Scholars Academic Journal of Pharmacy
Abbreviated Key Title: Sch Acad J Pharm
ISSN 2347-9531 (Print) | ISSN 2320-4206 (Online)
Journal homepage: http://saspublisher.com/sajp/

OPEN ACCESS

Pharmacognosy

Analytical Characterization of Vandetanib Bulk drug by FTIR Spectroscopy

Balu S. Khandare*, Atish C. Musle, Sanket S. Arole, and Pravin V. Popalghat

Pharmaceutical Analysis Department of Kasturi Shikshan Sanstha College of Pharmacy, Shikrapur Pune, Maharashtra, India

DOI: 10.36347/SAJP.2019.v08i10.001 | **Received:** 11.10.2019 | **Accepted:** 18.10.2019 | **Published:** 21.10.2019

***Corresponding author:** Balu S. Khandare

Abstract **Original Research Article**

A simple, precise, accurate, sensitive and economic spectroscopic method has been developed for estimation of Vandetanib from bulk by least square treatment of Fourier transform infrared spectrometric method with help of data obtained at wave number corresponding to C-F group at 1211.10cm^{-} , aromatic C=C at 1499.76 cm^{-1}, C-H alkane at 2905.45 cm^{-1}, CH2 bend at 1415.56 cm , alkenes out of plane bend at 991.28 cm^{-1}, aromatics out of plane bend at 842.14cm^{-1}, C=C Alkene at 1617.78 cm^{-1} , C-O at 1145.57 cm^{-1} , N-H stretch at 1574.19 cm^{-1}, C-N amines 1332.42 cm^{-1}, C-Br at 772.18 cm^{-1}.In order to validate method Linearity, Accuracy and precision studies were carried out and result were satisfactory obtained. The drug at each of the 80 %, 100 % and 120 % levels showed good recoveries that is in the range of 97.00 to 99.00% for the method, hence it could be said that the method was accurate. Limit of detection (LOD) and limit of quantitation (LOQ) were determined for the method. The method was validated by the International Conference on Harmonization. All validation parameters were within the acceptable limit. The developed method was successfully applied to estimate the amount of vandetanib in pharmaceutical formulation.

Keywords: Vandetanib, FTIR, validation, Assay, Precision, % Recovery.

INTRODUCTION

Vandetanib(N(4-bromo-2-fluorophenyl))6-methoxy-7[(1-methyl-4-piperidinyl)methoxy]4-quinazolinamine) is a recently identified protein kinase inhibitor, which shows antitumor efficacy by inhibiting tumor cell proliferation and survival via epidermal growth factor receptor (EGFR) and RET inhibition, as well as inhibiting tumor angiogenesis via vascular EGFR-2 (VEGFR-2) inhibition [1, 2]. Its preclinical and clinical activity against several tumor types including advanced and metastatic papillary thyroid cancer, non small cell lung cancer (NSCLC), and advanced colorectal cancer (CRC) either in monotherapy or in combination with other anticancer agent as first or second line therapy has been demonstrated [3].

In the present study, we developed a novel analytical method and validations of Fourier transform infrared spectroscopy for determination of Vandetanib in bulk.

A few spectrophotometric, RP-HPLC methods are reported to estimate the Vandetanib in combination with other drugs are revealed as per the literature survey [4].

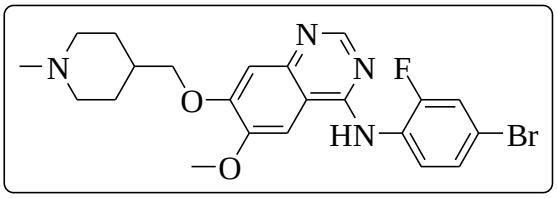

Fig-1: Chemical Structure of Vandetanib

The Vandetanib was kindly supplied as a gift sample by Mylan laboratories pvt. Ltd., Hyderabad (India). All rest of chemicals used were of HPLC grade, double distilled water used throughout. Standard volumetric glassware's were used for performing all the dilutions. A citizen analytical balance (Sartorius) was used for weighing the bulk.

FTIR analysis was performed in FTIR spectrometer Bruker Alpha II by using circular KBr pellet as well as nujol mull technique using Opus 7.5 [14-18].

