

Research Article



Accelerated Stability Study, Swing Study and Photostability Study on Terbinafine Hydrochloride Creams

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ABSTRACT

Accelerated stability study, swing study and photostability study had been performed on terbinafine hydrochloride creams by using stability-indicating RP HPLC method. Accelerated stability study had been performed according to WHO requirements. Samples of terbinafine hydrochloride cream were tested for any physical change, pH value and content of active ingredient. The results showed that there was no change in physical characteristics and small and acceptable changes of pH value had been noticed and the potency loss from the initial assay value did not exceed 5%. Swing study had been performed on terbinafine hydrochloride samples and the results were the same as accelerated stability study. A photostability study had been performed according to ICH requirements and the result showed that there was 14% potency loss from the initial assay value.

Keywords: Terbinafine hydrochloride, accelerate stability study, photostability study.

INTRODUCTION

Terbinafine hydrochloride is a synthetic potent antimycotic agent of the allylamine class, (fig 1). It selectively inhibits fungal squaline epoxidase causing a fungicidal action due to the intracellular accumulation of the toxic sterol squaline, it also exerts a fungistatic action by depletion of ergosterol^{1,2}.

Terbinafine hydrochloride now is the drug of choice in dermatophyte nail and skin infections because of its fungicidal mode of action over a short treatment duration.³

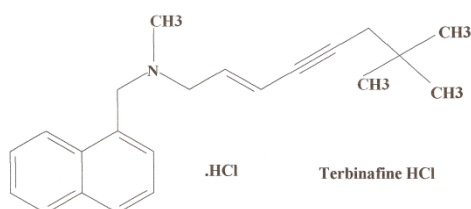


Figure 1: Chemical structure of terbinafine hydrochloride.

Accelerated stability studies are designed to increase the rate of chemical –degradation and /or physical change of drug substance or drug product by using exaggerated conditions and predicating the shelf life under normal conditions. The design of accelerated studies may include elevated temperature, high or low humidity and intense light, low tem and freezing /thaw cycling as appropriate⁴.

Stability studies need to be performed by using stability-indicating methods as recommended by ICH guide⁵ and stability indicating method is a validated analytical method that accurate and precisely measure active ingredient (drug product-drug substance) free from process impurities, excipients and degradation products⁶.

Stability –indicating RP HPLC method had been developed for determination of terbinafine hydrochloride in bulk drug substance⁷ and semi solids dosage forms (creams)⁸

The chromatographic separation in this method was performed using C18 column and a mobile phase consisting of methanol and acetonitrile (60:40v/v) with (0.15% triethylamine and 0.15% phosphoric acid) at a flow rate of 0.4ml/min. The eluents were monitored by UV photo diode array detector at wave length of 224 nm.

In this work we used the previous stability-indicating method to perform accelerated stability study, swing study and photostability study on terbinafine hydrochloride creams.

MATERIALS AND METHODS

Materials

Reference terbinafine (assigned purity 99.9%) was kindly supplied by alphares company (local private pharmaceutical company) which offered also samples of terbinafine hydrochloride cream and all solvents and reagents which were needed to the studies.

Samples of terbinafine hydrochloride cream for other two local private pharmaceutical companies (alsaed, albalsam) were purchased from local pharmacy. The creams were claimed to contain 1% terbinafine hydrochloride.

HPLC apparatus VWR Hitachi La Chrom Elite model with auto sampler and diode array detector.

Standard solution preparation

Approximately (10) mg of terbinafine hydrochloride (RS) accurately weighed was transferred to (100) ml volumetric flask and diluted with methanol to the volume. Then (10) mg of this solution was transferred to (100) ml volumetric flask and diluted to the volume with



methanol. The final concentration of this solution was considered to be (0.01) mg/ml of terbinafine hydrochloride.

Sample preparation

A quantity of the cream containing (1) mg of terbinafine hydrochloride was extracted with (25) ml methanol with the help of sonicating, then this solution was transferred quantitatively to (100) ml volumetric flask and methanol was added to make up to volume. After sonicating for (5) minutes a portion of the solution was filtered through a filter having a porosity of 0.45 μ m. The final concentration of terbinafine hydrochloride was considered to be (0.01) mg/ml.

Methods

Chromatographic conditions

The chromatographic conditions which were used in the method for analyzing terbinafine hydrochloride in cream samples are displayed in table (1).

Table 1: Chromatographic conditions of HPLC method

Column	Intersil : L10DS(4.6mm.15cm) particle size 5 μ m
Mobile phase	Methanol - acetonitril (60:40 v/v) with (0.15% triethylamine and 0.15% phosphoric acid) pH=7.68
Detection and wave length	Photo diode array detector monitored at 224 nm
Flow rate	0.4 ml/minute
Injection volume	10 μ l
Oven temperature	25°C

Method for accelerated stability study

Samples of terbinafine hydrochloride had been subjected to accelerated stability study according to the following WHO requirements⁹:

Storage conditions 40 \pm 2°C / 75 \pm 5%RH.

