SHORT COMMUNICATIONS

SPECTROPHOTOMETRIC DETERMINATION OF ANTINEOPLASTIC DRUG GEFITINIB IN TABLET DOSAGE FORM USING INORGANIC SOLVENT

ABSTRACT

In the present research work, a simple, accurate and precise spectrophotometric method has been developed for the determination of gefitinib in bulk and its tablets dosage form. Gefitinib was dissolved in 0.1 N hydrochloric acid and absorbance was measured at 252.0 nm. The calibration curve obeyed Beer's law in the concentration range of 3-15 µg mL^{-1} with correlation co-efficient of 0.9989. The detection limits and quantitation limits were found to be 0.69 µg mL^{-1} and 2.08 µg mL^{-1}, respectively. The recovery ranged between 98.00 and 101.89 %. The validation parameters such as accuracy, precision, linearity, limit of detection and limit of quantitation of developed method were validated according to international conference on harmonization (ICH) Q2-R1 guidelines and successfully analyzed gefitinib from tablet dosage form.

Keywords: Spectrophotometric method, gefitinib, tablet formulation, ICH guidelines, Analytical method validation

INTRODUCTION

Gefitinib is chemically *N*-(3-chloro-4-fluoro-phenyl)-7-methoxy-6-(3-morpholin-4-yl propoxy) quinazolin-4-amine. The mass of gefitinib is 446.90 Dalton, and its empirical formula is $C_{22}H_{24}ClFN_4O_3$. It is used for the treatment of lung cancer in patients who have been treated with chemotherapy in past. Gefitinib is the selective inhibitor of tyrosine kinase[1-2]. It is official in the Indian Pharmacopoeia 2018 and is assayed by liquid chromatographic method[3]. Literature survey reveals few analytical methods[4-7] for the determination of gefitinib alone as well as in combinations. The aim of current investigation was to develop precise and accurate ultraviolet spectrophotometric method for the quantitation of gefitinib tablets using inorganic solvent.

MATERIALS AND METHODS

Gefitinib was procured as a gift sample for Neon Laboratories Ltd., Mumbai, India and gefitinib tablets were procured from a local pharmacy. Hydrochloric acid analytical grade was purchased from S. D. Fine Chemicals, Mumbai, India. The analysis of samples was carried out on UV-Visible spectrophotometer (1800, Shimadzu Corporation, Japan). An electronic balance (AX200, Shimadzu, Ltd., Japan) and ultrasonic bath (LeelaSonic- 150, Leela Electronics, India) was used in the research work. Calibrated glassware was used in the research work.

Preparation of stock and working standard solutions

10 mg of gefitinib was accurately weighed and transferred into a 100 mL volumetric flask. The drug was dissolved in sufficient amount of 0.1 N HCl and finally diluted up to 100 mL with the same solvent to obtain a final concentration of 1000 µg mL^{-1} (stock solution). An appropriately diluted stock solution gave 100 µg mL^{-1} of working standard solution.

Method validation

The developed method was validated in accordance with ICH Q2 (R1) guideline[8]. Linearity was assessed by constructing a calibration curve over the range 3 – 15 µg mL^{-1} of gefitinib. Calibration curves were developed by plotting absorbance vs. concentration (n=3) and correlation coefficient and regression equation were calculated. The recovery experiment was performed by spiking standard solutions of gefitinib (4, 5, 6 µg mL^{-1}) into previously analysed sample of 5 µg mL^{-1} at the level of 80, 100 and 120 %. In the precision, repeatability of the method was confirmed by measuring the absorbance of 10 µg mL^{-1} solution of gefitinib at 252.0 nm for six times and % RSD was calculated. Intraday precision was carried out by determining three different concentrations of gefitinib (3, 10, 15 µg mL^{-1}) for three times on a same day and interday precision was checked by determining the same concentrations for three times on three consecutive days and % RSD was calculated. Detection limits (LOD) and quantitation limits (LOQ) were calculated in accordance to the equation given in ICH Q2 (R1) guideline. Specificity of gefitinib was determined by using synthetic mixture having

Table I: Validation parameters

Parameter	Results
Detection wavelength (nm)	252.0
Regression equation	y = 0.067 x + 0.009
Beer's law limits (µg mL^{-1})	3 - 15
Limit of detection (µg mL^{-1})	0.69
Limit of quantification (µg mL^{-1})	2.08
Precision (% RSD)	
• Repeatability	0.6776
• Intraday	0.14 - 1.66
• Inter-day	0.25 – 1.84
Accuracy (% Recovery)	98.00-101.89
Robustness	Robust
Specificity	Specific

