings highlighted its therapeutic potential in diseases driven by macrophage overactivation.

Clinical investigations further established the efficacy and safety of vimseltinib in patients with TGCT. In early phase clinical trials, the drug showed promising antitumor activity with significant reductions in tumor size and improvements in pain, mobility, and physical function.[5] The phase III MOTION trial, a randomized double-blind placebo-controlled study, demonstrated superior objective response rates and symptomatic improvement with vimseltinib treatment compared with placebo in patients with symptomatic TGCT not amenable to surgery.[6] Based on these findings, vimseltinib received approval from the United States Food and Drug Administration (FDA) in 2025 for the treatment of adult patients with symptomatic TGCT associated with severe morbidity or functional limitation.[7]

Address for Correspondence: B. Pavani, Associate Professor, Department of Pharmaceutical Analysis, Vasavi Institute of Pharmaceutical Sciences, Kadapa 516247.; **E-Mail:** pavanianalysis@gmail.com

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Apart from TGCT, vimseltinib is also being investigated for potential applications in other malignancies and inflammatory disorders involving macrophage dysregulation. Its favorable pharmacological profile, oral administration, and improved kinase selectivity make it a promising next-generation targeted therapeutic agent.[8] Consequently, vimseltinib represents an important advancement in precision oncology and macrophage-targeted therapy.

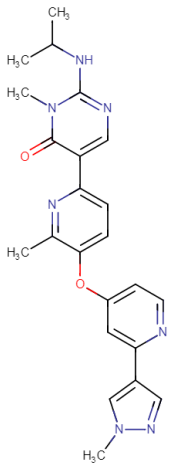

Figure 1: Structure of Vimseltinib

High Performance Liquid Chromatography (HPLC) plays a crucial role in the validation of Vimseltinib (MK-6482), a novel drug used in the treatment of cancers associated with von Hippel-Lindau (VHL) disease. In the review of literature, more economical methods were observed[10-13], hence a simple, cost-effective stability-indicating simultaneous estimation of Vimseltinib by RP-HPLC in pharmaceutical dosage form must be developed and validated as per the guidelines of ICH (Q2 specification).

Materials and Methods:

Vimseltinib (API), Vimseltinib tablets (Welireg), Acetonitrile, Methanol, Ortho Phosphoric Acid, Distilled water. All of the solvents and chemicals were of UPLC quality and obtained from Rankem Chemicals Pvt Ltd.

Instrumentation:

The Method Development and Validation was performed by Waters UPLC Accquity equipped with TUV Detector and Empower 2 Software. Analytical weighing Balance, Ultrasonicator, pH Meter, Hot air oven.

Chromatographic Condition:

An Isocratic Elution carried out by using Acetonitrile and 0.1% OPA 30:70 v/v as the Mobile Phase, Diluent used was Combination of Acetonitrile and Water in 1:1 ratio. CHS C18 (50mm x 2.1 mm, 1.8m) column was used to determine the Method at a flow rate of 1ml/min, by maintaining the column Temperature at 30 0C. In addition, with an injection volume of 10µL and the wavelength detected at 251nm.

API Formulation

Preparation of Standard stock solutions and Working Solution: A 50 mLvolumetric flask is filled with precisely weighed 7 mg of vimseltinib. After adding 3/4 of the diluents, the flask was sonicated for ten minutes. The flask containing 140 µg/mLof Vimseltinib solution was filled with diluents and labeled as Standard stock solution. Additionally, 1 mLof the stock solution was pipetted out, transferred into a 10 mLvolumetric flask, and diluted to create 14 µg/mLof vimseltinib.

Sample Formulation

Preparation of Sample stock solutions and Working Solution: After weighing ten tablets and calculating their average weight, the weight of one tablet was transferred into a 100 mLvolumetric flask, 80 mLof diluent was added, and the mixture was sonicated for 25 minutes. The volume was then filled with diluent and filtered through UPLC filters to create a 140 µg/mLVimseltinib solution. To create 14µg/mLof vimseltinib, 1 milliliter of the filtered sample stock solution was transferred to a 10 milliliter volumetric flask and diluted.

