World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
Original Article

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

Byasabhusan Das[1], Paul Richards M[2], B. A. Vishwanath[3], Suchitra D[2], Najma Amreen[4]

[1]Professor and HOD, [4]Research Scholar, Department of Pharmaceutical Analysis, Anwarul Uloom College of Pharmacy, Hyderabad, Telangana
[2]Professor, Department of Pharmaceutical Chemistry & [3]Principal and Chairman, Department of Pharmaceutics, Aditya Bangalore Institute of Pharmacy Education and Research, Yelahanka, Kogilu, Bangalore -64, India

Received: 21-10-2020 / Revised Accepted: 27-11-2020 / Published: 30-11-2020

ABSTRACT

A high performance liquid chromatographic strategy for the assessment of Terbinafine HCl from formulation was created. Terbinafine HCl was chromatographed on a BDS Hypersil C18 column 150 cm long and having an inner measurement of 4.6 mm. Mobile phase involving Mobile phase A - Buffer of K_2HPO_4, Mobile phase B of Methanol, Mobile phase C of Acetonitrile within the volume proportion of 15:35:50. The pH of the buffer adjusted to7.5. The detection was carried out using an ultraviolet detector set at a wavelength of 223 nm. The technique was extended for the stability studies of Terbinafine HCl.

Keywords: Terbinafine HCl, Stability Studies, HPLC

INTRODUCTION

Terbinafine hydrochloride 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)-N-methyl-1-naphthyl methyl amine hydrochloride N,6,6-trimethyl-N-(naphthalen-1-ylmethyl) hept-2-en-4-yn-1-amine and clinically 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 of the active drug may not be broad, a poisonous item might be shaped in the decomposition cycle.

METHOD DEVELOPMENT

In method Selection two profile are considerably selected both for Analytical and Stability profile

Address for Correspondence: Byasabhusan Das, Professor and HOD, Department of Pharmaceutical Analysis, Anwarul Uloom College of Pharmacy, Hyderabad, Telangana; E-mail: richie2626@gmail.com

How to Cite this Article: Byasabhusan Das, Paul Richards M., B. A. Vishwanath, Suchithra M., Najma Amreen. Stability indicating RP-HPLC method development and validation of Terbinafine in pure and pharmaceutical formulations. World J Pharm Sci 2020; 8(12): 102-106.

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. A Sharp, symmetrical, well resolute peak obtained and peak tailing is <1.1 and nearly 100% recovery observed. So this method can be used for routine analysis after done with four different trials and observed in figure no 2.

METHOD VALIDATION

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.

Sample	**Assay (mg/Bulk powder)**	**Statistical Analysis**	
Reference Standard-1	99.41	Mean	99.32
Reference Standard-2	98.92	SD	0.361
Reference Standard-3	99.62	%RSD	0.361
Working Standard-1	98.91	Mean	98.433
Working Standard-2	98.53	SD	0.501
Working Standard-3	97.92	%RSD	0.512

Linearity: A series of solutions are prepared using Terbinafine HCl working standard at concentration levels from 1ppm to 250ppm and values are in table no 2.

Concentration (ppm)	**Area count**			**Area Count**		
	Injection 1	Injection 2	Injection 3	Average	Std	% RSD
1	82.8186	83.8248	83.4221	83.3552	0.51	0.61
2.5	199.3884	202.9979	199.5562	200.6475	2.04	1.02
5	403.2846	400.9775	405.8040	403.3554	2.41	0.60
10	798.1102	799.8001	799.7963	799.2355	0.97	0.12
25	1936.5588	1941.8846	1939.2061	1939.2165	2.66	0.14
50	3565.4805	3562.7278	3576.7202	3568.3095	7.41	0.21
100	7094.2305	7094.0806	7096.6421	7094.9844	1.44	0.02
150	10637.4000	10638.8000	10651.6000	10642.6000	7.83	0.07
200	13728.2000	13710.4000	13708.9000	13715.8333	10.74	0.08

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.

