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Spectrophotometric Determination of Vandetanib in Bulk by Area Under Curve and First Order Derivative Methods

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Abstract: It is a simple, precise and economical UV-spectrophotometric method has been developed for the estimation of Vandetanib from bulk. Two method was developed First method (A) applied was area under curve (AUC) in this method area was integrated in wavelength from 323.59-333.36nm. Second method (B) was first order derivative spectrometric method. In this method absorbance at λmin=311.27nm, λmax=340.54nm and zero cross=328.37nm was measured. Calibration curves were plotted for the method by using instrumental response at selected wavelength and concentration of analyte in the solution. Both the method linearity was observed in the concentration range of 5-30µg/ml at the λmax=328.44nm. 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 both methods, 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.
Key words: UV, validation, Assay, Precision, % Recovery, Vandetanib, area under curve.

Introduction:

Vandetanib(N(4-bromo-2-fluorophenyl))6-methoxy-7[(1-methyl-4-piperidinyl)methoxy]4-quinazolinamine) is a recently identified small molecule 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]

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In the present study, we developed a novel analytical method and validation of first derivative method for Vandetanib in bulk using UV spectroscopy.

Literature survey reveals that a few spectrophotometric, RP-HPLC methods are reported for the estimation of Vandetanib in combination with other drugs. [4]

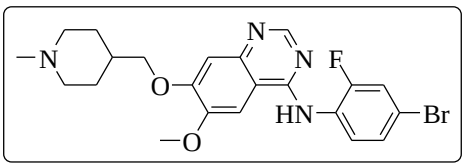

Fig 01: Chemical Structure of Vandetanib

Materials and methods:

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. A double beam UV-Visible spectrophotometer, (UV 1800, Shimadzu limited, Japan) having two matched cells with 1cm light path. A citizen analytical balance (Sartorius) was used for weighing the bulk sample.

Preparation of standard stock solutions:

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.

Selection of wavelength for analysis of Vandetanib:

Accurately pipetted 1.0 mL volume of standard stock solution of Vandetanib was transferred into a 10 mL volumetric flask, diluted to a mark with methanol to give concentration of 10 µg/mL. The resulting solution was scanned in the UV range (200–400 nm) using shimadzu UV-VIS spectrophotometer instrument. The maximum absorbance of solution was measured at the wavelength 328.44nm (Figure 2).

Preparation of calibration curve:

From the standard stock solution fresh aliquots were pipette out and suitably diluted with methanol to get final concentration in the range of 5-30 (µg/ml). The solutions were scanned under 200-400 nm wavelength range and a sharp peak was obtained at 328.44nm (figure 2). Calibration curve was plotted by taking absorbance on y-axis and concentration of solution on x-axis (figure 03 and 04). For both the methods A and B. The drug follows linearity in the concentration range 5-30µg/mL with a correlation coefficient of Method A value (R^2) 0.9997 and Method B value (R^2) 0.994.

