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Research Article

UV Spectrophotometric Method for Estimation of Voriconazole in Bulk Form

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Abstract

This study presents a validated UV spectrophotometric method for the precise estimation of voriconazole in bulk formulations. Voriconazole, an essential antifungal agent, demands accurate quantification for its pharmaceutical applications. The proposed method leverages the sensitivity of UV spectroscopy to determine voriconazole concentrations effectively.

The method's validation adheres to regulatory guidelines, ensuring reliability and accuracy. Spectrophotometric analysis was performed within a specific wavelength range, demonstrating linearity, precision, accuracy, and robustness across different concentrations of voriconazole.

Parameters such as specificity, sensitivity, and stability were evaluated to affirm the method's suitability for routine analysis.

The results indicate the method's efficacy in quantifying voriconazole in bulk and semi-solid forms with high precision and sensitivity. This validated UV spectrophotometric method presents a valuable tool for pharmaceutical analysis, facilitating quality control and assurance in voriconazole formulations.

Keywords: Voriconazole, UV spectrophotometry, Anti-fungal, semi-solid formulation, Beer's Lambert's law.

INTRODUCTION:

Voriconazole, chemically known as (2R, 3S)-2-(2, 4-Difluorophenyl)-3-(5-fluoropyrimidin-4-yl)-1-(1H-1,2,4-triazole-1-yl) butan-2-ol [1].

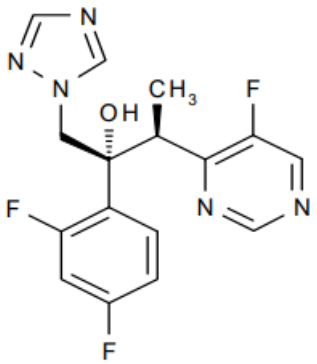

Figure 1: Voriconazole structure [2]

Voriconazole is a second-generation triazole antifungal agent indicated for use in the treatment of fungal infections including invasive aspergillosis, oesophageal candidiasis, and serious fungal infections. The use of this drug is increasing, because it represents an alternative to amphotericin B treatment in invasive fungal infections [12].

DRUG PROFILE OF VORICONAZOLE [3,4,5]:

Mechanism of action: It works principally by inhibiting cytochrome P-450-mediated 14 α-lanosterol demethylation, which is an essential step in fungal ergosterol biosynthesis.

Medical Uses: Voriconazole is primarily used to treat various invasive fungal infections, including Aspergillosis, Candidiasis, Fusariosis, and Scedosporiosis.

Administration and Dosage:

Voriconazole is available in oral and intravenous formulations.

a. Oral tablets or suspensions are typically administered with or without food, as directed by a healthcare professional.

b. Intravenous (IV) administration is often used in severe infections or when oral intake is not feasible.

Pharmacokinetics:

i. Voriconazole is well-absorbed orally, with good bioavailability.

ii. It undergoes extensive hepatic metabolism primarily via the cytochrome P450 enzyme system, mainly CYP2C19 and CYP3A4.

iii. The drug has a relatively short half-life, requiring multiple dosing throughout the day.

Adverse Effects:

Common side effects include visual disturbances (blurred vision, colour perception

changes), headache, gastrointestinal disturbances (nausea, vomiting, diarrhoea), and rash.

Serious adverse effects may include hepatotoxicity, neurotoxicity, and cardiac effects (prolongation of QT interval).

Voriconazole can interact with numerous medications, including other antifungals, immunosuppressants, and certain antibiotics, necessitating careful monitoring and dosage adjustments.

MATERIALS AND METHODS:

Voriconazole (central Research Laboratory in Vignan Pharmacy College), Analytical balance equipment (infra600), a double-beam UV visible spectrophotometer (Lab India), Analytical grade reagents and chemicals are used.

SOLUBILITY [6]:

Table1: Voriconazole solubility in various solvent.

Solvent	Observed Solubility
Acetone	Freely soluble
Ethanol	Soluble
Methanol	Soluble
DMSO	Soluble
Water	Insoluble

UV ANALYSIS[7,8,9,10]:

A. Preparation of Standard Stock Solution:

1 mg/mL Standard drug solution of voriconazole was prepared by transferring 25 mg of drug into 25 mL volumetric flask which was initially dissolved with methanol and make up to the mark with distilled water.

