

RESEARCH ARTICLE

Development and Validation of UV Spectrophotometric Method For The Estimation of Finasteride Drug

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ABSTRACT

A simple, accurate, precise, reproducible, highly sensitive, an economic spectrophotometric method has been developed for the estimation of finasteride. UV spectrophotometric method is based on the measurement of absorption at a maximum wavelength of 255 nm. The developed method was validated with respect to linearity, accuracy (recovery), precision (inter and intraday variations), Limit of Detection (LoD) and Limit of Quantitation (LoQ). Beer's law was obeyed in the concentration range of 5–25 µg/mL with a correlation coefficient of 0.9933. Results of the analysis were validated statistically and by recovery study. Hence the developed and validated method can be used for estimation of finasteride.

Keywords: Development, Finasteride, UV Spectroscopy, Validation.

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INTRODUCTION

Finasteride ((5 α , 17 β)-N-(1, 1-dimethylethyl)-3-oxo-4-azaandrost-1-ene-17-carboxamide) is a selective inhibitor of type II- 5 α - reductase in-silico.¹ Thus, the inhibition of type II -5 α -reductase suppresses the metabolism of testosterone to dihydrotestosterone (DHT), resulting in a significant decrease in plasma and intraprostatic DHT concentrations. Hence it is used as an antiandrogen agent. At low doses, it is used in benign prostatic hyperplasia (BPH) and at higher doses used in prostate cancer. Additionally, it is registered in many countries for male pattern baldness. Finasteride blocks the peripheral conversion of testosterone to dihydrotestosterone (DHT), resulting into decrease scalp DHT concentration to the levels found in the hairy scalp, reduce serum DHT, increase hair regrowth, and slow hair loss.² In recent years, stringent quality control in the pharmaceutical industries has given rise to a growing need for simple, selective and sensitive analytical methods for their determination in pure and in dosage forms. The literature review revealed that there are few methods based on HPLC, HPTLC, RP-HPLC, polarography, and spectroscopy for its estimation in bulk and dosage form. Spectrophotometry has always provided analytical techniques characterized by instrumental simplicity, moderate cost, and portability. These features make spectrophotometric techniques particularly suitable for the determination of trace concentrations of clinically important compounds.³ If a suitable method, for a specific need, is not available, then it becomes essential to develop a simple, sensitive, accurate, precise, rapid, and reproducible method for the estimation of drug samples.

Finasteride is not official in I.P and B.P. The drug is official in Martindale, The Extra Pharmacopeia and United States Pharmacopoeia and the latter describes HPLC procedure for assay in pure drug and tablets

The present work describes the development and validation of the UV spectrophotometric method, which can quantify the finasteride (Figure 1). An attempt was made to develop a simple, accurate, precise, and rapid spectrophotometric method for the estimation of finasteride.

MATERIALS AND METHOD

Apparatus

All the spectral absorption measurements were made using JASCO 4500 (UV-Visible) (UV-Vis) spectrophotometers equipped with 10-mm matched quartz cells, a scanning speed of 400 nm/min, and a bandwidth of 2.0 nm.

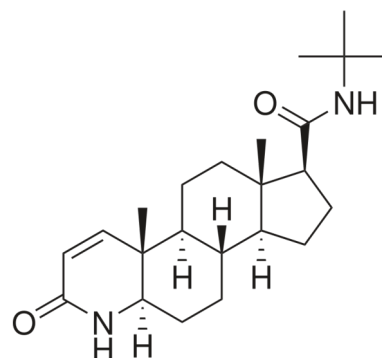


Figure 1: Structure of finasteride

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Chemicals

Finasteride, methanol, double distilled water (DDW) were purchased from Yarrochem products, Mumbai.

ANALYTICAL METHOD VALIDATION

Preparation of standard finasteride solution

Accurately weighed finasteride (10 mg) was transferred to 10 mL volumetric flask and dissolved in methanol to obtain a standard stock solution having a concentration of finasteride drug (FSD) as 1000 µg/mL.

