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Spectrophotometric Determination and Validation for Terbinafine Hydrochloride in pure and in Tablet Dosage Form

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ABSTRACT

Terbinafine Hydrochloride is a synthetic allylamine antifungal. It is highly lipophilic in nature and tends to accumulate in skin, nails, and fatty tissues. The aim of this study was to develop simple, sensitive, cost effective, accurate, precise and rapid ultraviolet (UV) Spectrophotometric method for the estimation of Terbinafine Hydrochloride in pure form and its formulations. For the estimation of Terbinafine Hydrochloride, solvent system employed was methanol and wavelength of detection was 282 nm. The developed method was used to estimate the total drug content in commercially available tablet formulations of Terbinafine Hydrochloride.

Key Words: Spectrophotometric Determination, Methanol, distilled water, Terbinafine hydrochloride, Validation.

INTRODUCTION

Terbinafine Hydrochloride is an allylamine antifungal agent and acts by inhibiting squalene epoxidase, thus blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. Chemically it is (2E)-N, 6, 6-trimethyl-N-(naphthalene-1-yl methyl) hept-2-en-4-yn-1-amine hydrochloride. The empirical formula of Terbinafine Hydrochloride is $C_{21}H_{25}N$ HCl and its molecular weight is 327.92., CAS Number: 78628-80-5., Brands; TEBIF (250mg), structural formula (Fig. I) .Terbinafine Hydrochloride is White or almost white crystal powder. It is slightly soluble in water and acetone, freely soluble in anhydrous ethanol and methanol [1].Survey of literature shows several HPLC determination spectrometric determinations in presence of its photodegradation products. The present investigation has been undertaken to develop simple UV Spectrophotometric in pure form and its formulations [2-6].

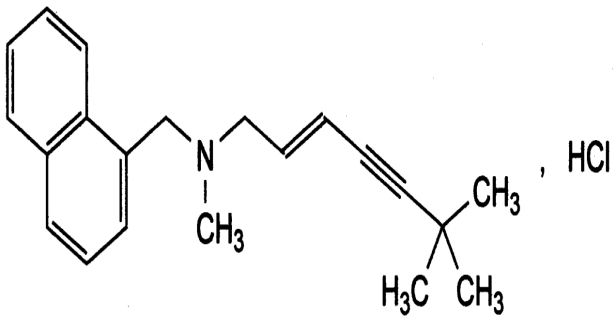

Figure I: Structural formula of Terbinafine Hydrochloride

MATERIALS AND METHODS

Terbinafine Hydrochloride pure drug was obtained as a gift sample from **Systopic** Laboratories Pvt. Ltd. NEW DELHI, India. **TEBIF** (250mg) tablets were purchased from the local market. Reagents in this assay were of analytical grade.

Apparatus

Spectral analysis were made on Perkin Elmer, U.S.A, Model: Lambda 19 was employed with Wavelength Range: 185-3200 nm., Scan Speed: 40 nm/min., Photometric accuracy: ± 0.003 .all the glass wares were rinse thoroughly with double distilled water and dried in hot air oven.

Preparation of standard stock solution (100µg/ml)

A 25 mg of Terbinafine Hydrochloride standard was weighed and transferred to a 25 ml volumetric flask and dissolved in 15 ml methanol. From this solution 2.5 ml was transferred to volumetric flask of 25 ml capacity. Volume was made up to the mark to give a solution containing 100µg/ml Terbinafine Hydrochloride.

