Stability of Omeprazole in SyrSpend SF Alka (Reconstituted)

Paul A. Whaley, BS
Mark A. Voudrie II, MS, PMP
Bridget Sorenson, CAPM

ABSTRACT

Omeprazole is used in the treatment of dyspepsia, peptic ulcer disease, gastroesophageal reflux disease, laryngopharyngeal reflux, and Zollinger–Ellison syndrome. Omeprazole is marketed by AstraZeneca under a number of names, most notably Prilosec and Losec, as well as being available from a number of generic manufacturers. Omeprazole is available in both tablet and capsule form, with varying strengths of each. The need for other administration options for those patients who cannot take tablets or capsules has led compounding pharmacies to seek other alternatives. One possible alternative is the use of a suspending agent to create an oral solution or suspension. In the past, this has been accomplished using a sodium bicarbonate solution as the vehicle. However, sodium bicarbonate/omeprazole combination imparts a bitter and unpleasant taste. SyrSpend SF Alka (reconstituted) is a vehicle for making a suspension which has a pleasant taste, thus increasing palpability and compliance. The objective of this study was to determine the stability of omeprazole in SyrSpend SF Alka (for reconstitution). The studied sample was compounded into a 2-mg/mL suspension and stored in a low-actinic plastic prescription bottle at temperatures between 2ºC and 8ºC. Six samples were assayed at each time point out to 92 days by a stability-indicating high-performance liquid chromatography method. The method was validated for its specificity through forced degradation studies. The shelf life of this product is at least 92 days, based on data collected when refrigerated and protected from light.

INTRODUCTION

Omeprazole is a proton pump inhibitor used in the treatment of dyspepsia, peptic ulcer disease (PUD), gastroesophageal reflux disease (GORD/GERD), laryngopharyngeal reflux (LPR), and Zollinger–Ellison syndrome.[1] It is used to treat a wide range of the patient population, including both infant and geriatric patients. These two groups in particular may experience difficulty in swallowing whole capsules or tablets. In the past, sodium bicarbonate has been used with omeprazole to create an oral solution. Sodium bicarbonate does little to mask the bitter taste of omeprazole. An alkaline suspending agent containing a sweetener masks the bitter taste and increases the palpability of omeprazole. This is of particular importance when considering the treatment of infants, as the masking of the taste increases end-user compliance. Some compounding vehicles contain alcohol and sorbitol. SyrSpend SF Alka (for reconstitution) (Fagron [formerly Gallipot], St. Paul, Minnesota) is a sorbitol- and alcohol-free alkaline suspending agent which could serve as an appropriate vehicle for compounding an omeprazole oral suspension.

The objective of this study was to examine the stability of omeprazole when prepared in an oral suspension using SyrSpend SF Alka (for reconstitution). The suspension was stored in a low-actinic plastic prescription bottle at a concentration of 2 mg/mL under *United States Pharmacopeia (USP)* refrigerated (2ºC to 8ºC) storage conditions. Stability was assessed by percent recovery studies performed at varying time points throughout 92 days.

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

MATERIALS AND METHODS

Chemical Reagents

Omeprazole raw powder was obtained from Gallipot (Lot 0906145D12; St. Paul, Minnesota). High-performance liquid chromatographic (HPLC)-grade acetonitrile (Lot CZ629; Burdick and Jackson, Kalamazoo, Michigan), 85% phosphoric acid ACS-grade (Lot 201103115; CCI, New Delhi, India), monosodium phosphate monohydrate (Lot 107148; Fisher Scientific, Pittsburgh, Pennsylvania), disodium phosphate heptahydrate (Lot B0131737; Acros Organics, Geel, Belgium), and octanesulfonic acid (Lot 038K0815; Sigma Aldrich, St. Louis, Missouri) were used in the 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 250-mL syringe. The second LC system, used for forced degradation studies, was a Varian Prostar (Palo Alto, California) equipped with a tertiary gradient solvent delivery system, a photodiode array detec-

tor (PDA), and an 84-vial programmable autosampler with a 100-mcL sample loop, and 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 buffer (50 mM phosphate), acetonitrile, and Octanesulfonic acid (700 mL:300 mL:4.0999 g). The mobile phase's pH was adjusted to 7.00 with 85% phosphoric acid and was delivered at 1.0 mL/min. Chromatographic separation was achieved using a 150 × 4.6 mm Phenomenex (Torrence, California) Gemini C18 column with 5-mcm particle packing. The mobile phase was used as solvent in diluting the standard and assay preparations to 80 mcg/mL. The assay was monitored at 301 nm following a 10-mcL injection.

