World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Stability indicating RP-HPLC method development and validation of Terbinafine in pure and pharmaceutical formulation

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World Journal of Advanced Research and Reviews, 2023, 18(03), 264–270

Publication history: Received on 15 December 2022; revised on 30 January 2023; accepted on 02 February 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.18.3.0156

Abstract

A high performance liquid chromatographic strategy for the assessment of TerbinafineHCl from formulation was created. TerbinafineHCl was chromatographed on a Inertsil ODS-3V (250×4.6, 5µm) and having an inner measurement of 3.9 mm. Mobile phase involving Mobile phase Acetonitrile : 2% IPA (80:20), Mobile phase. The pH of the buffer adjusted to 3.5. The detection was carried out using an ultraviolet detector set at a wavelength of 260 nm. The technique was extended for the stability studies of TerbinafineHCl.

Keywords: Terbinafine HCl; Stability Studies; RP-HPLC; PDA Detection; Tablet dosage forms; ICH guidelines

1. Introduction

Terbinafine hydrochloride[1-4] is a white fine crystalline powder and it is freely miscible in methylene chloride and methanol, miscible in ethanol, and slightly soluble in water. Bioavailability readily absorbed, Protein binding >99%. (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-Nmethyl-1-naphthyl methyl amine hydrochloride N,6,6-trimethyl-N-(naphthalen-1-ylmethyl) hept-2- en-4-yn-1-amine and clinically[5-7] used as antifungal agent with half life 36 hours. Instability of a medication item can prompt a diminished in its bioavailability, instead of to loss of medication or to development of poisonous degradation items. This decrease in bio-accessibility can bring about a considerable bringing down in the helpful viability of the measurement structure. Chemical degradation[8-10] of the active drug may not be broad; a poisonous item might be shaped in the decomposition cycle.

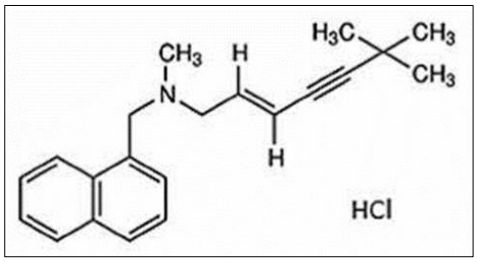

Figure 1 Chemical structure of Terbinafine hydrochloride

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1.1. Method Development

In method Selection two profile are considerably selected both for Analytical and Stability profile and in step 2 starting conditions to hold all analytes and has a limit factor 10 -15 and in step 3 Selectivity optimization and system optimization to accomplish satisfactory without peak spacing for the molecule size and stream rate these parameters might be changed without influencing capacity factors and last with the method validation.fig.01.

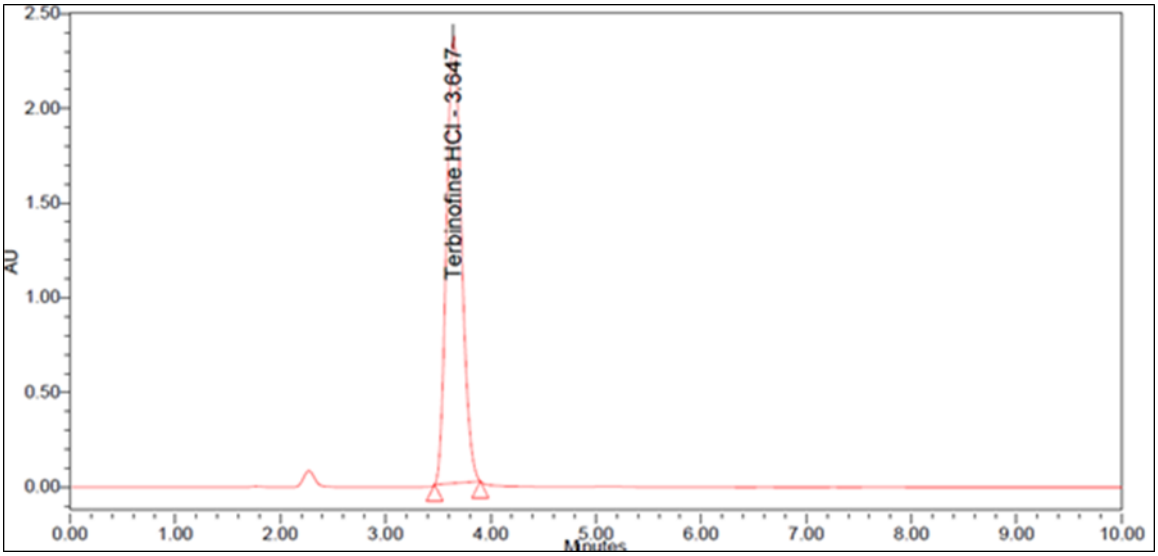

Figure 2 Typical Chromatogram of Terbinafine hydrochloride

1.2. Method Validation

1.2.1. Specificity

Reference and working standard solutions are prepared as per test method and injected and it is in table no 1. Acceptance Criteria: % Difference between Reference Standard and Working Standard should not be more than 1.0 and peak purity should be as per the acceptance criteria. Three point peak purity should not be less than 0.9500.

