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UV-Spectrophotometric determination of minoxidil and its application to the assay in pharmaceutical dosage forms

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ABSTRACT

A selective and sensitive spectrophotometric method for determination of Minoxidil has been validated by three simple, precise and economical UV methods have been developed for the estimation of Minoxidil in Pharmaceutical solution. Minoxidil has the absorbance maxima at 285 nm (Method A), and in the first order derivative spectra, showed sharp peak at 267 nm (Method B). Method C applied was in the wavelength range of 280-288 nm. All the process was carried out in methanol as the solvent. Linearity for detector response was observed in the concentration range of 5-40µg/mL for Method A, Method B and Method C. The proposed methods were successfully applied for the determination of Minoxidil in there commercial preparation. The method allows rapid analysis of pharmaceutical formulation with accuracy and precise. Analysis was validated by statistically and recovery studies which was found satisfactory.

Keywords: Absorption Maxima, Area under curve, Derivative Spectroscopy, Minoxidil.

INTRODUCTION

Minoxidil is chemically 2, 4-diamino-6-piperidinopyrimidine-3-oxide (Fig. 1) white crystalline power soluble in methanol but insoluble in water, acetone and alkaline solution [1]. Minoxidil has been used as a peripheral vasodilatator drug orally administrated, applied in the treatment of refractory hypertension patients [2]. Excessive oral administration of this drug to patient should cause liquid retention and hirsutism. Initially described as an antihypertensive drug, minoxidil have also shown new applications in dermatology, especially in the treatment of androgenic alopecia [3]. In this case, this drug has been topically applied in order to stimulate hair growth by inducing vasodilatation and increasing the local irrigation and blood flow [4]. The reference method for minoxidil quantification given by the US Pharmacopeias uses liquid chromatography [5]; however, other different methods have been proposed for its determination in pharmaceutical formulas and in human plasma, which include high-performance liquid

chromatography (HPLC) with UV detection [6,7] and electrochemical detection [8,9], GC[10], radioimmunoassay[11], and electrolysis[12].

Present work emphasizes on the quantitative estimation of Minoxidil in their dosage form by UV Spectroscopic methods.

MATERIALS AND METHODS

Minoxidil was obtained as a gift sample from Encube Ethicals Pvt. Ltd., Mumabi and Pharmaceutical solution of Minoxidil were procured from market GROMANE® from Zydus. All the chemicals use are AR Grade. UV Visible spectrophotometer (Shimadzu Model 1800) was employed with spectral bandwidth of 1 nm attach with computer loaded with Shimadzu UV PC software (UV probe) version 2.31.

2.1 Preparation of standard stock solutions and calibration curve

Standard stock solution of pure drug containing 2 μg ml^{-1} of minoxidil prepared in methanol distilled water system. The working standard solutions of the drug were obtained by dilution of the stock solution in the distilled water. Series of solutions with concentration range of 5-40 μg ml^{-1} of RAM were used to prepare calibration curve. Linearity for detector response was observed in the concentration range of 5-40 μg ml^{-1} for Method A, Method B and Method C.

2.2 Preparation of samples

1 ml of sample (2% minoxidil topical solution contains 20 mg of minoxidil in 1 ml solution) weighed by syringe and transferred into a 100-ml volumetric flask, sonicated with 10 ml methanol for 3-5 min then makeup the volume with double distilled water and filtered. 1 ml of solution was transferred by pipette into a 100-ml volumetric flask then completed to volume with double distilled water to yield a sample solution having a concentration assumed to be 2 μg ml^{-1} of minoxidil.

2.3 Method A: Absorption Maxima Method

By appropriate dilution of stock solution and scanned in the spectrum mode from 400 nm to 200 nm the λmax 285 nm was selected for the analysis. The calibration curve was prepared and the concentration of the sample solution can be determined. The result shown in table no. 2

2.4 Method B: Area under Curve Method

Area under Curve in the range of 280-288 nm figure 3 was selected for the analysis. The calibration curve was prepared. By using the calibration curve, the concentration of the sample solution can be determined. The result shown in table no. 2

2.5 Method C: First Order Derivative Spectroscopic method

First order derivative spectra of drug showed a sharp peak at 267 nm which was selected for its quantitation. The concentration of the drug present in the pharmaceutical solution was determined against the calibration curve in quantitation mode. The result shown in table no.2.

Validation of the Developed Methods

The developed methods for estimation of minoxidil validated as per ICH guidelines.

3.1 Linearity:
The linearity was evaluated by analyzing different concentration of standard solution of minoxidil. The Beer Lambert's law was obeyed in the concentration range of 5-40 µg ml^{-1} for both method with regression coefficient of 0.9991, 0.9998 and 0.9999 for method A, B and C respectively.

3.2 Limit of Detection and Limit of Quantitation:
LOD and LOQ were calculated from the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the six replicate determinations, y intercept was calculated and the standard deviation of the y intercept was computed. From these values, the parameters Limit of Detection (LOD) and Limit of Quantitation and (LOQ) were determined on the basis of response and slope of the regression equation. The result was given table no 1.

