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UV Spectrophotometric Method for Simultaneous Determination of Tamsulosin and Finasteride in Combined Dosage Form

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ABSTRACT

A simple, rapid and specific UV spectrophotometric method with good sensitivity was developed and validated for the simultaneous determination of tamsulosin and finasteride in bulk and pharmaceutical formulations. In methanol, the lambda max of finasteride and tamsulosin was fixed as 235 and 225nm respectively, using a Shimadzu UV–Visible spectrophotometer (model UV-1800) with quartz cells. In this proposed method both these drugs obeyed linearity individually and in mixture within the concentration range of 1- 10 µg ml^{-1} for tamsulosin and 12.5 - 100 µg ml^{-1} for finasteride, with a correlation coefficient value of 0.9992 and 0.9994 for tamsulosin and finasteride respectively. The low relative standard deviation values indicate good precision and high recovery values indicate accuracy of the proposed method. The proposed method had been applied to the determination of drugs in commercial formulations. Assay results were in good agreement with label claim. The method was validated according to the ICH guidelines.

Keywords: UV spectrophotometric method, finasteride, tamsulosin, simultaneous determination.

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INTRODUCTION

Finasteride [1] (FIN) chemically is, N- (1,1-dimethylethyl) –3-oxo-4-aza-5-androst-1-ene- 17-carboxamide (Figure.1) is a type II 5 alpha reductase inhibitor, slowly reduces prostatic volume. Prostate growth and function is influenced by dihydrotestosterone, 5 alpha-reductase enzyme converts testosterone to dihydrotestosterone. Inhibition of 5 alpha reductase results in decreased level of dihydrotestosterone leading to reduction of prostate size. Tamsulosin [2] (TAM) chemically is, 5- [(2R)-2[[2-(2-Ethoxy Phenoxy) ethyl] amino]Propyl}- 2-methoxy benzene sulfonamide (Figure.2) is a selective alpha 1 adrenoceptor blocking agent. Smooth muscle tone is mediated by the sympathetic nervous stimulation of alpha1 adrenoceptors, which are abundant in the prostate, prostatic capsule, prostatic urethra, and bladder neck. Blockade of these adrenoceptors can cause smooth muscles in the bladder, neck and prostate to relax, resulting in an improvement in urine flow rate and reduction in symptoms of benign prostatic hyperplasia (BPH) [3, 4]

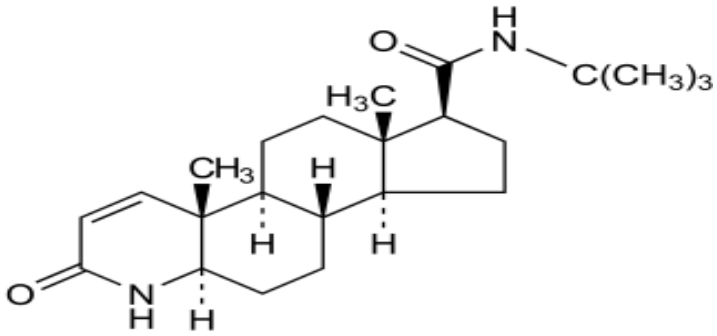

Figure 1. Finasteride

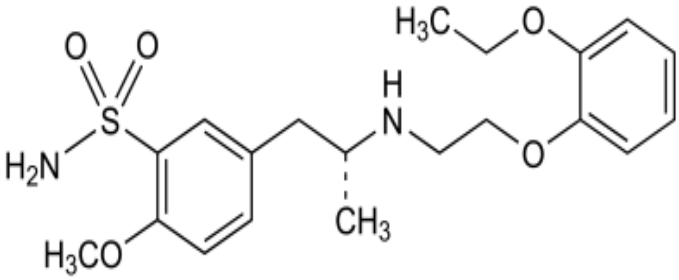

Figure 2. Tamsulosin

According to the literature survey it was found that few analytical methods such as Visible, UV, polarographic analysis, HPLC methods were reported for finasteride and tamsulosin [5-11]. The objective of this study was to develop and validate a simple and specific UV spectrophotometric method for the simultaneous determination of finasteride and tamsulosin in formulation. This method exhibited a precise, accurate and cost effective assay for these drugs in mixture.

