JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

First order Derivative Spectrophotometric Method for Determination of Minoxidil and Finasteride in Pharmaceutical Dosage Form

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Article history:

Received 09 FEBRUARY 2018,
Accepted 31 MARCH 2018
Available online 10 APRIL 2018

Citation:
Roy A., Hinge M., Desai S. Formulation and First order Derivative Spectrophotometric Method for Determination of Minoxidil and Finasteride in Pharmaceutical Dosage Form **J Pharm Sci Bioscientific Res**. 2018. 8(1):112-116

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ABSTRACT:

A simple, reliable, accurate and precise first order derivative method has been developed and validated for simultaneous determination of Minoxidil and Finasteride in Pharmaceutical dosage form. In methanol and water, the quantitative determination was carried out using first order spectra of Minoxidil at 300 nm (ZCP of FIN) and Finasteride and at 228.63nm (ZCP of MIN), respectively. The linearity for MIN and FIN was obtained in the concentration range 5-25 µg/ml and 0.1-0.5 µg/ml with 0.9990 and 0.9971 correlation coefficient, respectively. Method was validated according to ICH guideline.

KEY WORDS: Minoxidil (MIN), Finasteride (FIN), First order derivative method

INTRODUCTION:

Minoxidil (MIN) chemically known as 6-(Piperidin-1-yl) pyrimidine-2, 4-diamine 3-oxide. (Figure 1) it is an antihypertensive agent. It is used in the treatment of male pattern hair loss, Minoxidil increase hair growth by prolonging anagen through the proliferative and anti-apoptotic effects on DPCs. acting on alteration of androgenic effect on genetically programmed hair follicles and direct stimulation of resting hair follicles.

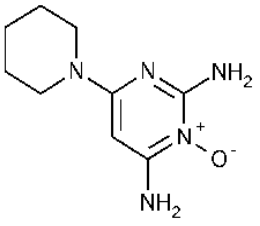

Figure 1 Structure of Minoxidil

Finasteride (FIN) chemically known as N-(1, 1-dimethylethyl)-3-oxo-(5α, 17β)-4-azaandrost-1-ene-17-carboxamide belongs to the class antiandrogen (Figure.2). It is an orally active testosterone 5-alpha-reductase inhibitor. It is used for treatment of benign prostatic hyperplasia. It is also used in the treatment of male pattern hair loss, In men with androgenic alopecia, the mechanism of action has not been fully determined, but finasteride has shown to decrease scalp dihydrotestosterone (DHT) concentration to the levels found in hairy scalp, reduce serum DHT, increase hair regrowth, and slow hair loss.

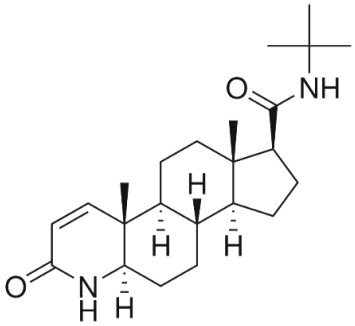

Figure 2 Structure of Finasteride

Literature survey revealed second order derivative spectroscopy and RP-HPLC analytical methods have been reported for Minoxidil and Finasteride in combined dosage form but no first order derivative spectroscopy method have been reported for estimation of Minoxidil and Finasteride in Pharmaceutical dosage form. The present study involves development and validation of simple, precise, sensitive and accurate ultra-violet (UV) spectrophotometric method for estimation of Minoxidil and Finasteride in Pharmaceutical dosage form. Validation of proposed method is carried out according to ICH guidelines.

MATERIALS AND METHOD

Double beam UV-visible spectrophotometer (Simadzu-1800, Software –UV Probe, Version 2.42) having two matched quartz cells with 1 cm light path. Single pan Electronic analytical balance (REPTECH). Pure samples of Minoxidil and Finasteride were obtained as a gift samples from INTAS Pharmaceuticals, Ahmedabad, India. Distilled water and Methanol UV Grade was purchased from Thomas Baker, Mumbai, India.

SOLVENT SELECTION

In Methanol and Water Minoxidil and Finasteride gives linear spectra at their measured wavelength. So Methanol and Water is the preferred solvent.