3.2 Precision
To check the degree of repeatability of the methods, suitable statistical evaluation was carried out. The standard deviation, coefficient of variance was calculated. The results were reported in Table 3.

3.3 Intermediate Precision
The intra and inter-day precision was calculated by assay of the sample solution on the same day and on different days at different time intervals, respectively. The results are presented in Table 3.

3.1 Accuracy
Accuracy of the method was studied by recovery experiments. The recovery experiments were performed by adding known amounts of the drugs. The recovery was performed at three levels, 80%, 100% and 120% of the label claim of the tablet. The result shown in table no. 4.

3.5 Ruggedness:
Ruggedness studies were carried out using only one parameter, i.e. different analyst. Results showed that the % RSD was less than 2, for different analysts. This study signifies the ruggedness of the method under varying conditions of its performance. The result shown in table no.4

RESULTS AND DISCUSSION

The methods discussed in the present work provide a convenient and accurate way for analysis of minoxidil in its pharmaceutical dosage form. Absorbance maxima of minoxidil were found to be 302 nm (Method A) and the wavelength range for quantitation for area under curve (Method B) was 296-298 nm. The .first order derivative spectroscopic method, sharp peak at 291nm (Method C) were selected for the analysis. Linearity for detector response was observed in the concentration range of 1-12 µg/ml for Method A, Method B and Method C. Standard deviation and coefficient of variance for five determinations of tablet sample using all the methods was found to be less than ± 2.0 indicating the good precision of both the methods. The validation of the proposed method was further confirmed by recovery studies, the %recovery values vary from 98.0 – 101.0 %. Based on the results obtained, it is found that the proposed methods are accurate, precise, reproducible & economical and can be employed for routine quality control of minoxidil tablet dosage forms.

Table No-1: Optical Characteristics of Minoxidil.

Parameters	Method A	Method B	Method C
λ max (nm)	285	267	280-288 nm
Beer's-Lambert's range	5-40 µg/mL	5-40 µg/mL	5-40 µg/mL
Coefficient of Correlation	0.9991	0.9998	0.9999
a. Slope(m)	0.074	0.580	0.005
b. Intercept(c)	0.001	0.011	0.001
LOD (µg/mL)	0.092	0.047	0.122
LOQ (µg/mL)	0.278	1.442	0.400

Table No-2: Results of Analysis of Pharmaceutical formulation

Method	Label Claim mg\ml	Amount of drug estimated	% Label Claim ±SD
A	20	19.98	99.90 ±0.152
B	20	19.58	97.90 ±0.087
C	20	19.99	99.95 ±0.135

Table No-3: Intraday and Interday data of Pharmaceutical formulation of Minoxidil

Method	Label Claim mg\ml	Intraday Precision % COV(n=5)	Interday Precision% COV(n=5)	
			Day I	Day II
A	20	0.632	0.599	0.611
B	20	0.496	0.388	0.399
C	20	0.532	0.526	0.525

Table No-4: Ruggedness Data

Method	Label Claim mg\ml	Analyst I*	% RSD	Analyst I*	% RSD
A	20	19.92	0.10	19.91	1.14
B	20	19.97	0.11	19.97	0.11
C	20	19.92	0.10	19.96	0.85

Table No-5: Recovery data of Ramipril

Method	Level of % Recovery	Concentration Taken (µg/ mL)	Concentration estimated (µg/ mL) (±SD)	%Analytical Recovery
Method A	80	36	35.97±0.014	99.55
	100	40	39.88±0.024	98.40
	120	44	43.94±0.016	99.45
Method B	80	36	35.95±0.0024	99.77
	100	40	39.92±0.025	102.40
	120	44	5.47±0.021s	99.45
Method B	80	36	4.49±0.0024	99.77
	100	40	5.12±0.025	102.40
	120	44	5.47±0.021s	99.45

