Research Article
ISSN: 0974-6943

Vishnu P. Choudhari et al. / Journal of Pharmacy Research 2009, 2(6),1065-1067

Available online through
www.jpronline.info

Simultaneous determination of Finasteride and Tamsulosin in pharmaceutical preparations by ratio derivative spectroscopy

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Received on: 27-02-2009; Accepted on: 29-04-2009

ABSTRACT

Simple, accurate, precise, and sensitive spectrophotometric method for simultaneous estimation of Tamsulosin(TAM) and Finasteride(FINA) in combined tablet dosage form have been developed and validated. The ratio derivative spectroscopic method involves measurement of first derivative amplitude of ratio spectra at 240.01nm for FINA and 229.91 nm for TAM as two wavelengths for estimation. Beer's law is obeyed in the concentration range of 2-10 and 25-125 µg/mL for TAM and FINA, respectively.

Keywords: Tamsulosin, Finasteride, Ratio Derivative Spectroscopy.

INTRODUCTION

Tamsulosin (TAM) (1) is chemically known as 5-[(2R)-2-[[2-(2-ethoxyphenoxy) ethyl] amino] propyl]-2-methoxybenzenesulfonamide, which an alpha-adrenoceptor blocker with enhanced specificity for the alpha-adrenoceptors of the prostate, is commonly used to treat benign prostatic hyperplasia (BPH). Finasteride (FINA) (2) is chemically known as (5a, 17ß)-N-(1, 1-Dimethylethyl)-3-oxo-4- azaandrost-1-ene-17-carboxamide. Finasteride is a competitive and specific inhibitor of Type II 5a-reductase, an intracellular enzyme that converts the androgen testosterone into Dihydro testosterone (DHT). For the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate to improve symptoms, reduce the risk of acute urinary retention, and reduce the risk of the need for surgery including transurethral resection of the prostate. The literature survey revealed that the many more HPLC and Spectroscopic methods for TAM and FINA are reported as a single drug formulation. But to my knowledge, only one method was reported for determination of combination of FINA and TAM (3), therefore it is felt necessary to develop simple ratio derivative UV spectrophotometric methods for this combination.

Several analytical methods that have been reported for the determination of TAM (4-7) in biological fluids and pharmaceutical formulations which include liquid chromatography coupled with mass spectrometry, HPLC, chiral liquid chromatography and capillary electrophoresis. For FINA several analytical methods have been reported which includes Bromometric assay, spectrophotometry, and liquid chromatography (8-13). This paper describes simple, accurate, precise and sensitive ratio derivative UV spectrophotometric method for simultaneous determination of TAM and FINA in combined tablet dosage form. The proposed methods are optimized and validated as per the International Conference on Harmonization (ICH) guidelines (14).

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MATERIALS AND METHODS

DRUGS AND CHEMICALS

Spectroscopic grade Methanol was used for specrtrophotometric method. All the solvents and reagents used were purchased from LOBA Chemie Pvt. Ltd., Mumbai. Tablet used for analysis were VELTAM – F form two batches (Batch no DH 1189 and DH 1338) manufactured by Intas Pharmaceuticals, Dehradhun, India having FINA USP 5mg and TAM 0.4 mg per tablet.Pure drug sample of FINA % purity 99.78 was kindly supplied as a gift sample by Ranbaxy Laboratories Ltd. and pure drug sample of TAM % purity 99.915 was gifted by Aarti drugs Pvt. Ltd. Mumbai. These samples were used without further purification.

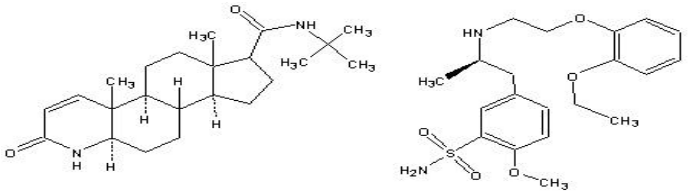
INSTRUMENTS

An UV-Visible double beam spectrophotometer (Varian Cary 100) with 10MM matched quartz cells were used for spectrophotometric method. All weighing were done on electronic balance (Model Shimadzu AUW-220D).

