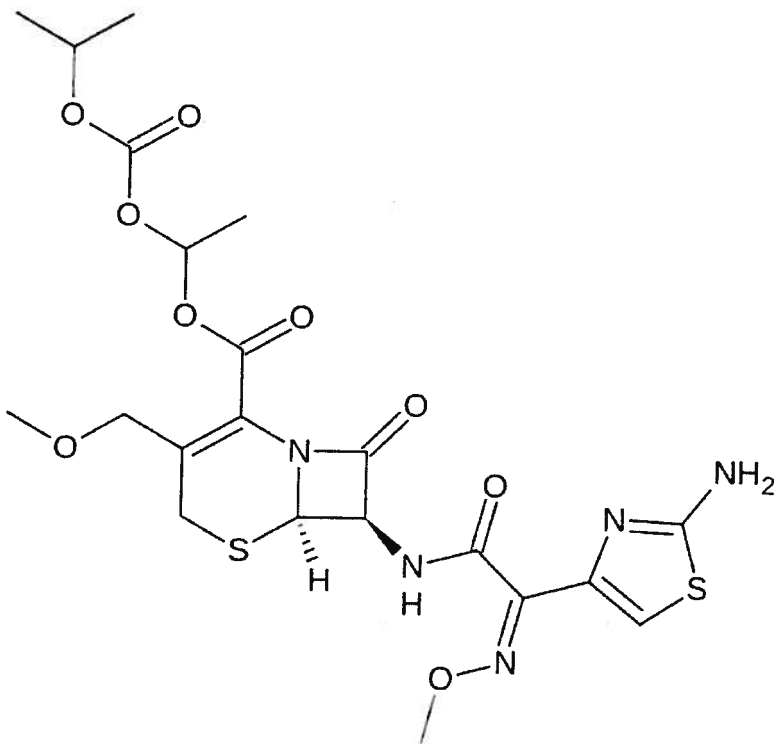
Stability Report

Cefpodoxime Proxetil



$C_{21}H_{27}N_5O_9S_2$

Materials

Flavors		**Lot#**	**Expiration**
Sweetening Enhancer		1368116	9/2012
Bitterness Supressor		B037013	3/2021
Bubblegum		W158177	7/2019
Grape		T0613	6/2021
Raspberry		R1130	11/2019
Watermelon		T0213	3/2021
FLAVORx, INC **9475 Gerwig Lane, Columbia, MD 21046**			
Standards	**Part #**	**Lot #**	
Cefpodoxime Proxetil	K558-100mg	16A6E891	
AK Scientific, Inc. **30023 Ahern Avenue** **Union City, CA 94587**			
Reagents	**Part #**	**Lot #**	
Acetonitrile	A955-4	130449	
Ammonium Acetate	A114-50	130362	
Fisher Scientific			
Water			
House Deionized Water System			
Glacial Acetic Acid	338826-100mL	32196LMV	
Sigma Aldrich			
Pharmaceutical	**NDC #**	**Lot #**	**Expiration**
Cefpodoxime Proxetil for Oral Suspension, USP	0781-6169-52	CP4857	6/2014
Manufactured For:			
Sandoz Inc.,			
Princeton, NJ 08540			
Manufactured By:			
Sandoz GmbH			
Austria			

Results

Table 1: Average % Potency Relative to Bottle Value

Sample	Average % Potency Relative to Bottle Value (20mg/mL) vs. Time after FLAVORx Flavor Addition (± 95%)		
	Day 0	Day 7	Day 14
Control	124.58 (0.19)	121.56 (0.80)	114.77 (0.22)
Bubblegum	119.57 (0.28)	120.31 (0.58)	113.85 (0.42)
Grape	126.61 (0.36)	122.59 (1.01)	117.91 (0.25)
Raspberry	127.13 (0.42)	126.96 (0.39)	117.88 (0.39)

Table 2: Average % Potency Relative to Control Sample

Sample	Average % Potency Relative to Control vs. Time after FLAVORx Flavor Addition (± 95%)		
	Day 0	Day 7	Day 14
Control	-	-	-
Bubblegum	95.98 (0.30)	98.97 (0.63)	99.20 (0.31)
Grape	101.63 (0.27)	100.85 (0.40)	102.74 (0.23)
Raspberry	106.33 (0.35)	105.53 (0.53)	103.54 (0.28)

Table 3: Sample pH over 14 day period

Sample	pH Day of Testing		
	Day 0	Day 7	Day 14
Control	4.43	4.44	4.45
Bubblegum	4.54	4.56	4.53
Grape	4.54	4.55	4.52
Raspberry	4.52	4.54	4.52

Note: The acceptable pH range for this drug as reconstituted is 4-5.5.