1.2.2. Limit of identification and Limit of Quantitation

The LOD found at 0.2 ppm concentration as the signal-to-noise ratio proportion is pretty much equivalent to 3:1 at this concentration. The LOQ found at 0.666 ppm concentration as the signal-to-noise ratio proportion is pretty much equivalent to 10:1 at this concentration. Precision System Precision: Standard solution were set up according to test strategy and infused multiple times.

1.2.3. Method Precision

Six preparations were arranged separately utilizing single batch of TerbinafineHCl working norm according to test strategy and infused every solutions in copy and values are table no 3.

1.2.4. Accuracy

Prepared solutions in triplicate at levels 80%, 100% and 120% of test concentration using TerbinafineHCl working Standard as per the test method and injected each solution in triplicate and overall statistical analysis in Table no 3.

1.2.5. Linearity

From the 2^0 stock solution, pipette out 1, 2, 3, 4, &5 ml of solution and transferred into 10ml volumetric flask and make up the volume up to the mark with diluent. The solutions were degassed and passed through 0.45µm membrane filter for filtration. The concentration of the solutions was 10, 20, 30, 40 & 50µg/ml and injected.

Table 1 Linearity Studies of Terbinafine

Linearity Level	Concentration (µg/ml)	Area		Mean
		Set 1	Set 2	
1	10	662923	675749	669336
2	20	1259872	1368568	1314220
3	30	1853392	1886025	1869708
4	40	2524548	2535918	2530233
5	50	3127561	3160218	3143889

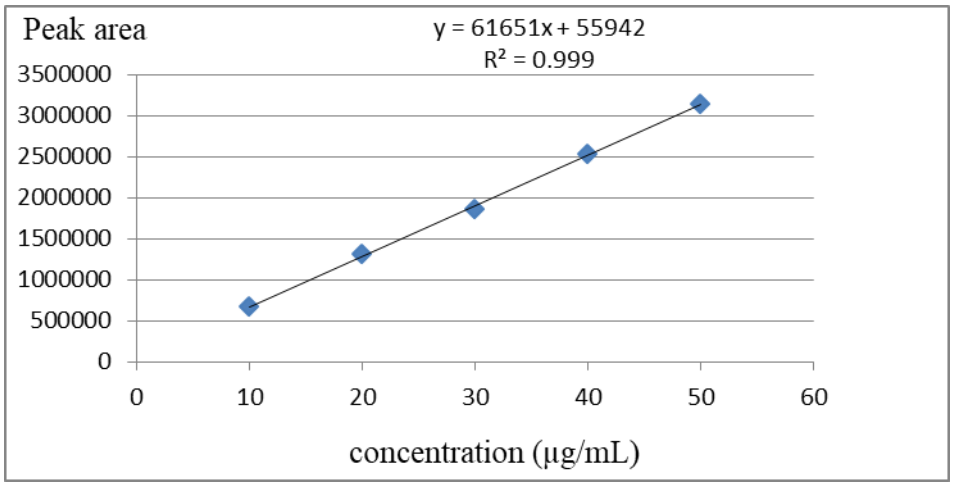

Figure 3 Linearity plot of Terbinafine

- Discussion

The linearity study was performed for range of 10-50 µg/ml. The correlation coefficient was found to be 0.999. Correlation coefficient should not be < 0.999.

1.2.6. Precision

From the 2^0 stock solution, pipette out 3ml of the solution and transferred into six 10ml volumetric flask and make up the volume up to the mark with diluent. The solution was degassed and passed through 0.45µm membrane filter for filtration. The concentration of the solution was 30µg/ml and all the solutions were injected.

Table 2 Precision Studies of Terbinafine

S.No	Concentration (µg/ml)	Amount Found(µg/ml)	Percentage %	Average %	S.D	%RSD
1	30	29.4	98%	98.4%	1.22	1.23
2		28.9	96.3%			
3		29.6	98.6%			
4		29.9	99.6%			
5		29.5	98.3%			
6		29.9	99.6%			

- Discussion

Precision studies were performed and the %RSD of Terbinafine was found to be 1.23. The %RSD of responses of six replicate injections were within the limits (should not be > 2).