Preparation of working standards for calibration

Methanol as a solvent

Stock solution of finasteride was diluted with methanol to get a series of concentrations 5, 10, 15, 20, 25 µg/mL.

Estimation of the calibration curve of FSD in Methanol

Calibration curve of finasteride in methanol was plotted using a concentration range of 5–25 µg/mL at the estimated wavelength, and the coefficient of regression was calculated.

Estimation of λ_{max}

To determine λ_{max} of FSD, it was accurately weighed (10 mg) and separately dissolved in 10 mL methanol to make a concentration of 1000 µg/mL. These solutions were then suitably diluted to 10 mL using methanol to get final solutions of concentration 10 µg/mL. The UV spectrum of finasteride diluted in both Water and Methanol were recorded over the wavelength range 200–400 nm and depicted in Figure 2 and 3.

Validation of UV -Vis spectroscopic method

The UV spectroscopic method for the estimation of FSD in methanol was validated with respect to linearity. The method employed was validated for linearity, precision accuracy, limit of detection, and limit of quantification.⁵⁻¹⁴ Validation was performed as per ICH guidelines.⁴

Linearity

The linearity of response was determined by analyzing at least three samples for each concentration in the range of 5-25 µg/ml. The absorbance of solution (methanol) was measured at 255 nm using a UV-visible spectrophotometer. The standard curve was obtained through analysis of the calibration standards of FSD and plot of mean absorbance of FSD versus corresponding

FSD concentration (µg/ml). The linearity of standard curve was evaluated using least-squares linear regression analysis depicted in Figure 3 and 4.

Precision

The precision of the method was evaluated in methanol by repeatedly analyzing three different concentrations (2, 4, and 6 µg/mL) of a standard solution of FSD at different time intervals on the same day (Intraday precision) and on three different days (Interday precision). At least three replicates of each of three concentrations (2, 4, and 6 µg/mL) representing the entire range of calibration curves were analyzed in the batch to establish the method's intraday and interday precision expressed as % relative standard deviation (RSD).

Accuracy

To ascertain accuracy of the proposed method, three different concentrations (2, 4, and 6 µg/mL) of FSD were prepared and the absorbance was recorded in triplicates. From the data obtained, standard deviation (SD) and % RSD were calculated. Accuracy was evaluated by comparing the predicted value of concentration with actual concentration and was expressed as predicted %.

Limit of detection (LoD)

The limit of detection is the minimum quantity of the drug, which can be detected by the method. The limit of detection is calculated using equation 1.

$$\text{LoD} = 3.3 (\sigma/S) \quad (1)$$

Where σ is the standard deviation of the constant and S is the mean of slope of the calibration curve equation.

Limit of quantification (LoQ)

The limit of quantification is the minimum quantity of the drug that can be quantified by the method. The limit of quantification is calculated using equation 6.

$$\text{LoQ} = 10 (\sigma/S) \quad (2)$$

RESULT AND DISCUSSION

Calibration curve of FSD in Methanol

The calibration curve for FSD in methanol follows Beers-Lambert's law. The graph of absorbance against concentration for FSD was found to be linear in the concentration range of 5-25 µg/ml at 255 nm.

The coefficient of regression of the calibration curve was found to be 0.9999. % RE gives the difference between a true