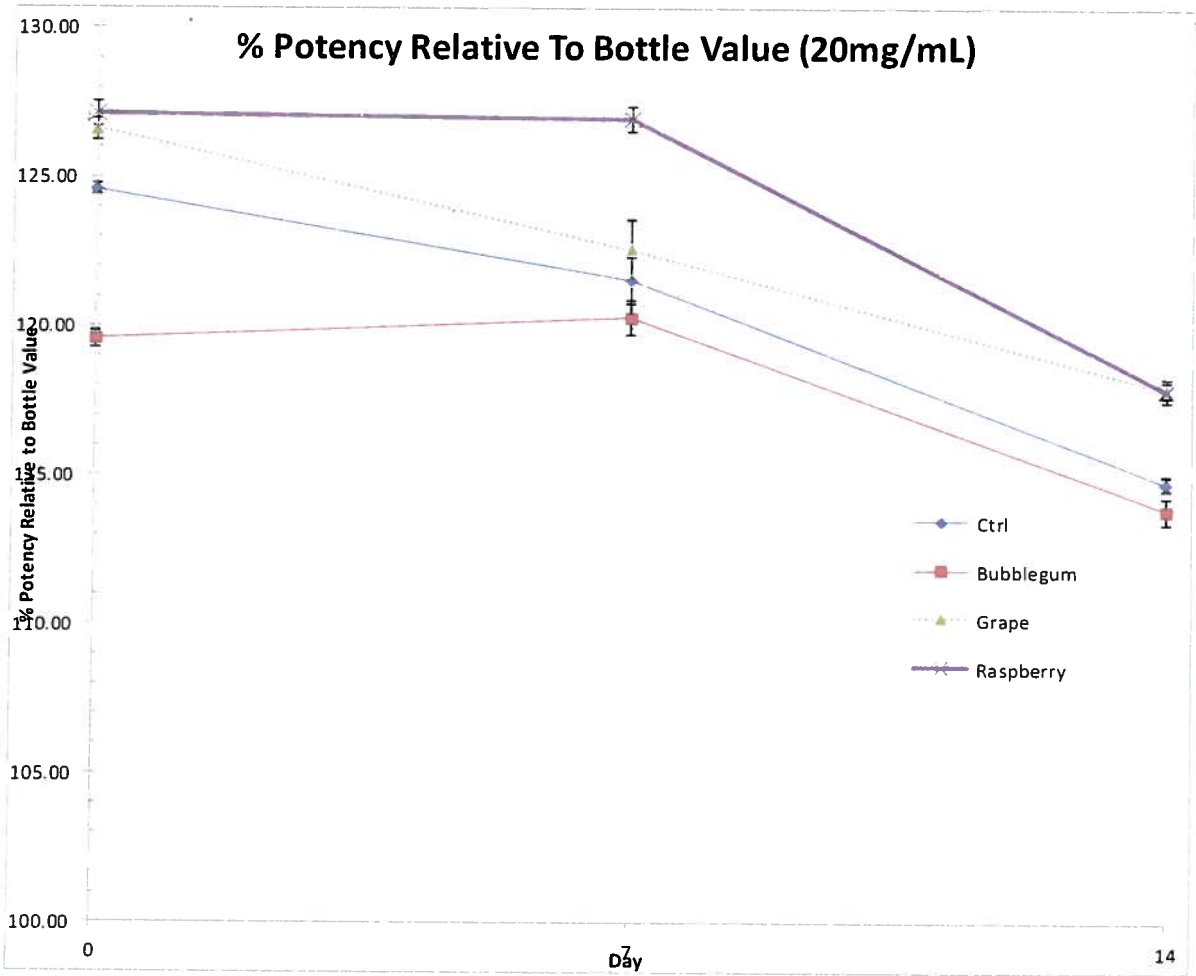


Figure 1: Average % Potency relative to Bottle Value over the 14 day shelf life of the medication. Lines do not represent a fit to an algorithm; they are presented for data clarity. Error bars represent ±95% confidence interval.