Selection of analytical wavelength

8 - 24 µg/ml solutions of Terbinafine Hydrochloride were prepared in methanol and spectrum was recorded between 200-400 nm. Spectrums for above concentration were obtained with n = 6. The overlain derivative spectrum of Terbinafine Hydrochloride at different concentration was recorded at 282nm. (Fig. II)

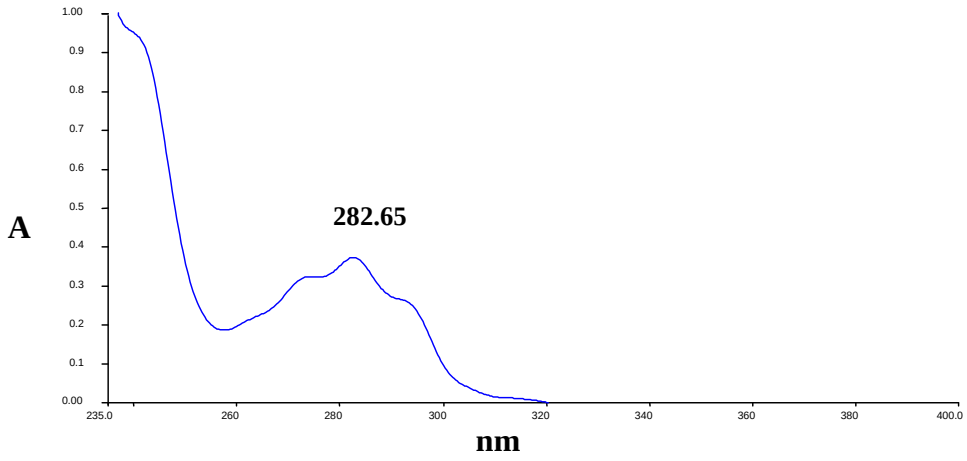

Fig II .Spectrum of Terbinafine Hydrochloride (16 ppm) in Methanol

Calibration curve for Terbinafine Hydrochloride (8 - 24 µg/ml)

Appropriate volume of aliquots from standard Terbinafine Hydrochloride stock solutions were transferred to different volumetric flasks of 10 ml capacity. The volume was adjusted to the mark with the methanol to obtain concentration of 8, 12, 16, 20 and 24µg/ml. Absorbance at 282 nm was measured and the plot of absorbance vs. concentration was plotted. The straight-line equation was determined. (Fig.III)

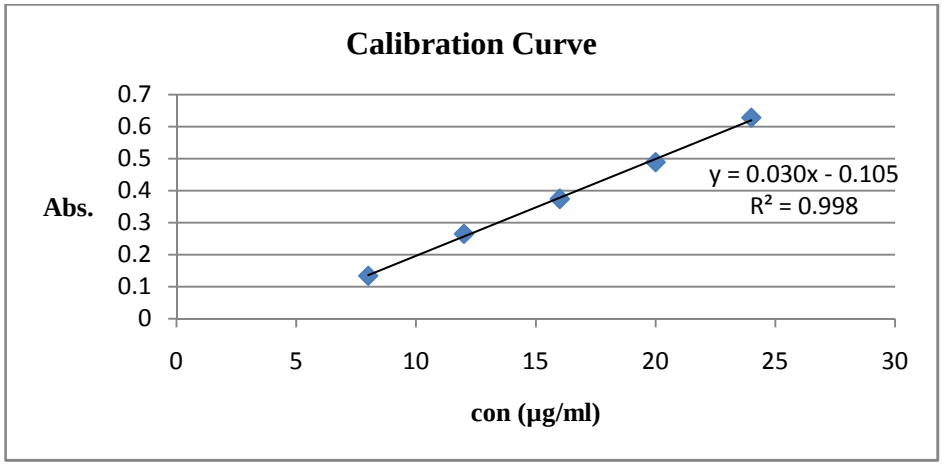

Figure III: Calibration curve of Terbinafine Hydrochloride at 282nm.

Table I: Result of calibration readings at 282 nm for Terbinafine Hydrochloride in Methanol

Concentrations(µg/ml)	Absorbance (n=6)
8	0.134448
12	0.265298
16	0.374342
20	0.488705
24	0.627505

Table II: Statistical data for Terbinafine Hydrochloride by Spectrophotometry method

Sr. No.	Parameters	Values
1	Absorption maxima (nm)	282
2	Beer's law limit (µg/ml)	8-24
3	Regression equation	Y=0.030x - 0.105
4	Correlation Coefficient	0.998

Determination of Terbinafine Hydrochloride in its Pharmaceutical Dosage Form.

