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Secundum Artem

Current & Practical Compounding Information for the Pharmacist.

STABILITY OF EXTEMPORANEOUSLY PREPARED PEDIATRIC FORMULATIONS USING ORA-PLUS WITH ORA-SWEET AND ORA-SWEET SF - PART II

INTRODUCTION

The most commonly used oral dosage forms today include tablets and capsules. Many patients cannot easily swallow these products so alternate formulations must be prepared, or compounded, by the pharmacist. When a modification is made to a commercial dosage form or when a new formulation is prepared, the pharmacist must be aware of its stability and should be able to project a reasonable expiration date. Stability studies must be completed for each drug product in the vehicle intended to be used in order to assign a valid expiration date.

The purpose of this study was to determine the stability of baclofen, captopril, diltiazem hydrochloride, dipyridamole, flecainide acetate, labetalol hydrochloride, metoprolol tartrate, verapamil hydrochloride and spironolactone/hydrochlorothiazide in 1:1 mixtures of Ora-Sweet:Ora Plus and Ora-Sweet SF:Ora Plus.

STABILITY STUDIES FOR ORAL LIQUIDS

Stability studies must follow certain guidelines to provide valid, accurate and meaningful information. General guidelines for a good study and for successful publication include:

1. A complete description of the materials, test conditions and methods must be provided for peer review. All materials must be "in-date", equipment calibrated and in good working condition and procedures spelled out completely in the protocol.
2. A stability-indicating analytical method must be used. The assay method must be capable of distinguishing between the parent drug, degradation products and other components of the product (the excipients).
3. An initial determination of the actual drug concentration must be made. This is necessary because the following time point results are compared to the time zero (t_o) concentration.
4. A sufficient number of test samples must be run. At minimum, duplicate analysis of three separate samples should be performed; more if feasible.
5. Conclusions must fit the obtained data. It is improper to expand the results into areas not covered by the project. For example, stability studies done in glass containers cannot be extrapolated or applied to plastic containers.

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STABILITY STUDY DESIGN

This study resulted from a survey mailed to community and hospital pharmacies to determine the active drugs and concentrations most frequently requested for extemporaneous compounding. Thirty different drugs were selected and studied in 1:1 mixtures of Ora Sweet:Ora Plus and Ora Sweet SF:Ora Plus over a 60 day time period. Ten of these are presented in this issue of Secundum Artem.

For each drug and each vehicle, approximately 800 mL of product was prepared. Sufficient powder was weighed, or a sufficient number of tablets/capsules was obtained to provide the active ingredient. The tablets were pulverized, or capsules emptied, and the powder comminuted in a mortar with a pestle. A portion of the vehicle was used to levigate the powder and a uniform paste prepared. Additional vehicle was added to the mortar in small portions and the product poured into a 1000 mL graduated container. The mortar was rinsed repeatedly with additional vehicle and added to the graduated container to make 800 mL. The product was placed in a 1000 mL beaker, covered and mixed for at least 30 minutes until uniform using a magnetic stirrer.

Six 120-mL amber clear plastic (polyethylene terephthalate) prescription ovals were filled. These containers were fitted with caps lined with low-density polyethylene foam. Three bottles were stored at 5°C and three bottles at 25° in the absence of light. An initial 5 mL sample was removed from the bulk product and samples were removed from each individual bottle after 1, 2, 7, 10, 14, 28, 35 and 60 days. Prior to sample removal, the bottles were agitated on a rotating mixer for 30 minutes. The pH was determined initially and after 30 and 60 days' storage at each temperature. The oral liquids were examined at each sample time for any change in appearance or odor. After the samples were obtained, they were stored at

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-70˚C until analyzed by a validated, stability-indicating, high performance liquid chromatographic method.