MATERIALS AND METHDS

Chemicals: 0.1N Hcl, 0.1N NaOH, Water, Acetonitrile, Methanol. Drugs: Tamsulosin and Finasteride pure powder were gift samples supplied from Intaas Pharmaceutical Limited, India. Formulation, Urimax F (0.4mg TAM + 5mg FIN per capsule), manufactured by Cipla Pharmaceutical Ltd, India, was purchased from the local pharmacy in Hyderabad, India.Instrument: Shimadzu UV–Visible spectrophotometer (model uv-1800).

Method

Selection of solvent and wavelength (λ max):

The absorbance of the both drugs i.e TAM and FIN was found maximum in methanol solvent compared to other solvents and the lamba (λ) max of tamsulosin and finasteride was fixed as 225nm and 235nm (Figure.3, 4) respectively.

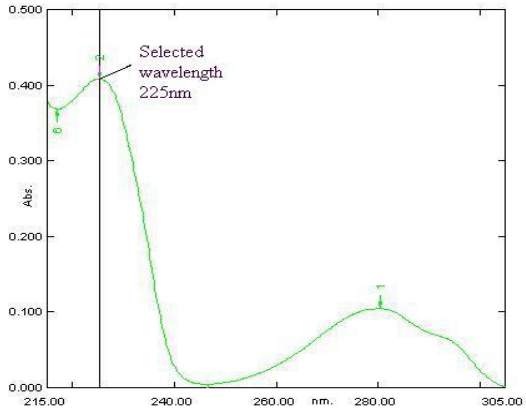

Figure 3. Spectrum of Tamsulosin showing selected wavelength

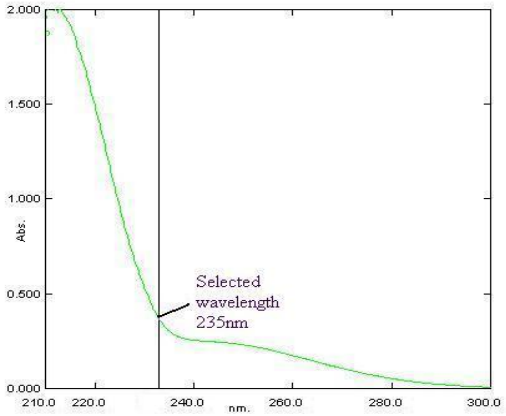

Figure 4. Spectrum of Finasteride showing selected wavelength

Preparation of FIN Stock Solution:

Standard finasteride stock solution was prepared by dissolving 125 mg of drug in 100ml of methanol to get a concentration of 1250 μg ml^{-1}.

Preparation of TAM stock solution:

Standard tamsulosin stock solution was prepared by dissolving 10mg of drug in 100ml of methanol to get a concentration of 100 µg ml^{-1}.

Application of Vierodt's Method: [12]

In quantitative estimation of two components by Vierodt's (Simultaneous equation) method two wavelengths i.e, 225nm of TAM and 235nm of FIN were selected as their respective λ max from the overlain spectrum, at which both drugs have maximum absorbance. A set of two simultaneous equations were formed using absorptivity coefficients at selected wavelengths. The concentrations of two drugs in the mixture were calculated using the following two simultaneous equations.