B. Preparation of working stock solution:

10 mL of solution was taken from the above standard stock solution and added to a 100 mL volumetric flask and makeup to the mark with distilled water to get a concentration of 100 µg/mL. From this solution 1 mL, 2 mL, 3 mL, 4 mL, and 5 mL, was transferred in to 10mL volumetric flast and makeup to the mark. The concentrations obtained were 10 µg/mL, 20 µg/mL, 30 µg/mL, 40 µg/mL, and 50 µg/mL and was scanned with UV spectrophotometer in the range of 200- 400nm using methanol as blank. A voriconazole calibration plot was created using collected data. This procedure is repeated for 3 times

METHOD VALIDATION:

Method validation is a process that is used to demonstrate the suitability of an analytical method for an intended purpose. The method was validated for linearity, precision, accuracy, robustness, ruggedness, LOD & LOQ.

Linearity: Linearity of a method is its ability to obtain test results that are directly proportional to the sample concentration over a given range.

1. From the standard stock solution, the various dilutions in concentrations 5 µg/ml, 10 µg/ml, 20 µg/ml, 30 µg/ml, 40 µg/ml, 50 µg/ml were prepared.
2. The solutions were scanned at 256nm and absorbance was recorded and shown in Table 2.
3. From this, a calibration curve was obtained by plotting absorbance versus concentration of voriconazole and the linearity was represented in figure 3.
4. The correlation coefficient was found to be 0.9993.

Precision: Precision of an analytical method expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at three levels: repeatability, intermediate precision and reproducibility.

Precision is expressed in terms of %Relative Standard Deviation.

$$\% \text{ RSD} = \frac{\text{Standard Deviation}}{\text{Mean}} \times 100$$

1. The Repeatability of the method was checked by scanning 30µg/ml solution for 6 times represented in [Table 3].
2. Intraday precision was determined by checking the absorbance of (30µg/ml) on the same day (morning, afternoon, evening) and the results are represented in [Table 4].
3. Inter-day precision was determined by checking the absorbance of (20µg/ml) on three different days and the obtained results were represented in [Table 5].

Accuracy: The accuracy of an analytical method expresses the closeness of agreement between the value accepted either as a conventional true value or an accepted reference value and the value obtained.

1. An Accuracy study was conducted by spiking at three concentration levels (80%, 100%, and 120%).
2. At each level, triplicate samples were scanned and the percentage recovery was determined and presented in [Table 6].

Robustness: The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

1. To determine the robustness of the method one parameter wavelength variation was made slightly different from the selected wavelength.
2. No significant difference was found in the absorbance and hence proposed method was considered as robust and reports were reported in [Table 7].

Ruggedness: The Ruggedness of an analytical procedure is the degree of reproducibility of results by analysing the same sample under a variety of conditions like laboratories, instruments, analysts, reagents etc.

1. The ruggedness of the developed method was checked by analysing the samples by different analysts at different days at similar operational conditions.
2. The statistical analysis showed no significant differences between results obtained by employing different analysts and results are shown in [Table 8].

Sensitivity: The limit of detection (LOD) and Limit of quantification (LOQ) of the drug was calculated by using equations according to ICH guidelines.

Limit of Detection: It is the lowest amount of the drug in the sample that can be detected, but not necessarily quantified, under the stated experimental conditions.

Limit of Quantification: It is an amount of analyte that can be quantified with a specified limit of accuracy and precision

