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Original Research Article

Quantitative estimation of fenticonazole nitrate by zero-order derivative area under curve spectrophotometric methods in bulk and in-capsule dosage form

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ABSTRACT

The purpose of this study is to establish Zero-order UV-Spectrophotometric - absorbance and Zero Order-Area under curve (AUC) methods for estimation of Fenticonazole Nitrate in bulk and vaginal capsules. Fenticonazole Nitrate is an antifungal drug and it is completely insoluble in water. Methanol was used as solvent for solubilization of Fenticonazole Nitrate. Maximum absorption for Fenticonazole Nitrate was found to be at wavelength 253 nm when dissolved in Methanol. The methods are based upon measurement of absorbance at 253nm and integration of area under curve for analysis of Fenticonazole Nitrate in the wavelength range of 242-262 nm. The drug followed linearity in the concentration range of 5 - 30μg/mL with correlation coefficient value r^2> 0.99 for both methods. The proposed methods were validated for accuracy (% recovery), precision, repeatability and ruggedness, as per ICH guidelines. The proposed methods were applied for qualitative and quantitative estimation of Fenticonazole Nitrate in vaginal capsules and results were found in good agreement with the label claimed. Developed methods can be used for routine analysis of Fenticonazole Nitrate in bulk and Vaginal Capsules.

1. Introduction

Fenticonazole Nitrate (FTZ) is an Imidazole antifungal drug used in the treatment of vulvovaginal candidiasis. It is active against the range of organism including dermatophyte pathogens, *Malassezia furfur,* and *Candida albicans*.[1] The interesting mechanism of action of Fenticonazole is inhibition of the secretion of protease acid by Candida albicans, damage to the cytoplasmic membrane; and by blocking cytochrome oxidases and peroxidises[2] Fenticonazole Nitrate chemically is 1-[2(2,4-dichlorophenyl)-2 {[4 (phenyl sulfanyl) phenyl]methoxy}ethyl]1H-imidazole. The chemical structure of Fenticonazole Nitrate is shown in Figure 1 Fenticonazole is official reported in EP with their characteristics, Identification test, Assay and Impurity detection.[3] Some literature of Fenticonazole is also exist in Merck index and Martindale.[4,5] The information of related substance with their identification test are reported in BP.[6] In literature, few liquid chromatography procedures have been reported for the analysis of Fenticonazole Nitrate.[7–11] The present UV-Spectrophotometric methods were designed for estimation of Fenticonazole Nitrate using Methanol as a solvent. The current works emphasize simple, precise, sensitive and effective UV Spectroscopy method for estimation of Fenticonazole Nitrate in bulk and in-Vaginal capsules. The method was validated as per ICH guidelines.

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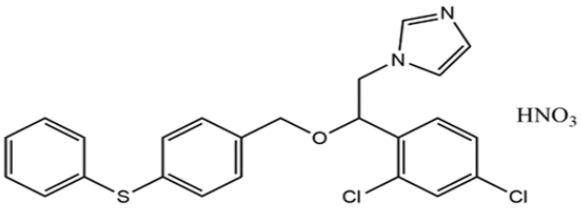

Figure 1: Thechemical structure of fenticonazole nitrate

1.1. Chemical and Reagents

Fenticonazole Nitrate was gifted by Akum Lifescience ltd. Haridwari. All Chemicals and reagents are AR Grade and purchased from Rankem Chemicals Pvt. Ltd.Mumbai and Vaginal Capsule (Fentin 600mg) was purchased from local market.

1.2. Instrument

1. Spectrophotometer: UV-2450 Shimadzu, Japan
2. Software: UV Probe 2.21
3. Sample cell: 1cm quartz cuvette
4. Lamp: Deuterium Lamp Wavelength range 200 – 400nm
5. Spectral Slit width: 1.0nm
6. Weighing Balance: Shimadzu AUX-120

2. Experimental

2.1. Preliminary solubility studies and selection of solvent

Solubility of FTZ was found in Methanol and Dimethylformamide (DMF). The Fenticonazole Nitrate is completely soluble in methanol. So for further study Methanol is used as a solvent.

2.2. Preparation of stock standard solution

Stock standard solution of FTZ was prepared by dissolving accurately weighed 10mg of FTZ into 100ml of Methanol, to obtain concentration of 100μg/mL. sonicated for 5 min. The working standards were prepared by dilution of the stock standard solution.

2.3. Determination of λ max and calibration curve

A fixed volume of 1.0mL of FTZ from stock solution was transferred to 10mL volumetric flask, diluted to mark with Methanol to obtain concentration of 10μg/mL. The resultant solution was scanned in UV range (400-200nm) in 1.0cm cell against solvent blank. The spectrum showed an absorption maximum at 253nm.