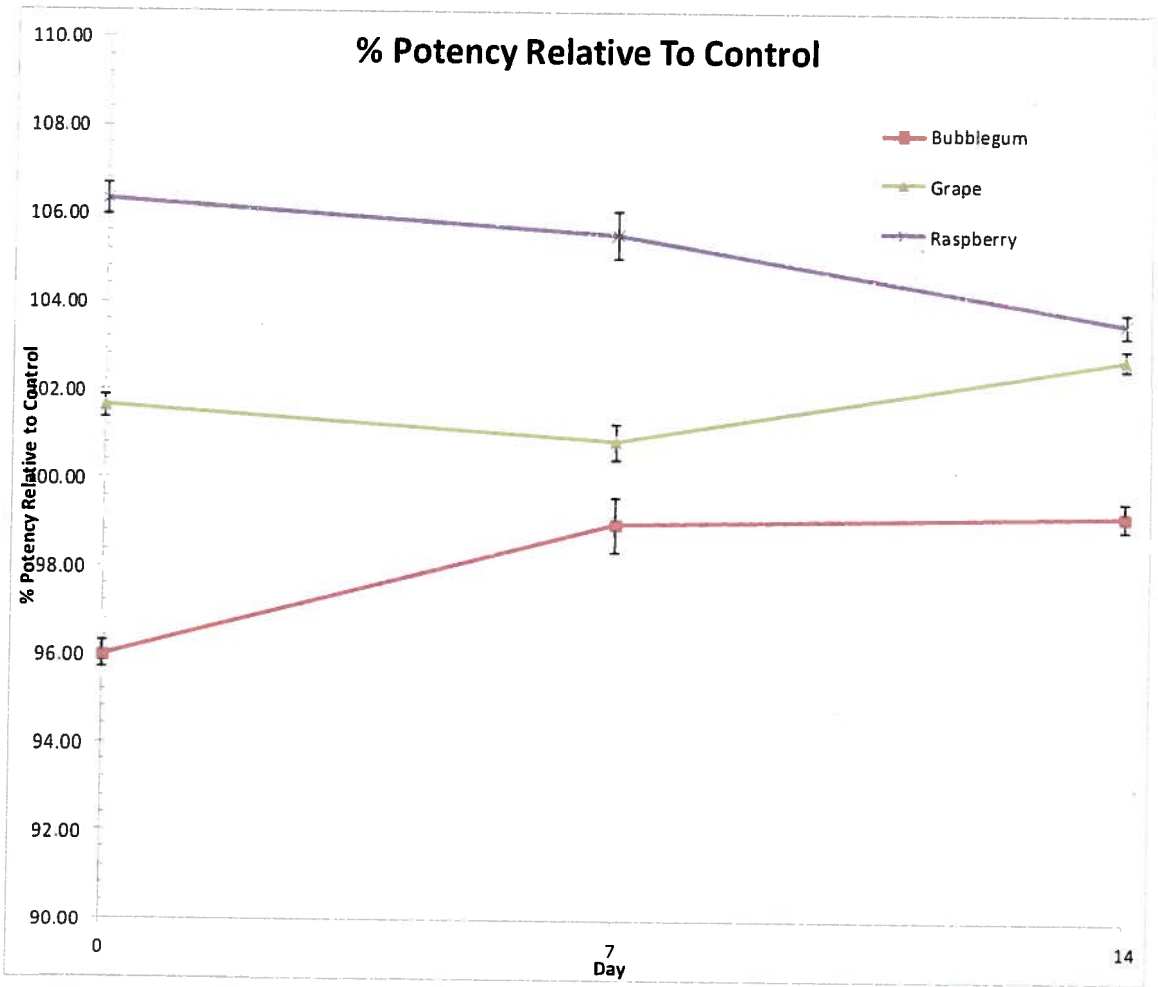


Figure 2: Average % Potency relative to the Control Sample over the 14 day shelf life of the medication. Lines do not represent a fit to an algorithm; they are presented for data clarity. Error bars represent ±95% confidence interval.