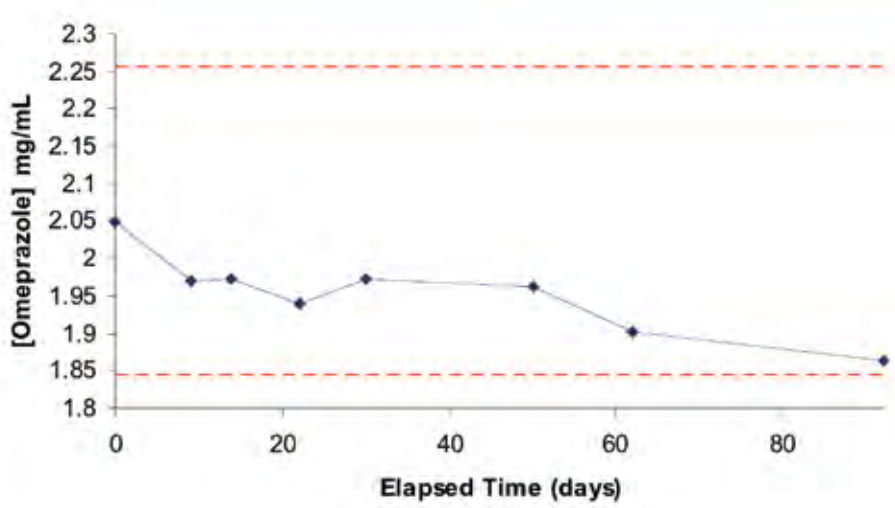
Validation of Forced-degradation Studies to Determine Stability-indicating Characteristics of the High-performance Liquid Chromatographic Method

Omeprazole samples were stressed and assayed to determine the specificity of the HPLC method to any possible degradation product produced during storage of an oral suspension. Omeprazole was diluted to 80 mcg/mL in a solution of acid (0.1M HCl), in addition to exposure to ultraviolet light at 365 nm and heat at 70°C. Time under each stressor varied due to the relative stability of omeprazole to each individual degradation pathway. Any extraneous peaks found in the chromatogram were labeled and the resolution (*USP*) was determined between the degradant and the omeprazole. A resolution of 1.5 was considered full separation. Purity calculations were performed in Galaxie on the omeprazole peak using the controlled unstressed standard as a reference.

Preparation of Omeprazole Suspension Samples

Omeprazole suspension was prepared by adding 240 mg of omeprazole powder to a plastic prescription bottle. SyrSpend SF Alka was reconstituted by adding 100 mL water per 6.43 g of SyrSpend SF Alka. Of the reconstituted suspension, 120 mL was added to the prescription bottle containing the omeprazole powder. The bottle was shaken until the omeprazole was uniformly dispersed. The flask was stored at *USP*-controlled refrigerated temperature (2°C to 8°C) for the stability study.

FIGURE. Plot of omeprazole concentration in SyrSpend SF Alka (reconstituted).



Note: Dashed lines represent upper and lower limits of Omeprazole specification.

Stability Study

The sample of omeprazole suspended in reconstituted SyrSpend SF Alka at a concentration of 2 mg/mL was submitted for stability. The sample was packaged in a low-actinic plastic prescription bottles and stored at USP-controlled refrigerated temperature (2°C to 8°C) using a digitally controlled laboratory refrigerator from Forma Scientific (Edison, New Jersey). Time points for the study were initial (T=0), 9 days (T=9), 14 days (T=14), 22 days (T=22), 30 days (T=30), 50 days (T=50), 62 days (T=62), and 92 days (T=92). The evaluation parameter was percent recovery assay. The stability of omeprazole 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 25 mL with mobile phase. The average and standard deviation of all replicate injections at each time point was used to calculate the percent recovery.