Method Validation

As per ICH guidelines, the developed method is validated for validating the analytical procedures. The validation parameters include system suitability, accuracy, linearity, limit of detection (LOD), limit of quantification (LOQ), precision, robustness, specificity and Degradation Studies were performed.

System suitability parameters:

The working standard solution was injected six times into UPLC system as and the chromatographic study was performed as per the developed and optimized conditions. The system suitability parameters were evaluated from standard chromatograms obtained by calculating the % RSD of retention times, theoretical plates and peak areas from six replicate injections.

Specificity: Checking of the interference in the optimized method. We should not find interfering peaks in blank and placebo at retention times of these drugs in this method. So this method was said to be specific.

Precision:

The method and system precision were demonstrated by preparing the standard solution at a known concentration and six repeatable injections were given to ensure the repeatability of the proposed method. The intermediate precision was also performed by preparing six working sample solutions by injecting each solution six times. The area was noted, mean, standard deviation, and percentage of RSD were calculated. The results were satisfactory and below 2% as per the limit.

Linearity:

The linearity of the drug was studied by preparing serial dilutions in the range of 5–30 µg/ml. The correlation between peak area response and drug concentration was shown on a graph. It was observed to be linear for the specified drug concentration.

Accuracy:

Accuracy was performed in triplicate for various concentrations of Vimseltinib equivalent to 50%, 100% and 150% of the standard amount were injected into the HPLC system per the test procedure.

Sensitivity:

Limit of detection and Limit of Quantification

LOD and LOQ were calculated from the average slope and standard deviation from the calibration curve as per ICH guidelines.

Based on the response's standard deviation and calibration curve's slope, the LOD and LOQ can be estimated. The formulae given below can be used to calculate LOD and LOQ:

$$LOD = 3.3\sigma/S$$

$$LOQ = 10\sigma/S$$

where S is calibration curve of the slope and σ is the response of the standard deviation.

Robustness: Small deliberate changes in method like Flow rate, mobile phase ratio, and temperature are made but there were no recognized change in the result and are within range as per ICH Guidelines.

Assay:

The assay and % purity were calculated for brand Romvimza with label claim 14mg. The observed value was compared with that of standard value without interference from the excipients used in the tablet dosage form

Degradation Studies

These studies are performed at various stress conditions to describe the stability of the pure drug substance and are helpful in determining a suitable storage conditions. These studies include base, peroxide, acid, neutral hydrolysis, photo, and thermal degradation.

Oxidation:

To 1 ml of stock solution of Vimseltinib, 1 ml of 20% hydrogen peroxide (H2O2) was added separately. The solutions were kept for 30 min at 60^0c. For UPLC study, the resultant solution was diluted to obtain 14µg/ml solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Acid Degradation Studies:

To 1 ml of stock solution Vimseltinib, 1ml of 2N Hydrochloric acid was added and refluxed for 30mins at 60^0c. For UPLC study, the resultant solution was diluted to obtain 14µg/ml solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Alkali Degradation Studies:

To 1 ml of stock solution Vimseltinib, 1 ml of 2N sodium hydroxide was added and refluxed for 30mins at 60^0c. For UPLC study, the resultant solution was diluted to obtain 14µg/ml solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Dry Heat Degradation Studies:

The standard drug solution was placed in oven at 105°C for 6h to study dry heat degradation. For UPLC study, the resultant solution was diluted to obtain 14µg/ml solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Photo Stability studies:

The photochemical stability of the drug was also studied by exposing the 300µg/ml solution to UV Light by keeping the beaker in UV Chamber for 7days or 200 Watt hours/m2 in photo stability chamber. For UPLC study, the resultant solution was diluted to obtain 14µg/ml solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Neutral Degradation Studies:

Stress testing under neutral conditions was studied by refluxing the drug in water for 6hrs at a temperature of 60º. For UPLC study, the resultant solution was diluted to obtain 14µg/ml solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Result and Discussion

Table 1 Optimized Condition

Parameter	***Condition***
Mobile phase	Acetonitrile: 0.1% OPA (30:70 v/v)
Flow rate	0.3 ml/min
Column	CHS C18 (50mm x 2.1 mm, 1.8m)
Detector wave length	254 nm
Column temperature	30°C
Injection volume	1µL
Diluent	Water and Acetonitrile in the ratio 50:50

