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RP-HPLC STABILITY INDICATING METHOD DEVELOPMENT AND VALIDATION FOR THE DETERMINATION OF LENVATINIB DRUG IN THE BULK AND ITS APPLICATION TO THE PHARMACEUTICAL DOSAGE FORM

D. SUCHITRA[1]*, CH. PRASHANTI[2], M. SUKANYA[3], K. SHRAVAN KUMAR[4]

[1] Assistant professor, Department of Pharmaceutical Analysis and Quality Assurance, Vision college of Pharmaceutical Sciences and Research, Boduppal, Hyderabad.

[2,3] Assistant professor, Department of Pharmaceutical Chemistry, Vision college of Pharmaceutical Sciences and Research, Boduppal, Hyderabad.

[4]Professor, Department of pharmaceutics, Vision College of Pharmaceutical Sciences and Research, Boduppal, Hyderabad.

Corresponding Author: Dr. D. Suchitra ***suchirakhi@gmail.com**

ABSTRACT

Objective: The main objective of the Stability-indicating method is to monitor results during stability studies to guarantee quality, safety, and efficacy. Thus, the present study is mainly focused on developing a simple, accurate, rapid, and economic stability-indicating assay method for the determination of the Lenvatinib drug by the RP-HPLC method.

Methods: The optimization and separation of degradation products were carried on a Waters HPLC instrument equipped with empower 2 software for data processing and integration. The selected drug was separated on the Inertsil ODS C18 column with configurations of 250mm × 4.6mm, 5µm particle size, and mobile phase composition of phosphate buffer [pH 3.8, adjusted with OPA] and Acetonitrile in 55:45v/v ratio. The detection was carried out at 257nm by maintaining the mobile phase flow rate at 1.0ml/min.

Results: The drug was eluted at 3.388min with all the efficiency parameters meeting the acceptance criteria. The developed method was validated as per ICH guidelines and showed a good linear relationship between analyte response and concentration over a concentration range of 6-14µg/ml with 0.999 coefficient and all other validation parameters gave satisfactory results and are in compliance with the specifications. Stress testing was done by exposing the Lenvatinib drug to extreme conditions of Acid, alkali, oxidative, thermal, and photolytic degradation, and the results proved the stability-indicating power of the developed method by successfully separating the degradation products from the parent component.

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Conclusion: A simple, accurate, rapid, and economic stability-indicating assay method for the determination of Lenvatinib drug by RP-HPLC method was successfully developed and proved as appropriate for the analysis by validation. It can be successfully applied for the quantitation, separation of degradation products, an assay of the pharmaceutical dosage form of Lenvatinib drug for regular laboratory analysis.

Key Words: Reverse-phased high performance liquid chromatography, method development, method validation and Stability-indicating assay method.

INTRODUCTION

Lenvatinib mesylate chemically named as 4- [3-chloro-4-(cyclopropyl carbamoyl amino) phenoxy]-7-methoxy quinoline-6-carboxamide methanesulfonate [1], was approved by US FDA on February 13, 2015, for treating Differentiated Thyroid Cancer and approved for the treatment of patients with Advanced Renal Cell Carcinoma in combination with everolimus drug on May 13, 2016 [2]. In 2018, it has been approved in Germany for the treatment of advanced hepatocellular carcinoma in adults who have not received any systemic treatment [3]. Lenvatinib is a white powder (white, non-hygroscopic, crystalline powder), available in 4mg and 10mg capsules. It is soluble in DMSO, Acetonitrile, sparingly soluble in acetic acid, slightly soluble in water, N, N-dimethylformamide, methanol, N-methyl pyrrolidone, and pyridine, and practically insoluble in ethanol (dehydrated).

Lenvatinib is a multikinase inhibitor used for the treatment of various types of thyroid cancer which previously could not be treated with radioactive iodine and is progressing. It acts as a vascular endothelial growth factor receptor (VEGFR2) antagonist and also as a fibroblast growth factor receptor antagonist (FGFR). Lenvatinib blocks the activation of VEGFR2 and inhibits the vascular endothelial growth factor receptor signal transduction pathway, decreases vascular endothelial cell migration and proliferation, and causes vascular endothelial cell apoptosis [1].