Twenty tablets were weighed; accurately average weight was found and finely powered. A quantity equivalent to 250 mg Terbinafine Hydrochloride was accurately weighed and transferred to volumetric flask of 25 ml capacity. 15 ml of methanol was transferred to this volumetric flask and sonicated for 15 min. The flask was shaken and volume was made up to the mark with methanol. The above solution was filtered through whatman filter paper (0.45µ). From this solution 2.5 ml was transferred to volumetric flask of 25 ml capacity. Volume was made up to the mark to give a solution containing 100µg/ml. From this solution 1.6 ml was transferred to volumetric flask of 10 ml capacity. Volume was made up to the mark to give a solution containing 16µg/ml. The resulting solution was analyzed by proposed method.

Table III: Assay Results of Marketed Formulation

Formulation	Actual concentration µg/ml	% Terbinafine Hydrochloride
Tablet	16	99.98

VALIDATION OF THE METHOD

Accuracy

Accuracy is the closeness of the test results obtained by the method to the true value. To study the accuracy 20 tablets were weighed and powdered and analysis of the same was carried out. Recovery studies were carried out by addition of standard drug to the sample at 3 different concentration levels taking into consideration percentage purity of added bulk drug samples. Accuracy was determined by calculating the recovery. The method was found to be accurate with 99.06%-99.82 % recovery of Terbinafine Hydrochloride [7-10].The results are shown in Table no IV.

Precision

Variation of results within the same day (intraday), variation of results between days (interday) was analyzed. Intraday precision was determined by analyzing Terbinafine Hydrochloride for three times in the same day at 282 nm. Inter day precision was determined by analyzing Terbinafine Hydrochloride daily for three days at 282 nm. Precision was calculated as repeatability and intra and inter day variation for the drug. The method was found to be

precise with Coefficient of variation (CV) (0.12-0.25) for intraday (n=3) and CV (0.14-0.29) for interday (n=3) for Terbinafine Hydrochloride [7-10].The results are shown in Table no IV.

Sensitivity

Limit of Detection (LOD) and Limit of Quantification (LOQ) were determined by kSD/s, where k is a constant (3.3 for LOD and 10 for LOQ), SD is the standard deviation of the analytical signal, and s is the slope of the concentration /response graph [7-10].The results are shown in Table no IV.

Table IV: Summary of Validation Parameters of Spectrophotometry

Parameters	Terbinafine Hydrochloride
Recovery%	99.82-100.2
Repeatability (RSD, n=6)	0.001217-0.005842
Precision(CV) Intra-day (n=3) Inter-day (n=3)	 0.12-0.25 0.14-0.29
Sensivity (LOD and LOQ(µg/ml))	0.35 and 0.81

RESULTS AND DISCUSSION

From the optical characteristics of the proposed method, it was found that Terbinafine Hydrochloride obeys linearity within the concentration ranges 8-24µg/ml. The developed estimation method proved to be accurate (accuracy varies between 99.97-100.2%) and precise with CV(0.12-0.25) for intraday (n=3) and CV(0.14-0.29) for interday (n=3).The method has been validated for the range 8-24 µg/ml using methanol. The method was found to be reproducible, specific as no interference observed when the drug was estimated in presence of excipients, rugged as there was no change in absorbance up to 24 hours of preparation of solution in methanol. The LOD and LOQ for Terbinafine Hydrochloride were found to be 0.35µg/ml and 0.81µg/ml respectively.

CONCLUSION

The developed UV Spectrophotometric method for the estimation of Terbinafine Hydrochloride was found to be simple and useful with high accuracy, precision, repeatability. Sample recoveries in all formulations using the above method was in good agreement with their respective label claim or theoretical drug content, thus suggesting the validity of the method and non-Interference of formulation excipients in the estimation. In the selected solvent system (methanol), drug was stable for more than 24 hours, thus suggesting that samples need not be estimated immediately after collection. The developed method was found to be stability specific and was validated as per ICH guidelines and statistical method.

Acknowledgement

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