Table 1: The concentrations of the various drugs used in this study were as follows:

Drug	Concentration (mg/mL)
Baclofen	10
Captopril	0.75
Diltiazem Hydrochloride	12
Dipyridamole	10
Flecainide Acetate	20
Labetalol Hydrochloride	40
Metoprolol Tartrate	10
Verapamil Hydrochloride	50
Spironolactone and Hydrochlorothiazide	5/5

STABILITY OF EXTEMPORANEOUS FORMULATIONS

Physical observations did not reveal any significant changes during the study period, including visual and olfactory observations. pH determinations are provided with each table; there was less than 0.5 pH unit change throughout the entire study period for all the preparations.

Baclofen[1-3]

Baclofen 10 mg/mL Oral Liquid

Rx	Baclofen 10 mg Tablets	#120
	Vehicle qs	120 mL

Baclofen is a skeletal muscle relaxant that occurs as white to off-white crystals and is slightly soluble in water, with pK_a values of 5.4 and 9.5. It is available in injection form (0.5 mg/mL and 2 mg/mL), with a pH in the range of 5-7, indicative of a reasonably stable drug. In this study, baclofen appears to be stable over 60 days in both vehicles studied with only 4% loss of potency at room temperatures. These results agree with a study of 5 mg/mL baclofen in simple syrup, where 95.9% in suspension and 94.5% in solution remained after 35 days. At pH 4 and 25˚C, baclofen in solution has a projected stability based on pseudo first order rate constants of 5.7 years.

Table 2: Percent of the initial concentration of baclofen (10 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	105.2	102.7	103.0	101.4
14	99.2	98.4	99.7	102.0
28	101.3	98.2	98.9	100.0
60	98.7	96.0	98.8	101.6

The initial pH of the Ora Sweet:Ora Plus mixture was 4.7.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.7.
There was less than 0.5 pH unit change throughout the study.

Captopril[4-12]

Captopril 0.75 mg/mL Oral Liquid

Rx	Captopril 100 mg Tablet	#1
	Vehicle qs	134 mL

Captopril is an angiotensin-converting enzyme inhibitor occurring as a white to off-white, crystalline powder with a slight acid-sulfhydryl odor and is freely soluble in water and in alcohol. It has two pK_a values of 3.7 and 9.8. Commercially, captopril is available only as oral tablets of captopril and captopril in combination with hydrochloroth-

iazide.

Captopril has limited stability at the 0.75 mg/mL concentration. Several studies in the literature report on the stability of captopril in various vehicles. The stability of captopril is evidently concentration, vehicle- and temperature-dependent. Longer storage times than those presented here have been reported; however, the vehicles (water and water with sodium ascorbate added) generally are not acceptable for routine oral administration to patients. If a patient or caregiver needs to store captopril solution for a long time, it would be best to dispense the tablets with instructions to crush and mix the tablets with water immediately prior to administration. If unusual dosages are required, capsules can be filled with the proper quantity of captopril and dispensed to the patient with instructions to empty the contents into a liquid and administer.

Label the prescription with an expiration date of 7 days at 25˚C or 14 days at 5˚C for the Ora-Sweet:Ora-Plus vehicle and 5 days at 25˚C or 10 days at 5˚C if Ora-Sweet SF and Ora-Plus were used.

Table 3: Percent of the initial concentration of captopril (0.75 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	98.7	97.4	99.3	98.0
14	93.2	87.2	90.2	81.9
28	86.4	78.8	82.4	63.4
60	72.7	55.3	62.3	30.4

The initial pH of the Ora Sweet:Ora Plus mixture was 4.1.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.1.
There was less than 0.5 pH unit change throughout the study.

Diltiazem Hydrochloride[13-16]

Diltiazem Hydrochloride 12 mg/mL Oral Liquid

Rx	Diltiazem Hydrochloride 90 mg Tablets	#16
	Vehicle qs	120 mL

Diltiazem hydrochloride is a benzothiazepine-derivative calcium-channel blocking agent occurring as a bitter-tasting, white to off-white crystalline powder that is soluble in water and alcohol. Diltiazem is available commercially only as various tablets and capsules, both immediate and extended release.