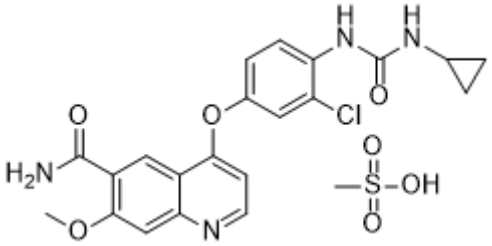

Fig. 1. Chemical structure of Lenvatinib Mesylate

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Upon storage any drug substances or drug products undergoes degradation. Changes in drug stability can risk patient safety by the formation of degradants. Instability of the drug product may cause loss or increase in the concentration of an active pharmaceutical ingredient, alteration in bioavailability, loss of content uniformity, or loss of package integrity. Therefore, it becomes necessary to know the purity profile under various experimental conditions. Thus, FDA recommends that all the assay procedures for stability should be stability-indicating. As indicated by ICH guidelines, stress testing must be done to investigate the degradation products which can further help in establishing the degradation pathways, retest period for the drug substance or shelf life for the drug products, recommended storage conditions, and developing and validating suitable stability-indicating analytical procedures [4].

From the extensive literature survey, it was observed that many researchers reported methods like RP-HPLC [5-7], Stability indicating UPLC [8,9], Bio-analytical method [10], LC-MS/MS [11] for individual and few combinations of Lenvatinib drug with Dasatinib [12-14]. According to current good manufacturing practices, all drugs must be tested with a stability-indicating assay method before release. To date there are no simple RP-HPLC stability-indicating assay methods for the determination of Lenvatinib drug is available in the literature. Therefore, it felt necessary to develop a new method for routine quality control analysis of the Lenvatinib drug.

MATERIALS AND METHODS

Materials: The standard drug Lenvatinib was a gift sample obtained from Dr. Reddy's Laboratories, Hyderabad, and the formulation Lenvima 10mg capsules manufactured by Eisai Pharmaceuticals Pvt Ltd., collected from a local market. The chemicals Acetonitrile [Merck], Methanol [Merck], and Water used for dissolution and mobile preparation were of HPLC grade.

Instrument used:

The present work was carried on a Waters HPLC [Alliance 2695 separation module] instrument which is equipped with Empower 2 software for data processing. The optimization and separation of the degradants were achieved on Inertsil ODS C18 analytical column. The eluate was detected at 257nm using 996 Photo-diode array detectors. Dissolution and degassing of the prepared solutions were achieved on an Enertech digital ultra sonicator. The pH of the buffer solution was adjusted using a Lab India pH meter.

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Methods

Preparation of standard and working standard solutions: About 10mg of Lenvatinib standard drug was weighed and transferred into a 10ml volumetric flask. Added 7ml of diluent, sonicated for about 15min to enhance dissolution and to remove air bubbles. Later, made up to the mark to 10ml to obtain 1000µg/ml and filtered the solution through a 0.45µ membrane filter by vacuum filtration.

From this pipetted out 0.1ml Lenvatinib standard solution, transferred to 10ml volumetric flask and made up to final volume with diluent to obtain 10µg/ml concentration.

Preparation of Potassium dihydrogen Phosphate Buffer (0.02M-pH-3.8):

Weighed accurately about 2.72172g and transferred to 1000ml volumetric flask containing water and degassed in digital ultra-sonicator for 15minutes and then filtered through 0.45 µ filter under vacuum filter. Finally adjusted the pH to 3.8 with diluted ortho phosphoric acid solution.

Preparation of Mobile phase: An accurately measured 55ml of phosphate buffer of 0.02M strength whose pH was adjusted to 3.8 using dilute orthophosphoric acid and 45ml of Acetonitrile were mixed in a 100ml volumetric flask. Sonicated for about 15min for enhancing dissolution and to remove air bubbles and filtered through 0.45µ membrane filter by vacuum filtration.

Preparation of sample solution: Emptied 10 Lenvima (10mg) capsules into a mortar and crushed into powder using a pestle. Taken an accurately weighed powder equivalent to 10mg into 10ml volumetric flask and diluted with mobile phase up to the mark. Sonicated for about 15 min to degas and enhance the dissolution and filtered through 0.45µ membrane filter by vacuum filtration. From this, pipetted out 0.1 ml of sample solution into 10 ml volumetric flask and made up to final volume to obtain 10µg/ml. Injected the standard and sample solutions into the HPLC system in triplicates and calculated the %Assay.

