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Method development and validation for the estimation of voricanazole by uv spectroscopy

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ABSTRACT

A simple, accurate, precise and economic spectrophotometric method has been developed for the determination of voricanazole in their bulk powder and pharmaceutical dosage form. Voricanazole showed maximum absorbance at 256 nm with 0.1 N Hydrochloric acid as solvent. Beer's law was obeyed in the concentration range 10-60 µg/mL with regression coefficient of 0.999. The concentration of active component were then determined from the calibration curve obtained by measuring the amplitude at 256 nm for Voricanazole. Accuracy and precision of the developed methods have been tested in addition recovery studies have been carried out in order to confirm their accuracy. The slope, intercept and correlation coefficient was found to be 0.0372, 0.0279 and0.9995. This method is simple, precise, accurate, sensitive and reproducible and can be used for the routine quality control testing of the marketed formulations.

Keywords: Spectrophotometry, Voricanazole, 0.1N HCl.

1. INTRODUCTION

Voricanazole (Figure 1) (2*R*, 3S)-2-(2, 4-difluorophenyl)-3-(5-fluoropyrimidin-4-yl) -1-(1*H*-1, 2, 4-triazol-1-yl) butan-2-ol, Voriconazole is a triazole antifungal medication used to treat serious fungal infections. Voriconazole has a low aqueous solubility, its maximum solubility being in acidic conditions. Absorption of voriconazole is essentially complete but the elimination of voriconazole is characterized by nonlinear pharmacokinetics. Voriconazole is a substrate for CYP2C9, CYP2C19, and CYP3A4. Therefore, CYP2C19 genotype and/or co administration of drugs that modulate CYP2C19 or CYP3A4 activities could affect voriconazole plasma concentrations.

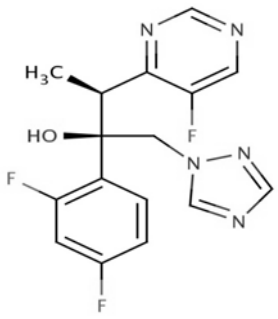

Figure -1: Structure of voriconazole.

Literature survey revealed that a number of methods have been reported for estimation of Voricanazole. However, there is no analytical method reported for the estimation of Voricanazole with 0.1N HCl as solvent in a dosage formulation. Present work describes simple, accurate, reproducible, rapid and economical methods for simultaneous estimation of Voricanazole in tablet formulation.

2. MATERIALS AND METHODS

2.1. Instruments

Instrument: PerkinElmer, double beam UV-VIS spectrophotometer. Bath sonicator of model 1.5l5OH, sisco.

2.2. Chemicals and reagents

0.1N Hcl and Milli Q Pore Water

2.3. Optimization

2.3.1. Scanning and determination of maximum wavelength (λmax)

In order to ascertain the wavelength of maximum absorption (λmax) of the drug solution (25µg/ml) in Milli Q Pore Water were scanned using UV-Visible spectrophotometer within the wavelength region of 200–400nm against reagent blank. The resulting spectrum was presented in

figure 2 and the absorption curve showed characteristic absorption maximum at 256 nm for Voriconazole.

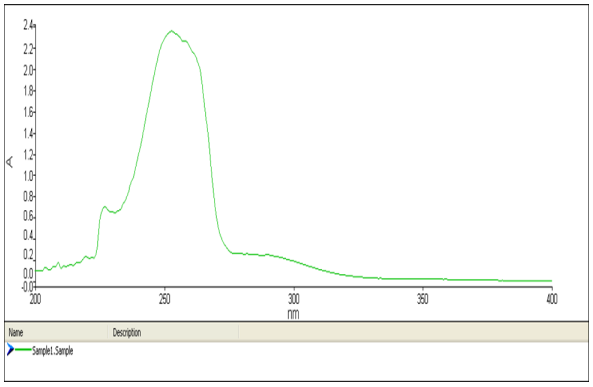

Figure - 2: Absorbance spectrum of Voriconazole (20µg/ml).

2.4. Preparation of stock solution

10µg voriconazole is taken and made up to 10ml with HCl and shake it.

2.5. Preparation of standard solution

From the stock solution further dilutions of 10, 20, 30, 40, 50, 60, µg/ml were prepared.

2.6. Preparation of sample solution

Ten tablets of voriconazole (200mg voriconazole) were weighed and powdered. Weighed the tablet powder equivalent to average weight of the tablet and transferred into 100ml volumetric flask and 100ml 0.1N HCl was added and diluted to volume with mobile phase. The solution was filtered through whatmann filter paper.