Time period 6 months

Testing frequency 0, 1,2,3,6 months

Method for swing study

Samples of terbinafine hydrochloride cream were incubated at a temperature of 40°C for 2 days then at a temperature of (2-8°C) for 2 days and this procedure had been repeated three times¹⁰.

Method for photostability study

Photostability study had been performed according to ICH requirements¹¹ where samples should be exposed to light providing an overall illumination of not less than 1.2 million lux hours and an integrated near ultraviolet energy of not less than 200 watt hours/square meter and this level can be obtained by exposing drug product outside of its immediate pack to disseminated day light for 50 days.

RESULTS AND DISCUSSION

Results of accelerated stability study

After subjecting samples of terbinafine hydrochloride cream for the three local private pharmaceutical companies to accelerated stability study according to WHO requirements the samples were tested for any physical change, pH value and the content of active ingredient by using stability-indicating RP HPLC method.

The results showed that there was no change in the physical characteristics of the cream and there were small and acceptable changes of pH value and the potency loss from the initial assay value did not exceed 5% (4%). The results of pH test and the content of active ingredient are shown in tables (2, 3).

Table 2: Results of the assay of terbinafine hydrochloride in cream samples by using RP HPLC method during the accelerated stability study

Time Product	0	1 M	2 M	3 M	6 M	
Nailfin	1	100.23	100.19	99.96	98.92	95.56
	2	100.07	99.6	99.37	98.20	95.44
Terbina	1	101.09	99.68	98.14	97.32	97.32
	2	99.36	100.09	99.11	98.50	95.15
balmisil	1	100.83	99.34	98.89	97.72	95.92
	2	100.66	100.06	99.12	97.06	96.48

Table 3: Results of pH test of terbinafine hydrochloride samples during the accelerated stability study

Time Product	0	1 M	2 M	3 M	6 M	
Nailfin	1	6.50	6.53	6.51	6.49	6.45
	2	6.61	6.59	6.57	6.53	6.50
Terbina	1	6.21	5.88	5.81	6.79	5.74
	2	6.34	5.82	5.98	5.80	5.76
balmisil	1	5.57	5.39	5.52	5.43	5.36
	2	5.56	5.43	5.50	5.42	5.53

Results of swing study

After subjecting the samples of terbinafine hydrochloride for the three local private pharmaceutical companies to swing test the samples were tested for any physical change, pH value and the content of active ingredient by using stability-indicating RP HPLC method.

The results showed that there was no change in the physical characteristics of the cream and there were small and acceptable changes of pH value and the potency loss from the initial assay did not exceed 5%.

The results of swing study are displayed in table (4).



Table 4: Results of swing test of terbinafine hydrochloride samples.

Standard Product		Initial pH	Final pH	Initial Con%	Final Con%
Nailfin	1	6.55	6.51	100.23	99.28
	2	6.61	6.57	100.01	100.53
Terbina	1	6.21	6.38	100.97	99.92
	2	6.34	6.40	99.63	101.6
Balmisil	1	5.57	5.52	101.83	98.54
	2	5.56	5.50	100.66	97.74

Results of photostability study

After subjecting terbinafine hydrochloride cream sample to photostability study according to ICH guide it was noticed that there were two peaks for degraded products and a potency loss of about 14% from the initial assay value.

The results of photostability study are displayed in figure (2).

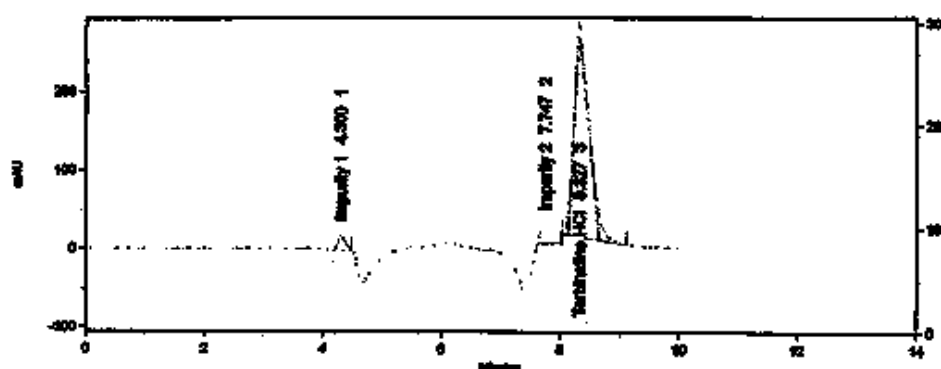


Figure 2: HPLC chromatogram for terbinafine hydrochloride cream sample after subjecting to photostability study.

CONCLUSION

All samples of terbinafine hydrochloride cream which were subjected to accelerated stability study and swing study were stable but for samples of terbinafine hydrochloride which had been subjected to photostability study there was 14% potency loss of the initial assay value.

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