Method development

For optimization of the present method, several trials were done on different columns using mobile phases of various compositions by regulating the flow rate at 1.0ml/min at 257nm UV detection. Injected the working standard solution of Lenvatinib into the HPLC system,

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recorded the optimized chromatogram showing all the efficiency parameters meeting the specification limits, and proceeded for method validation.

Chromatographic conditions

The quantitative determination and separation of the degradants were achieved on a Waters HPLC [Alliance 2695 separation module] instrument. Total analysis of data was obtained from Empower 2 software. The method was optimized on the Inertsil ODS C18 column using mobile phase composition of Phosphate buffer (pH 3.8, adjusted by adding dilute orthophosphoric aid) and Acetonitrile in the ratio 55:45v/v respectively. The mobile phase was degassed, filtered, and pumped through the analytical column at a flow rate of 1.0ml/min. The eluate showed a retention time of 3.388min which was detected at 257nm by the PDA detector.

Method validation

To assure that the developed analytical method will meet the predetermined specifications and quality characteristics, the method was validated according to the ICH guidelines, using different analytical parameters like Linearity, accuracy, precision, specificity, LOD, LOQ, and robustness [15,16].

(a) System suitability

Before validating the developed method, a system suitability study was done to ensure that the HPLC system, reagents, chemicals, and column used are capable to give accurate and precise results. This was established by injecting the 10µg/ml concentration standard solution of Lenvatinib six times and recorded the chromatograms. Noted the data of all the efficiency parameters and the %RSD was calculated for all the areas of six replicate injections.

(b) Linearity

In the present study, the linearity of the method was studied by injecting the five concentration standard solutions of Lenvatinib over a concentration range of 6-14µg/ml. A calibration graph was plotted between analyte concentration on X-axis and analyte response on Y-axis. Through linear regression analysis, the parameters such as slope, intercept and correlation coefficient are reported.

(c) Precision

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In this study, the validation of the precision was performed at two different levels.

i) Intra-day assay precision: The intra-day assay precision was evaluated by assaying six replicate injections at 100% of the standard concentration(10µg/ml), during the same day, over a short time interval, under the same experimental conditions. Recoded the chromatograms and calculated the mean, standard deviation, and %Relative standard deviation.

ii) Inter-day variation: The inter-day variation was demonstrated by assaying six replicate injections at 100% of the standard concentration(10µg/ml), on different days under the same experimental conditions. From the areas obtained in the chromatograms, the mean, standard deviation, and % Relative standard deviation were calculated.

(d) Accuracy

In the present study, the accuracy was assessed by the recovery of the spiked analytes. The pre-analyzed sample solution of 10µgm/ml was added to the known quantity of standard solutions of Lenvatinib at 3 concentration levels of 5µg/ml, 10µg/ml, and 15µg/ml. The prepared solutions were injected in triplicate into the HPLC system, recorded the chromatograms. Calculated the %RSD values and percent recoveries of the areas from the amount added and amount found values.

(e) LOD and LOQ

The detection limit and quantitation limit were measured by using the standard deviation of y-intercept and slope of regression lines.

LOD = 3.3 × Standard deviation of y-intercept / Slope

LOQ = 10 × Standard deviation of y-intercept / Slope

(f) Robustness

To examine the effect of operational parameters on the analysis results, in the present study, a deliberate change was made in the flow rate conditions and percent organic composition

(i) Variation of flow conditions:

The sample was analyzed at 0.9ml/min and 1.1ml/min instead of the optimized flow rate condition of 1.0ml/min, by keeping the remaining conditions unchanged. Injected 20µl of

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standard Lenvatinib solution into the HPLC system, recorded the chromatograms, and compared the efficiency parameters with the optimized chromatogram.

(ii) Variation of mobile phase organic composition:

The sample was analyzed by pumping the mobile phase composition of phosphate buffer: Acetonitrile in the ratio of 60:40% and 50:50% rather than 55:45% v/v. Injected 20µl of standard Lenvatinib solution into the HPLC system under unchanged other operating conditions. Recorded the chromatograms and compared the efficiency parameters with the optimized chromatogram.