1.3. Forced Degradation Studies

1.3.1. Acid Hydrolysis (Acid degradation)

Weighed accurately about 5mg of standard sample into a 25ml volumetric flask, and add 2ml of 1N HCL solution and heat the solution at 80^{0}C for 1hr. At the end of the exposure, cool the solution and then neutralize with 2ml of 1N NaOH solution and make up the volume with the diluents and degassed. Filter the solution with 0.45micron filters and inject into the system.

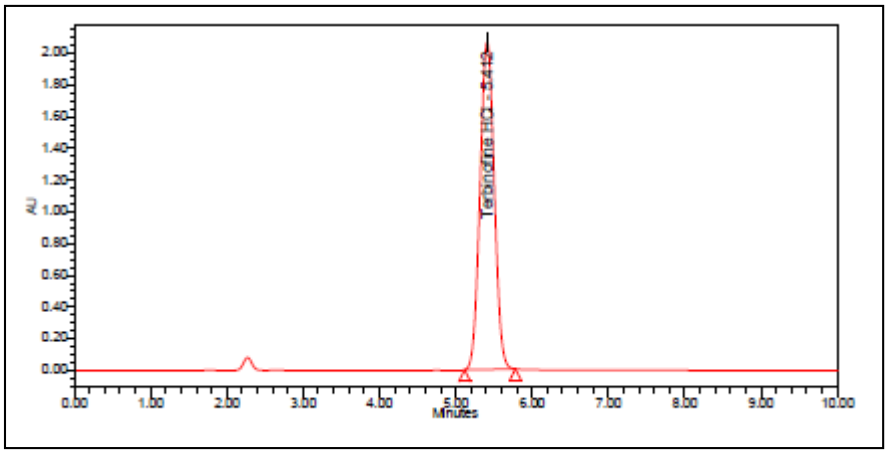

Figure 4 Chromatogram of Acid Degradation studies

1.3.2. Base Hydrolysis (Base degradation)

Weighed accurately about 5mg of the standard sample into a 25ml volumetric flask, and add 2ml of 1N NaOH solution and heat the solution at 80^{0}C for 1hr. At the end of the exposure, cool the solution and then neutralize with 2ml of 1N HCL solution and make up the volume with the diluents and degassed. Filter the solution with 0.45micron filters and inject into the system.

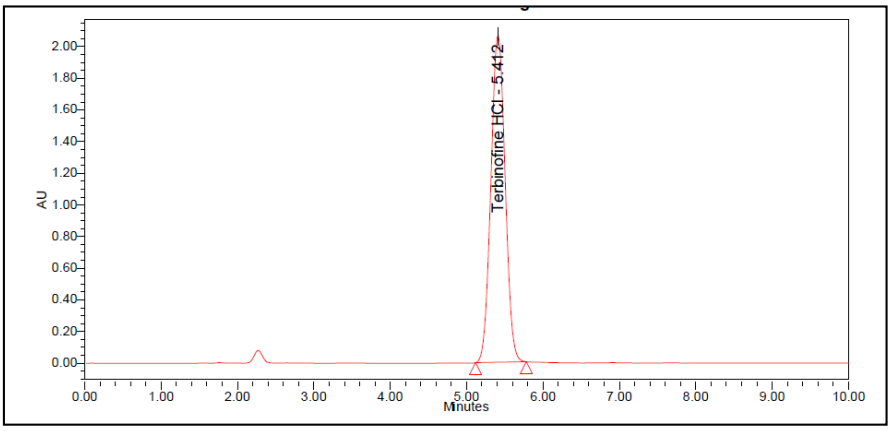

Figure 5 Chromatogram of Base Degradation studies

1.3.3. Oxidative Hydrolysis (Peroxide degradation)

Weighed accurately about 5mg of the standard sample into a 25ml volumetric flask, and add 2ml of hydrogen peroxide solution and heat the solution at 80^{0}C for 1hr. At the end of the exposure, cool the solution and make up the volume with the diluents and degassed. Filter the solution with 0.45micron filters and inject into the system.