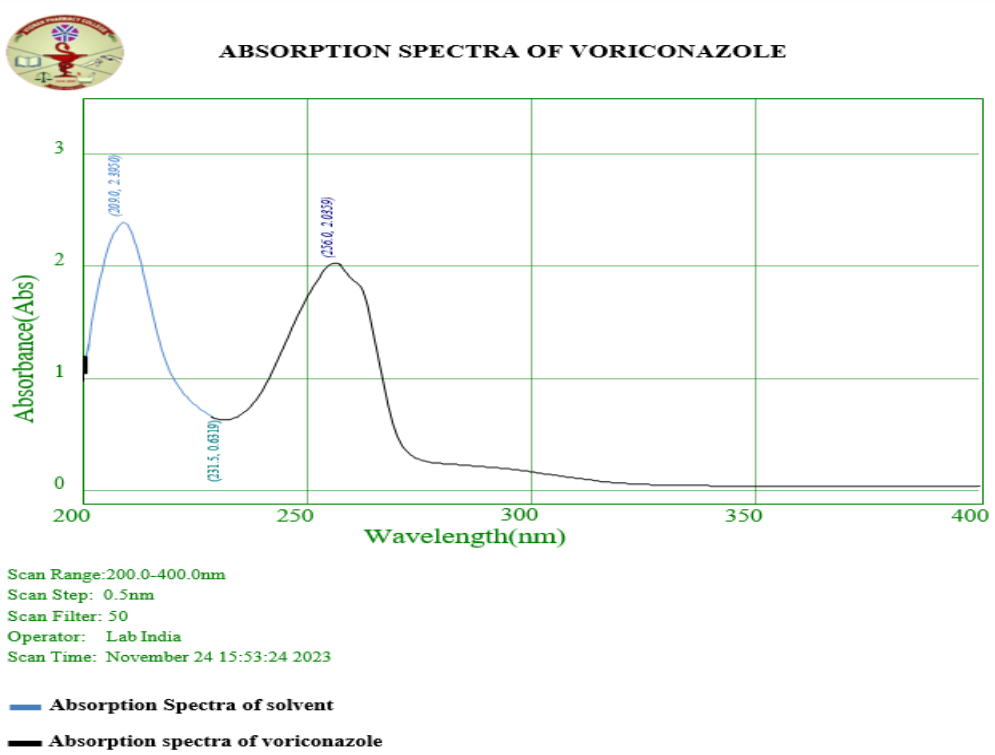

Figure 2: Absorption spectra of voriconazole

CALIBRATION CURVE OF VORICONAZOLE [11,12]:

The calibration curve of voriconazole was plotted by taking absorbance V/s concentration. The λ max of voriconazole was found to be 256nm. The absorbance values are given in Table 1 Standard calibration curve of voriconazole followed Beer Lambert's law between 10-50 µg/ml as shown in Fig 4.

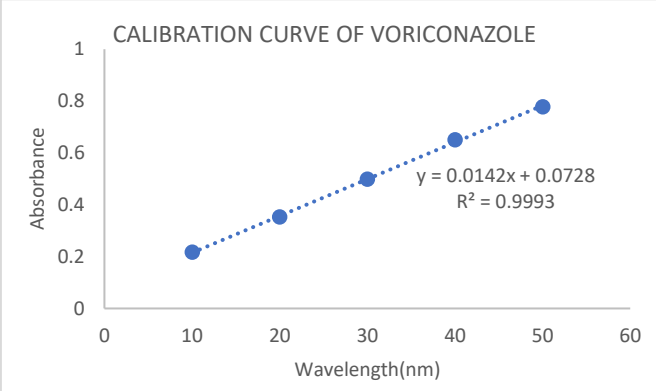

Figure 3: Calibration curve of Voriconazole

The equation of line was found to be y = 0.0142x+ 0.0728, R^2 = 0.9993 for the calibration plot of voriconazole in methanol.

