Stability of Minoxidil in Espumil Foam Base

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ABSTRACT

Minoxidil is a drug used to stimulate hair growth and to slow balding. It is marketed under a number of trade names, including Rogaine, and is available in varying strength dose forms from a number of generic manufacturers. Minoxidil is available in oral and topical forms. In topical form, it can be applied by a metered-spray or a rub-on applicator. A hydroalcoholic compounding vehicle can minimize greasiness, itching, burning, and contact dermatitis where low concentrations of ethanol and propylene glycol are present. Espumil Foam Base contains low concentrations of these ingredients and also can form a foam on topical application. Espumil's unique delivery by foam-activating packaging assures simple application to difficult-to-treat areas, and it vanishes quickly after application, keeping it in place and avoiding healthy skin areas. The objective of this study was to determine the stability of minoxidil in Espumil Foam Base. The studied sample was compounded into a 50-mg/mL solution and stored in a plastic foam-activating bottle at room temperature conditions. Three samples were assayed at each time point out to 90 days by a stability-indicating high-performance liquid chromatography method. The method was validated for its specificity through forced-degradation studies. The beyond-use-date is at least 90 days, based on data collected when this formulation was stored at room temperature, protected from light.

INTRODUCTION

Minoxidil is an antihypertensive vasodilator medication that has been shown to stimulate hair growth and slow balding. Minoxidil is available in oral and topical forms as a spray, liquid, or lotion.[1] Espumil Foam Base (Fagron US-formerly Gallipot, St. Paul, Minnesota) is an alternative, innovative pharmaceutical compounding vehicle that minimizes greasiness, itching, burning, and contact dermatitis due to low concentrations of ethanol and propylene glycol. Its unique delivery system assures simple application of medication to difficult-to-treat areas. Espumil Foam Base vanishes quickly after application, avoiding healthy skin areas.

Pharmacists frequently compound preparations extemporaneously on prescription for individual patients in lieu of commercially-supplied products in many situations allowed by State Boards of Pharmacy and U.S. Food and Drug Administration regulations.

The objective of this study was to examine the stability of minoxidil in Espumil Foam Base. The solution was stored in a plastic foam-activating bottle at a concentration of 50 mg/mL at room temperature. Stability was assessed by percent recovery studies performed at varying time points throughout 90 days.

MATERIALS AND METHODS

Chemical Reagents

Minoxidil raw powder (Lot 12D17-V06-005410) was received from Fagron US-formerly Gallipot, St. Paul, Minnesota. Espumil Foam Base (Lot 12H08-U05-005818) was received from Fagron US-formerly Gallipot. High-performance liquid chromatographic-grade methanol (Lot K38E16; JT Baker, Center Valley, Pennsylvania), and acetic acid (Lot B0522653; Acros Organics, Geel, Belgium) were used in this study. High-performance liquid chromatographic-grade water was supplied by filtering deionized water from a Millipore (Billerica, Massachusetts) Elix through a Millipore Simplicity.

Equipment and Chromatographic Conditions

Two different types of high-performance liquid chromatography (HPLC) systems were used. The first, used for validation and the stability study, was a Perkin Elmer 200-Series (Perkin Elmer, Waltham, Massachusetts) equipped with a quaternary gradient solvent delivery system, a dual wavelength UV/VIS detector, and a 100-vial programmable autosampler with a Peltier tray, 200-mcL sample loop, and 250-mL syringe. The second HPLC system, used for forced-degradation studies, was a Varian Prostar (Varian, Palo Alto, California), equipped with a tertiary gradient solvent delivery system, a photodiode array detector, and an 84-vial programmable autosampler with a 100-mcL sample loop, and a 250-mcL syringe. The Perkin Elmer HPLC was operated and data was collected using Perkin Elmer Totalchrom chromatography software, while the Varian HPLC used Galaxie chromatography software. The mobile phase for the HPLC method was water, methanol, acetic acid (800:200:1) and was delivered at 1.0 mL/min. Chromatographic separation was achieved using a 150 × 4.6 mm Phenomenex (P/No. 00F-4435-EO; Tor-

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rence, California) Gemini C18 column with 5-mcm particle packing. The mobile phase was used as solvent in diluting the standard and assay preparations to 40 mcg/mL. The assay was monitored at 279 nm, following a 20-mcL injection.

Validation of Forced-degradation Studies to Determine Stability-indicating Characteristics of the High-performance Liquid Chromatographic Method

Minoxidil samples were stressed and assayed to determine the specificity of the HPLC method to any possible degradation product during storage of a compounded suspension. Minoxidil was diluted to 40 mcg/mL in solutions of base (1.0M NaOH), acid (1.0M HCl), and hydrogen peroxide (7.0%), in addition to exposure to ultraviolet (UV) light at 365 nm and heat at 70°C for 3 hours. Any extraneous peaks found in the chromatogram were labeled and the resolution (*United States Pharmacopeia*) was determined between the degradant and the minoxidil. A resolution of 1.5 was considered full separation. Purity calculations were performed on Galaxie on the minoxidil peak using the controlled, unstressed standard as a reference.

Preparation of Minoxidil Samples

The minoxidil sample was prepared by adding 12.6 g of minoxidil powder to a 250-mL volumetric flask and then brought to volume with Espumil Foam Base. The contents were stirred on a stir plate with 50°C heat for approximately 10 minutes. The contents were transferred to a plastic foam-activating bottle and stored at room temperature for the stability study.