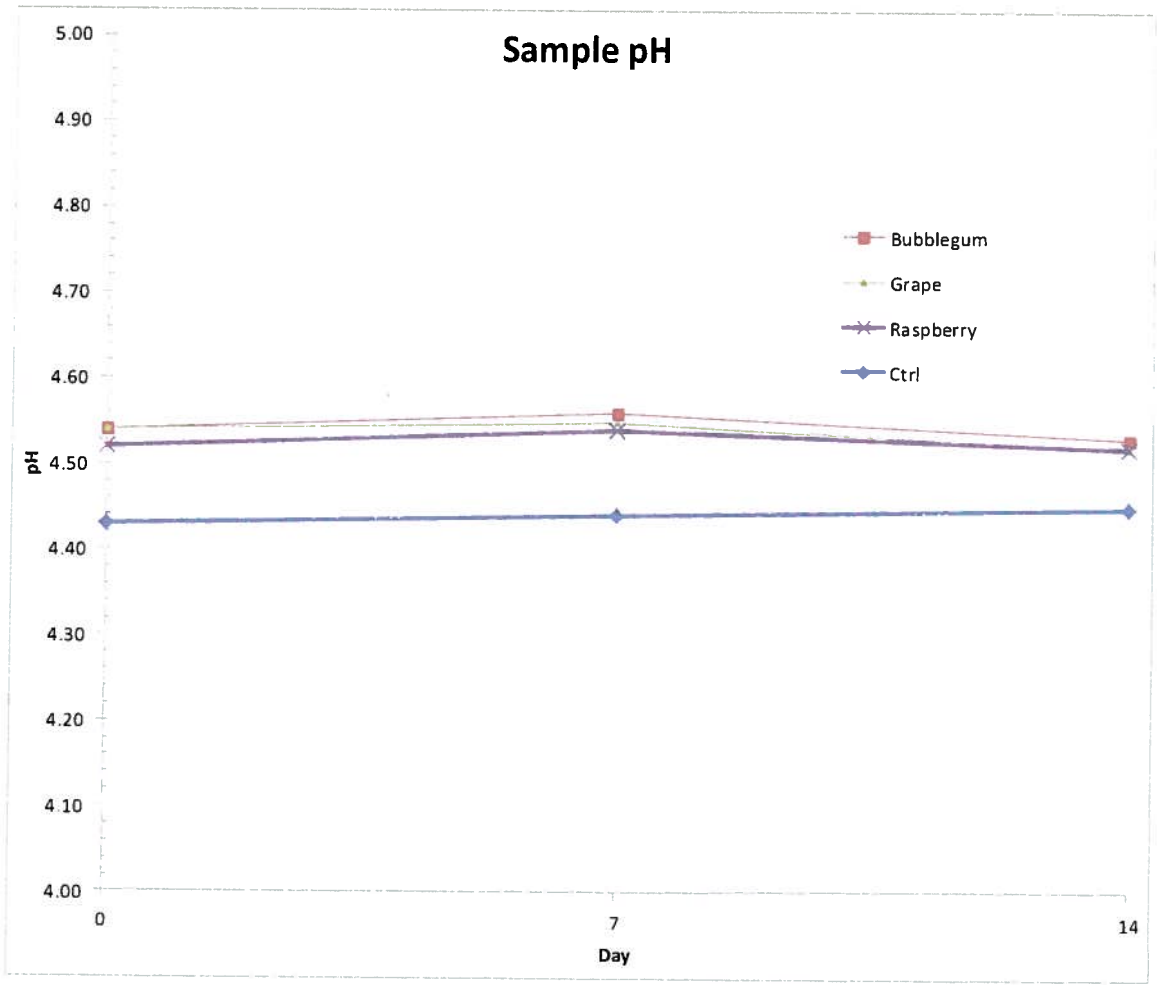


Figure 3: Sample pH recorded on each day of testing. Lines do not represent a fit to an algorithm; they are presented for data clarity.

