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NOTE

Reverse Phase HPLC Determination of Terbinafine Hydrochloride in Tablets

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A reverse phase HPLC method is developed for the determination of terbinafine HCl in pharmaceutical dosage forms. Chromatography was carried out on an ODS column using a mixture of acetonitrile and phosphate buffer (40 : 60 v/v) as the mobile phase at a flow rate of 1 mL/min. Detection was carried out at 283 nm. The retention time of the drug was 7.106 min. The method produced linear responses in the concentration range of 0.5–50 μg/mL of terbinafine HCl. The method was found to be applicable for determination of the drug in tablets.

Key words: Terbinafine, Estimation, Tablets, HPLC.

Terbinafine[1] is 1-napthalene methanamine, N-[(2E)-6,6-dimethyl 2-hepten-4-yl]-N-methyl, which exerts a primary fungicidal activity, has been proved to have a safe profile. The drug is also free from clinically significant interactions. A literature survey reveals the reports of a few spectrophotometric, high performance liquid chromatographic and capillary electrophoresis[2–5] methods for the determination of terbinafine HCl in human plasma, urine, hair, nails and milk. In the present investigation, the authors propose a simple, sensitive and reproducible HPLC method for the determination of terbinafine HCl.

HPLC grade acetonitrile (Qualigens), potassium dihydrogen phosphate, disodium hydrogen phosphate and orthophosphoric acid (AR grade, Qualigens) were used for preparing the mobile phase. Pure samples of terbinafine HCl (Ranbaxy) and commercial samples of tablets containing the drug namely daskil (Novartis), fungoteck (FDC) were employed in the study.

Chromatographic conditions: A gradient HPLC system (Waters) with Waters 1525 binary HPLC pump, a RP C18 column (150 × 4.6 mm i.d., W03281S024, particle size 5 μm) and a 2487 UV dual absorbance detector was employed. The system was run by Waters Breeze software. A freshly prepared 40 : 60 v/v mixture of acetonitrile and phophate buffer (3.02 pH) was used as the mobile phase. Both acetonitrile and phosphate buffer were filtered through a 0.45 μm membrane filter and sonicated before use. The flow rate of the mobile phase was maintained at 1 mL/min. The detection was carried out at 283 nm.

Estimation of terbinafine hydrochloride: About 50 mg of terbinafine HCl was weighed accurately and transferred into a 50 mL volumetric flask and dissolved in 25 mL methanol. The solution was sonicated for 15 min and then the volume was made up with a further quantity of methanol to get a 1 mg/mL solution. Subsequent dilutions of this solution ranging from 0.5–40 μg/mL were made in 10 mL

volumetric flasks with the mobile phase. 20 μL of the solution was injected each time into the column. Each of the dilutions was injected 5 times into the column and the corresponding chromatograms were obtained. From these chromatograms, the retention times and the areas under the peaks of the drug were noted. The regression equation of the drug concentrations was computed. This equation was later used to estimate the amount of terbinafine HCl in pharmaceutical dosage forms.

To check the intra-day and inter-day variation of the method, solutions containing 8, 12, 20 μg/mL of terbinafine HCl were subjected to the proposed HPLC method of analysis and the recoveries were noted.

Estimation of the drug in tablet dosage forms: Two commercial brands of tablets (daskil of Novartis, fungoteck of FDC) were chosen for testing the suitability of the proposed method to estimate terbinafine in tablet formulations. For this, 20 tablets were weighed and powdered. An accurately weighed portion of this powder equivalent to 50 mg of terbinafine was transferred into a 50 mL volumetric flask containing 25 mL methanol. The contents were allowed to stand for 1/2 h with intermittent sonication to ensure complete solubility of the drug and then filtered through a 0.45 μm membrane filter. Appropriate volume of this filtrate equivalent to 10 μg/mL of the drug was taken in a 10 μL volumetric flask. The contents of the flask were made up to volume with the mobile phase and mixed well. 20 μL of the solution was then injected into the column. The mean peak area of the drug of five such determinations was calculated and the drug content in the tablets was quantified using the regression equation obtained for the pure sample.

The present study was aimed to develop a sensitive, precise and accurate HPLC method for the analysis of terbinafine in pharmaceutical dosage forms. For this, a binary mixture of acetonitrile and phophate buffer (40 : 60 v/v) was found to be the most suitable mobile phase as the chromatographic peaks obtained with this system were better defined and resolved and all were almost free from tailing. Under the above mentioned conditions, the retention time obtained for terbinafine was 7.106 min.

The peak areas of the drug were reproducible as indicated by low coefficient of variation (1.1%) shown in Table-1.

TABLE-1
CALIBRATION OF THE PROPOSED METHOD

Concentration of terbinafine (μg/mL)	Coefficient of variation (%)
0.5	1.10
1.0	1.02
2.0	0.40
5.0	0.28
10.0	0.68
20.0	0.83

A good linear relationship (r = 0.998) was observed between the concentrations of terbinafine and respective peak areas. The regression curve was constructed by linear regression fitting and its mathematical expression was $y = 0.0006731 + 0.9767x$ (where 'y' is peak area and 'x' is the concentration of terbinafine hydrochloride). The regression characters are given in Table-2. The

intra-day and inter-day drug variation studies by the proposed method showed low coefficient of variation, as shown in Table-3. The drug content in the tablets was quantified using the proposed method of analysis. The mean amount of terbinafine obtained in tablet dosage forms is shown in Table-4. This reveals that the method is quite precise. The absence of additional peaks in the chromatogram indicated non-interference of the common excipients used in the tablets.

TABLE-2
REGRESSION CHARACTERS OF THE PROPOSED HPLC METHOD

Parameters	Value
Standard deviation on slope (δb)	0.00052
Standard deviation on intercept (δa)	0.00538
Standard error of estimation (δe)	0.00811
Relative standard deviation (%)	0.48450
% Range of error at 95% confidence limit	0.40510
% Range of error at 99% confidence limit	0.59940
Slope (a)	0.97670
Intercept (b)	0.00067
Correlation coefficient (r)	0.99800

TABLE-3
INTRA- AND INTER-DAY PRECISION OF THE PROPOSED METHOD

Concentration of terbinafine HCl (μg/mL)	Observed concentration of terbinafine HCl (μg/mL)			
	Intra-day		Inter-day	
	Mean (n = 5)	RSD (%)	Mean (n = 5)	RSD (%)
8	7.96	1.04	8.02	0.89
12	12.04	0.52	11.98	1.44
20	20.02	0.98	24.95	0.94

TABLE-4
ASSAY OF TERBINAFINE HYDROCHLORIDE IN TABLET DOSAGE FORMS

Brand name of the tablet	Labelled amount of drug (mg)	Mean (± S.D.) amount found the proposed method (n = 5)	Mean (± S.D.) % labelled amount (n = 5)
Daskil	250	252.6 ± 0.44	101.0 ± 0.78
Fungoteck	250	249.3 ± 0.31	99.72 ± 0.13

It can be concluded that the proposed HPLC method is sensitive and reproducible for the analysis of terbinafine HCl in pharmaceutical dosage forms in a short analysis time. The method was duly validated by evaluation of the required parameters.

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