Diltiazem appears to be stable for at least 60 days in both vehicles at both 5˚C and 25˚C. Different stability profiles have been reported using different vehicles containing different sugars, i.e., dextrose, sucrose, fructose, sorbitol, mannitol, lactose. The most stable preparations appear to be prepared at pH 5.

Table 4: Percent of the initial concentration of diltiazem hydrochloride (12 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	101.3	100.4	100.8	99.9
14	98.3	97.1	97.2	98.1
28	97.5	97.3	98.3	96.4
60	94.3	95.1	96.3	94.2

The initial pH of the Ora Sweet:Ora Plus mixture was 4.2.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.2.
There was less than 0.5 pH unit change throughout the study.

Dipyridamole[17]

Dipyridamole 10 mg/mL Oral Liquid

Rx	Dipyridamole 50 mg Tablets	#24
	Vehicle qs	120 mL

Dipyridamole is a non-nitrate coronary vasodilator occurring as an intensely yellow, bitter tasting, crystalline powder or needles. It is slightly soluble in water and very soluble in alcohol. Its commercial availability is limited to oral tablets.

Dipyridamole is stable for at least 60 days in both vehicles and at both temperatures. A 10 mg/mL suspension containing 0.5% citric acid in methylcellulose has been reported to be stable for 30 days in the refrigerator.

Table 5: Percent of the initial concentration of dipyridamole (10 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	100.6	99.3	99.8	102.1
14	97.8	96.9	98.1	97.1
28	96.3	95.4	96.7	96.2
60	93.6	92.1	94.1	92.5

The initial pH of the Ora Sweet:Ora Plus mixture was 4.2.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.3.
There was less than 0.5 pH unit change throughout the study.

Flecainide Acetate[18-19]

Flecainide Acetate 20 mg/mL Oral Liquid

Rx	Flecainide Acetate 100 mg Tablets	#24
	Vehicle qs	120 mL

Flecainide acetate is a local anesthetic-type antiarrhythmic agent structurally related to procainamide. It occurs as a white crystalline powder with a solubility of 48.4 mg/mL in water and 300 mg/mL in alcohol at 37˚C, and has a pK_a of 9.3. It is available as oral tablets.

Flecainide is stable, with less than 2% loss at any of the conditions, when formulated with these vehicles. One report lists a 45 day stability under refrigerated and room temperature storage conditions.

Table 6: Percent of the initial concentration of flecainide acetate (20 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	100.5	101.3	100.8	99.8
14	98.3	99.1	99.0	99.7
28	98.5	98.7	99.1	99.3
60	98.5	99.0	98.7	98.6

The initial pH of the Ora Sweet:Ora Plus mixture was 4.3.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.3.
There was less than 0.5 pH unit change throughout the study.

Labetalol Hydrochloride[20-23]

Labetalol Hydrochloride 40 mg/mL Oral Liquid

Rx	Labetalol Hydrochloride 300 mg Tablets	#16
	Vehicle qs	120 mL

Labetalol hydrochloride is an alpha- and beta- adrenergic blocking agent, commercially available as a racemic mixture of its 4 stereoiso-

mers. It occurs as a white or off-white crystalline powder and is sparingly soluble in water (about 20 mg/mL) and freely soluble to soluble in alcohol. It has a pK_a of 9.3. Labetalol is available as an aqueous solution for injection with a long expiration date (2 years). It is most stable in solutions having a pH of 2-4.

Labetalol demonstrated less than a 4% loss of potency in the formulations and conditions used in this study. One report of labetalol hydrochloride 7-10 mg/mL in distilled water, simple syrup, apple juice, grape juice and orange juice were stable for at least four weeks at both room and refrigerator temperatures. Labetalol hydrochloride is most stable in solutions with a pH of 3-4.

