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Research Article

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VALIDATED UV SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF DUTASTERIDE IN TABLET DOSAGE FORM

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ABSTRACT

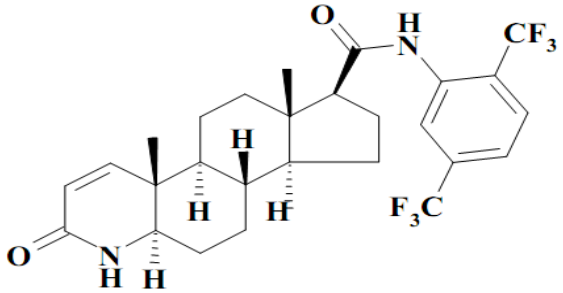
The objective of this present investigation is to develop a simple, sensitive and accurate spectrophotometric method for the determination of Dutasteride in raw material and tablet dosage form. The λ_{max} of was found to be 241 nm. The linear dynamic response was found to be in the concentration range of 12-28 µg/ml and coefficient of correlation was found to be 0.997. The %RSD value was below 2.0 for intraday and interday precision indicated that the method was highly precise. The LOD and LOQ were found to be 0.125 and 0.345 µg/ml respectively which revealed that method was highly sensitive. The percentage recovery value was higher than 100 %, indicating the accuracy of the method and absence of interference of the excipients present in the tablet formulation. The proposed method was simple, fast, accurate, precise and reproducible and hence can be applied for routine quality control analysis of Dutasteride in bulk and pharmaceutical tablet formulations.

Keywords: Spectrophotometry, Dutasteride, estimation and validation.

INTRODUCTION

Dutasteride is a potent and specific dual 5α-reductase inhibitor for the treatment of benign prostatichyperplasia (BPH) and lower urinary tract symptoms (LUTS)[1, 2]. It was approved by USFDA in October 2002 and it has been approved in several countries.[3, 4] Dutasteride inhibits the conversion of testosterone to 5α-dihydrotestosterone (DHT). DHT is the androgen, which is primarily responsible for the initial development and subsequent enlargement of the prostate gland.

Figure 1. Chemical structure of Dutasteride



Chemically Dutasteride is 17β-N-(2,5-bis(trifluoromethyl) phenyl-carbamoyl)-4-aza-5-androst-1-en-3-one[5] (Figure **1**). The drug is not official in any pharmacopoeia till date. A survey of literature has not revealed any UV spectrophotometric method for the determination of the drug in bulk or pharmaceutical formulation. The other analytical methods that have been reported for its determination in bulk and pharmaceutical formulation include HPLC[6] and HPTLC[7]. A liquid chromatography tandem mass spectrometry (LC-MS/MS) method using sophisticated LC–MS/MS apparatus has also been reported for quantification of the drug from human plasma.[8]

So in this present study, a simple, economical, precise and accurate analytical method has been developed for the estimation of Dutasteride in pure form and in solid dosage form.

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MATERIALS AND METHODS

Chemicals & Reagents

Standard Dutasteride was received as a gift sample from HealthCare Pharmaceuticals Ltd. and the commercially available Dutasteride tablets claimed to contain 0.5 mg of active ingredients were procured from local market of India. Analytical grade methanol and water used as solvent.

Instruments

UV-Visible double beam spectrophotometer (UV-1601 PC SHIMADZU Limited, Japan), Micropipette of Variable volume 10-1000µL (Gene Pete Co.) and Digital balance (Citizen Co.) were used in the study process.

Method

Wavelength selection

In order to ascertain the wavelength of maximum absorption (λ_{max}) of the drug, different solutions of the drugs (12µg/ml and 28µg/ml) in a mixture of methanol-water (50:50) were scanned using spectrophotometer

within the wavelength region of 200 – 380 nm against mixture of methanol-water (50:50) as blank. The resulting spectra were shown in Figure 2 and the absorption curve showed characteristic absorption maxima at 241 nm for Dutasteride.

Preparation of standard solution for calibration curve

10 mg Standard Dutasteride was accurately weighed and transferred to 100 ml volumetric flask and dissolved in about 50 ml mixture of methanol-water (50:50) by shaking on a thermostatically controlled water bath for 30 min and diluted up to the mark with the same solvent to get a stock solution of 100 µg/ml. Appropriate amounts of the stock solution were diluted with the same solvent, yields concentrations of 12-28µg/ml which were used for the construction of calibration curve.