***Method Precision*:** Six preparations were arranged separately utilizing single batch of Terbinafine HCl working norm according to test strategy and infused every solutions in copy and values are table no 3 .

OBSERVATION / RESULTS				
Concentration	Injection	Area	Statistical Analysis	
100ppm	Injection-1	6873.20	Mean	6879.0333
	Injection-2	6875.71	SD	8.51
	Injection-3	6870.72	%RSD	0.1
	Injection-4	6875.41		
	Injection-5	6888.23		
	Injection-6	6891.21		

Accuracy: Prepared solutions in triplicate at levels 80%, 100% and 120% of test concentration using Terbinafine HCl working Standard as per the test method and injected each solution in triplicate and overall statistical analysis in Table no 4.

Overall Statistical Analysis		
Mean	**SD**	**%RSD**
101.44	1.54	1.5

Robustness: Prepared test solution in triplicate as per test method and injected different variable conditions with flow rate 0.9 ml/min and 1.1 ml/min, wavelength for 221 nm and 225 nm, temp of 27 degrees and 33 degrees with pH 7.4 and pH 7.6. The results indicating that the test method was robust for all variable conditions.

Ruggedness: Six preparations of the working standard were individually prepared as per the test method and injected each solution in duplicate using different column, system, analyst on different day was used overall RSD should be not more than 2.0 %.

Stability of sample solution: Sample solution was prepared as per test method and analyzed initially and at different time intervals by keeping the solutions at room temperature and outlined in Table no 5.

OBSERVATION/RESULTS		
Time in hours	**Area**	**%RSD**
Initial	7091.2352	0.139545
1	7091.2350	
2	7091.2321	
3	7091.0832	
4	7091.0821	
5	7091.0772	
6	7091..0771	
7	7091.0770	
8	7091.0691	
9	7091.0693	
10	7091.0682	
24	7091.0081	

Oxidative Degradation Study: The process of oxidation relies upon the measure of oxygen present noticeable all around and the idea of the material it contacts. Genuine oxidation occurs on an atomic level - we just observe the huge scope impacts as the oxygen makes free radicals on a superficial level split away and outlined in Table no 6.

TERBINAFINE HCL UNCOATED TABLET FORMULA

Tablet Formula		
S.NO.	**Ingredients**	**mg/Tab**
1	Terbinafine Hcl	280
2	Avicel PH 101	38
3	PVP K29/32	12
4	SSG / XL	12
5	Mg.Stearate	4
6	Aerosil	4
Total tab weight		350
Tolling used		10mm

Placebo formula		
S.NO.	**Ingredients**	**mg/Tab**
1	Avicel PH 101	318
2	PVP K29/32	12
3	SSG / XL	12
4	Mg.Stearate	4
5	Aerosil	4
Total tab weight		350
Tolling used		10mm

Accelerated stability study: When contrasted with the Ac-disol assay values, XL assay values are less. When contrasted with the Ac-disol disintegration values, XL disintegration values are less. When contrasted with the Ac-disol moisture content values, XL moisture content values are more.

Mobile phase preparation: Prepared a filtered and degassed mixture of 15% of 0.01M K_2HPO_4, previously adjusted with H_3PO_4 to p^H 7.5 ± 0.1, 50% of ACN and 35% of methanol.

Preparation of Dipotassium hydrogen phosphate buffer: Precisely about 870.97 mg of Dipotassium hydrogen phosphate was gauged and moved to 1000 mL of water and blended well and pH acclimated to 7.5 with phosphoric acid, sifted and degassed through 0.45µ membrane filter paper and sonicated for 30 minutes.

Preparation of Diluent: Prepared a filtered and degassed combination of 15% HPLC grade water, half ACN and 35% methanol.