Standard solution of Vandetanib was prepared by transferring accurately weighed 10 mg of drug into a 100ml volumetric flask and the volume was made up to 100ml using methanol as a solvent to get the concentration of 100µg/ml. Various working concentrations were made by further diluting with same medium [6-10].

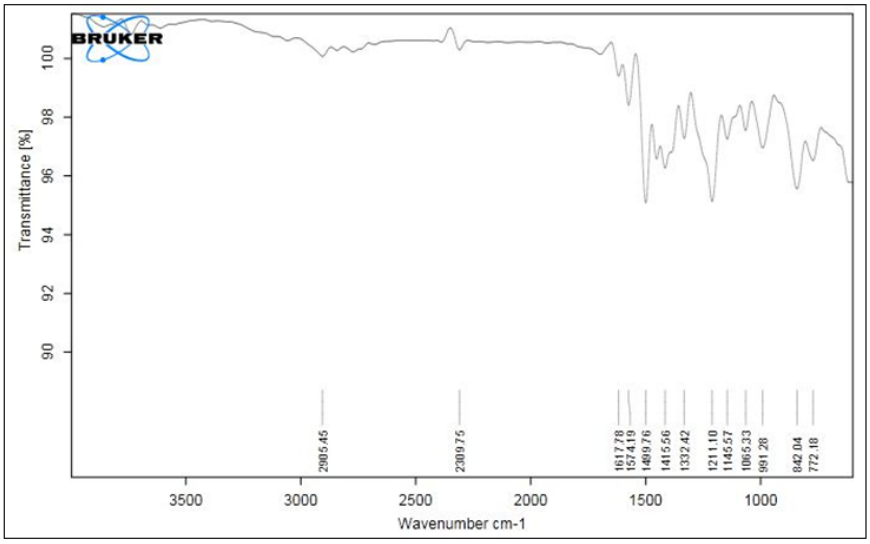

Fig-2: FTIR analysis of Bulk Vandetanib Drug

Table-1: FTIR functional group interpretation of Vandetanib

FUNCTIONAL GROUP	TYPE OF VIBRATION	FREQUENCY (cm^{-1})
C-H	Alkanes (stretch)	2905.45
	-CH2- (bend)	1415.56
	Alkenes (out of plane bend)	991.28
	Aromatics (out of plane bend)	842.04
C=C	Alkene	1617.78
C-O	Ethers	1145.57
N-H	Amines (stretch)	1574.19
C-N	Amines	1332.42
C-F	Fluoride	1211.10
C-BR	Bromide	772.18
C=C	Aromatic	1499.76

The objective of validation of an analytical procedure is to demonstrate whether the procedure is suitable for its intended purpose.

For the selectivity and linearity the Vandetanib was diluted with methanol to obtain final dilutions. The calibration curve for Vandetanib was obtained by plotting the peak area versus concentration.

The LOD is the lowest concentration of an analyte that can be detected by analytical process and the LOQ refers to the smallest concentration which can be quantified with analytical procedure.

The LOD and LOQ can be determined by instrumental and statistical methods.

For the instrumental methods LOD is the lowest amount to be detected by detector and LOQ is the lowest amount to be quantified by detector.

For statistical methods the LOD and LOQ can be determined by using statistical formula LOD=3.3 σ/Slope LOQ= 10σ/Slope where is standard deviation

Accuracy of the analytical method is the closeness of the mean results obtained by the method to the true value of the analyte. It is also termed as trueness.

The accuracy for the analytical procedure was determined at 80%, 100% and 120% levels of standard solution and results were expressed in terms of % recoveries. Three determinations at each level were performed and % RSD was calculated.

Precision of the analytical process is the closeness of the individual measures when the process is applied repeatedly.

The proposed method was validated for various parameters such as Linearity, Accuracy, Precision, Limit of detection (LOD) and Limit of Quantitation (LOQ) according to ICH Q2 (R1) guideline [6].