In Method I absorbance at 253nm was considered for analysis while for Method II two wavelengths 242-262 nm were selected for determination of Area under Curve [AUC]. Optical Characteristics of FTZ presented in.Table 1. Zero order UV-spectrum showing maximum absorbance and AUC are shown in.Figure 2

Table 1: Optical characteristics and linearity of fenticonazole nitrate

Parameters	Method 1	Method 2 (AUC)
Linearity Range	5-30	5-30
Wavelength / AUC Range	253	242-262
Slope	0.025	0.106
Intercept	0.028	0.030
Correlation Coefficient	0.999	0.998
LOD (μg)	0.311787	0.32600
LOQ (μg)	0.944811	0.987891

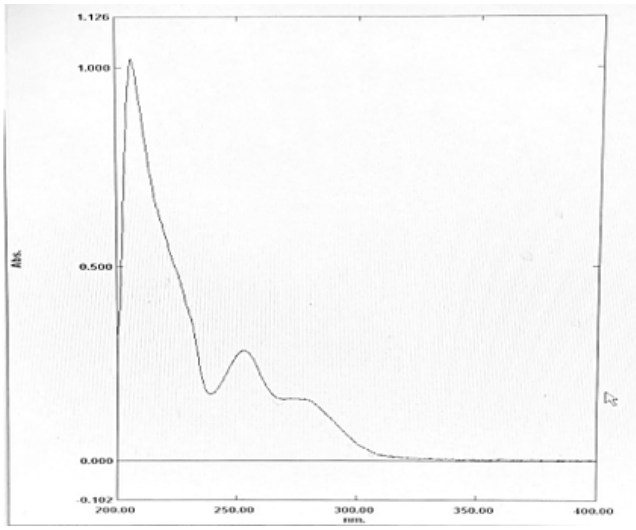

Figure 2: Method I. UV-spectrum of fenticonazole nitrate in methanol showing λmax (253 nm)

An appropriate volume of stock solution in the range of 0.5–3.0mL were transferred in series of 10mL volumetric flask, volume was made up to 10mL with Methanol to get concentration of 5–30μg/mL and absorbance was measured at 253nm (method I) and Zero order- AUC was recorded in between the wavelength range of 242-262 nm (Method II) against the blank. Calibration curves were prepared by plotting concentration versus absorbance and AUC as shown in.Figure 3

3. Analysis of Capsule formulation

Ten capsules were accurately weighed and average weight determined, an amount of power drug equivalent to 10

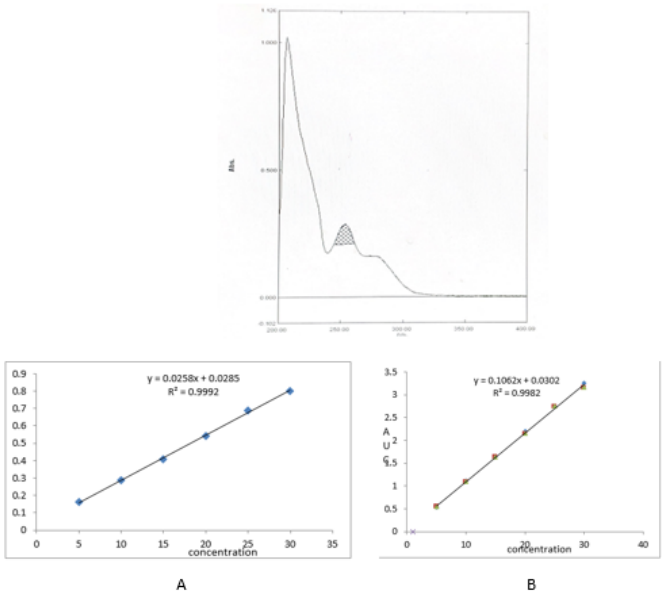

Figure 3: Method II. UV-spectrum of Fenticonazole Nitrate in Methanol showing selection of wavelength for integration of AUC Range (242-262) **A:** Linearity Curve of Fenticonazole Nitrate by Zero-Order Spectrometry **B:** Linearity curve fenticonazole nitrate by zero order auc spectrometry

mg of Fenticonazole Nitrate was transfer into 100 mL volumetric flask containing 100 ML of Methanol, sonicated for 5 min. The volume was made up to the mark with same solvent and filtered through 0.45μm Whatman filter paper. A suitable volume of solution was further diluted with Methanol to obtain concentration 20μg/mL of Fenticonazole Nitrate for tablet assay. These sample solutions were scanned at selected wavelengths in Method I and Method-II and the results were obtained. From the respected linear regression equations, the concentrations were determined. The procedure was repeated for six times and the results are shown in.Table 2

3.1. Validation

The method was validated for accuracy, precision, and ruggedness according to ICH guidelines.