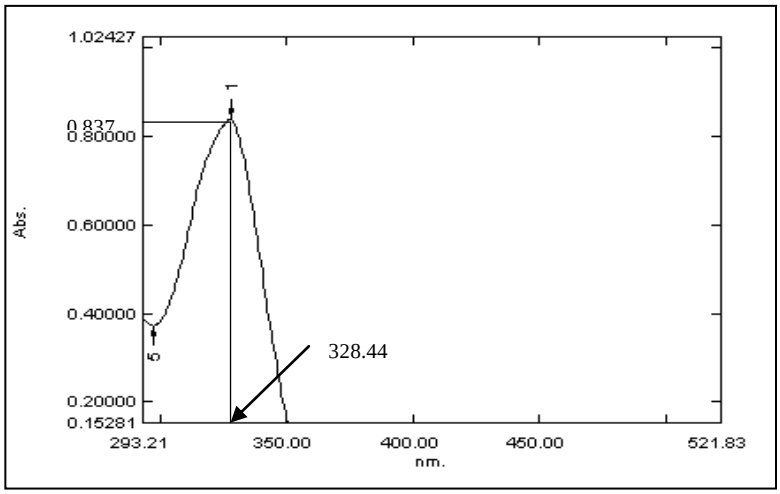

Fig 02: Determination of C_{max} of Vandetanib std. stock solution

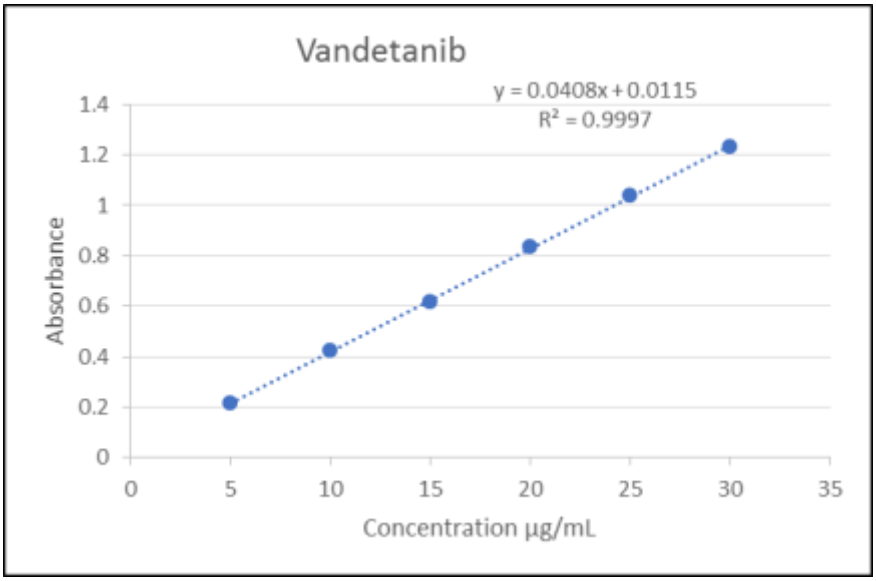

Fig 03: Calibration curve AUC of Vandetanib

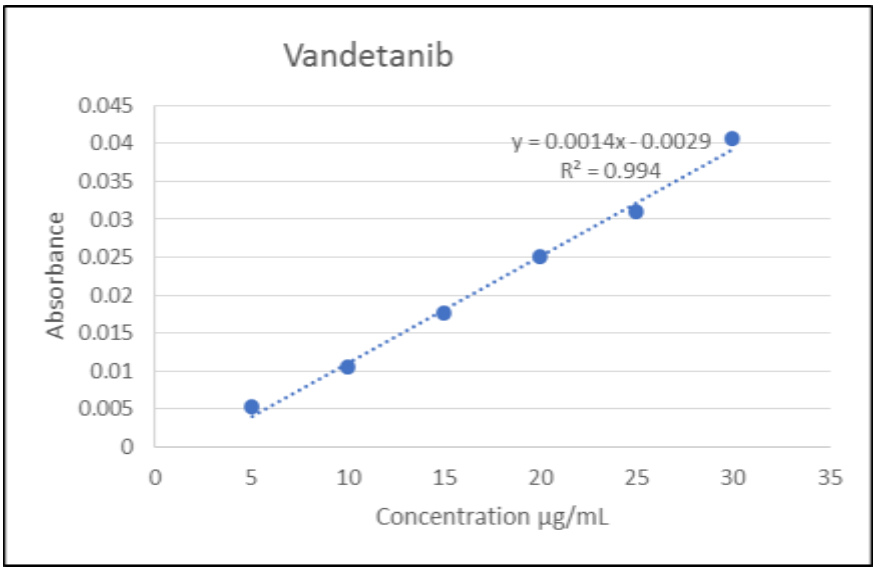

Fig 04: Calibration curve First order derivative of Vandetanib

Area under curve (Method A):