$C_x = A_2\, ay_1 - A_1\, ay_2 / ax_2\, ay_1 - ax_1\, ay_2$ --- (1)

$C_y = A_1\, ax_2 - A_2\, ax_1 / ax_2\, ay_1 - ax_1\, ay_2$ --- (2)

Where,

C_x and C_y are the concentrations of x and y

A_1 is the absorbance of mixture at λ_1 ,A_2 is the absorbance of mixture at λ_2 ,ax_1 is the absorptive value of x at λ_1 ,ax_2 is the absorptive value of x at λ_2 ,ay_1 is the absorptive value of y at λ_1 ,ay_2 is the absorptive value of y at λ_2

Preparation of Test Solutions and Estimation of Finasteride and Tamsulosin in formulation

For analysis of commercial formulations, 20 capsules (Urimax F containing 0.4mg TAM and 5mg FIN) were weighed, powdered and weight equivalent to 12.5 mg of finsateride and 1mg of tamsulosin was taken and transferred into a volumetric flask and made up to 100ml with methanol, sonicated for 5min, filtered and further diluted with methanol to get the concentrations within the linearity range of respective drugs and measured the absorbance's at 235 nm for finsateride and 225 nm for tamsulosin respectively.

RESULTS AND DISCUSSION

The analytical method was validated with respect to parameters such as linearity, precision, accuracy, limit of detection (LOD), limit of quantitation (LOQ) and ruggedness.

Linearity

To construct Beer's law plot for finasteride and tamsulosin different aliquots of finasteride (1-8ml) with different concentrations (12.5, 25, 37.5, 50, 62.5, 75, 87.5 and 100 µg ml^{-1}) and tamsulosin (0.1-1ml) with different concentrations (1, 2, 3, 4, 5, 6, 7, 8, 9 and 10µg ml^{-1}) (Figure .5, 6), were prepared by serial dilutions with methanol from the individual stock solutions. Then

absorbance of the solutions was measured at 235 nm for finasteride and 225 nm for tamsulosin respectively. The linearity values were shown in Table 1.

Table 1. Linearity

Parameters	Tamsulosin	Finasteride
Concentration range (µg ml^{-1})	1 – 10	12.5 - 100
Slope	0.059	0.006
Intercept	0.003	0.007
Correlation coefficient (r^2)	0.9992	0.9994

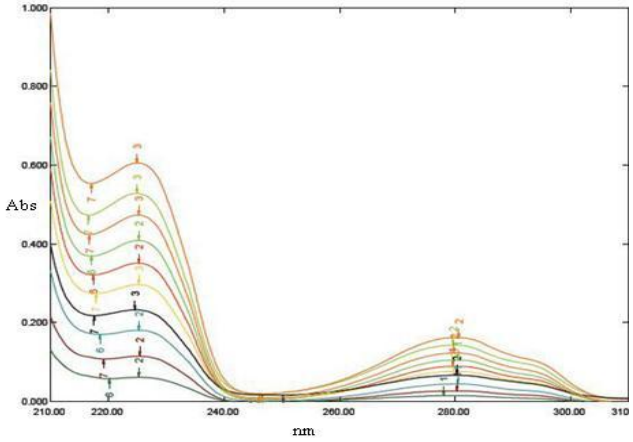

Figure 5.Overlay spectra of standard tamsulosin (1-10 µg/ml)

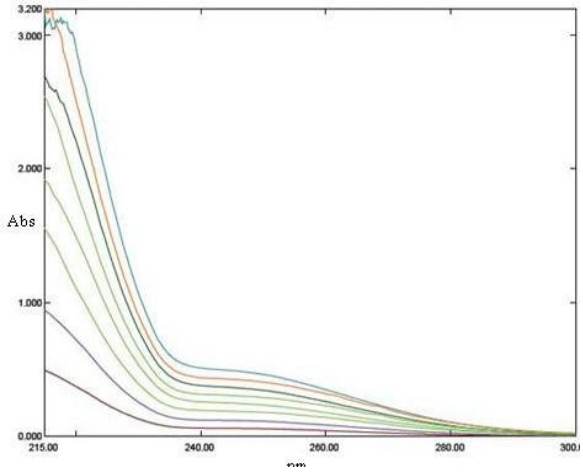

Figure 6.Overlay spectra of standard finasteride drug (12.5-100 µg/ml)

Recovery studies

The recovery studies were carried out at three different levels i.e. 80%, 100% and 120% level. To ensure the reliability of the above method, recovery studies were carried out by mixing a known quantity of standard drug with the pre analysed sample formulation and the contents were reanalyzed by the proposed method. The percent recovery values were in between 98.0-99.8%, which indicates that the method is accurate and reveals that commonly used excipients and

additives present in the pharmaceutical formulations did not interfere in the proposed method. The percentage recovery values were shown in Table 2.