Table 7: Percent of the initial concentration of labetalol hydrochloride (40 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	100.6	101.3	98.9	99.3
14	99.0	99.3	100.7	100.1
28	99.3	99.9	100.1	99.7
60	97.8	98.4	98.2	96.9

The initial pH of the Ora Sweet:Ora Plus mixture was 4.5.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.4.
There was less than 0.5 pH unit change throughout the study.

Metoprolol Tartrate[24-26]

Metoprolol tartrate 10 mg/mL Oral Liquid

Rx	Metoprolol Tartrate 100 mg Tablets	#12
	Vehicle qs	120 mL

Metoprolol is a 1-selective adrenergic blocking agent, commercially available as oral tablets and an injection. It is commercially available as a racemic mixture and occurs as a white, crystalline powder with a bitter taste and is very soluble in water and freely soluble in alcohol. It has a pK_a of 9.68.

Metoprolol exhibits less than 3% loss in potency under the conditions used in this study. Several reports support the stability of metoprolol in various vehicles and at various pH levels, including one study at pH 4, 7 and 9.

Table 8: Percent of the initial concentration of metoprolol tartrate (10 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	101.3	100.8	99.8	101.3
14	100.2	99.2	98.0	97.5
28	101.0	98.3	98.8	97.8
60	99.6	97.8	98.3	98.0

The initial pH of the Ora Sweet:Ora Plus mixture was 4.3.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.2.
There was less than 0.5 pH unit change throughout the study.

Verapamil Hydrochloride[27-28]

Verapamil Hydrochloride 50mg/mL Oral Liquid

Rx	Verapamil Hydrochloride 80 mg Tablets	#75
	Vehicle qs	120 mL

Verapamil hydrochloride is a phenylalkylamine-derivative calcium-channel blocking agent commercially available as a racemic mixture. It occurs as a white or practically white, crystalline powder with a bitter taste and is soluble in water and sparingly soluble in alcohol. In the commercially available injection dosage form (2.5 mg/mL), it has a pH of 4-6.5.

Verapamil shows less than 4% loss in both formulations in this study. The optimum pH range of verapamil has been reported to be from pH 3.2-5.6.

Table 9: Percent of the initial concentration of verapamil hydrochloride (50 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	99.7	100.4	100.1	99.0
14	98.4	98.4	99.7	98.6
28	99.0	97.0	99.5	97.9
60	98.0	96.5	98.4	97.9

The initial pH of the Ora Sweet:Ora Plus mixture was 4.4.
The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.2.
There was less than 0.5 pH unit change throughout the study.

Spironolactone/Hydrochlorothiazide[29-33, 34-35]

Spironolactone/Hydrochlorothiazide 5/5 mg/mL Oral Liquid

Rx	Spironolactone-Hydrochlorothiazide 25mg/25mg	#24
	Vehicle qs	120 mL

Spironolactone is an aldosterone antagonist occurring as a light cream-colored to light tan, crystalline powder with a faint to mild mercaptan-like odor. It is practically insoluble in water and soluble in alcohol. Hydrochlorothiazide is a thiazide diuretic occurring as a white or practically white, practically odorless, crystalline powder and has a slightly bitter taste. It is slightly soluble in water and soluble in alcohol, with pK_a values of 7.9 and 9.2. Hydrochlorothiazide oral solution is commercially available in a strength of 50 mg/5 mL, indicative of a reasonably stable oral liquid product.

In the spironolactone/hydrochlorothiazide formulations, there was less than 3% loss of hydrochlorothiazide and less than 4% loss of spironolactone in these vehicles. Numerous reports are available concerning spironolactone which shows an optimum pH for stability of approximately 4.5. Hydrochlorothiazide exhibits very poor water solubility and in these preparations is present primarily in a suspended form, which enhances its stability.

Table 10: Percent of the initial concentration of spironolactone in spironolactone/hydrochlorothiazide (5/5 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	98.9	97.3	101.3	100.2
14	96.5	96.9	98.1	97.1
28	97.8	96.2	97.9	96.4
60	96.5	97.5	98.9	97.4

The initial pH of the Ora Sweet:Ora Plus mixture was 4.4.