SELECTION OF WAVELENGTHS (ZERO CROSSING POINTS)

The Normal spectral data was processed to obtain first order derivative spectrum at the range of 400-200 nm. It was observed that Minoxidil shows zero crossing point (ZCP) at 228.63 nm, 249.01, 261.97, 274.37 and 288.45 out of which 228.63 nm was selected because at this wavelength Finasteride gives considerable absorbance. Finasteride shows ZCP at 300 nm. ZCP of value of MIN was found to be 300 nm for estimation of FIN and ZCP value of FIN was found to be 228.63 nm for estimation of MIN because adequate absorbance produce at this wavelength.

PREPARATION OF STANDARD STOCK SOLUTION

Standard Minoxidil and Finasteride stock solution was prepared by dissolving 10 mg of drug in 10 ml volumetric flask separately to get concentration 1000 µg/ml in Methanol.

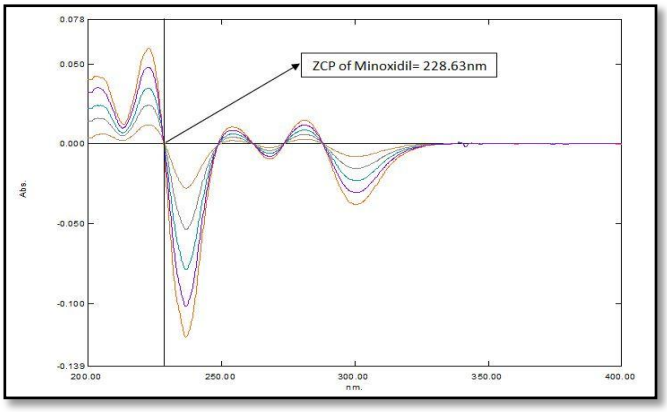

Figure 3 Overlain spectra of MIN

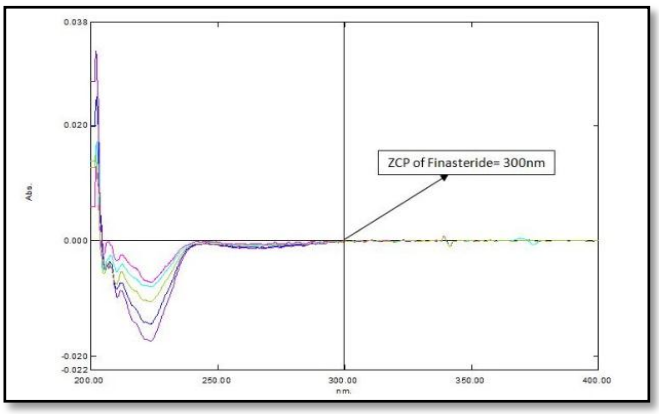

Figure 3 Overlain spectra of FIN

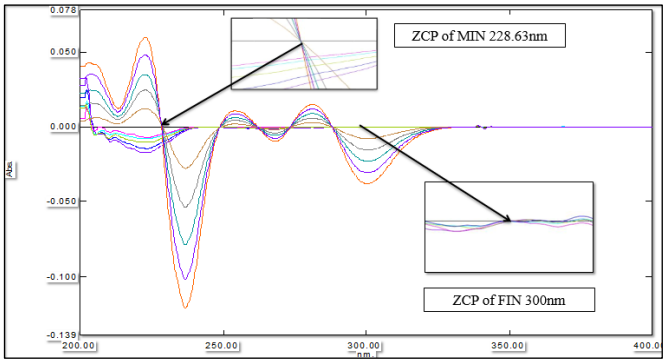

Figure 4 Overlain spectra of MIN & FIN

PREPARATION OF SAMPLE SOLUTION

Pipette out 1 ml from the standard stock solution of Minoxidil and Finasteride in other 10 ml Volumetric flask and volume was made up to the mark with distilled water (100 µg/ml). Pipette out 1 ml from the sample solution of Finasteride in other 10 ml Volumetric flask and volume was made up to the mark with distilled water (10 µg/ml). From Minoxidil sample solution, aliquots of 0.5,1.0,1.5,2.0 and 2.5ml and 0.1, 0.2, 0.3, 0.4 and 0.5 for Finasteride were transferred to the 10 ml of volumetric flask separately and volume was made up to mark with water

to get concentration for Minoxidil 5,10,15,20 and 25 µg/ml and 0.1, 0.2, 0.3, 0.4 and 0.5 µg/ml for Finasteride.