Figure No-1: Structure of Minoxidil

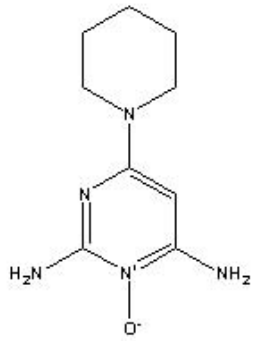


Figure No-2:UV Spectra of Minoxidil

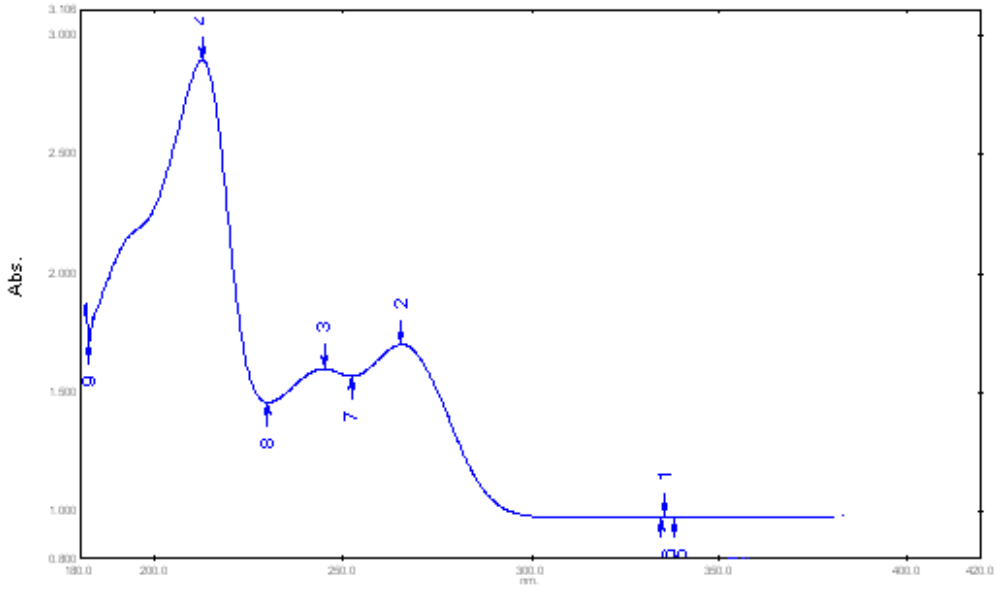


Figure No-3:UV-Visible spectrum of Minoxidil in distillsed water indicating AUC

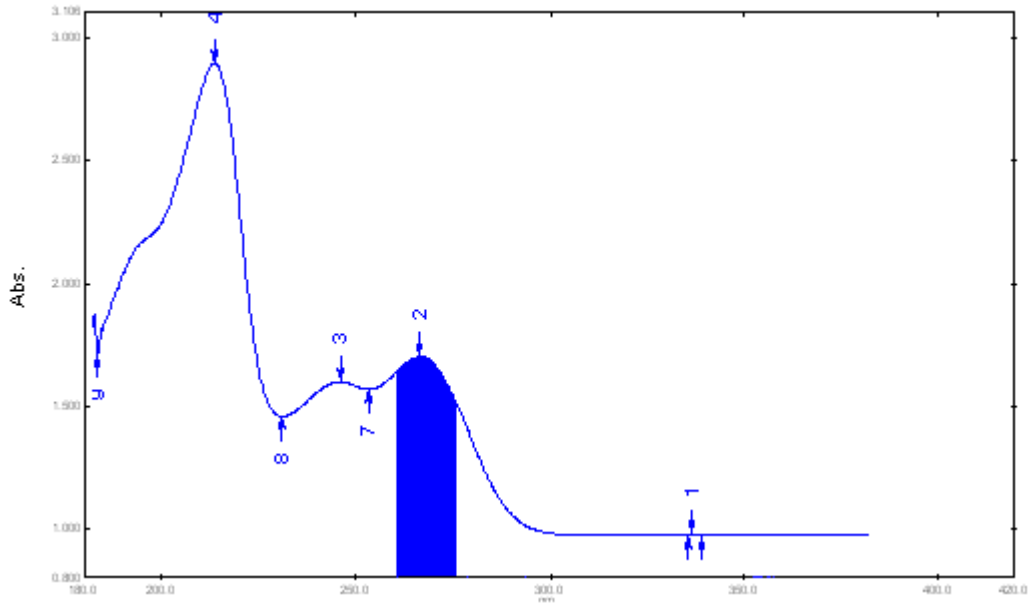
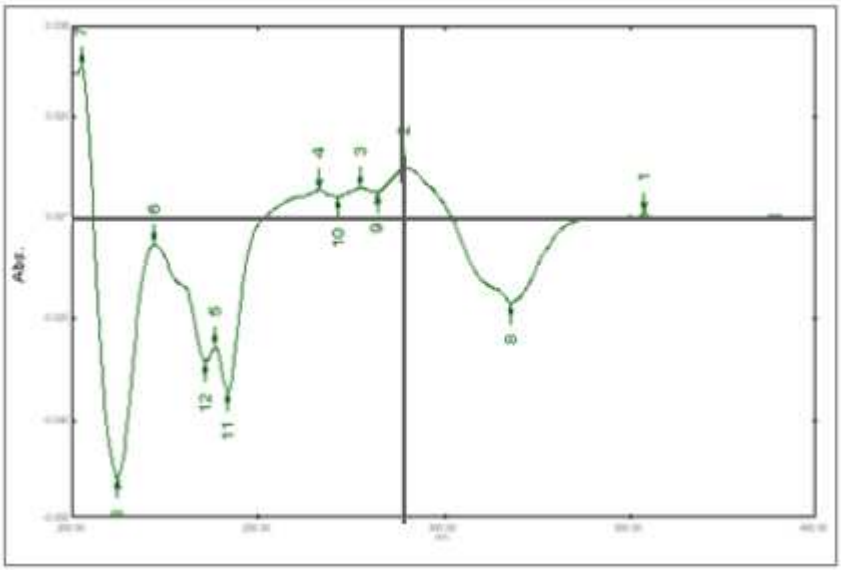


Figure No-4:First order derivative spectrum of Minoxidil.



CONCLUSION

The proposed UV-visible Spectrophotometric methods were found to be simple, stability, sensitive, selective, accurate, precise and economical and can be used in the determination of minoxidil in bulk and pharmaceutical dosage forms in a routine manner.

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