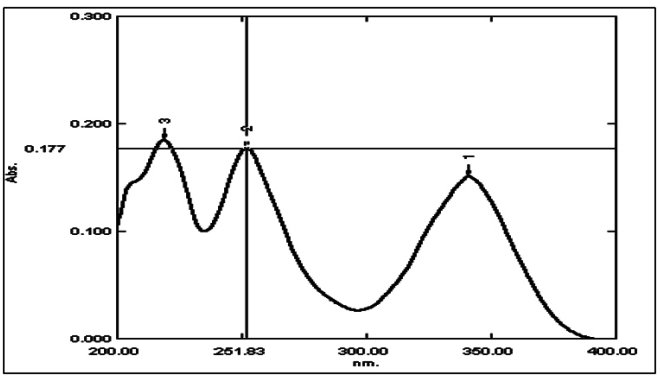

Fig. 1: Ultraviolet spectrum of gefitinib (3 µg mL^{-1}) in 0.1N HCl

standard gefitinib drug and commonly used excipients in the manufacturing of tablet formulation. Robustness was performed by making small deliberate changes in two internal factors - detection wavelength and solvent compositions, and results were examined. The % RSD was calculated for changes in each condition. Solution stability studies were carried out at room temperature. The absorbances of the solutions kept under the room temperature were measured periodically and compared with initial solution. The significant variation was observed after six hours at room temperature.

Assay of marketed formulation

Accurately weighed and powdered 20 tablets of gefitinib (labelled claim: 250 mg) was prepared. The quantity of tablet powder equivalent to 100 mg of gefitinib was weighed on an electronic balance and transferred into a 100 mL volumetric flask containing 50 mL 0.1 N HCl, the flask was shake for 15 min to dissolved the drug completely and diluted up to the mark with 0.1 N HCl. The resultant solution was mixed and filtered through Whatman filter paper No. 1. An aliquot of 1.0 mL from the resultant solution was transferred to 100 mL volumetric flask and diluted with 0.1 N HCl to obtain 100 µg mL^{-1} concentration. The absorbance of the resultant solution was measured at 252.0 nm using an appropriate blank. The concentration of sample solution was calculated from the calibration curve of gefitinib.

RESULTS AND DISCUSSION

The standard solution of gefitinib (3 µg mL^{-1}) was prepared in 0.1 N HCl and was scanned in the range of 200 to 400 nm against 0.1 N HCl as solvent blank. The analytical wavelength for the measurement of gefitinib was selected at 252.0 nm. The zero order ultraviolet spectrum of gefitinib is shown in Fig. 1. Linearity of the developed method was found to be 3 – 15 µg mL^{-1}, with satisfactory value of correlation coefficient (r^2) of 0.9986. Accuracy of method was determined by performing recovery studies and was in the range of 98.00 – 101.89 %, indicating that the method is accurate. The precision data for the method was found within the limits, indicating that the method is precise. Detection limit and quantitation limit values were found to be 0.69 µg mL^{-1} and 2.08 µg mL^{-1}, which indicates that the method is sensitive and specific. The % RSD was found within the limits for robustness study which indicates that the method is robust. The percent contents of gefitinib was found to be 99.68 % which indicates that the drug product was in accordance with the labeled claims. Results of validation parameters are summarized in Table I.

CONCLUSION

The results of validation parameters and drug contents indicate that the developed method is reproducible, accurate, and precise. Hence, the proposed spectrophotometric method can be regularly used for the determination of gefitinib tablets without interference of excipients in the quality control laboratory.

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Shailesh K. Koradia[a]*, Dhwani R. Patel[b], Prachi A. Rana[b], Binny A. Rudani[b] and Unnati S. Chaudhari[b]

[a] Department of Pharmaceutical Quality Assurance, Krishna School of Pharmacy & Research, Drs. Kiran & Pallavi Patel Global University, Krishna Edu Campus, Vadodara – Mumbai National Highway # 8, Varnama, Vadodara- 391 243, Gujarat, India

[b] Department of Pharmaceutical Quality Assurance, Babaria Institute of Pharmacy, BITS Edu Campus, Vadodara – Mumbai National Highway # 8, Varnama, Vadodara- 391 243, Gujarat, India

***For Correspondence: E-mail: shaileshkoradia.ksp@kpgu.ac.in**

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