

**NOTE****UV Spectrophotometric Estimation of Voriconazole in Bulk and Tablet Dosage Form**

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A new simple, rapid, sensitive and precise spectrophotometric method in ultra violet region has been developed for determination of voriconazole in bulk and tablet dosage form. Voriconazole exhibited maximum absorbance at 256 nm with apparent molar absorptivity of  $1.636E + 04$  in 0.1 N HCl. Beer's law was found to be obeyed in the concentration range 10-70 mcg/mL. Regression equation was found to be  $0.034105x - 0.46707$  and coefficient of correlation was 0.9986. The proposed method is sensitive, accurate, reproducible and useful for the routine estimation of voriconazole in bulk.

**Key Words: Spectrophotometer, Voriconazole.**

The FDA for the treatment of deadly fungal infections has approved voriconazole. The medication is indicated for the primary treatment of acute invasive aspergillosis. It has also been approved as salvage therapy for rare but serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium* spp. Unlike other agents, voriconazole has been approved in both oral and intravenous formulations. Voriconazole<sup>1</sup> (UK-109, 496) is a novel broad-spectrum triazole antifungal agent that has a structure and a spectrum of action similar to those of fluconazole and itraconazole, respectively and is chemically as (2R,3S)-2-(2,4-difluorophenyl)-3-(5-fluoro-4-pyrimidinyl)-1(1H-1,2,4-triazol-1-yl)-2-butanol with an empirical formula of C<sub>16</sub>H<sub>14</sub>N<sub>5</sub>F<sub>3</sub> and a molecular weight is 346.50.

The chemical structure of voriconazole was derived from that of fluconazole by replacement of one triazole moiety by a fluoropyrimidine group and  $\alpha$ -methylation. This modification resulted in an enhanced spectrum of antifungal activity and increased *in vitro* potency. Voriconazole binds to the cytochrome P-450 enzyme lanosterol 14- $\alpha$ -demethylase, which prevents the conversion of lanosterol to ergosterol.

The primary mode of action of voriconazole is the inhibition of fungal cytochrome P-450-mediated 14- $\alpha$ -LAN sterol demethylation, an essential step in fungal ergo sterol biosynthesis. The accumulation of 14- $\alpha$ -methyl sterols correlates with the subsequent loss of ergo sterol in the fungal cell wall and may be responsible for the antifungal activity of voriconazole<sup>2</sup>.

Literature reveals that for estimation of voriconazole, several microbiological<sup>3</sup> and HPLC<sup>4-6</sup> methods have been developed. There was no UV method developed thus in the present investigation an attempt was made to develop a simple and economic spectrophotometric method with greater precision, accuracy and sensitivity for the analysis of voriconazole in tablet dosage form.

A thermospectronic model of Emerk UV/Vis spectrophotometer with 1 cm matched quartz cells was used. Pure voriconazole was gift from Shree Pharmaceuticals, Indore and 20 % HCl and distilled water were used in the study. Calibration method used for the estimating of voriconazole in tablet dosage form<sup>7</sup>.

**Standard preparation:** About 10 mg of voriconazole was accurately weighed and dissolved in 100 mL of 0.1 N HCl to give stock solution of (100 µg/mL). Different aliquots were taken from stock standard in a series of 10 mL volumetric flask and the volume was made up with 0.1 N HCl to get concentration of range of 10-100 µg/mL. One of the above solutions was scanned in UV range using 0.1 N HCl as a blank and wavelength of maximum absorption was found to about 256 nm. The absorption solutions of different concentration were measured at 256 nm using 0.1 N HCl as a blank. Calibration curve was plotted between absorbance *vs.* concentration. Optical characteristics such as  $\lambda_{\max}$ , Beers law, Sandell's sensitivity, molar extinction coefficient, regression equation, slope and intercept are presented in Table-1.

TABLE-1  
OPTIMUM CONDITION, OPTICAL CHARACTERISTICS AND STATISTICAL  
DATA OF THE REGRESSION EQUATION FOR THE STANDARD  
VORICONAZOLE PRECISION AND ACCURACY DATA

| Parameter  | Value                   |
|--|-------------------------|
| $\lambda_{\max}$ (nm)                              | 256                     |
| Beer's law limit (µg/mL)                           | 10 to 70                |
| Molar absorbtivity (L/mol cm)                      | 1.636E + 04             |
| Sandell sensitivity ((µg/cm <sup>2</sup> /0.001AU) | 2.12E - 02              |
| Correlation coefficient (R)                        | 0.9986                  |
| Regression equation (y = mx + c)                   | Y = 0.034105x - 0.46707 |
| Intercept (a)                                      | -0.46707                |
| Slope (b)  | 0.034105                |

**Sample preparation:** For analysis of voriconazole in tablet, the commercial brands of 50 mg tablet were weighed, triturated and mix uniformly powder equivalent to 50 mg (potency claimed) was taken in to 100 mL volumetric flask and volume was made up with mobile phase. The resulting solution was filtered through Whatmann filter paper No. 41 and filtrate was diluted to have concentration in between the linearity range obtained. The results obtained are given in Table-2.

TABLE-2  
RESULTS OF THE ESTIMATION OF VORICONAZOLE IN TABLET

| Tablet formulation (Vfend, Pfizer) | Label claim (mg/tablet) | Amount found (mg/tablet) $\pm$ SD | Recovery studies Amount added | Amount found | Recovery (%) |
|------------------------------------|-------------------------|-----------------------------------|-------------------------------|--------------|--------------|
| Batch A                            | 20                      | 19.95 $\pm$ 0.09                  | 2.5                           | 22.42        | 99.67        |
| Batch B                            | 20                      | 19.87 $\pm$ 0.07                  | 5.0                           | 24.88        | 99.50        |
| Batch C                            | 20                      | 20.00 $\pm$ 0.07                  | 7.5                           | 27.46        | 99.84        |

Mean concentration of six replicates.

The proposed method for determination of voriconazole showed beer's law in range of 10 to 70 mcg/mL and molar absorptivity of (1.636E + 04 L/mol cm). Linear regression of absorbance on concentration gave the equation (0.03410x - 0.46707) with correlation coefficient ( $r^2$ ) 0.9986. To evaluate the validity and reproducibility of the method, known amount of pure drug was added to the previously analyzed pharmaceutical preparation and the resultant mixture was analyzed.

The developed method was found to be accurate and precise. Statistical data suggested that it could be used for the routine analysis of voriconazole in bulk form.

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