(g) Application of the developed method for assay determination of Lenvatinib formulation

Injected the prepared Lenvatinib standard and sample (Lenvima) solutions into the HPLC system in five replicate injections, noted the chromatograms, measured the areas, and calculated the %Assay by using the formula-

$$\%ASSAY = \frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Weight of standard}}{\text{Dilution of standard}} \times \frac{\text{Dilution of sample}}{\text{Weight of sample}} \times \frac{\text{Purity}}{100} \times \frac{\text{Weight of tablet}}{\text{Label claim}} \times 100$$

Stress testing studies

FDA recommends that all the assay procedures for stability should be stability-indicating. Before performing stability studies, a stability-indicating method is necessary to determine the possible degradants generated during storage conditions so that they can be separated, identified, and detected for assuring the quality, safety, and efficacy of the drugs. According to the ICH guidelines, the stress testing studies are performed by exposing the drug to severe conditions than those used for Accelerated stability testing. The samples generated from forced degradation can be used to develop the stability-indicating method which can be applied later for the analysis of samples generated from accelerated and long-term stability studies.

In the present investigation, stress testing was performed by exposing the drug to severe conditions of Acid, alkali, peroxide, thermal, and photolysis. Later these stressed samples

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were analyzed by injecting the samples into the HPLC system after suitable dilution. Finally calculated the percent degraded amount and percent active amount to assess the peak purity of the Lenvatinib drug.

(i) Acid Degradation: To investigate the acid hydrolysis of the Lenvatinib drug, 1000µg/ml standard solution was mixed with 1ml of 2N HCl and refluxed at 60℃ for 30 min. Later, neutralized the generated samples with 1ml of 2N NaOH and diluted with mobile phase to get 10µg/ml concentration. Cooled the solution and filtered through 0.45µ membrane filter by vacuum filtration. Injected the sample into the HPLC system, recorded the chromatogram to check for the degradation.

(ii) Alkali degradation: Standard solution (1000µg/ml) was mixed with 1ml of 2N NaOH and refluxed at 60℃ for 30min. Neutralized the obtained sample with 1ml 2N HCl and diluted with mobile phase to obtain 10µg/ml concentration. Cooled and filtered the solution using a 0.45µ membrane filter by vacuum filtration. Injected the sample into the HPLC system, recorded the chromatogram to check for the alkali degradation.

(iii) Oxidation: To the standard solution of Lenvatinib(1000µg/ml), 1 ml of 20% hydrogen peroxide was added and kept aside for 30 min at 60ºC. The resultant solution was diluted with a mobile phase to obtain 10µg/ml solution. Cooled and filtered the solution with a 0.45µm membrane filter. Injected into the HPLC system, and recorded the chromatogram to assess the stability of the drug.

(iv) Thermal Degradation: The Lenvatinib drug solution(1000µg/ml) was placed in an oven at 60ºC for 6h. The resultant solution was diluted to obtain 10µg/mL solution. Cooled the solution and filtered through a 0.45µm membrane filter. Injected into the HPLC system, and the chromatograms were recorded for the assessment of sample stability.

(v) Photolysis: For the photolytic study, the standard solution of Lenvatinib(1000µg/ml) was exposed to UV light for 1 day in a photostability chamber. The resultant solution was diluted to obtain 10µg/mL solution and filtered with a 0.45µm membrane filter. Injected the sample into the HPLC system, and observed the chromatograms for the stability assessment.

Results and discussions

Method development

For creating a new procedure for the quantification and separation of degradation products of Lenvatinib drug in bulk and pharmaceutical dosage form, attempts were made by using two

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different analytical columns such as Phenomenex Luna ODS C18 and Inertsil ODS C18 with column configurations of 250mm×4.6mm, 5µm particles size. At last, the Inertsil ODS C18 column was found to produce satisfactory results. Various mobile phase compositions with varying proportions of organic phase at different pH of buffer adjusted with dilute orthophosphoric acid were tested by maintaining the constant flow rate of 1.0ml/min at 257nm UV detection. Ultimately, the Phosphate buffer of pH – 3.3 adjusted with dilute orthophosphoric acid: Acetonitrile (60:40v/v) was found to give satisfactory results. To assure that the developed method is suitable for use, further proceeded for method validation as per ICH guidelines. The optimized chromatogram of the Lenvatinib drug was given in Figure 2 and the data of all the efficiency parameters were summarized in Table 1.

Analytical Method validation:

a) System suitability: The efficiency parameters such as retention time, peak asymmetry, and theoretical plates obtained for the six replicate injections were found to meet the acceptable limits. The calculated %RSD was found to be 0.3 indicating the suitability of the instrument, chemicals, and all the reagents used for the optimization of the method and can generate precise and accurate results. The observed data were summarized in Table 2.

