Stability of Captopril in SyrSpend SF

Christine M. Geiger, MS
Bridget Sorenson, BS, CAPM
Paul A. Whaley, BS

ABSTRACT

Captopril is an angiotensin-converting enzyme inhibitor available as a tablet. Patients who are unable to take tablets have led compounding pharmacies to seek alternative dosage forms including solutions and suspensions. The objective of this study was to determine the stability of captopril in sorbitol-free, alcohol-free SyrSpend SF suspending agent. The studied samples were compounded into a 0.8-mg/mL suspension and stored in low-actinic plastic bottles at temperatures between 2°C to 8°C. Six samples were assayed at each time point out to 32 days by a stability-indicating high-performance liquid chromatography method. The samples remained within 90% to 110% of the initial concentration throughout day 14 of the study. Based on the data collected, the beyond-use date of these preparations is 14 days when protected from light and refrigerated.

INTRODUCTION

Captopril is an angiotensin-converting enzyme (ACE) inhibitor used for the treatment of hypertension and congestive heart failure.[1] Captopril is commonly marketed by Bristol-Myers Squibb under the trade name Capoten and is available generically from several manufacturers. Captopril is available as tablets[1] in strengths of 12.5 mg, 25 mg, 50 mg, and 100 mg for oral administration.[2] Captopril is a white to off-white crystalline powder that may have a slight sulfurous odor. An oral preparation containing a sweetener may increase the palatability of an oral dose form. Some patients are unable to use suspending agents containing sorbitol or alcohol. SyrSpend SF (Fagron US [formerly Gallipot], St. Paul, Minnesota) is an alcohol- and sorbitol- free suspending agent which could serve as a suitable suspending agent for compounding captopril oral suspensions.

The objective of this study was to examine the stability of captopril in an oral suspension using SyrSpend SF. The suspension was stored in a low-actinic plastic bottle at a concentration of 0.8 mg/mL at refrigerated storage conditions. Stability was assessed by percent recovery studies performed at varying time points throughout 32 days.

MATERIALS AND METHODS

Chemical Reagents

Captopril powder (Lot AA14409-002569) was received from Fagron US [formerly Gallipot]. SyrSpend SF (Lot 1006242R14) also was received from Fagron US [formerly Gallipot]. High-performance liquid chromatographic (HPLC)-grade methanol (Lot DF870; Honeywell, Muskegon, Michigan), 85% phosphoric acid (Lot 2011052000; CCI, Columbus, Wisconsin), and tetrahydrofuran (Lot WW0200; Spectrum, Gardena, California) were used in this study. HPLC-grade water was supplied by filtering deionized water from a Millipore Elix through a Millipore Simplicity (Billerica, Massachusetts).

Equipment and Chromatographic Conditions

Two different types of HPLCs were used. The first, used for validation and the stability study, was a Perkin Elmer 200-Series (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 a 250-mcL syringe. The second HPLC system, used for forced degradation studies, was a Varian Prostar (Palo Alto, California) equipped with a tertiary gradient solvent delivery system, a photodiode array detector (PDA), 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 is 0.34% phosphoric, 2.63% tetrahydrofuran, 29.20% methanol, and 68.14% water. The mobile phase was adjusted to a pH of 2.6 with 85% phosphoric acid and was delivered at 1.2 mL/min. Chromatographic separation was achieved using a 150 × 4.6 mm Phenomenex (Serial No. 610040-9; Torrence, California) Gemini C18 column with 5-mcm particle packing. The mobile phase was used as a solvent to dilute the standard and assay preparations to 50 mcg/mL. All preparations were filtered prior to injection. The assay was monitored following a 100-mcL injection.

The authors are affiliated with Dynalabs, LLC, located in St. Louis, Missouri.

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

Captopril samples were stressed and assayed at 220 nm to determine the specificity of the HPLC method to any possible degradation product during storage of an oral suspension. Captopril was diluted to 50 mcg/mL in solutions of acid (0.1M HCl), base (0.1M NaOH), hydrogen peroxide (3.5%), in addition to exposure to ultraviolet light at 365 nm and heat at 70°C for three hours. Any extraneous peaks found in the chromatogram were labeled and the resolution (*United States Pharmacopeia*) was determined between the degradant and the captopril. Purity calculations were performed in Galaxie on the captopril peak using the controlled unstressed standard as a reference.

Preparation of Captopril Suspension Samples

The captopril suspension was prepared by adding 100 mL of SyrSpend SF via volumetric pipette and 157.0 mg of captopril to a low actinic prescription bottle. Another 100-mL aliquot of SyrSpend SF was added to achieve a final concentration of 0.793 mg/mL captopril (concentration corrected for loss on drying and assay). The suspension was stored at refrigerated conditions between 2°C to 8°C for the duration of the study.