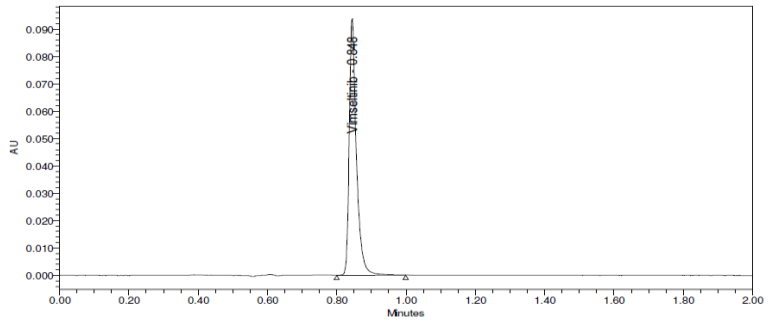

Figure 2: Optimized Chromatogram

System Suitability:

Table 2: System Suitability

S no	RT	area	Plate Count	Tailing
Injection-1	0.851	101865	9113	1.5
Injection-2	0.853	102387	9139	1.5
Injection-3	0.853	102601	9173	1.5
Injection-4	0.853	102280	9158	1.5
Injection-5	0.853	101961	9125	1.5
Injection-6	0.855	103988	9195	1.5
Mean		102514		
Std. Dev		771.8		
RSD		0.8		

Standard solution was injected six times, and their corresponding chromatograms were obtained. The theoretical plate count exceeded 2,000, the USP tailing was under 2, and the percent RSD was under 2%, according to observations. All of the requirements for system suitability were met and fall within acceptable ranges.

Linearity:

Six concentrations ranging from 3.5 to 21 µg/ml were prepared and linearity was estimated in a duplicate manner. The linearity equation for Vimseltinib was y = 7260.5x + 329. For the alibration curve over the concentration range, the data have shown a good correlation.

Table 3: Linearity Data

Concentration (ppm)	****Peak area***
0	*0*
3.5	25354
7	51761
10.5	76544
14	102283
17.5	128311
21	151698
y :	7260.5x + 329
R^2	0.999
Slope	7260.5
Intercept	329

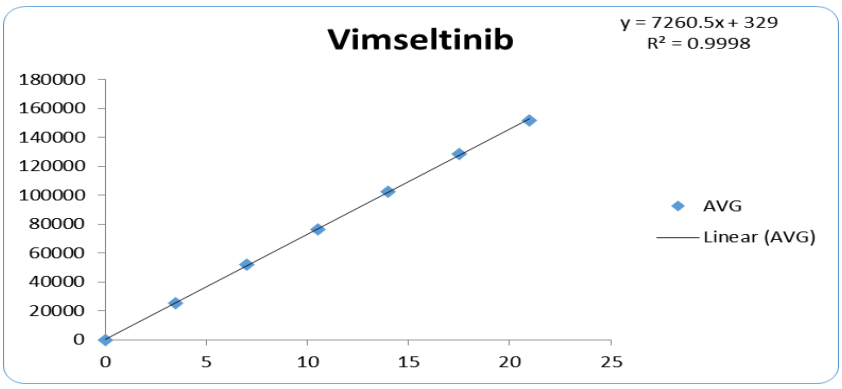

Figure 3: Calibration Curve of Vimseltinib

Accuracy:

Three doses were given at each level, and the mean % recovery was calculated. Vimseltinib's recovery rate was observed to be between 99% and 100%, which is within the acceptable ranges

Table 4: Accuracy Data

% Level	*Amount Spiked (µg/mL)*	*Amount recovered (µg/mL)*	*% Recovery*	*Avg %*	*Mean %Recovery*
50%	***7***	6.97	99.60	*99.60*	***99.52%***
		7.00	100.02		
		6.94	99.19		
100%	***14***	13.94	99.57	*99.64*	
		13.97	99.77		
		13.94	99.58		
150%	***21***	20.87	99.38	*99.33*	
		20.82	99.15		
		20.89	99.46		

Precision:

Table 5: Precision Data

S. No	*Method Precision*	*Intermediate Precision*
Injection-1	101727	101813
Injection-2	102666	100764
Injection-3	101838	102232
Injection-4	101992	102216
Injection-5	102359	100622
Injection-6	102668	102101
Mean	102208	101625
S.D	414.5	738.5
%RSD	0.4	0.7