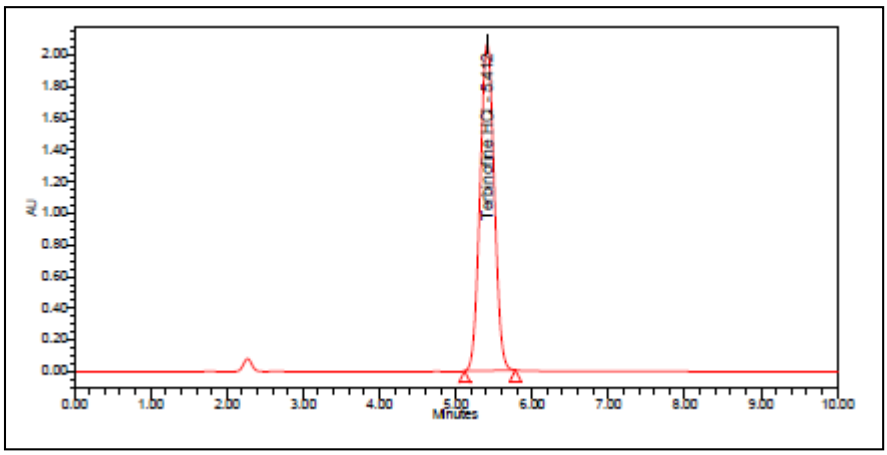

Figure 6 Chromatogram of Hydrogen Peroxide Degradation studies

1.3.4. Hydrolysis (Water degradation)

Weighed accurately about 5mg of the standard sample into a 25ml volumetric flask, and add 2ml of water and heat the solution at 80^{0}C for 1hr. At the end of the exposure, cool the solution and make up the volume with the diluents and degassed. Filter the solution with 0.45micron filters and inject into the system.

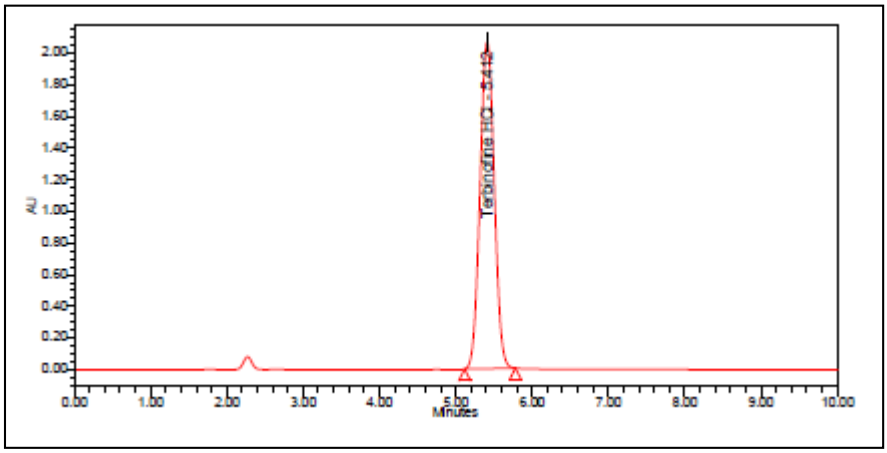

Figure 7 Chromatogram of Water Degradation studies

Table 3 Forced Degradation Studies of Terbinafine

Degradation Mechanism	% Degration
Acid Degradation	1.4%
Base Degradation	0.65%
Peroxide Degradation	1.35%
Hydrolysis Degradation	3.2%

2. Discussion

Table 4 Summarized data

S.No	Parameters	Accepted Criteria	Results
1	Linearity	The correlation coefficient must be higher than 0.998	R^2 = 0.999
2	Precision	The %RSD for 6 replicate samples should be NMT 2.0%	1.23%
3	Intermediate precision	The %RSD of 6 replicate samples should be NMT 2.0%	0.56%
4	Accuracy (50%, 100%, 150%)	The % recovery at each level mean recovery should be within 98.0 – 102.0%	% recovery 100.4%, 100.6%, 98.9%
5	LOD		0.29
6	LOQ		0.90
7	Robustness		
	Effect of variation in wavelength	Should comply with system suitability parameters	255nm %RSD = 1.3% 265nm %RSD = 2.0%
	Effect of variation in temperature		25°C %RSD = 0.26% 35°C %RSD = 0.47%
	Effect of variation in flow rate		0.9ml/min %RSD = 0.63% 1.1ml/min %RSD = 0.59%
8	Forced Degradation Studies		
	Acid Degradation		1.4%
	Base Degradation		0.65%
	Peroxide Degradation		1.35%
	Hydrolysis Degradation		3.2%

3. Conclusion

The validated HPLC method employed proved to be simple, specific, accurate, precise, and stability indicating. The developed method was able to discriminate between Terbinafine hydrochloride and its possible degradation products. Statistical analysis proves that the method is suitable for the analysis of Terbinafine hydrochloride as bulk drug and in pharmaceutical formulation without any interference from the excipients. Hence, this proposed method can be used for the routine analysis of Terbinafine hydrochloride in pure, tablet form and in its degraded products.

Compliance with ethical standards

Acknowledgments

The authors are thankful to Management and Principal, A. M. Reddy Memorial College of Pharmacy, Narsaraopet, A.P. for providing necessary facilities for this entire research work d alongside

Disclosure of conflict of interest

All the authors declare not interested on conflict of interest.

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