Assay: The assay estimation of tablets demonstrated decline when contrasted with the initial values in all the conditions. Test an incentive at quickened condition (40°C/75%RH) following two months was discovered to be lower (98.36%) when contrasted with the particular worth (98.44%). The assayvalue for moderate condition (30°C/65%RH) and long haul (25°C/60%RH) were discovered to be 98.24% and 100.14%, separately. All the assay values of Ac-disol are higher when contrasted with the Plasdone XL values. The outcomes were within the cutoff points when contrasted and the particular qualities according to the Protocol. The point by point results are incorporated in Table 7.

S.No	Period	°C/%RH Condition	Sample Innovator (Ac-disol)	Sample ISP (XL)
1	Time Zero		101.170	98.440
2	One month	Time 40^{0}C/75%RH	100.912	99.291
3		Time 30^{0}C/65%RH	99.951	98.322
4		Time 25^{0}C/60%RH	100.750	99.881
5	Two months	Time 40^{0}C/75%RH	99.691	98.360
6		Time 30^{0}C/65%RH	100.060	98.242
7		Time 25^{0}C/60%RH	100.491	100.140

Uniformity of weight: The results were within the limits (±5% on average weight) as per the Protocol. The detailed results are incorporated in Table 8.

Thickness: The results were within the limits (4.6 - 5.4 mm) as per the Protocol. The detailed results are incorporated in Table 9 Thickness results (mm) Initial day – 2 months stability.

S.No	Period	°C/%RH Condition	Sample Innovator		Sample ISP	
			LW (%)	HW (%)	LW (%)	HW (%)
1	Time Zero		-0.591	0.591	-0.281	1.591
2	One month	Time 40°C/75%RH	-1.112	1.420	-1.652	2.782
3		Time 30^{0}C/65%RH	-2.050	1.692	-2.291	4.220
4		Time 25^{0}C/60%RH	-2.872	2.671	-1.420	2.951
5	Two months	Time 40°C/75%RH	-1.551	1.900	-1.511	1.982
6		Time 30^{0}C/65%RH	-1.601	1.660	-1.330	1.961
7		Time 25^{0}C/60%RH	-1.922	2.341	-1.151	1.720

S.No	Period	°C/%RH Condition	Sample Innovator		Sample ISP	
			LT (mm)	HT (mm)	LT (mm)	HT (mm)
1	TimeZero		5.071	5.232	5.090	5.270
2	One month	Time 40^{0}C/75%RH	5.060	5.281	5.122	5.291
3		Time 30^{0}C/65%RH	5.130	5.351	5.171	5.311
4		Time 25^{0}C/60%RH	5.131	5.301	5.192	5.340
5	Two months	Time 40^{0}C/75%RH	5.111	5.182	5.121	5.200
6		Time 30^{0}C/65%RH	5.080	5.181	5.122	5.181
7		Time 25^{0}C/60%RH	5.062	5.180	5.131	5.231