In area under curve method involves to calculation of integrated value of absorbance with selected wavelength. Area calculation calculated in bounded by the curve and horizontal axis. Horizontal axis represent baseline. Where, α is area of bounded portion by curve data and a straight line connecting the starting and end point and β is the area of portion bounded by straight line connecting starting and end point on curve data and horizontal axis, λ_1 and λ_2 are wave length showing starting and end point from figure 5. In this AUC method area was integrated between the wavelength ranges from 323.59-333.36nm (figure 5). Also, calibration curves of vandetanib was prepared in various concentration ranges i.e. 5-30µg/mL at their respective AUC range.[5,6]

$$\textbf{Area calculation } (\alpha + \beta) = \frac{\lambda 1}{\lambda 2} A d\lambda$$

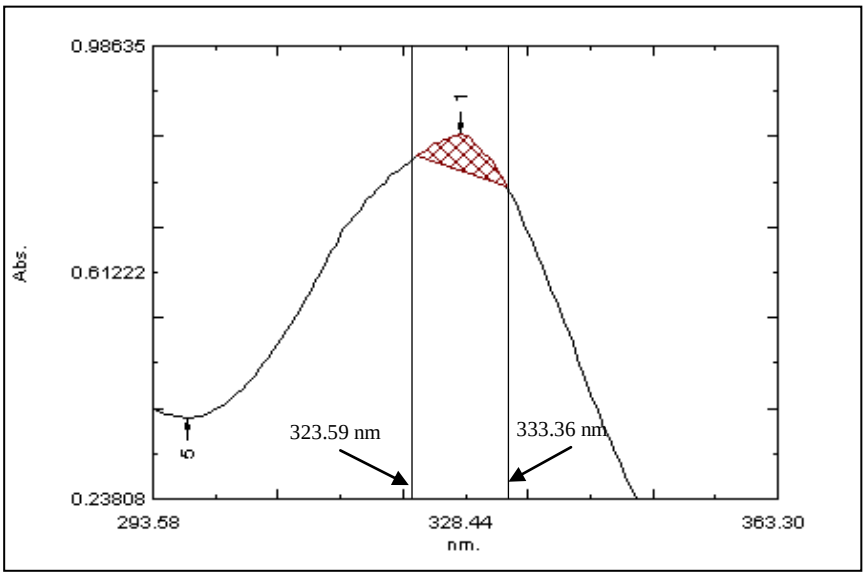

Fig 05: Area under curve graph of 20µg/mL Vandetanib

First Order Derivatives Spectrophotometry (Method B):

In this method solution of Vandetanib (5-30 µg/ml) were prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. The absorption spectra obtained were derivatised from first fourth order. First order derivative spectra were selected for analysis of drug. From spectra of drug the absorbance was measured at λmax=311.27 nm, λmin=340.54 nm and zero cross =328.44 nm, amplitude difference (dA) with respect to wavelength difference (dλ) was measured for the respective concentration of standard and was plotted against concentrations and regression equation was calculated.[7,8]

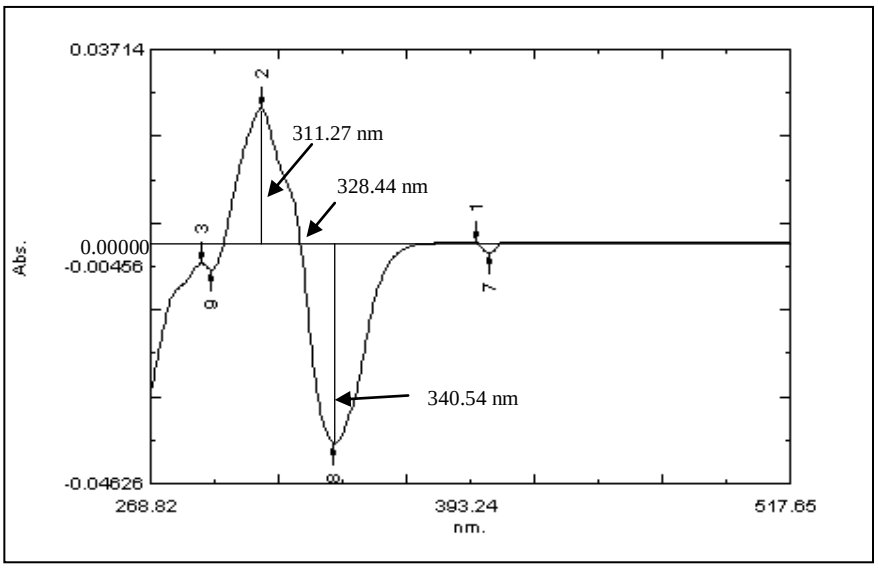

Fig 06: First Order Derivative spectra of Vandetanib

Validation of the developed method:

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

Table 01: Linearity results of Vandetanib in methanol

Concentration (µg/ml)	Method A (Area under curve)	Method B (First order derivative)
5	0.214	0.00523
10	0.424	0.0105
15	0.614	0.0175
20	0.837	0.0250
25	1.037	0.0310
30	1.231	0.0405

Table 02: Result of Precision

Precision	Method A (%RSD)	Method B (% RSD)
Repeatability	0.445	0.437
Intraday	0.633	0.614
Interday	0.885	0.785

Linearity:

Fresh aliquots were prepared from the stock solution (100µg/ml) in different concentrations. The samples were scanned in UV-visible spectrophotometer against reagent blank. It was found that the selected drug shows linearity between the 5-30µg/ml (Table 01).

Repeatability:

The precision of the method was checked by repeatedly injecting (n=6) standard solutions of vandetanib (20 µg/mL). Area under curve of each of these solutions was measured in the range of 323.59-333.36nm. Percentage relative standard deviation (%RSD) was calculated (Table 2).

In first order spectrophotometry derivative method concentration of the solution was determined by measuring absorbance at λmin= 311.27nm, λmax=340.54nm and zero cross=328.44nm.

Intermediate precision (reproducibility):

The intra-day and inter-day precision of the proposed method was determined by analysing 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).

Accuracy (Recovery studies):

The accuracy for the analytical procedure was determined at 80%, 100% and 120% levels of standard solution. Area under curve was measured in the range of 323.59- 333.36nm also first derivative measured in the range 311.27-340.54nm 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).

Table 03: Recovery Study of Vandetanib

Accuracy level	Method A Mean % recovery	%RSD	Method B Mean % recovery	%RSD
80%	98.93	0.836	99.85	0.825
100%	98.06	0.662	98.42	0.745
120%	97.29	0.498	99.23	0.798

Table 04: LOD and LOQ of Vandetanib

Method	Method A	Method B
LOD	0.3591	0.4895
LOQ	1.4323	1.3425

Limit of detection and Limit of quantitation:

The objective of validation of an analytical procedure is to demonstrate whether the procedure is suitable for its intended purpose. 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. (Table 4).

Result and Discussion:

In spectroscopic technique was developed simple and specific method for the determination of vandetanib in bulk form. The generated regression equations were,

Method A - $\int_{333}^{323} A d\lambda 0.0409x + 0.0121$ $R^2 = 0.9997$

Method B- $\int_{340}^{311} A d\lambda 0.0014x + 0.0029$ $R^2 = 0.994$

Where $\int_{333}^{323} A d\lambda$ is area under curve between 323.59-333.36nm, $\frac{dA}{d\lambda}$ is amplitude difference, x is concentration and R^2 is correlation coefficient. The R^2 values were 0.9997 and 0.994 for Method A and B respectively indicated that developed methods were linear. The proposed methods were found to be precise as % RSD values for intraday as well as interday precision were satisfactory. The drug at each of the 80 %, 100 % and 120 % levels showed good recoveries that is in the range of 97.00to 99.00% for both methods, hence it could be said that these methods were accurate. The LOD and LOQ were calculated as 0.3591µg/ml and 1.4323µg/ml for method A and 0.4895µg/ml and 1.3425µg/ml for method B respectively. Thus, the developed method is found to be robust and rugged which can be applied as a rapid tool for routine analysis of vandetanib in the bulk and in the pharmaceutical dosage form. The validation parameters for method A and method B are summarized in Table 05.