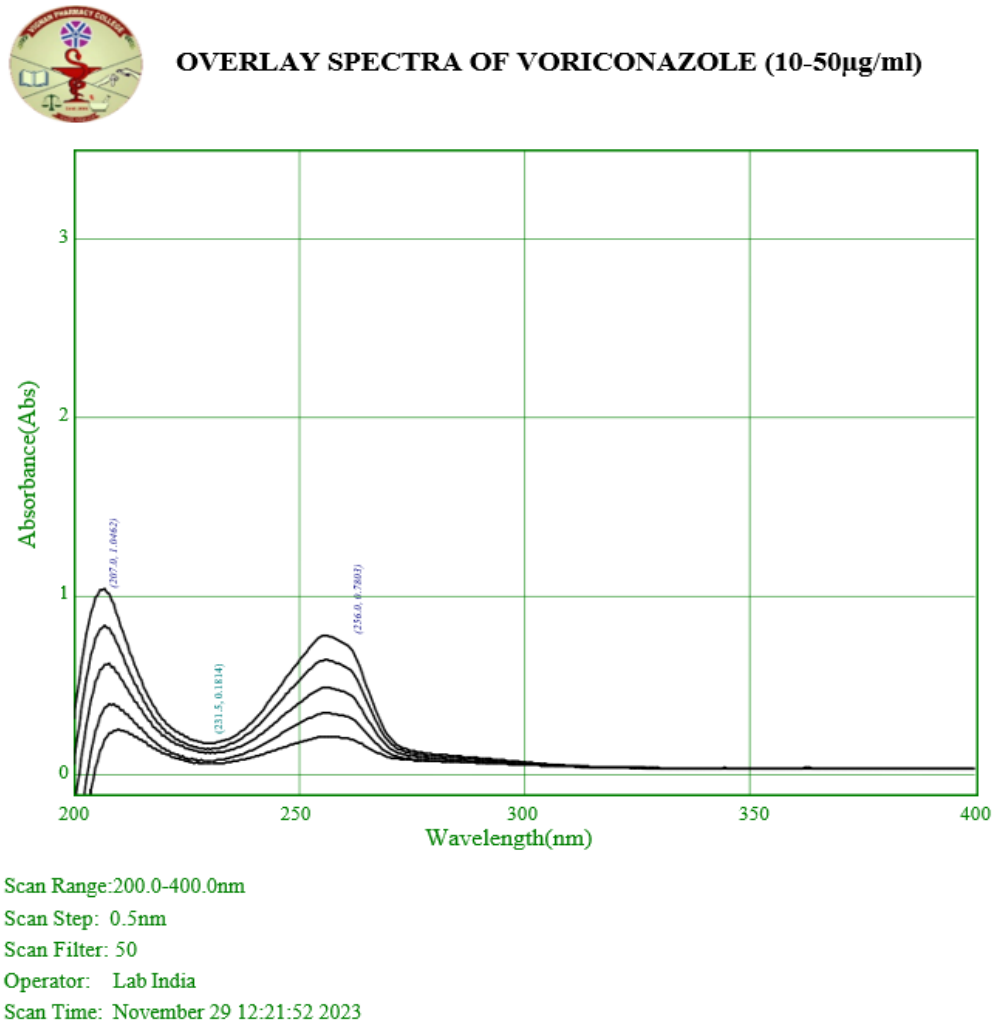

Figure 4: Overlay Spectra of Voriconazole at different concentrations(10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml)

Table 2: Linearity data of voriconazole

Concentration(µg/ml)	Absorbance
10	0.2160
20	0.3526
30	0.4977
40	0.6504
50	0.7771

Table 3: Repeatability data

Concentration (µg/ml)	Absorbance
30	0.4211
30	0.4220
30	0.4241
30	0.4252
30	0.4263
30	0.4171
% RSD	0.74%

Table 4: Intraday Precision

Concentration (µg/ml)	% RSD			Mean% RSD
	Morning	Afternoon	Evening	
30	0.413	0.408	0.406	0.88

Table 5: Inter-day Precision

Concentration (µg/ml)	% RSD			Mean% RSD
	Day1	Day2	Day3	
30	0.413	0.408	0.406	0.88

Table 6: Accuracy data

% Level of Addition	Amount added (µg/ml)	Amount Found (µg/ml)	% Recovery	% Mean Recovery
80	16	15.81	98.83	99.21
100	20	19.80	99.01	
120	24	23.61	99.79	

Table 7: Robustness Results

centration(µg/mL)	Absorbance		
	λ1	λ2	λ3
30	0.4313	0.4211	0.4323
30	0.4233	0.4220	0.4321
30	0.4254	0.4241	0.4377
30	0.4254	0.4252	0.4340
30	0.4257	0.4263	0.4347
30	0.4245	0.4263	0.4335
%RSD	0.65%	0.74%	0.47%

Table 8: Ruggedness Results

Concentration (µg/mL)	Absorbance	
	Analyst 1	Analyst 2
30	0.4211	0.4398
30	0.4220	0.4392
30	0.4241	0.4548
30	0.4252	0.4571
30	0.4263	0.4427
30	0.4263	0.4410
%RSD	0.74%	1.79%

Table 9: LOD and LOQ

LOD (µg/mL)	LOQ (µg/mL)
0.0482	0.0854

RESULT:

The method was developed and validated as per ICH guidelines. Voriconazole exhibited maximum absorbance at 256 nm and obeyed Bee's Lambert's law in the range of 10-50 µg/ml. The linear equation y = 0.0142x+0.0728, R^2 = 0.9993.

CONCLUSION:

A validated UV Spectrophotometric method has been developed for the estimation of voriconazole in bulk form. This method can be used for routine analysis of voriconazole in bulk form.

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Conflict of interest:

The authors declare there is no conflict of interest.

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