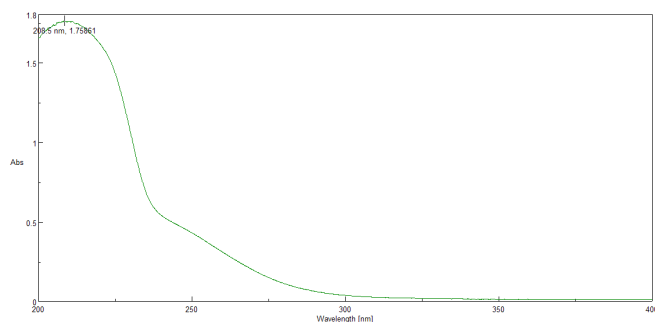


Figure 2: UV Spectrum for 100 ppm diluted in water

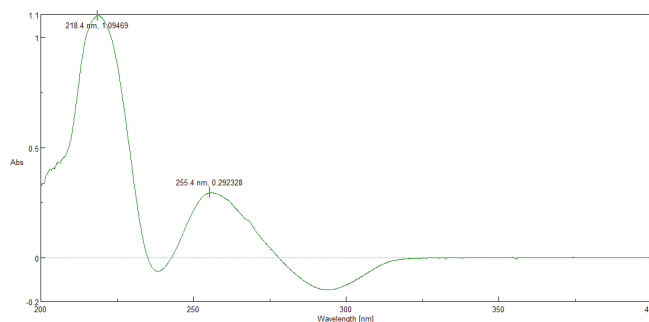


Figure 3: UV Spectrum for 100 ppm diluted in methanol

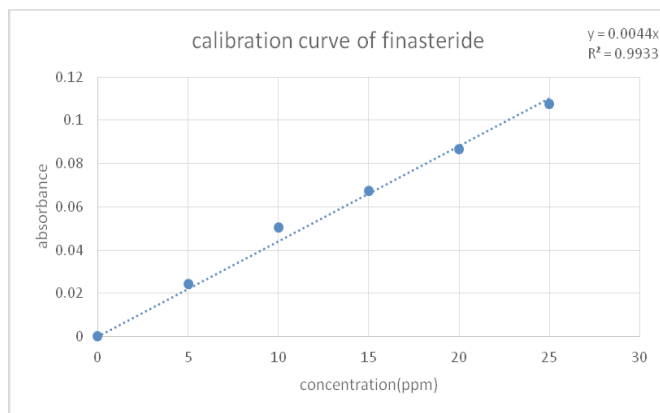


Figure 4: Predicted concentration and % RE in concentration estimation of FSD by UV- Vis spectroscopy.

value and approximate value. The lower magnitude of error (<2%) indicates a high prediction power of the regression equation (Table 1).

Accuracy

Accuracy is the measurement of the exactness of an analytical method or the closeness of agreement between the experimental values and the true value. Accuracy was measured using minimum three determinations per three concentrations.

The percentage RSD of a standard solution of FSD of concentration 2, 4, and 6 $\mu\text{g}/\text{mL}$ were calculated as shown in Table 2. The % mean accuracy of calculated concentration levels for all the samples ranged from 99.95 to 100.05%, which is within acceptable limit 85–115%.

Precision

Precision is performed to an estimated random error of the analytical method. The repeatability and reproducibility of a method can be evaluated by carrying out several independent measurements of the same analyte. The preciseness of this method was evaluated by estimating %RSD at different concentration levels during validation.

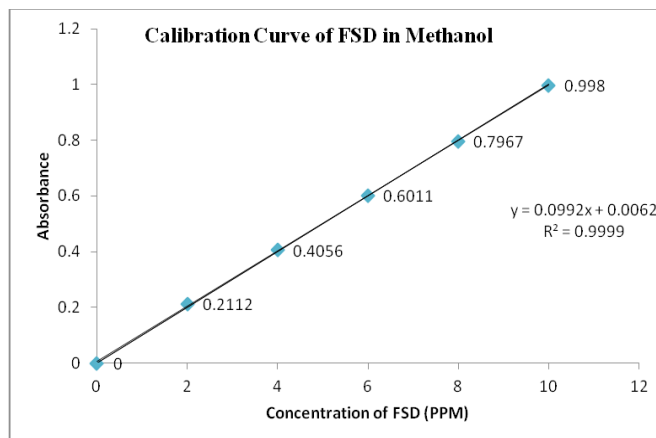


Figure 5: Calibration curve of FSD in Methanol

Intra Day Precision

The repeatability of the method was evaluated in triplicate on the same day for three different concentrations of FSD in Methanol (2, 4, and 6 $\mu\text{g}/\text{mL}$). The % RSD at different concentration levels are summarized in the Table 3, Since the % RSD for intraday precision at concentration 2, 4 and 6 $\mu\text{g}/\text{mL}$ was found to be less than 2, the method was found to be precise.