Table No. 05: Optical Parameters/ Summary of Vandetanib

Parameter	Result for Method A	Result for Method B
Range	323.59-333.36	311.27-340.54
Linearity range	5-30 (µg/mL)	5-30 (µg/mL)
Standard regression equation	0.0408x +0.0115	0.0014x+0.0029
Correlation coefficient (R^2)	0.9997	0.994
Repeatability	0.445	0.437
Intraday	0.633	0.614
Interday	0.885	0.785
Accuracy (Mean % Recovery)	98.93	99.85
LOD	0.3591	0.4895
LOQ	1.4323	1.3425

Conclusion:

From the results and discussion, two spectrophotometric methods were developed and validated as per ICH guidelines Q2 (R1). In this paper described for the determination of vandetanib in bulk is simple, sensitive and reproducible. The proposed methods can be successfully applied for vandetanib without any interference in quality control.

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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, doi:10.4314/tjpr.v15i10.21.
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, doi:10.1016/j.jchromb.2013.01.037.
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, doi:10.1186/s13065-017-0274-4.
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, doi:10.4103/0973-1482.131393.
5. Dudhe P.B., Choudhary E. D. (2018) Development and Validation of First Order Derivative Method for Tenofovir alafenamide in Bulk using UV Visible Spectroscopy, International Journal of ChemTech Research, Vol.11, No.08 pp 267-273 [ISSN: 0974-4290], doi:10.20902/IJCTR.2018.110833.
6. Dudhe PB, Sonawane AM. Spectrophotometric Determination of Cycloserin in Bulk and Capsule Dosage form by Area Under Curve and First Order Derivative Methods. International Journal of PharmTech Research. 2016;9(8):131-9.
7. Dudhe PB, Kamble MC, Van S, Rajpurohit VJ, Komerwar A, Gondane SJ. Development and Validation of a Spectrophotometric Method for Glibenclamide in Bulk and Tablet Dosage Forms. International Journal of PharmTech Research. 2016;9(2):19-23.
8. PB D, Shelke PS, Chavare PD. Determination of Apixaban from Bulk and Tablet Dosage Form by Area Under Curve and First Order Derivative Spectrophotometric Methods.
9. Dudhe, P.B., Shinde A. P., Salgar K., (2014). Development and validation of analytical methods for Simultaneous estimation of domperidone and esomeprazole Magnesium in bulk and in pharmaceutical formulations Using UV-Visible spectroscopy, International Journal of PharmTech Research, 6, (5), 1501-1508, ISSN No.0974-4304.
10. PB D, Kamble MC, Komerwar A, Sonawane AM, Van S. Development and validation of first order derivative method for Metronidazole in bulk and tablet using UV Visible spectroscopy. International Journal of ChemTech Research, Vol.9, No.04, pp140-144,2016
11. Dudhe, P.B., Shivarkar N. A., Nagras M. A., (2012). UV-Spectrophotometric method development and validation of propranolol hydrochloride and flunarizine dihydrochloride in bulk drug and capsule dosage form, Contemporary Investigations and Observations in Pharmacy, 1(1), 19-23, ISSN No.2278-7429.
12. P.B Dudhe, Lahane AV, Borhade KD, Shelke PS, Chavare PD. Spectrophotometric Determination of Acetazolamide in Bulk and Tablet Dosage Form by Area Under Curve and First Order Derivative Methods.

13. Dudhe P.B., Chavare P. D., Shelke P. S. (2017) Spectrophotometric Determination of Febuxostat from Bulk and Tablet Dosage Form by Area Under Curve Method, International Journal of ChemTech Research, Vol.10, No.06 pp 183-189 [ISSN: 0974-4290]
14. Dudhe PB, Kamble MC. RP-HPLC Method Development and Validation for the Determination of Canagliflozin in Human Plasma.
15. Sonawane A.M, Dudhe P.B, Chalke NH, Bhagat KB. Development and Validation RP-HPLC Method for the Simultaneous determinetion of Loperamide Hydrochloride and Norfloxacin in Pharmaceutical Formulation. International Journal of Pharmaceutical Sciences and Research. 2016 aug 1;7(8):3441-5.

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