Physical Appearance/Observations

When reconstituted, the medication had a white, viscous appearance. When diluted in the sample preparation step prior to analysis each sample was cloudy. The smell and appearance of each sample, except bubblegum, was consistent over the two week trial. The bubblegum flavored sample had a yellow hue (see attached photograph) compared to the other samples by day 7 and persisted to day 14 without further change.

Standards Preparation

The initial standard solution was prepared to approximately 1.0 $mg \cdot mL^{-1}$. The remaining standard solutions were prepared by serial dilution from this standard. Each solution was thoroughly mixed and visually inspected to ensure no standard remained un-dissolved. The concentration range included 1.0 $mg \cdot mL^{-1}$, 0.2 $mg \cdot mL^{-1}$, 0.1 $mg \cdot mL^{-1}$, 0.05 $mg \cdot mL^{-1}$ and 0.01 $mg \cdot mL^{-1}$. An aliquot of each standard was transferred to a 2mL glass sample vial to be used with the HPLC.

Sample Preparation

The Cefpodoxime Proxetil for Oral Suspension was mixed thoroughly before reconstitution. The dry pharmaceutical was separated by weight into four separate vials prior to reconstitution. The four samples consisted of a control and the three flavor formulations to be tested, bubblegum, grape and raspberry. Flavors analyzed were chosen by FLAVORx. Each sample was reconstituted according to the manufacturer's directions accounting for addition of flavors per the FLAVORx formulary. As the amount of each sample was ¼ that of the original, all liquids used in the reconstitution were divided by four.

To prepare the samples for analysis by HPLC each sample needed to be diluted. To prepare these dilutions, 0.225 mL of each sample was quantitatively transferred into a 25mL volumetric flask. The flask was then brought to volume using a mixture of acetonitrile and water (1:1, v:v%). The final concentration was approximately .180 $mg \cdot mL^{-1}$. At this concentration Cefpodoxime Proxetil is completely soluble. Solubility at this concentration was determined by dilution of the pharmaceutical standard. After vigorous mixing and sonication the solutions still remained cloudy as a result of other excipients in the pharmaceutical formulation. A portion of the solution was removed and placed in a 2mL centrifuge tube. The tubes were centrifuged for 3 minutes. The supernatant of each sample was transferred to a 2mL glass sample vial to be used with the HPLC.

The samples were stored in a refrigerator at 4°C over the two week study. On each day of testing the samples were thoroughly mixed followed by a pH measurement.

Blank Preparation

A blank sample was prepared with the acetonitrile water mixture used in the dilutions.

Mobile Phase Composition:

The mobile phase consisted of 20mM ammonium acetate and acetonitrile. The ammonium acetate was brought to a pH of 5 using glacial acetic acid.

Column:

Phenomenex Gemini-NX 5µm C18, 250x4.60mm
Part #: 00G-4454-E0
S/N: 612008-10

Guard Column:

Phenomenex SecurityGuard Cartridge System
Part #: KJO-4282
Cartridge: Gemini-NX C18 4x3.0mm
Part #: AJO-8368

Conclusion

The results of this testing showed no significant variation in potency between the flavored samples and the control. All samples were calculated to have a higher amount of Cefpodoxime Proxetil than was stated by the manufacturer. Despite this result, all the samples followed the same trend showing consistency between the samples. The results above show that the formulation test with flavors stayed between 90% and 110% of the control throughout the trial. The pH of each sample was also consistent of the course of the trial and remained between 4.0 and 5.5 as required by USP. Based on this analysis, Cefpodoxime Proxetil for Oral Suspension from any manufacture that has the same formulation and concentration as the medication tested is appropriate to use with the flavors tested in this experiment.

Tested By: _____ Date 2/19/2014

Greg Winter

Reviewed By: _____ Date 9/7/2014

William R. LaCourse, Ph.D.

Control Bubblegum Grape Raspberry

The above photograph is included to show the color change observed in the bubblegum flavor formulation.