PROCEDURE

RATIO DERIVATIVE SPECTROPHOTOMETRIC METHOD (15)

Stock solution of each drug having concentration 1000µg/mL was prepared by dissolving FINA and TAM separately in methanol. Aliquots of stock solutions were further diluted in methanol and were



a) FINA b) TAM

Fig1: Chemical structures of a) FINA and b) TAM

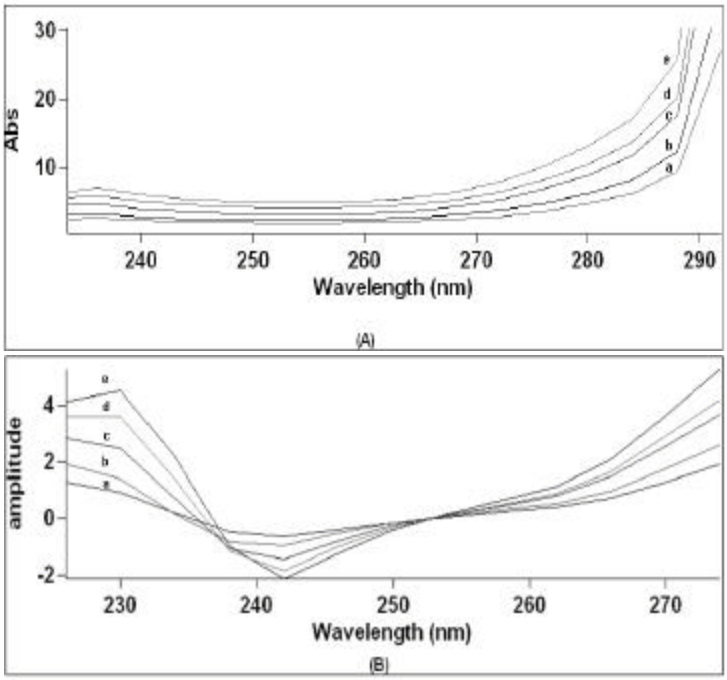
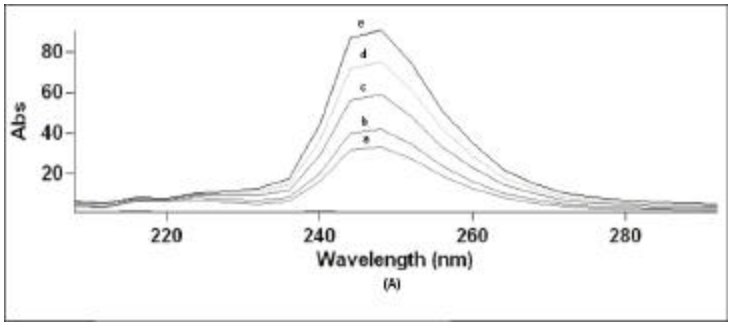


Fig 2. Ratio spectra (A) and first derivative of the ratio spectra (B) of (a) 2, (b) 4, (c) 6, (d) 8 and (e) 10 µg/mL solution of TAM when 75 µg/mL solution of FINA is used as divisor.



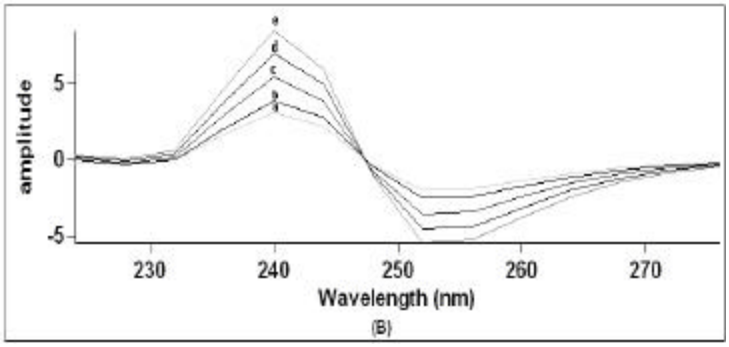


Fig 3. Ratio spectra (A) and first derivative of the ratio spectra (B) of (a) 25, (b) 50, (c) 75, (d) 100 and (e) 125 µg/mL solution of FINA when µg/mL solution of TAM is used as divisor.