2.7. Method validation

2.7.1. Linearity

To construct Beer's law plot for Voriconazole, different aliquots of Voriconazole were taken and diluted to 10 mL with Milli Q Pore Water to get the working standard solutions. The absorbances of each solution were measured at λmax 256 nm . The results were shown in table 1. The standard graph for Voriconazole was plotted by taking concentration of drug on x-axis and absorbance on y-axis and was shown in figure 3. The drug has obeyed Beer's law in the concentration range of 10- 60 µg /ml.

Table - 1: Linearity of voriconazole

Concentration(µg/ml)	Absorbance
10	0.408
20	0.752
30	1.163
40	1.503
50	1.901
60	2.256
Slope	0.0372
Intercept	0.0279
Correlation coefficient	0.9995

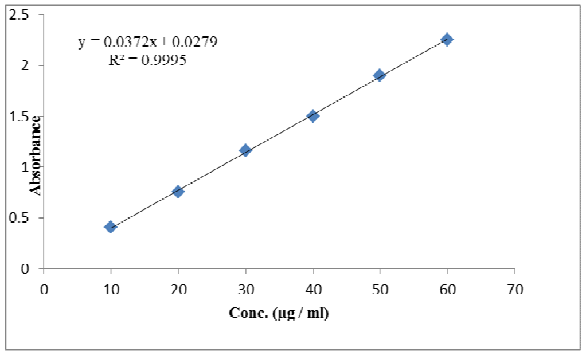

Figure - 3: Linearity for voriconazole.

Table – 2: Accuracy study results

Spike level	Absorbance	Added Amt (mg)	Amt recovered (mg)	Average Amt recovered (mg)	% Recovery
50	0.372	1.09	1.1	1.1	99%
	0.371		1.0		
	0.371		1.3		
100	0.742	2.14	2.1	2.1	101%
	0.742		2.2		
	0.740		2.1		
150	0.1120	3.05	3.2	3.0	98.49%
	0.1120		3.0		
	0.1118		3.5		

2.7.2 Accuracy

The accuracy, specificity, suitability and validity of the proposed methods were satisfied by conducting recovery studies. A known quantity of the drug was added to the pre analyzed sample formulation at 50%, 100% 150% levels. The percentage recovery was calculated and given in table 2.

2.7.3 Precision

2.7.3.1. Repeatability

The repeatability of the method was studied by measuring the absorbance at 256 nm of standard solutions of six replicate samples and measured the absorbance at 256 nm.

Table – 3: Precision study results

Concentration (µg/mL)	Absorbance at 256 nm	% Assay
20	0.742	98.6
20	0.740	98.4
20	0.741	98.5
20	0.742	98.6
20	0.741	98.5
20	0.743	98.8
Average		98.57
Standard deviation		0.136
%RSD		0.13

3. RESULTS AND DISCUSSION

From the optical characteristics of the proposed method, it was found that voriconazole obeys linearity within the concentration range of 10-60µg /ml for the drug absorbance at for voriconazole standard and tablets. Calibration curve was plotted using concentration vs absorbance. From the results shown in accuracy, it was found that the percentage recovery values of pure drug to the Placebo were in-between 98.61 – 101.63 %, which indicates that the proposed method is accurate and also reveals that the commonly used excipients and additives in the pharmaceutical formulations were not interfering in the proposed method. From the results shown in precision table, it was found that the % RSD is0.13, which indicates that the method has good reproducibility. The developed spectrophotometric method was validated by using linearity, range, accuracy and precision and the estimation was done by direct comparison method. The RSD for all parameters were found to be less than 2%.

The proposed method was found to be simple, precision & sensitive for the routine determination in tablet formulation. To study the validity and reproducibility of the proposed methods recovery studies were carried out. The methods are validated in terms of linearity accuracy and precision specificity and reproducibility. The proposed method can be successfully used for the estimation of voriconazole.

Interference studies accuracy, precision, linearity revealed that the common excipients used in the dosage form do not interfere with the estimation of voriconazole using the proposal method.

4. CONCLUSION

The proposed UV method is simple accurate precise and specific, highly sensitive for the measurement of voriconazole. The developed spectrophotometric method was validated by using linearity accuracy and precision and the estimation was done by direct comparison method. The mobile phase is simple to prepare and economical. These methods do not require any sophisticated apparatus in contrast to chromatographic method. Hence the proposed method can be successfully useful for the routine quality control analysis of the drug in marketed preparations

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