Estimation of Dutasteride from commercial preparation

For the analysis of the dosage form, forty tablets of Dutasteride (0.5 mg) were ground to fine powder and mixed thoroughly. Powder equivalent to 10 mg of the drug was transferred to a 100 ml volumetric flask and dissolved in about 50 ml mixture of methanol-water (50:50) by shaking on a thermostatically controlled water bath for 30 min. The solution was filtered through Whatman filter paper (No. 41) and diluted suitably using the same solvent so as to obtain a concentration in the range of linearity as previously discussed for the pure drug and absorbance was recorded at 241 nm against mixture of methanol-water (50:50) as blank. (Figure **2**, Table **1**)

Figure 2. UV spectrum of Dutasteride

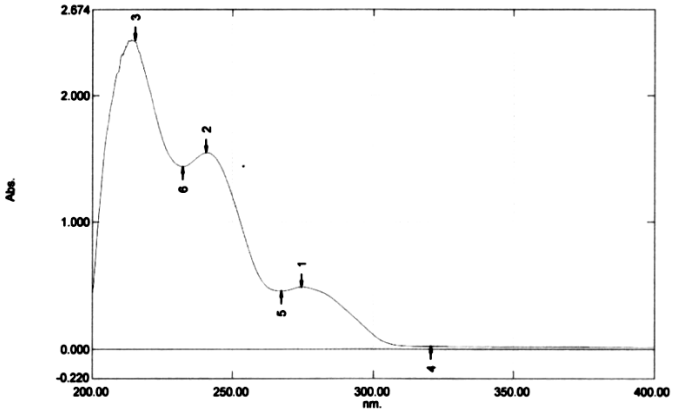


Table 1. Determinations of active ingredients in tablets

Sample	Label claimed	Amount found	% Labeled Claim*
Dutasteride	0.5 mg	0.514±0.36	102.8%

**Average of three determinations*

RESULTS AND DISCUSSION

All of the analytical validation parameters for the proposed method were determined according to International Conference on Harmonization (ICH) guidelines[9]. (Table **1**)

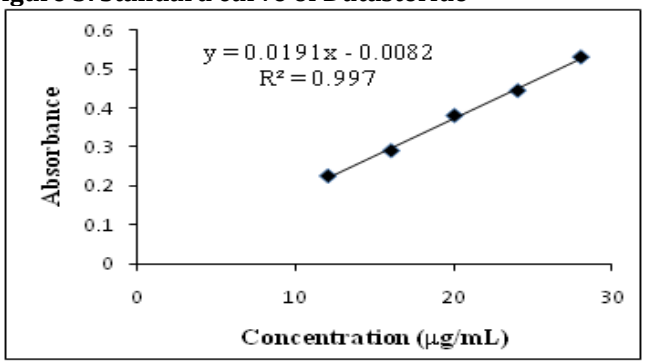
Table 2. Validation Parameters

Parameters	Results		
Absorption maxima(nm)	241		
Linearity range (µg/ml)	12 to 28		
Standard Regression equation	Y = 0.0191x + 0.0082		
Correlation coefficient	0.997		
LOD (µg/ml)	0.125		
LOQ (µg/ml)	0.345		
Precision	Concentration (µg/ml)	Intraday (%RSD)	Interday (%RSD)
	20	0.79	1.02

Linearity

The linearity of this method was determined at seven concentration levels ranging from 12µg/ml- 28µg/ml. The plot of absorbance Vs respective concentration of Dutasteride was found to be linear in the range of 12µg/ml- 28µg/ml. Beer's law was obeyed over this concentration range. The regression equation was found to be Y = 0.0191x + 0.0082 and the correlation coefficient (r) of the standard curve was found to be 0.997 (Figure **3**).

Figure 3. Standard curve of Dutasteride



Precision

The precision is a measure of the ability of the method to generate reproducible results. The precision of the assay was determined by repeatability (intraday) and intermediate precision (inter-day) and reported as RSD %. For this, 20 µg/ml of the solution was measured three times in a day and the same was repeated in next three days and then the %RSD was calculated. The precision (measurements of intraday and interday) results showed (Table **2**) good reproducibility with percent relative standard deviation (% RSD) was below 2.0%. This indicated that method was highly precise.

Recovery studies (Accuracy)

Recovery studies were performed to judge the accuracy of the method. Recovery studies were carried out by adding a known quantity of pure drug to the pre-analyzed formulation and the proposed method was followed. From the amount of drug found, percentage recovery was calculated. Recovery study was carried out at three levels 80%, 100% and 120% for the sample concentration of 20µg/ml. The percentage recovery value (Table **3**) was found to be higher than 100%, indicated that the accuracy of the method and absence of interference of the excipients present in the formulation.

Table 3. Recovery study

Level of Addition (%)	Formulation (µg/ml)	Addition of pure drug (µg/ml)	% Recovery of pure drug	Recovery (%) ± S.D.
80	20	16	101.14	
100	20	20	101.97	101.34±0.57
120	20	24	100.89	

Sensitivity

Limit of detection (LOD) and limit of quantification (LOQ) were calculated by the using the equation given in ICH guidelines. This may be expressed as LOD = 3.3 σ/S and LOQ = 10 σ/S, Where S is the standard deviation of the absorbance of the sample and M is the slope of the calibrations curve. The LOD and LOQ for Dutasteride were found to be 0.125µg/ml and 0.345 µg/ml respectively (Table **1**); this demonstrated that the method was highly sensitive.

CONCLUSION

It can be concluded that the proposed method was simple, rapid, accurate, sensitive, economic and reliable with good

precision and accuracy. The proposed method was also applied for the assay of Dutasteride in tablet formulation (in triplicate) and the results are shown in Table 4. The results obtained were in good agreement with the label claims. Hence, this method can be used for the routine determination of Dutasteride in pure sample and in tablet formulations.

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