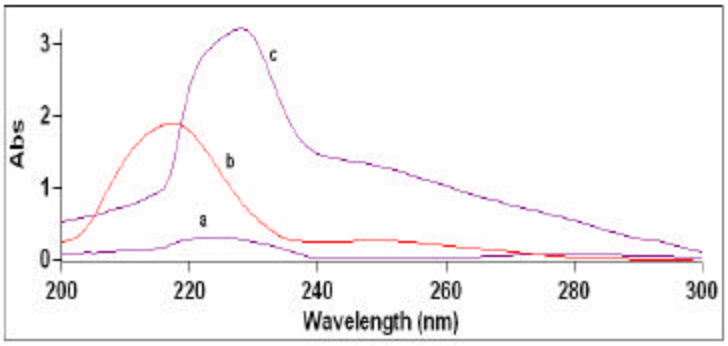


Fig 4.Overlain zero order absorbance spectra of (a) TAM (µg/mL) (b) FINA (75 µg/mL) (c) and their mixture

Table 1 . Optical Characteristics and Validation for the Method

Parameters	FINA	TAM
Working (nm)	240.01	229.91
Linearity	2-10 µg/mL	25-125 µg/mL
Molar absorptivity (l mole^{-1} cm^{-1})	171869.27	87829.65
Precision [a]		
Inter-day (%RSD)	0.18	0.16
Intra-day (%RSD)	0.15	0.13
LOD [a] ± SD	0.21 µg/mL	0.19 µg/mL
LOQ [a] ± SD	0.647 µg/mL	0.54 µg/mL
Regression values [a]		
Slope ± SD	0.05504	0.4715
Intercept ± SD	1.408	-0.249
Regression coefficient(r^2) ± SD	0.998	0.999

[a] *Denotes average of six estimations*

Table 2. Statistical Validation Data of Tablet Formulation and recovery study

Drug	Result of formulation analysis			Result of recovery study		
	Amount present	%Of amount Found ± SD	%RSD	Level of recovery	% of recovery	%RSD
FINA	5 mg	99.82± 0.552	0.553	80	99.32	0.228
				100	100.59	0.612
				120	99.49	0.351
TAM	0.4 mg	99.63±0.791	0.791	80	100.74	0.560
				100	101.23	0.286
				120	99.87	0.216

[a] *Denotes average of six estimations*

scanned in the wavelength range of 300–200 nm. The Beer's law was obeyed over the concentration range 2-10 µg/mL by TAM and over the concentration range 25-125 µg/mL by FINA.

Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 5 mg of FINA and 0.4 mg of TAM was transferred to 25 mL volumetric flask, 20 mL of methanol was added to the same flask, sonicated for 30 min and diluted to 25 mL with methanol. The sample solution was centrifuged for 5 minutes at 8000 rpm. The solution was further diluted with methanol to obtain the dilution within the Beer's law range.

THEORETICAL ASPECTS

The absorption spectrum of mixture is divided by the absorption spectrum of std. solution of one of compound and first derivative of ratio spectrum is obtained, resulting spectra is independent of conc. of divisor. The conc. of active compounds are then determined from calibration graph obtained by measuring amplitude at points corresponding to minima or maxima. Using appropriate dilutions of standard stock solution, the two solutions were scanned separately. The ratio spectra of different TAM standards at increasing concentrations were obtained by dividing each with the stored spectrum of the standard solution of FINA (75 µg/mL) as shown in Fig 2 (A) and the first derivative of these spectra traced, are illustrated in Fig 2 (B). Wavelength 229.91 nm was selected for the quantification of TAM in TAM + FINA mixture. The ratio and ratio derivative spectra of the solutions of FINA at different concentrations were obtained by dividing each with the stored standard spectrum of the TAM (6 µg/mL) (Fig. 3 (A) and 3 (B) respectively). Wavelength 240.01 nm was selected for the quantification of FINA in FINA + TAM mixture. Measured analytical signals at these wavelengths were proportional to the concentrations of the drugs. The amount of TAM and FINA in tablets was calculated by using following equations

At 229.91 nm: $C_{TAM} = d/d\lambda [A_{TAM} / A_{FINA}]$ – Intercept (C) / Slope (m) ... (1)

At 240.01 nm: $C_{FINA} = d/d\lambda [A_{FINA} / A_{TAM}]$ – Intercept (C) / Slope (m) ... (2)

RECOVERY STUDIES

The accuracy of the proposed method was checked by recovery studies, by addition of standard drug solution to preanalysed sample solution at three different concentration levels (80 %, 100 % and 120 %) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 2 µg mL^{-1} of TAM and 25 µg $mL^{-1}$of FINA.