Fresh aliquots were prepared from the stock solution (100µg/ml) in different concentrations. For the

Table-2: Linearity results of Vandetanib in methanol

Concentration (µg/ml)	Linearity
5	0.214
10	0.424
15	0.614
20	0.837
25	1.037
30	1.231

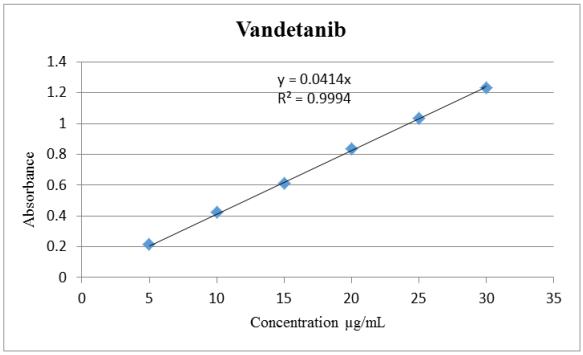

Fig-3: Calibration curve of Vandetanib

The precision of the method was checked by repeatedly injecting (n=6) standard solutions of vandetanib (20 µg/mL). Repeatability (precision) and reproducibility of the experiment are indicated by percentage relative standard deviation (% RSD). Percentage relative standard deviation (% RSD) was calculated for the method (Table-2). The intra-day and inter-day precision of the proposed method was determined by analyzing the corresponding responses 3 times on the same day and on 3 different days over a period of 1 week for 3 different concentrations of standard solutions of vandetanib (10, 15 and 20µg/mL).The results were reported in terms of relative standard deviation (% RSD). The results were tabulated in (Table-2). These experimental results confirmed good precision of the method when performed on the same or different days by different analyst.

Table-3: Result of Precision

Precision	(%RSD)
Repeatability	0.445
Intraday	0.633
Interday	0.885

The accuracy for the analytical procedure was determined at 80%, 100% and 120% levels of standard solution and results were expressed in terms of % recoveries. Three determinations at each level were performed and % RSD was calculated. The results were tabulated in (Table-3).

evaluation of linearity results linear regression analysis based on the minimum square method was used. The obtained value of the correlation coefficient over the range 5-30µg/ml is r^2=0.999

The result shows linear relation between analytical responses and drug concentration.

Table-4: Recovery Study of Vandetanib

Accuracy level	Mean % recovery	%RSD
80%	98.93	0.836
100%	98.06	0.662
120%	97.29	0.498

The LOD and LOQ was determined and the results were tabulated in Table-4.

Table-5: LOD and LOQ of Vandetanib

Method	Method A
LOD	0.3591
LOQ	1.4323

CONCLUSION

From the results and discussion, Fourier transform infrared spectroscopic method were developed and validated as per ICH guidelines Q2 (R1). All the validation parameters performed were found to be satisfactory, therefore the proposed methods can be successfully applied for vandetanib without any interference in quality control.

ACKNOWLEDGEMENTS

The authors are grateful to, the Principal and the Management of Kasturi Shikshan Sanstha's college of Pharmacy Shikrapur Pune. The authors are thankful to Mylan laboratories pvt. Ltd., Hyderabad (India) for providing gift sample.

REFERENCES

1. Darwish HW, Bakheit AH. A new spectrofluorimetric assay method for vandetanib in tablets, plasma and urine. Tropical Journal of Pharmaceutical Research. 2016;15(10):2219-25.
2. Andriamanana I, Gana I, Duretz B, Hulin A. Simultaneous analysis of anticancer agents bortezomib, imatinib, nilotinib, dasatinib, erlotinib, lapatinib, sorafenib, sunitinib and vandetanib in human plasma using LC/MS/MS. Journal of Chromatography B. 2013 May 1;926:83-91.
3. Amer SM, Kadi AA, Darwish HW, Attwa MW. Liquid chromatography tandem mass spectrometry method for the quantification of vandetanib in human plasma and rat liver microsomes matrices:

metabolic stability investigation. Chemistry Central Journal. 2017 Dec;11(1):45.
4. Lin H, Cui D, Cao Z, Bu Q, Xu Y, Zhao Y. Validation of a high-performance liquid chromatographic ultraviolet detection method for the quantification of vandetanib in rat plasma and its application to pharmacokinetic studies. Journal of cancer research and therapeutics. 2014 Jan 1;10(1):84.
5. Hagan A, Phillips GJ, Macfarlane WM, Lloyd AW, Czuczman P, Lewis AL. Preparation and characterisation of vandetanib-eluting radiopaque beads for locoregional treatment of hepatic malignancies. European Journal of Pharmaceutical Sciences, 2017; 101, 22-30.
6. Khandare B, Dudhe PB, Upasani S, Dhoke M. Spectrophotometric Determination of Vandetanib in Bulk by Area Under Curve and First Order Derivative Methods, International Journal of Pharm Tech Research, 2019, 12(2), 103-110.
7. Khandare BS, Bhujbal NS, Kshirsagar SS. Analytical Method Development and Validation of Vandetanib by Using RP-HPLC of Bulk Drug. Scholars Academic Journal of Pharmacy.;8(8):432-435.
8. Upasani MD, Dudhe P, Khandare B. Development and Validation of Adenosine by RP-HPLC Method in Bulk drug and Pharmaceutical dosage forms. Am. J. PharmTech Res. 2019;9(3):240-6.
9. KHANDARE B, Musle AC, Arole SS, Popalghat PV. Analytical method development and validation of olmutinib bulk drug as per ICH Q2 guidelines by using RP-HPLC Method. Journal of Drug Delivery and Therapeutics. 2019 Aug 30;9(4-A):608-11.
10. KHANDARE B, Musle AC, Arole SS, Popalghat PV. Spectrophotometric Determination of Olmutinib in Bulk by Area under Curve and First Order Derivative Methods and its Validation as per ICH guidelines. Journal of Drug Delivery and Therapeutics. 2019 Sep 8;9(4-A):349-54.
11. Khandare BS, Wagh KS. Formulation, Development and Evaluation of Fast Dissolving Oral Film of a Atenolol Drug and validation by RP-HPLC Method using ICH Q2 guidelines. Journal of Drug Delivery and Therapeutics. 2019 Sep 15;9(5):99-104.
12. Denys A, Czuczman P, Grey D, Bascal Z, Whomsley R, Kilpatrick H, Lewis AL. Vandetanib-eluting radiopaque beads: in vivo pharmacokinetics, safety and toxicity evaluation following swine liver embolization. Theranostics. 2017;7(8):2164.
13. Denys A, Czuczman P, Grey D, Bascal Z, Whomsley R, Kilpatrick H, Lewis AL. Vandetanib-eluting Radiopaque Beads:: javax. xml. bind. JAXBElement@ 320a723e: Pharmacokinetics, Safety and Toxicity Evaluation following Swine Liver Embolization. Theranostics. 2017;7(8):2164-76.
14. Sakugawa K, Ikeda A, Takemura A, Ono H. Simplified method for estimation of composition of alginates by FTIR. Journal of Applied Polymer Science. 2004 Aug 5;93(3):1372-1377.
15. Belfer S, Fainchtain R, Purinson Y, Kedem O. Surface characterization by FTIR-ATR spectroscopy of polyethersulfone membranes-unmodified, modified and protein fouled. Journal of Membrane Science. 2000 Jul 1;172(1-2):113-24.
16. Zorba T, Papadopoulou E, Hatjiissaak A, Paraskevopoulos K, Chrissafis K. Urea-formaldehyde resins characterized by thermal analysis and FTIR method. Journal of Thermal Analysis and Calorimetry. 2008 Apr 1;92(1):29-33.
17. Chalmers JM, Everall NJ, Ellison S. Specular reflectance: A convenient tool for polymer characterization by FTIR-microscopy?. Micron. 1996 Oct 1;27(5):315-28.
18. Kizil R, Irudayaraj J, Seetharaman K. Characterization of irradiated starches by using FT-Raman and FTIR spectroscopy. Journal of agricultural and food chemistry. 2002 Jul 3;50(14):3912-8.
19. Piel C, Albrecht A, Neubauer C, Klampfl CW, Reussner J. Improved SEC-FTIR method for the characterization of multimodal high-density polyethylenes. Analytical and bioanalytical chemistry. 2011 Jun 1;400(8):2607-13.
20. Haris PI, Severcan F. FTIR spectroscopic characterization of protein structure in aqueous and non-aqueous media. Journal of Molecular Catalysis B: Enzymatic. 1999 Sep 15;7(1-4):207-221.
21. Vasanthan N, Salem DR. FTIR spectroscopic characterization of structural changes in polyamide- 6 fibers during annealing and drawing. Journal of Polymer Science Part B: Polymer Physics. 2001 Mar 1;39(5):536-47.