



## Stability of Propranolol Hydrochloride in SyrSpend SF

**Christine M. Geiger, MS**  
**Mark A. Voudrie II, MS, PMP**  
**Bridget Sorenson, BS, CAPM**

### INTRODUCTION

Propranolol hydrochloride (HCl) is a non-selective beta-adrenergic receptor blocking agent. Oral forms are approved for use in patients with hypertension, abnormal heart rhythms, heart disease, angina, pheochromocytoma, migraines, and certain types of tremors.<sup>1</sup> It also improves survival post myocardial infarction.

Propranolol HCl is a bitter-tasting, odorless, white crystalline powder. The bitter taste is an issue for patients incapable of swallowing the tablets or capsules whole. A suspending agent containing a sweetener would provide a masking effect for the bitter taste thus increasing the palatability of an oral liquid dosage form and improving therapeutic compliance. Some patients are unable to use suspending agents containing sorbitol or alcohols. SyrSpend SF (Fagron US—formerly Gallipot, St. Paul, Minnesota) is an alcohol- and sorbitol-free suspending agent which could serve as a suitable alternative for compounding propranolol HCl oral suspensions.

The objective of this study was to examine the stability of propranolol HCl in an oral suspension using SyrSpend SF. The suspension was stored in a low-actinic plastic bottle at a concentration of 1 mg/mL at room temperature storage conditions. Stability was assessed by percent recovery studies performed at varying time points throughout 90 days.

### MATERIALS AND METHODS

#### Chemical Reagents

Propranolol HCl raw powder was purchased from Medisca (Lot 65892/E;

### ABSTRACT

Propranolol hydrochloride is a beta blocker used to treat high blood pressure, abnormal heart rhythms, heart disease, pheochromocytoma, and certain types of tremors. Propranolol is marketed by Wyeth (now a part of Pfizer) and AstraZeneca under the brand names Inderal, Inderal LA, Avlocardyl, Deralin, Dociton, Inderalici, InnoPran XL, Sumial, Anaprilium, Bedranol SR (Sandoz). It is also available generically from several manufacturers. Propranolol hydrochloride is available as tablet, capsule, and oral liquid dosage forms in several strengths. Some patients are unable to tolerate oral tablets and capsules, challenging compounding pharmacies to seek alternative dosing options; namely oral solutions and suspensions. The objective of this study was to determine the stability of propranolol hydrochloride in SyrSpend SF. The drug was compounded into a 1-mg/mL suspension using SyrSpend SF and subsequently stored in a low-actinic plastic prescription bottle at room temperature conditions. Six samples were assayed at each specific time point extending to 90 days by a stability-indicating high-performance liquid chromatography method. The method was validated for its specificity through forced-degradation studies. Based on the data collected, when protected from light at room temperature, the beyond-use date of propranolol hydrochloride in SyrSpend SF was shown to be at least 90 days.

Plattsburgh, New York). SyrSpend SF was received from Fagron US—formerly Gallipot (Lot 1110358V14; St. Paul, Minnesota). High-performance liquid chromatographic (HPLC)-grade acetonitrile (Lot DF818; Honeywell, Morristown, New Jersey), ammonium phosphate monobasic (Lot 082990A; Fisher Scientific, Pittsburgh, Pennsylvania), triethylamine (Lot B0521038; Acros Organics, Geel, Belgium), and phosphoric acid (Lot 2011052000; CCI, New Delhi, India) were utilized 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 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

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

50 mM ammonium phosphate monohydrate with 0.5% tetraethylamine and acetonitrile (750:250). The mobile phase was adjusted to pH 3.00 with 85% phosphoric acid and was delivered at 1.4 mL/min. Chromatographic separation was achieved using a 150 × 4.6 mm Phenomenex (Torrance, California) Gemini C18 column with 5- $\mu$ m particle packing. The mobile phase was used as solvent to dilute the standard and assay preparations to 50 mcg/mL. The assay was monitored following a 100- $\mu$ L injection.

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

Propranolol HCl samples were stressed and assayed at 290 nm to determine the specificity of the HPLC method to any possible degradation product produced during storage of an oral suspension. Propranolol HCl 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. Time under each stressor varied due to the relative stability of propranolol HCl to each individual degradation pathway. Any extraneous peaks found in the chromatogram were labeled and the resolution (*United States Pharmacopeia [USP]*) was determined between the degradant and the propranolol HCl. Purity calculations were performed in Galaxie on the propranolol HCl peak using the controlled unstressed standard as a reference.

### Preparation of Propranolol Hydrochloride Suspension Samples

The propranolol HCl suspension was prepared by adding 103.4 g of propranolol HCl to a low-actinic prescription bottle. Two aliquots of SyrSpend SF were added to the bottle using a volumetric pipette to achieve a final volume of 100 mL. The final concentration was 1 mg/mL propranolol

HCl. The suspensions were stored at room temperature for the duration of the study.