Stability Study

The sample of minoxidil in Espumil Foam Base at a concentration of 50 mg/mL was submitted for stability. The sample was packaged in a plastic foam-activating bottle and stored at room temperature. Time points for the study were initial (T=0), 7 days (T=7), 15 days (T=15), 35 days (T=35), 45 days (T=45), 64 days (T=64), and 91 days (T=91). The evaluation parameter was percent recovery assay. The stability of minoxidil in solution was defined by the percent recovery with respect to T=0 using the validated HPLC method. The sample stock was prepared three times by adding 2 mL of solution with a volumetric pipette to 100 mL with mobile phase. Each sample stock was further diluted by adding 2 mL of stock to 50 mL with mobile phase. The average and standard deviation of all replicate injections at each time point were used to calculate the percent recovery.

RESULTS

The stability of minoxidil in Espumil Foam Base is shown in Table 1. The result of 49.52 mg/mL at T=0 was set as the initial concentration for the study, and all subsequent time points were compared to this value. The accompanying Figure shows the data in terms of concentration and shows that the concentration of the sample remained within the specification (90%<[minoxidil]<115%) throughout the duration of the study.

TABLE 1. Stability of Minoxidil in Espumil Foam Base at Room Temperature for 92 Days.

ELAPSED TIME	PERCENTAGE RECOVERY
T=0	100.00
T=7	100.86
T-15	98.87
T=35	99.28
T=45	100.90
T=64	98.55
T=91	101.53

DISCUSSION

The HPLC method was shown to be stability indicating by forcibly degrading minoxidil and separating the degradant peaks from that of the main analyte. Minoxidil was stable to base, UV light, and heat; however, acid and oxidizer created some degradation. The degradants present in the acid and oxidizer were all completely separated from the analyte with acceptable resolution. Additionally, validation parameters listed in Table 2 show that all system suitability results met acceptance criteria.

Minoxidil (Fagron US-Formerly Gallipot) in Espumil Foam Base

The initial potency of the Minoxidil in Espumil Foam Base was 49.52 mg/mL, which is shown in the Figure. This concentration was 99.0% of the compounding target of 50 mg/mL. The T=0 result was set

FIGURE. Plot of minoxidil concentration in Espumil Foam Base.

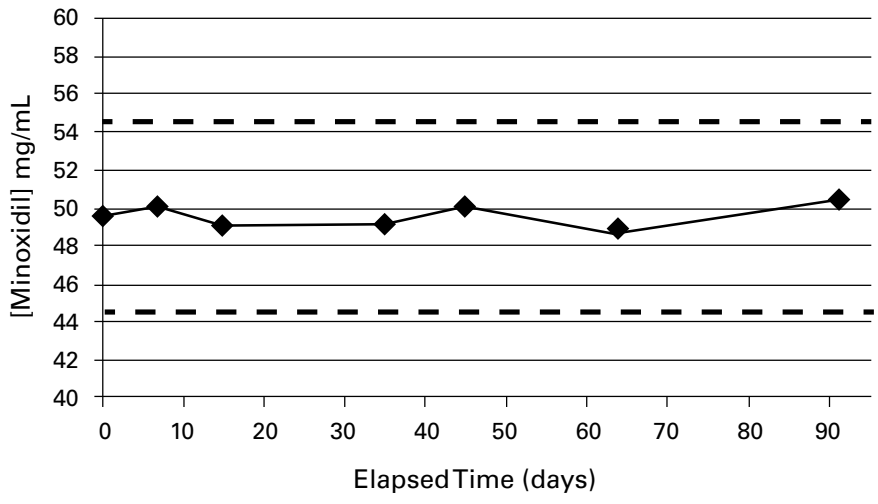

TABLE 2. Stability of Minoxidil in Espumil Foam Base at Room Temperature for 91 Days.

VALIDATION PARAMETER	RESULTS
Peak tailing	0.82
Theoretical plates	3082.51
Range	7.86 to 70.71 mcg/mL; R^2 = 0.9997
Extraction precision (Espumil Foam Base) *n*=6	% RSD = 0.86
Accuracy (mcg/mL)	% Target = 100.7
Specificity (resolution between main degradant peaks)	Res (*USP*) = 2.9

as the baseline for all other time points tested. The assay results varied between 48.80 mg/mL (T=64) and 50.77 mg/mL (T=91). Every replicate chromatogram for every time point was clear of degradant peaks and had the same chromatographic profile.

CONCLUSION

Minoxidil was stable in Espumil Foam Base for 91 days at room temperature conditions. The samples were still within specification at day 91; however, no general trend was observed during the course of the study. Therefore, the beyond-use date is concluded to be 90 days. This study is continuing to determine whether a longer beyond-use-date can be applied. The findings of this study show that Espumil Foam Base is an acceptable base for preparing individual compounded minoxidil formulations. This formulation has the added advantage of minimizing greasiness, itching, burning, and contact dermatitis because of low concentrations of ethanol and propylene glycol. The formulations would be viable alternatives to commercially available liquids or lotions.

REFERENCE

1. U.S. National Library of Medicine. National Institutes of Health. MedlinePlus. *Minoxidil Topical.* [MedlinePlus Website.] Available at: www.nlm.nih.gov/medlineplus/druginfo/meds/a689003.html. Accessed February 12, 2013.

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