(b) Linearity: The regression equation obtained upon plotting a calibration curve over a concentration range of 6 to 14µg/ml was y = 13586x + 2288.1. The obtained correlation coefficient(r^2 = 0.999) demonstrates the excellent relationship between the analyte concentration and analyte response. The obtained linearity data and the plotted calibration curve were presented in Table 3 and Figure 3 respectively.

(c) Precision

Inter-day variation: The calculated Mean, Standard Deviation, and %RSD values were presented in Table 4. The obtained %RSD value for the six replicative injections was less than 1.0% which confirmed the method's Precision.

Intermediate Precision: The calculated Mean, Standard deviation, and %RSD values of day 1 and day 2 were presented in Tables 5 and 6. The obtained %RSD values on two different days were observed to be less than 1% which illustrated the good precision of the analytical method.

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(d) Accuracy: The mean recovery values obtained for the three specification levels at 50%, 100%, and 150% were found to be 99.810% meeting the validation criteria proved the method's accuracy. The calculated results were summarized in Table 7.

(e) Limit of Detection and Limit of Quantitation: Calculated the LOD and LOQ using the standard deviation of intercept and slope of the calibration curve. The LOD was found to be 0.993µg/ml and LOQ was 3.008µg/ml. Thus, confirmed the sensitivity of the present developed method.

(f) Robustness

From the chromatographic data, it was observed that there is no significant change in the efficiency parameters like peak asymmetry and theoretical plates even upon varying the flow rate conditions of ±0.1ml/min and the organic mobile phase ratio of ±5%. Thus, the developed method was found robust. The results are summarized in Table 8.

(g) Assay of Marketed dosage form (Lenvima): Lenvima 10mg capsules were selected for the application of the developed method. The calculated %Assay in Lenvima 10mg capsules was 99.732% and is within the specification limits. Thus, confirmed that the developed method can be successfully applied for the Lenvatinib pharmaceutical dosage forms. The data of pure drug and formulation are summarized in Tables 9 and 10 respectively.

Forced Degradation studies: The Lenvatinib drug has undergone degradation in all the applied stress conditions. The Lenvatinib drug was found to be labile to acidic and alkaline conditions showing the highest degradation of about 23.04%and 14.48% respectively. It also showed significant degradation under oxidative, thermal, and photolytic conditions showing %degraded amount of about 8.27%, 6.53%, and 7.48% respectively. However, the generated degradation products are well separated from the parent component without any interference. This proved the method's specificity and stability-indicating nature of the developed novel RP-HPLC analytical method and can be adequately applied for the separation of the degradation products. The %degraded amount under all the stress conditions is tabulated in Table 10.

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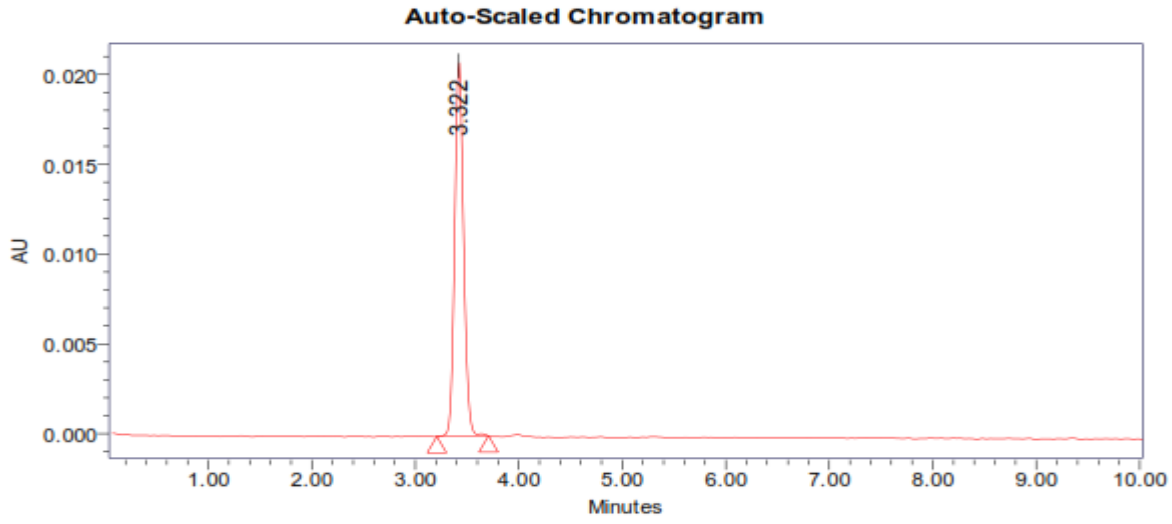