### STABILITY STUDY

The sample of propranolol HCl suspended in SyrSpend SF at a concentration of 1 mg/mL was submitted for stability. The sample was packaged in a low-actinic plastic prescription bottle and stored at room temperature. Time points for the study were initial (T=0), 20 days (T=20), 32 days (T=32), and 90 days (T=90). The evaluation parameter was percent recovery assay. The stability of propranolol HCl 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 volumetric 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 propranolol HCl in SyrSpend SF is shown in Table 1. The result of 1.08 mg/mL at T=0 was set as the initial

**TABLE 1. Stability of Propranolol Hydrochloride in SyrSpend SF at Room Temperature for 90 Days.**

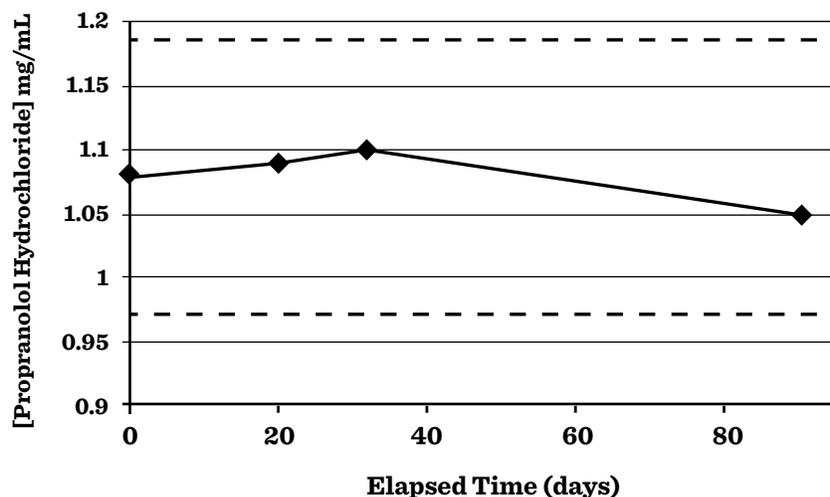
ELAPSED TIME	% RECOVERY
T=0	100.00
T=20	100.90 $\pm$ 2.69
T=32	102.13 $\pm$ 1.04
T=90	97.68 $\pm$ 1.674

concentration for the study, and all subsequent time points were compared to this value. The Figure that accompanies this article depicts the data in terms of concentration of the suspension that remained within the specification (90% < [propranolol HCl] < 110%) throughout the duration of the study.

### DISCUSSION

The HPLC method was shown to be stability indicating by forcibly degrading propranolol HCl and separating the degradant peaks from that of the main analyte. Propranolol HCl was stable to acid and heat; however, base and light created slight degradation. Oxidizer created significant degradation. The degradants present were all completely separated from the analyte

**FIGURE. Plot of propranolol hydrochloride concentration in SyrSpend SF Suspension.**



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

**TABLE 2. Summary of the Validation Parameters for the High-performance Liquid Chromatographic Method Used in the Stability Study of Propranolol Hydrochloride in SyrSpend SF.**

VALIDATION PARAMETER	RESULTS
Peak tailing	1.72 % RSD = 0.73
Theoretical plates	6420.13 % RSD = 0.98
Range	5.05 to 121.30 mcg/mL R <sup>2</sup> = 0.9994
Extraction precision (SyrSpend SF) <i>n</i> =6	% RSD = 4.50
Accuracy (mcg/mL)	% Target = 99.74%

RSD = relative standard deviation

with acceptable resolution. Additionally, validation parameters listed in Table 2 show that all system suitability results met acceptable criteria.

### Propranolol Hydrochloride USP Raw Powder (Medisca) in SyrSpend SF Suspension

The initial potency of the Propranolol HCl USP Raw Powder in SyrSpend SF suspension was 1.08 mg/mL, which is shown in the Figure that accompanies this article. This concentration was 108% of the compounding target of 1.0 mg/mL. The T=0 result was set as the baseline for all other time points tested. The assay results varied between 1.05 mg/mL (T=90) and 1.10 mg/mL (T=32). All sample preparations at each time point were within specification, with a high percent relative standard deviation of 2.69% (T=20). Every replicate chromatogram for every time point was clear of the degradant peaks and had the same chromatographic profile.

## CONCLUSION

When compounded from the raw powder, propranolol HCL was stable in SyrSpend SF for 90 days when stored at room temperature conditions. The samples were still within specifications at day 90, therefore, the beyond-use date is concluded to be 90 days.

The findings of this study show that SyrSpend SF is an acceptable oral syrup and suspending vehicle for preparing individually compounded propranolol HCl suspensions. 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 option for those patients who are unable to tolerate solid dosage forms.

## REFERENCES

1. INDERAL—propranolol hydrochloride tablet [product information]. [NIH Website.] September 2010. Philadelphia, PA: Wyeth Pharmaceuticals Inc. Available at: <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=b4f0efb8-b5e0-4efc-6e8d-525a93446ad8>. Accessed June 27, 2012.

Address correspondence to Bridget Sorenson, BS, CAPM, 2327 Choteau Avenue, Saint Louis, MS 63103. E-mail: bsorenson@dynamabs.us 📧