Table 2. Recovery studies

Drug	Amount added (µg ml^{-1})	Amount recovered (µg ml^{-1})	% Recovery
Finasteride	12.5	12.46	99.70
	10	9.78	98.68
	15	14.89	99.73
Tamsulosin	1	0.981	98.14
	0.8	0.789	99.40
	1.2	1.19	99.60

Precision

The precision of the method was established by carrying out the analysis of the analytes (n = 6) using the proposed developed method. The low value of standard deviation showed that the methods were precise. The results were shown in Table 3.

Table 3. Precision studies

Drug	Concentration (µg ml^{-1})	Intra-day conc. Measured		Inter-day conc. Measured	
		Mean(µg ml^{-1})	% *RSD	Mean(µg ml^{-1})	%*RSD
Finasteride	25	25.05	0.841	25.08	1.106
Tamsulosin	2	2.03	0.674	2.05	0.965

*mean of six observations, Relative standard deviation (RSD)

LOD and LOQ

The LOQ of tamsulosin and finasteride was found to be 1µg ml^{-1} and 12.5µg ml^{-1} respectively and the LOD was found to be 0.3µg ml^{-1} and 4µg ml^{-1} respectively.

Ruggedness

The ruggedness test of analytical assay method is defined as degree of reproducibility of assay results obtained by the successful applications of assay over different time, day and among multiple analysts. The % RSD values for assays performed in the same laboratory by two analysts were found to be less than 2, indicating the ruggedness of the method.

Assay

Then the amount of drug present in formulations was calculated using the simultaneous equation. The spectrum of formulation sample is shown in Figure 7. The results were shown in Table 4.

Table 4. Analysis of formulation

Drug name	Amount labeled (mg ml^{-1})	Amount estimated (mg ml^{-1})	% Label claim	% deviation
Finasteride	5mg	4.94	98.8	(-) 1.2
Tamsulosin	0.4mg	0.396	99.0	(-) 1.0

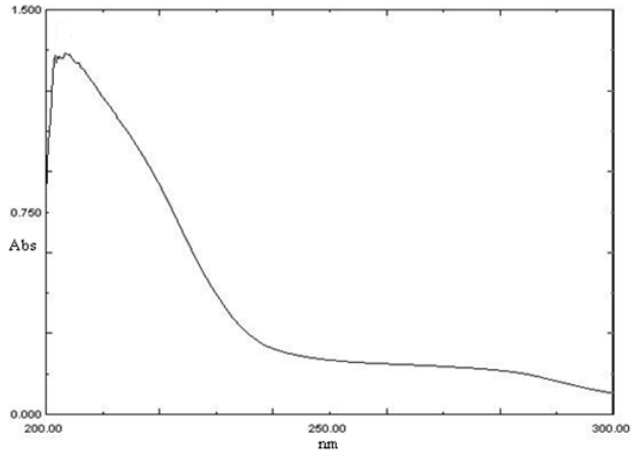

Figure 7. Spectrum of formulation (tamsulosin 2 µg ml^{-1} and finasteride 25 µg ml^{-1})

CONCLUSION

A convenient and rapid UV method has been developed for simultaneous estimation of finasteride and tamsulosin in available dosage form. The assay provides a linear response across a wide range of concentrations. Low intra-day and interday % RSD coupled with excellent recoveries. Hence, this method can be easily and conveniently adopted for routine analysis of Finasteride and Tamsulosin in pure form and its dosage forms.

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