RESULTS AND DISCUSSION

Under experimental conditions described, calibration curve, assay of tablets and recovery studies were performed. Using appropriate dilutions of standard stock solution the two solutions were scanned separately. The zero order overlain spectra are shown in Fig 4. A critical evaluation of proposed method was performed by statistical analysis of data where slope, intercept, correlation coefficient is shown in Table 1. As per the ICH guidelines, the method validation parameters checked were linearity, accuracy and precision. Beer's law obeyed in the concentration range 2-10 µg/mL and 25-125 µg/mL with correlation coefficient of 0.999 and 0.998 for TAM and FINA respectively. The proposed method was also evaluated by the assay of commercially available tablets containing TAM and FINA (n = 6). The % assay was found to be 99.63 % for TAM and 99.82 % for FINA as presented in Table 2. Results of recovery studies are shown in Table 2. For TAM, the recovery study results ranged from 99.87% to 101.23 % with % RSD values ranging from 0.216 % to 0.560 %. For FINA, the recovery results ranged from 99.32 % to 100.59 %, with % RSD values ranging from 0.228 % to 0.612 %. The accuracy and reproducibility is evident from the data as results are close to 100 % and standard deviation is low.

CONCLUSION

The validated Spectrophotometric method employed here proved to be simple, fast, accurate, and precise and sensitive thus can be used for routine analysis of TAM and FINA in combined tablet dosage form without prior separation.

ACKNOWLEDGEMENT

The authors are thankful to Dr.Reddy's Pharmaceutical Ltd., Hyderabad, India and Aarti Drugs Ltd., Mumbai for providing gift samples of FINA and TAM repectively. The authors are thankful to University of Pune for financial assistance.

REFERENCES

1. The Merck Index, Maryadele J.O. Neil.Eds,13th Ed Published by Merck Research Lab, Division of Merck & Co. White House Station, NJ, USA,2001,pg no 721,1615.
2. The United States Pharmacopoeia, NF 24,29th Ed., Asian Edition, The United States Pharmacopoeal Convention MD, 2006 pg no. 907.
3. Pande V V, Jadhav J N, Chandorkar J G, Journal of Pharmacy Research Vol.2.Issue 3. 2009 Pg no 507.
4. Rao, R. N., Talluri, M.V.N., Raju, A.N., Shinde.D.D., Ramanjaneyulu, G.S., J Pharm Biomed Anal 46 (1), 2007 pg no94.
5. Macek J., Klýma J., Ptacek P., J Chromatogr B, 809, 2004,pg no307.
6. Kulkarni S P., Amin P D, J Pharm Biomed Anal 23, 2000,pg no 983.
7. Matsushima H, Takanuki K, Kamimura H, Watanabe T, Higuchi S, J Chromatogr B, 695, 1997 pg no 317.
8. Sevgi T U, Spectrochimica Acta part A 67, 2007,pg no 778.
9. Basavaiah K., Somashekar B.C., Anilkumar U. R., Ramakrishna,V. Electica Quimica, volume 31, 2006, pg no 31.
10. Akheel A. Syed, Mungalimane K. Amshumali, J Pharm Biomed Anal., 25, 2001,pg no1015.
11. Demir H, Cucu A, Sakarya S, Analytica Chimica Acta 557, 2006, pg no252.
12. Basavaiah K, Somashekar B C, E-J of Chemistry Vol. 4, No.1, pg no109.
13. Constanzer M. L., Matuszewski B. K., Bayne W. F., J of Chromatogr, 566, 1991,pg no127.
14. ICH Harmonised Tripartite Guideline , Validation of Analytical Procedures: Text and Methodology Q2 (R1) Nov 2005.
15. Ei-Sayed A Y, EI-Salem N A, Recent Development of Derivative Spectrophotometry and their Analytical Applications ,Analytical Science 21,2005,pg no595.

Source of support: Nil, Conflict of interest: None Declared