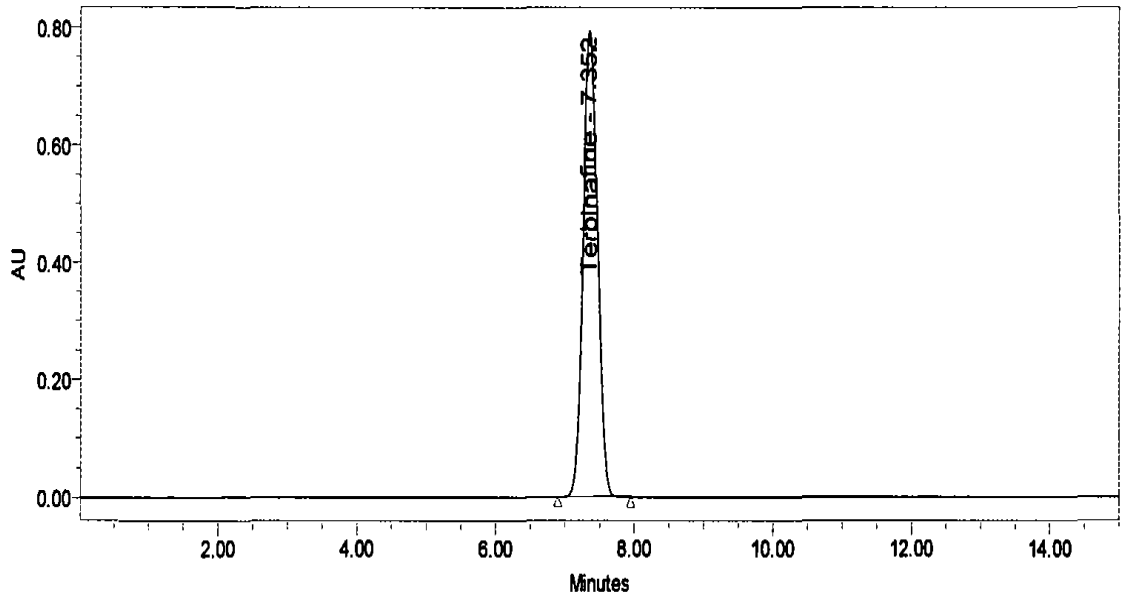

Figure 1: Chromatogram of Terbinafine HCl working standard

CONCLUSION

The chromatographic technique for the assurance of test methods of Assay for Terbinafine HCl bulk drug, raw materials and tablets were simple, reliable, sensitive and less time consuming. The advantage of the current test techniques was that it doesn't need any complicated mobile phase and it is basic isocratic method. The current technique can be confidently be utilized for fast and exact quantitation of Terbinafine HCl, uncommonly this strategy can be a significant enthusiasm for analytical chemistry, since it offers a particular quality control in the test methodology of Assay of Terbinafine HCl. The current work shows a validated, highly sensitive and selective method for assurance of Terbinafine HCl in pharmaceutical dosage forms. These validated method parameters were applied to the oxidative degradation investigations of Terbinafine HCl, which impact the stability of the active drug for example Terbinafine HCl. These oxidative degradation studies on Terbinafine HCl indicated that till the time of a half year there was no oxidative degradation of Terbinafine HCl in both dry powders and tablet formulations under ambient conditions and furthermore under accelerated stability conditions. Indicating that the excipients utilized alongside Terbinafine HCl doesn't influence the stability of the Terbinafine HCl.

REFERENCES

1. Kim CK, Yeon KJ, Ban E, Hyun MJ, Kim JK, Kim MK, Jin SE, Park JS; J Pharm Biomed Anal.2005 Mar 9;37(3):603-9.
2. Janake jonsson, Chromatographic theory and basic principles, 38 (1987) 1-2.
3. Elen Katz, Quantitative analysis using chromatographic techniques, John Wiley & sons, (1987) 55-59.
4. Krstulovic A.M, Reversed-phase high performance chromatography: theory, practice and biomedical applications, (1982) 167 –181.
5. Edgar Lederer, Michael Lederer, Chromatography: A review of principles and applications, Elsevier, (1954) XVII-XVIII.
6. Rossel MT, Lefebvre RA, J Chromatogr.1991 Apr 19,565(1-2):504-10.
7. James W. Munson, Pharmaceutical analysis: modern methods, part B, Marcel Dekker Inc. (1984) 7-39.
8. REMINGTON The Science and Practice of Pharmacy, 20th Edition, 2000 : P-1553
9. Merk Index (P-1633)
10. www.PDR.net (PDR-324 & 2282)
11. Janeway CA, Travers P, Walport M, Capra JD. Immunobiology: the Immune system in Health and Disease.4th ed. London: Current Biology Publication; 1999. p 602.
12. K.A.Connors, G.L. Amidon, and L. Kennon, Chemical Stability of Pharmaceuticals (Wiley & Sons, New York, NY, 1979), pp.88-98.
13. ICH Stability Testing: Photostability Testing of New Drug Substances and Products, ICH, Geneva, Switzerland, November 1996