4. Accuracy/Recovery Studies

To estimate the accuracy of both the proposed methods, recovery studies were executed out at 50, 100 and 150% of the test concentration as per ICH guidelines. To the pre-analyzed sample solution (10μg/ml), a known amount of drug standard was added at 50, 100 and 150% and solutions were reanalyzed by proposed methods. The experiments were performed three times at each level for each method. The results of the recovery studies are reported in the table below.

4.1. Precision

Precision of the methods were studied as intra-day, inter-day variations and repeatability. Precision was determined by analyzing the concentration of 15, 20, and 25μg/ml. To determine the degree of repeatability of the methods, statistical evaluation was carried out, and the results are reported in the table below.

4.2. Repeatability

Repeatability was determined by analyzing Fenticonazole concentration of 20μg/mL for six times and results are reported in below table.

4.3. Ruggedness

The ruggedness of the proposed method was determined by analysis of aliquots from homogenous slot by two analyst using same operational and environmental conditions and the results are reported in below table.

4.4. Sensitivity

The sensitivity of proposed methods was estimated in terms of estimating Detection Limit (DL) and Quantitation Limit (QL) which were calculated using formulae "DL = 3.3 ×N/B," and "QL = 10 × N/B" where "N" is average standard deviation of the absorbance or peak areas of the Fenticonazole (n = 3), taken as a measure of noise, and "B" is the slope of the corresponding calibration curve.

Table 2: Analysis of vaginal capsules

	Label claim(mg)	Conc (μg/mL)	%Amount found n=6	±SD	±RSD
Method 1	600	20	100.56	0.5428	0.5406
Method 2	600	20	100.06	0.1855	0.1853

Table 3: Average of three estimates

%Value	Initial Amount (μg/mL)	Ammount Added (μg/mL)	Method 1		Method 2	
			%Recovery	%RSD	%Recovery	%RSD
50%	10	5	100.8	1.1223	100.37	1.8608
100%	10	10	101	1.6602	101.32	1.4484
150%	10	15	100.93	0.5635	99.935	0.089

Table 4: Average ofthree estimates

Concentation (μg/mL)		Intra-Day %RSD		Inter-Day %RSD	
Method 1	Method 2	Method 1	Method 2	Method 1	Method 2
15	15	1.170	1.291	0.9854	1.2553
20	20	0.6587	0.2708	1.5568	1.2068
25	25	1.4253	1.3544	1.2564	1.3676

Table 5: Average of six estimations

Method	Concentration (μg/mL) n=6	%Amount Found	%RSD
Method 1	20	98.7	1.7277
Method 2	20	99.83	1.2410

Table 6: Average of six estimations

Method	Amount taken (μg/mL) n=3	%Amount found	
		Analyst 1	Analyst 2
Method 1	20	99.60	98.466
Method 2	20	98.883	98.396

5. Results and Discussion

In the present investigation, Methanol is used to enhance the aqueous solubility of poorly water-soluble drugs Fenticonazole Nitrate in bulk and in vaginal capsules. By selecting proper solvent. For the solubility studies, different solvent was tried but optimum solubility was achieved in Methanol. In Method I and II, linearity of Fenticonazole Nitrate was found to be in the range of 05 - 30μg/mL, with correlation coefficient (r2 > 0.99). Marketed brand of Vaginal capsules were analyzed. The amounts of Fenticonazole Nitrate determined by 'Method I' and Method II was found to be 100.56% and 100.06, respectively**.** In both these methods, precision was studied as repeatability, inter and intra-day variations at three different concentrations of Fenticonazole Nitrate and % RSD was found to be less than 2. The accuracy of method was determined by calculating mean percentage recovery. It was determined at 50, 100 and 150% level and % recovery was found to be in the range 100.80% - 100.93% and 100.37% – 99.94% for method I and II respectively. The ruggedness of the methods was studied by two different analysts using the same operational and environmental conditions and % RSD found to be less than 2. DL and QL were found to be 0.3117μg/ml and 0.9448 μg/ml, respectively for Method I and DL and QL were found to be 0.3260μg/ml and 0.9878μg/ml respectively for Method II indicating adequate sensitivity of the methods.

6. Conclusion

The proposed methods for analysis of Fenticonazole Nitrate in pharmaceutical formulations are ecofriendly; simple, precise and rapid so can be employed for routine analysis. From the proposed methods, we conclude that there is a good scope for other poorly water-soluble drugs to get solubilized by using organic solvents.

7. Source of Funding

None.

8. Conflict of Interest

Authors declare that there is no direct or indirect conflict of interest with this research work.

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