VALIDATION PARAMETERS

Linearity

Based on the result obtained under experimental conditions described, the graph obtained for first order derivative spectra showed in (Figure. 3 and 4). The absorbance of solution was measured at 300 nm for MIN and 228.63 nm for FIN. The calibration curve showed linear response in range of 5- 25 µg/ml for MIN and 0.1-0.5 µg/ml for FIN.

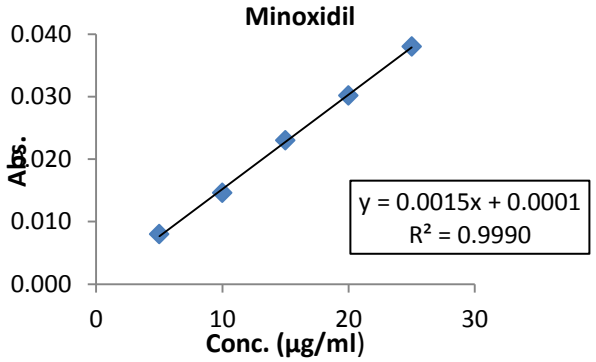

Figure 5 Calibration curve of Minoxidil

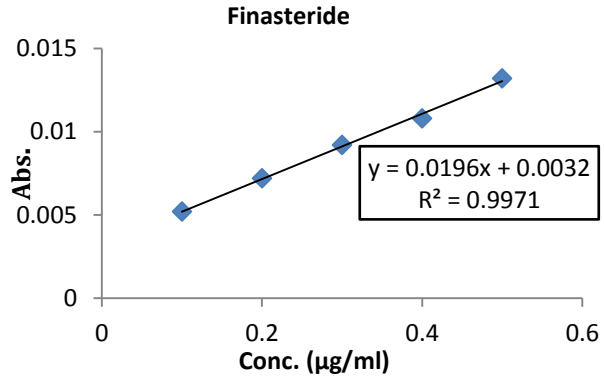

Figure 6 Calibration curve of Finasteride

Table 1 Result of Linearity

Sr. No.	Parameter	MIN (at 300 nm)	FIN (at 228.63 nm)
1	Concentration (µg/ml)	May-25	0.1-0.5
2	Slope	0.0015	0.0196
3	Intercept	0.0001	0.0032
4	Correlation co-efficient	0.999	0.9971

Precision

To determine precision of method MIN and FIN solution at concentration 15 and 0.3 µg/ml respectively was analyse six times for first derivative spectrophotometric method. The solution for standard deviation were prepared fresh every day. The precision values were shown in Table No. 4 and 5.

Table 2 Result of Repeatability of MIN and FIN

Drugs	Mean ± S.D. (n=6)	%R.S.D.
MIN (at 300 nm)	0.02298 ± 0.00004	0.1776
FIN (at 228.63 nm)	0.00899 ± 0.00001	0.1815

Table 3 Result of Precision of MIN.

Conc. (µg/ml)	Intraday Abs. ± S.D. (n=3)	% R.S.D.	Interday Abs. ± S.D. (n=3)	% R.S.D.
15	0.0229 ± 0.000061	0.2648	0.0230 ± 0.000100	0.4444
20	0.0303 ± 0.000061	0.2002	0.0310 ± 0.000152	0.4869
25	0.0376 ± 0.000010	0.2659	0.0382 ± 0.000152	0.3995

Table 4 Result of Precision of FIN.