Figure 2: Optimized chromatogram of Lenvatinib Standard drug

Table 1: Results of Optimized Chromatogram of Lenvatinib Standard

Drug	Rt	Peak Area	Peak Height	Peak Asymmetry	Theoretical plates
Lenvatinib	3.322	145867	32546	1.76	8457

Table 2: System suitability data of Lenvatinib

Drug	S. No.	Retention time(min)	Analyte response	Theoretical plates(N)	Peak Asymmetry
Lenvatinib	1	3.398	145965	8475	1.78
	2	3.324	146857	8495	1.79
	3	3.349	145985	8492	1.80
	4	3.322	145689	8569	1.80
	5	3.388	146697	8463	1.76
	6	3.364	145982	8458	1.80

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	***Mean (n=6)**		146195.8		
	±SD (n=6)		466.6152		
	% RSD (n=6)		0.319171		

*Mean of five determinations, SD: Standard Deviation, RSD: Relative Standard Deviation

Table 3: Chromatographic Data for Linearity Study

Concentration µg/ml	**Average Peak Area**
6	85784
8	112564
10	139867
12	165248
14	189586

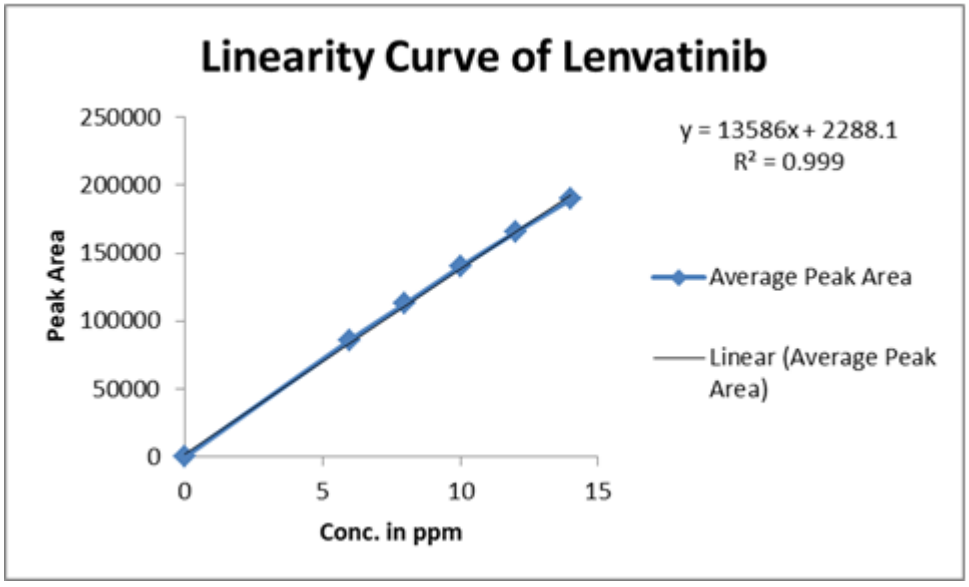

Figure 3: Calibration Curve of Lenvatinib

Table 4: Intra-day variation data of Lenvatinib

Drug	**Injection**	**Retention Time (min)**	**Peak Area**	**No. of Theoretical Plates**	**Peak Asymmetry**

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Lenvatinib	1	3.397	145865	8547	1.78
	2	3.390	145874	8498	1.78
	3	3.384	145842	8547	1.77
	4	3.378	145869	8572	1.77
	5	3.349	145698	8629	1.75
	6	3.364	145265	8569	1.78
	***Mean (n=6)**		145735.5		
	±SD (n=6)		239.9556		
	%RSD (n=6)		0.164651		

*Mean of six determinations, SD: Standard Deviation, %RSD: Relative Standard Deviation

Table 5: Day 1 results of intermediate precision for Lenvatinib

Drug	Injection	Retention Time (min)	Peak Area	No. of Theoretical plates	Peak Asymmetry
Lenvatinib	1	3.371	147856	8569	1.79
	2	3.376	147584	8574	1.79
	3	3.382	147965	8654	1.78
	4	3.359	147523	8542	1.79
	5	3.333	147854	8571	1.78
	6	3.341	147856	8534	1.79
	***Mean (n=6)**		147773		
	±SD (n=6)		176.3088		
	%RSD (n=6)		0.12		

