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Research Article

DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF TERBINAFINE HYDROCHLORIDE IN BULK AND IN TABLET DOSAGE FORM

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Abstract

Terbinafine Hydrochloride (TH) is a new potent antifungal agent. UV-spectrophotometric method has been developed for the determination of TH in bulk and in tablet dosage form. For the determination of Terbinafine Hydrochloride, solvent system employed was methanol and wavelength of detection was 223 nm. The aim of this study was to develop simple, sensitive, cost effective, accurate, precise, reproducible and rapid ultraviolet (UV) Spectrophotometric method for the determination of Terbinafine Hydrochloride in bulk and tablet dosage form. The linearity and range for Terbinafine Hydrochloride in methanol was found to be 1-3.5 µg/ml with coefficient of correlation (R^2) value 0.999. The method was validated for precision, accuracy and sensitivity (LOD and LOQ).

Key words: Distilled water, Methanol, Spectrophotometric Determination, Terbinafine Hydrochloride, Validation.

Introduction

Terbinafine Hydrochloride (TH) is a new potent antifungal agent. It belongs to an allyl amine class and has broad-spectrum activity against yeasts, dimorphic fungi, molds, and dermatophytes. The drug has been found to be a potent inhibitor of squalene epoxidase which is an enzyme present in fungal and mammalian cell systems important in ergo sterol biosynthesis. It is highly lipophilic base and it is used both orally and as a topical application for cutaneous mycoses, depending on the severity and specific nature of the mycoses. Molecular structure of Terbinafine HCl is shown in fig-1. Chemically TH is 1-naphthalenemethanamine, *n-(6, 6-dimethyl-2-hepten-4-ynyl)-n* methyl-, *(E)-, hydrochloride*, having molecular formula $C_{21}H_{25}N \cdot HCL$ and molecular weight 293. TH is very slightly or slightly soluble in water, freely soluble in anhydrous ethanol, methanol and in methylene chloride, slightly soluble in acetone[1-4]. Survey of literature shows several HPLC, HPTLC, non-aqueous voltametric and spectrometric method

have been used for assay of TH in raw material and dosage forms. These methods are simple and rapid but due to low sensitivity of them, their use is limited. Reported spectrophotometric method estimates TH in presence of its photodegradant[5-14]. The present investigation has been undertaken to develop simple UV Spectrophotometric method to determine TH in bulk and tablet dosage form.

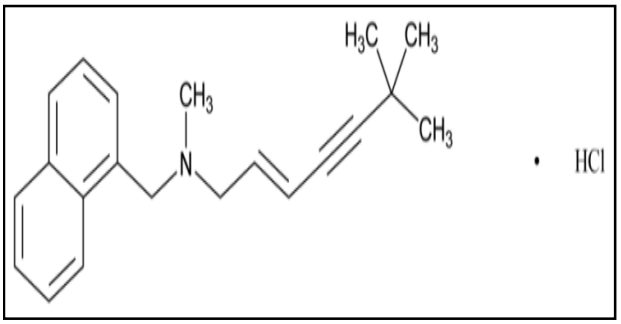

Fig-1: Chemical Structure of Terbinafine hydrochloride

Materials and method

TH pure drug was obtained as a gift sample from Cipla Ltd. Maharashtra India. Fintrix film coated tablets (250 mg) were purchased from local medical shop. Reagents used for this assay were of analytical grade.

Apparatus

Spectral analyses were made on UV-Vis spectrophotometer - Shimadzu Corporation with model no 1800, Software-UV-probe 3.43 and was employed with Wavelength Range: 190 to 1100nm and Photometric accuracy: ±0.002 Abs (0.5Abs), ±0.004 Abs (1.0Abs), ±0.006 Abs (2.0Abs). All the glass wares were rinse thoroughly with double distilled water and dried in hot air oven.

Preparation of standard stock solution

5 mg of TH was weighed and transferred to 25 ml volumetric flask. It was dissolved in small amount of methanol and then volume was adjusted to up to the mark to make final concentration of 200μg/ml.

Selection of analytical wavelength

From stock solution 5 μg/ml of solutions was prepared with methanol and spectrum was recorded between 200-400 nm. It was found that in methanol TH showed λmax of 222.85 nm with absorbance of 1.042.The overlain derivative spectrum of TH at concentration range 1-3.5 μg/ml was recorded at 223nm.

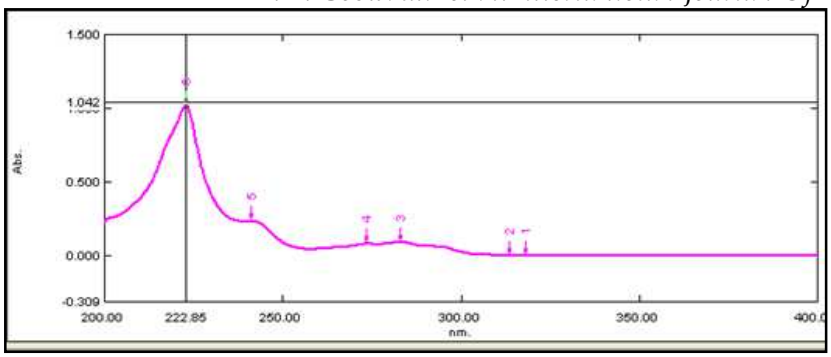

Fig-2: Spectrum of Terbinafine Hydrochloride (5 µg/ml) in Methanol

Calibration curve for Terbinafine Hydrochloride (1-3.5 **µg/ml)**

Appropriate aliquots from standard TH stock solutions were transferred to different volumetric flasks of 10 ml capacity. The volume was adjusted to the mark with the methanol to obtain working standard solutions in concentration range of 1, 1.5, 2, 2.5, 3 and 3.5 µg/ml. These solutions were scanned at 223 nm to measure absorbance and these absorbances were plotted against corresponding concentrations. The straight-line equation was determined.