Inter Day Precision

The reproducibility of the method was evaluated by carrying out the estimations in triplicates for three different concentrations of actarit in methanol (2, 4, and 6 $\mu\text{g}/\text{mL}$) on three consecutive

Table 1: Predicted concentration and % RE in concentration estimation of FSD by UV- Vis spectroscopy.

Actual Conc. ($\mu\text{g}/\text{ml}$)	Predicted conc. ($\mu\text{g}/\text{ml}$)*	% RE
2	2.02 \pm 0.04	0.7
4	4.02 \pm 0.12	0.5
6	6.03 \pm 0.04	0.5
8	7.94 \pm 0.57	0.7
10	9.94 \pm 0.07	0.6

Mean \pm SD (n = 3)

Table 2: Accuracy studies

Sr. No	Concentration ($\mu\text{g}/\text{mL}$)	Predicted conc ($\mu\text{g}/\text{ml}$) \pm SD	Accuracy (%)
1	2	1.99 \pm 0.01	100.05
2	4	4.00 \pm 0.04	99.95
3	6	6.00 \pm 0.03	99.97

Mean \pm SD (n = 3)

Table 3: Intraday precision (% RSD) and accuracy results for three determinations for estimation of FSD in a day.

Time	Actual concentration		
	LQC(2 $\mu\text{g}/\text{mL}$)	MQC(4 $\mu\text{g}/\text{mL}$)	HQC(6 $\mu\text{g}/\text{mL}$)
	Predicted concentration ($\mu\text{g}/\text{ml}$)		
10.00 am	2.00 \pm 0.015	4.00 \pm 0.043	6.00 \pm 0.036
1.00 pm	1.99 \pm 0.06	3.99 \pm 0.044	5.99 \pm 0.047
5.00 pm	1.98 \pm 0.07	3.98 \pm 0.062	5.97 \pm 0.068
Mean	1.99	4.00	6.001
S.D	0.015	0.002	0.003
%RSD	0.099	0.066	0.042
%Accuracy	100.10	99.95	99.96

Mean \pm SD (n=3)

Table 4: Interday precision (%RSD) for three determinations for estimation of FSD over three days

Time	Actual concentration		
	LQC(2µg/mL)	MQC(4µg/mL)	HQC(6µg/mL)
	Predicted concentration (µg/mL)		
1	2.00 ± 0.02	4.01 ± 0.05	6.00 ± 0.01
2	1.99 ± 0.03	3.99 ± 0.06	5.98 ± 0.03
3	2.01 ± 0.02	4.03 ± 0.02	6.02 ± 0.07
Mean	2.003	4.001	6.012
S.D	0.007	0.006	0.007
%RSD	0.34	0.109	0.19
%Accuracy	100.01	99.76	99.56

Mean ± SD, (n=3)

days (fresh samples were prepared every day). The % RSD at different concentration levels are summarized in Table 4.

LoD

The limit of detection is the minimum quantity of the drug, which can be detected by the method.

LoD for FSD in Methanol was found to be 0.24 µg/mL.

LoQ

The limit of quantification is the minimum quantity of the drug that can be quantified by the method. LoQ was found to be 0.74 µg/ml for the detection of FSD in Methanol. The method could detect and quantify FSD in concentration as low as 0.74 µg/mL.

CONCLUSION

The UV Spectrophotometric method was validated, and the developed method was found to be simple, economical, easy, accurate, precise, reproducible and highly sensitive and can be used for routine estimation of finasteride in bulk and other formulations.

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