Sensitivity:

Table 6: LOD and LOQ Data

Molecule	*LOD*	*LOQ*
Vimseltinib	0.01µg/ml	0.04 µg/ml

Robustness:

Table 7: Robustness data

Parameter	***Optimized condition and %RSD***		***Used condition***	***Obtained %RSD***
Flow rate (±0.1ml/min)	*0.3ml/min*	*0.8%*	0.2ml/min	0.7
			0.4 ml/min	1.3
MP Composition (5%v/v)	*30:70*		25:75	0.9
			35:65	1.0
Column Temp (±3^{0}c)	*30^{0}c*		27 ^{0}C	1.0
			33 ^{0}C	0.4

Assay

Table 8: % Assay Purity Data

Formulation	***Label claim(mg)***	***% Assay****
Romvimza	Vimseltinib 14 mg	99.50 %w/w

Degradation studies:

Table 9: Force Degradation Studies

S.No	Condition	% Drug Degraded	%Drug Recorded	***Peak Purity***
1	Acid	5.32	94.68	*Passes*
2	Alkali	5.41	94.59	*Passes*
3	Oxidation	7.25	92.75	*Passes*
4	Thermal	4.08	95.92	*Passes*
5	UV	2.85	97.15	*Passes*
6	Water	0.70	99.30	*Passes*

Conclusion:

In conclusion, the Vimseltinib UPLC analysis results show that this approach can accurately determine the drug's concentration and purity. The method's excellent repeatability, crisp peak resolutions, and dependable retention lengths make it ideal for routine quality control and pharmacokinetic research. When examining Vimseltinib's analytical properties, UPLC is an important tool for ensuring its efficacy and safety for clinical use.

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References:

1. *Smith BD, Kaufman MD, Wise SC, et al. Vimseltinib: A precision CSF1R therapy for tenosynovial giant cell tumors and diseases promoted by macrophages. Clin Cancer Res. 2022;28(6):1113-1123.*

2. *Cannarile MA, Weisser M, Jacob W, Jegg AM, Ries CH, Rüttinger D. Colony-stimulating factor 1 receptor (CSF1R) inhibitors in cancer therapy. J Immunother Cancer. 2017;5:53.*

3. *Smith BD, Wise SC, Kaufman MD, et al. Discovery of vimseltinib, a highly selective switch-control kinase inhibitor of CSF1R. Clin Cancer Res. 2022;28(6):1113-1123.*

4. *Tap WD, Gelderblom H, Palmerini E, et al. The MOTION study: A randomized phase III study of vimseltinib in tenosynovial giant cell tumor. Future Oncol. 2023;19(10):715-726.*

5. *Wagner AJ, Gelderblom H, Rutkowski P, et al. Clinical activity of vimseltinib in patients with tenosynovial giant cell tumor. J Clin Oncol. 2021;39(15_suppl):11508.*

6. *Gelderblom H, Wagner AJ, Tap WD, et al. Vimseltinib versus placebo for tenosynovial giant cell tumour (MOTION): a multicentre, randomized, double-blind, placebo-controlled, phase III trial. Lancet. 2024;403(10445):2709-2719.*

7. *U.S. Food and Drug Administration. FDA approves vimseltinib for tenosynovial giant cell tumor. Silver Spring (MD): FDA; 2025.*

8. *Dou F, Lu D, Gao J. Vimseltinib: A novel CSF1R inhibitor for treatment of tenosynovial giant cell tumors. Intractable Rare Dis Res. 2025;14(2):143-144.*

9. *Drugbank: Vimseltinib*

10. *Bhingaradiya, S., V. L. S. Dantinapalli, and S. Elumalai. "Stability Indicating Method Development And Validation Of Vimseltinib By Using UPLC In Bulk And Pharmaceutical Dosage Form.". International Journal of Pharmaceutics and Drug Analysis, vol. 14, no. 1, Feb. 2026, pp. 14-19.*

11. *Pavani B, Malothu N, Rao AA, Guntupalli C. QBD Driven Bioanalytical Method Development and Validation of Tepotinib using RP-UPLC.*