Conc. (µg/ml)	Intraday Abs. ± S.D. (n=3)	% R.S.D.	Interday Abs. ± S.D. (n=3)	% R.S.D.
0.3	0.0079 ± 0.000020	0.2518	0.0103 ± 0.000050	0.4878
0.4	0.0098 ± 0.000021	0.2116	0.0108 ± 0.000050	0.4640
0.5	0.0124 ± 0.000025	0.2025	0.0137± 0.000052	0.3873

Recovery studies

The recovery studies were carried out at three different levels i.e. 80%. 100% and 120%. The percentage recovery values were shown in Table No. 2

Table 5 Result of Recovery Study

Drug	Amount Added (µg/ml)	Amount Recovered (µg/ml)	% Recovery
Minoxidil	10	9.96	99.66
	18	17.98	99.95
	20	19.85	99.77
	22	21.95	99.93
Finasteride	0.2	0.19	99.82
	0.36	0.35	99.82
	0.4	0.39	99.61
	0.44	0.43	99.72

Assay procedure

It was employed for analysis of Minoxidil and Finasteride in topical formulation i.e. Morr F 5% containing Minoxidil 5% and Finasteride 0.1%. In this method the higher percentage of recovery and non-interference of the formulation excipients in analysis method for both drugs in their combined dosage form. The %RSD value Indicated suitability of this method for routine analysis of Minoxidil and Finasteride in their combined dosage form. Table No.4.

Table 6 Result of Assay of Marketed Formulation.

Formulation	Actual concentration µg/ml of the solution		Amount obtained µg/ml of the solution (n=3)		% MIN ± S.D. (n=3)	% FIN ± S.D. (n=3)
	MIN	FIN	MIN	FIN		
Morr F 5%	15	0.3	14.986	0.296	99.19 ± 0.674	99.53 ± 0.0978

LOD and LOQ

The limit of detection (LOD) and limit of quantification (LOQ) of developed method were determined by injecting progressively low concentration of the standard solution. The LOD of Minoxidil and Finasteride was found to be 0.0272 µg/ml and 0.00327 µg/ml respectively. LOQ was found to be 0.08242 µg/ml and 0.00991 µg/ml respectively.

Table 7 Summary of Validation Parameters

PARAMETER	MIN	FIN
ZCP (nm)	228.63	300
Linearity (µg/ml) (n=5)	5-25 µg/ml	0.1-0.5 µg/ml
Regression Equation (y = mx + c)	y = 0.0015x + 0.0001	y = 0.0196x + 0.0032
Correlation coefficient	0.9990	0.9990
Repeatability (% R.S.D) (n=6)	0.1776	0.1815
Intraday precision (% R.S.D) (n=3)	0.0229 – 0.0376	0.0079 – 0.0124
Interday precision (% R.S.D) (n=3)	0.0230 – 0.0382	0.0103 – 0.0137
LOD (µg/ml) (n=5)	1.14315	0.01786
LOQ (µg/ml) (n=5)	3.4641	0.05413
% Recovery	98.93 – 99.95	99.61– 99.82
Assay % w/w (n=3)	99.19 ± 0.674	99.53 ± 0.0978

RESULT AND DISCUSSION

The developed first order derivative method for simultaneous estimation of MIN and FIN in pharmaceutical dosage form was found reliable. Linearity for MIN at 300nm (ZCP of FIN) and FIN at 228.63nm (ZCP of MIN) are shown in Table. Calibration graph of absorbance versus concentration for MIN and FIN were plotted; and the linear regression equations obtained at 300nm, Y= 0.0015X + 0.0001 and at 228.63nm, Y= 0.0196X + 0.0032, respectively. The validation of developed method was performed as per ICH guideline as shown in respective tables. Recovery study was carried out showing accuracy with % recovery of 98.93 - 99.95 % for MIN and 99.61 – 99.82 % for FIN. The LOD was found to be 1.14315 µg/ml and 0.01786 µg/ml and LOQ was found to be 3.46410 µg/ml and 0.05413 µg/ml for MIN at 300 nm (ZCP of FIN) and FIN at 228.63 nm (ZCP of MIN), respectively. Pharmaceutical dosage form was analysed by the developed method and the assay was found to be 99.19 % and 99.53% for MIN and FIN, respectively. Summary of all the validation parameters is shown in the table.

CONCLUSION

The developed first order derivative UV spectroscopic method has been found simple, accurate and precise, as indicated by the low relative standard deviation. Thus, the developed method can be used easily for the estimation of pharmaceutical dosage form.

ACKNOWLEDGEMENT

I am thankful to INTAS Pharmaceuticals, Ahmedabad for the gift samples and ROFEL, Shri G.M. Bilakhia College of Pharmacy, Vapi for all the facilities and support throughout the study.

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