Stability Study

The sample of captopril suspended in SyrSpend SF at a concentration of 0.7931 mg/mL was submitted for stability. The sample was packaged in a low actinic plastic prescription bottle and stored at refrigerated conditions between 2°C to 8°C. Time points were initial (T=0), 12 days (T=12), 14 days (T=14), and 32 days (T=32). The evaluation parameter was percent recovery assay. The stability of captopril in suspension was defined by the percent recovery with respect to T=0 using the validated HPLC method. The sample stock was prepared six times by adding 1 mL of suspension with a volumetric pipette to a 20-mL flask and diluting to volume with mobile phase. The average and standard deviation of all replicate injections at each time point were used to calculate the percent recovery.

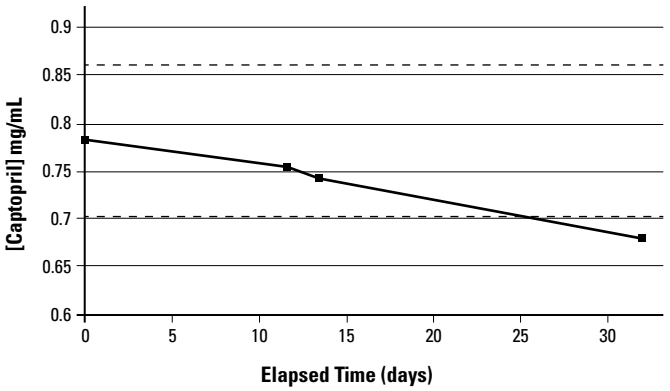
RESULTS

The stability of captopril in SyrSpend SF is shown in Table 1. The result of 0.7808 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 Figure depicts the data in terms of concentration of the suspension that remained within the specifications (90%<[captopril]<110%) throughout the duration of the study.

TABLE 1. Stability of Captopril in SyrSpend SF Refrigerated (2°C to 8°C) for 32 Days.

ELAPSED TIME	% RECOVERY
T=0	100.00
T=12	96.72 ± 0.26
T=14	95.06 ± 0.56
T=32	86.02 ± 0.77

FIGURE. Plot of captopril concentration in SyrSpend SF suspension.



Note: Dashed lines represent upper and lower limits of captopril specifications.

DISCUSSION

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

TABLE 2. Summary of the Validation Parameters for the High-performance Liquid Chromatographic Method Used in the Stability Study of Captopril.

VALIDATION PARAMETER	RESULTS	
Peak tailing	0.92	% RSD = 0.39
Theoretical plates	2188.24	% RSD = 0.66
Linear range	4.97 to 119.18 mcg/mL R^2 = 0.9995	
Extraction precision (SyrSpend SF) *n*=6	% RSD = 1.44	
Accuracy (mcg/mL)	%Target = 99	

RSD = relative standard deviation

The initial potency of captopril in SyrSpend SF suspension was 0.78081 mg/mL, which is shown in the Figure. This concentration was 98.45% of the compounding target of 0.793079 mg/mL. The T=0 result was set as the baseline for all other time points tested. The assay results varied between 0.67167 (T=32) and 0.78081 (T=0) for refrigerated conditions. All sample preparations at each time point were within specification with the exception of those at T=32, with a high relative standard deviation of 0.77% (T=32). Every replicate chromatogram for every time point was clear of degradant peaks and had the same chromatographic profile.

CONCLUSION

Captopril was stable in SyrSpend SF for 14 days when stored under refrigerated conditions (2°C to 8°C) when compounded from powder. The sample was still within specification at day 14; therefore, the beyond-use date is concluded to be 14 days. By day 32, the sample was no longer within specifications. The findings of this study show that SyrSpend SF is an acceptable oral syrup and suspending vehicle for preparing individual captopril formulations when stored refrigerated between 2°C to 8°C. This formulation has the added advantage of helping to mask the bitter taste while remaining alcohol, sorbitol, and sugar free. The formulation would be a viable alternative to commercially available tablets when that dosage form is found to be inappropriate.

REFERENCES

1. MedlinePlus: A Service of the U.S. National Library of Medicine, National Institutes of Health. *Captopril*. [MedlinePlus Website.] Updated as of October 15, 2012. Available at: http://www.nlm.nih.gov/medlineplus/druginfo/meds/a682823.html. Accessed March 28, 2013.
2. RxList: The Internet Drug Index. *Capoten (Captopril Tablets, USP)*. [RxList Website.] Updated as of October 9, 2012. Available at: http://www.rxlist.com/capoten-drug.htm. Accessed March 28, 2013.

Address correspondence to Bridget Sorenson, BS, CAPM, 2327 Chouteau Avenue, Saint Louis, MO 63103. E-mail: bsorenson@dynalabs.us