TABLE 1. Stability of Omeprazole in Reconstituted SyrSpend SF Alka Refrigerated (2°C to 8°C) for 90 days.

Elapsed Time	% Recovery
T=0	100.00
T=9	96.24 ± 1.80%
T=14	96.32 ± 3.87%
T=22	94.69 ± 1.71%
T=30	96.32 ± 0.66%
T=50	95.76 ± 4.45%
T=62	92.87 ± 1.79%
T=92	90.98 ± 2.72%

RESULTS

The stability of omeprazole in reconstituted SyrSpend SF Alka is shown in Table 1. The result of 2.0483 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 included with this manuscript shows the data in terms of concentration and that the concentration of the suspension remained within the specification (90%<[omeprazole]<110%) throughout the 62 days of the study.

The HPLC method was shown to be stability indicating by forcibly degrading omeprazole and separating the degradant peaks from that of the main analyte. Omeprazole was stable to light, with slight

degradation under acid stress. There was significant degradation created by heat. The degradants present in the acid and heat conditions 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.

Gallipot SyrSpend SF Alka (Reconstituted) Omeprazole Suspension

The initial potency of the omeprazole suspension was 2.0483 mg/mL, as shown in the Figure included with this manuscript. This concentration was 102.4% of the compounding target of 2 mg/mL. The T=0 result was set as the baseline for all other time points tested. The assay results showed an overall downward trend to a low point of 1.8635 mg/mL at T=92. Every replicate chromatogram for every time point was clear of degradant peaks and had the same chromatographic profile.

CONCLUSION

Omeprazole was stable in SyrSpend SF Alka (reconstituted) for 92 days when stored under refrigerated (2°C to 8°C) conditions. The sample was still within specification at day 92. However, the overall trend is that of decreasing concentration during the course of the study. The beyond-use-date should be set to 60 days. The findings of this study show that SyrSpend SF Alka (reconstituted) is an acceptable suspending vehicle for preparing individual compounded omeprazole formulations. This formulation has the added advantage of helping to mask the bitter taste while remaining alcohol and sorbitol free. The formulations would be viable alternatives to commercially available capsules when that dosage form is found to be inappropriate.

REFERENCE

1. U.S. National Library of Medicine. *Omeprazole.* [National Center for Biotechnology Information Website.] May 16, 2011. Available at: www.ncbi.nlm.nih.gov/pubmedhealth/PMH0000936. Accessed January 16, 2012.

TABLE 2. Summary of the Validation Parameters for the High-Performance Liquid Chromatographic Method Used in the Stability Study of Omeprazole in SyrSpend SF Alka (Reconstituted).

Validation Parameter	Results	
Peak Tailing	1.33	% RSD = 1.99
Theoretical Plates	4398.5	% RSD = 0.67
Linear range (301 nm)	20 to 200 mcg/mL R^2=0.9998	
Extraction Precision *n*=6	%RSD = 1.23	
Accuracy (50, 100, 180 mcg/mL)	%Target = 98.61%, 98.53%, 99.67%	
Specificity (resolution between main degradant peaks)	Res (USP) = 11.27	

TABLE 2. Summary of the Validation Parameters for the High-Performance Liquid Chromatographic Method Used in the Stability Study of Omeprazole in SyrSpend SF Alka (Reconstituted).

VALIDATION PARAMETER	RESULTS	
Peak Tailing	1.33	% RSD = 1.99
Theoretical Plates	4398.5	% RSD = 0.67
Linear range (301 nm)	20 to 200 mcg/mL R^2=0.9998	
Extraction Precision n=6	%RSD = 1.23	
Accuracy (50, 100, 180 mcg/mL)	%Target = 98.61%, 98.53%, 99.67%	
Specificity (resolution between main degradant peaks)	Res (USP) = 11.27	
Extraction Precision n=6	%RSD = 1.23	
Accuracy (50, 100, 180 mcg/mL)	%Target = 98.61%, 98.53%, 99.67%	
Specificity (resolution between main degradant peaks)	Res (USP) = 11.27	

Address correspondence to Paul Whaley, BS, Method Development Chemist, Dynalabs, LLC, 2327 Chouteau Avenue, St. Louis, MO 63103. E-mail: pwhaley@dynalabs.us