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*Mean of six determinations, SD: Standard Deviation, %RSD: Relative Standard Deviation

Table 6: Day 2 results of intermediate precision for Lenvatinib

Drug	S. No.	Retention Time(min)	Peak Area	No. of Theoretical plates	Peak Asymmetry
Lenvatinib	1	3.310	146589	8569	1.79
	2	3.388	146985	8574	1.78
	3	3.378	146857	8564	1.79
	4	3.333	146524	8574	1.79
	5	3.341	146982	8569	1.78
	6	3.396	146856	8547	1.79
	Mean(n=6)		146798.8		
	Standard Deviation(n=6)		197.192		
	% RSD(n=6)		0.373433		

*Mean of six determinations, SD: Standard Deviation, %RSD: Relative Standard Deviation

Table 7: Lenvatinib Accuracy data

Drug	Spiking level	Peak Area	*Average Area (n=3)	*Known Amount (ppm)	*Amount obtained (ppm)	*Percentage Recovery (n=3)	Average Recovery (n=9)
Lenvatinib	50%	69986	70031.67	5	4.986	99.720%	99.810%
		69985					
		70124					
	100%	138265	138413.33	10	10.019	100.190%	
		138521					
		138454					
	150%	205859	205138	15	14.930	99.533%	
		204658					
		204897					

*Mean of three determinations

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Table 8: Results of Robustness study

Parameter used for sample analysis	Peak Area	Retention Time(min)	Theoretical plates	Tailing factor
Optimized Flow rate of 1.0 mL/min	145867	3.388	8457	1.76
At 0.9 mL/min	146854	3.595	8152	1.74
At 1.1 mL/min	135262	3.122	7985	1.73
More organic phase (about 5 % Increase in Acetonitrile)	143652	3.119	8142	1.72
Less organic phase (about 5 % decrease in Acetonitrile)	142546	3.545	7985	1.75

Table 9: Peak results for assay standard

Drug	Injection	Retention Time	Analyte Response	Theoretical plates	Peak asymmetry
Lenvatinib standard	1	3.379	145857	8546	1.76
	2	3.303	145874	8574	1.77
	3	3.322	145685	8759	1.76
	4	3.327	145876	8598	1.76
	5	3.310	145682	8564	1.77
	***Mean(n=5)**		145794.8		
	Standard Deviation(n=5)		101.8759		
	% RSD(n=5)		0.069876		

*Mean of five determinations, %RSD: Relative Standard Deviation

Table 10: Peak results for Assay sample

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Drug	Injection	Retention Time(min)	Analyte Response	Peak Asymmetry	Theoretical plates
Lenvatinib sample	1	3.310	146425	1.78	8457
	2	3.388	146874	1.77	8495
	3	3.398	146524	1.78	8475
	4	3.349	146895	1.76	8496
	5	3.364	146857	1.79	8468
	***Mean(n=5)**		146715		
	Standard Deviation(n=5)		222.7252		
	% RSD(n=5)		0.151808		

*Mean of five determinations, %RSD: Relative Standard Deviation

Table 11: Results of Stress testing Studies for Lenvatinib

S. No.	Stress Condition	Peak Area	% of Degraded Amount	% of Active Amount	Total % of Amount
1	Standard	145867.00	0	100%	100%
2	Acidic	112259.24	23.04	76.96	100%
3	Basic	124687.11	14.48	85.48	100%
4	Oxidative	133803.79	8.27	91.73	100%
5	Thermal	136341.88	6.53	93.47	100%
6	Photolytic	134956.14	7.48	92.52	100%

CONCLUSION

The present created method is considered as novel as this is the first stability indicating RP-HPLC method for the quantification of Lenvatinib drug. The lesser analysis time of elution at 3.322min proved the rapidity and the calculated LOD and LOQ values of 0.99µg/ml and

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3.008µg/ml confirmed that the developed method is highly sensitive. The successful separation of all the generated degradants from the active component of the Lenvatinib drug without any interference confirmed the stability-indicating nature of the developed method. The checked validation parameters produced satisfactory results with great accuracy and precision and all other parameters meeting its specification limits assured that the developed method is appropriate for the analysis of Lenvatinib drug. Thus, it can be routinely employed in the pharmaceutical industries for the quantification of Lenvatinib drugs in bulk and pharmaceutical dosage forms.

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