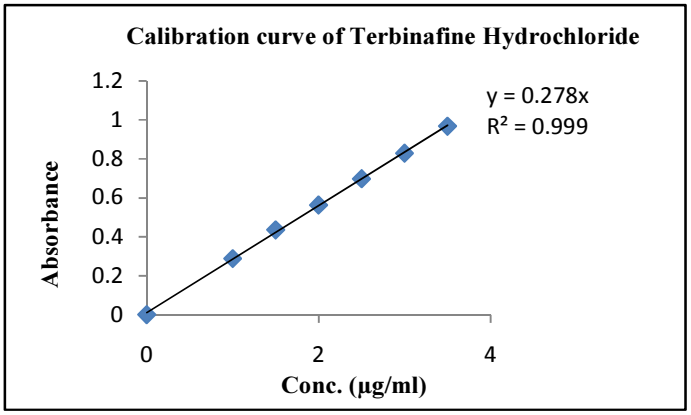

Fig-3: Calibration curve of Terbinafine Hydrochloride at 223nm

Table-1 Result of Calibration curve of Terbinafine Hydrochloride in methanol.

Conc. (µg/ml)	Absorbance
1	0.28818
1.5	0.43568
2	0.56339
2.5	0.69797
3	0.82907
3.5	0.96796

Table-2: Optimum condition and Stastical data for regression equation of TH.

Parameters	Values
λmax	223 nm
Linearity (Beer's law limit in µg/ml)	1-3.5
Regression equation	y = 0.278x
Slope	0.278
Correlation co-efficient (R^2)	0.999

Analysis of tablet formulation

The proposed method was used to determine TH in tablet. 14 tablets were weighed and powdered. The amount of powdered drug equivalent to 5 mg of TH was weighed accurately and transferred into a suitable flask. The tablet powder was dissolved in small amount of methanol and sonicated for 15 min. The flask was shaken and volume was made up to the mark with methanol to give 200µg/ml. The resultant solution was then filtered through a Whatman filter paper (0.45µ). From this filtrate 0.15 ml of solution was transfer to 10 ml capacity volumetric flask. The volume was made up to the mark with methanol to give a solution of concentration 3µg/ml. The absorbance of this solution was measured at 223 nm. The drug content of the preparation was calculated using a standard calibration curve.

Table-3: Assay Results of Marketed Formulation.

Formulation	**Actual concentration µg/ml**	**% Terbinafine Hydrochloride**
Film coated Tablet	**3**	**99.92%**

Validation of the Method:

Accuracy

The accuracy of an analytical method is the extent to which test results generated by the method and the true value agree. To study the accuracy 14 tablets were weighed and powdered and analysis of the same was carried out. For accuracy of method, recovery studies were carried out by applying a known amount of standard TH at a level of 80%, 100% and 120 % to the sample solution (standard addition method). Three determinations were performed at

each level and the results obtained were compared with the expected results. The method was found to be accurate with 98.18 -99.1 % recovery of TH[15-19]. The results are shown in Table no 4.

Precision

Repeatability of sample was assessed using six replicates of the same concentrations (1.5 µg/ml). The intraday and interday precision of the proposed method was determined by estimating the corresponding responses three times on the same day and on three different days over a period of one week and results are reported in terms of percentage relative standard deviation. The proposed method was found to be precise as indicated by percent RSD not more than 2%. RSD for intraday was found to be 0.04821%, for interday 0.06059 % and the method was found to be reproducible with % RSD of 0.0885-0.169 %[15-19]. The results are shown in Table no 4.

Sensitivity

The limit of detection (LOD) is the lowest concentration of analyte in a sample that can be detected but not necessarily quantified. The limit of quantitation LOQ is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy.LOD and LOQ can be determined as k x σ / S, where k is a constant (3.3 for LOD and 10 for LOQ), σ is SD and S is slope of regression equation[15-19]. The results are shown in Table no 4.

Table-4: Summary of Validation Parameters of Spectrophotometry

Parameters	Values
% Recovery	98.18-99.10%
Repeatability (% RSD)	0.0885- 0.169
Precision (%RSD) Intraday Interday	 0.04821 0.06059
LOD (µg/ml)	0.107
LOQ (µg/ml)	0.325

Results and Discussion

From the optical characteristics of the proposed method, it was found that Terbinafine Hydrochloride obeys linearity within the concentration ranges 1-3.5µg/ml. The developed spectrophotometric method proved to be accurate

(between 98.18-99.10%) and precise as indicated by percent RSD not more than 2%. RSD for intraday 0.04821%, for interday 0.06059 % and the method was found to be reproducible with % RSD of 0.0885-0.169 %. The method was found to be simple, 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. Sensitivity was determined in terms of LOD and LOQ for which were found to be 0.107µg/ml and 0.325µg/ml respectively.

Conclusion

The proposed UV spectrophotometric method was found to be simple, precise, accurate, reproducible and convenient. Statistical analysis confirms that the proposed method is an appropriate method for their quantification in the formulation. Therefore, they can be useful for routine analyses and quality- control assays of TH in pharmaceutical formulations.

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