The initial pH of the Ora Sweet SF:Ora Plus mixture was 4.2. There was less than 0.5 pH unit change throughout the study.

Table 11: Percent of the initial concentration of hydrochlorothiazide in spironolactone/hydrochlorothiazide (5/5 mg/mL) remaining after packaging in plastic prescription containers and storage at 5˚C or 25˚C for up to 60 days.

Time	Ora-Sweet:Ora Plus		Ora-Sweet SF:Ora Plus	
(Days)	5˚	25˚	5˚	25˚
1	100.5	101.3	99.7	99.9
14	99.5	100.1	98.9	99.8
28	98.6	98.5	99.6	98.4
60	99.0	98.1	98.4	97.5

SUMMARY

It appears that baclofen, diltiazem hydrochloride, dipyridamole, flecainide acetate, labetalol hydrochloride, metoprolol tartrate, verapamil hydrochloride and spironolactone/hydrochlorothiazide can be mixed with Ora-Sweet:Ora-Plus (1:1) or Ora-Sweet SF:Ora-Plus (1:1) and used over a 60 day period, since at least 90% of the original concentration is retained. Pharmacists should be able to compound formulations extemporaneously at the concentrations presented here in 1:1 mixtures of Ora-Sweet:Ora-Plus or Ora-Sweet SF:Ora-Plus and be assured of physical and chemical stability of at least 60 days when packaged in light-resistant containers of the materials used in this study. For captopril, however, an expiration date of 7 days at 25˚C or 14 days at 5˚C for the Ora-Sweet:Ora-Plus vehicle and 5 days at 25˚C or 10 days at 5˚C if Ora-Sweet SF and Ora-Plus would be appropriate.

REFERENCES

1. Baclofen. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health- System Pharmacists, Bethesda MD, 1996, pp 951-954.
2. Johnson CE, Hart SM. Stability of an extemporaneously compounded baclofen oral liquid. Am J Hosp Pharm. 1993; 50:2353-5.
3. Ahuja S. Baclofen. In: Florey K, ed. Analytical profiles of drug substances. Vol. 14. Washington, DC: American Pharmaceutical Association; 1985:527-48.
4. Captopril. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health- System Pharmacists, Bethesda MD, 1996, pp 1128-1136.
5. Pereira CM, Tam YK. Stability of captopril in tap water. Am J Hosp Pharm. 1992; 49:61205.
6. Pramar Y, Das Gupta V, Bethea C. Stability of captopril in some aqueous systems. J. Clin Pharm Ther. 1992; 17:185-9.
7. Nahata MC, Morosco RS, Hipple TF. Stability of captopril in three liquid dosage forms. Am J Hosp Pharm. 1994; 51:95-6.
8. Kadin H. Captopril. In: Florey K, ed. Analytical profiles of drug substances. Vol 11. Washington, DC: American Pharmaceutical Association; 1982:79-137.
9. Extemporaneous oral liquid dosage preparations. Toronto, Ontario: Canadian Society of Hospital Pharmacists; 1988:26.
10. Allen Jr LV and Erickson II MA. Stability of baclofen, captopril, diltiazem hydrochloride, dipyridamole and flecainide acetate in extemporaneously compounded oral liquids. Am J Health-Syst Pharm. 1996; 53:2179-84.
11. Nahata MC, Morosco RS. Stability of captopril in liquid containing ascorbic acid or sodium ascorbate. Am J Hosp Pharm 1994; 51:1707-8.
12. Chan DS, Sato AK, Claybaugh JR. Degradation of captopril in solutions compounded from tablets and standard powder. Am J Hosp Pharm 51; 1994:1205-8.
13. Diltiazem Hydrochloride. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health-System Pharmacists, Bethesda MD, 1996, pp 1136-1140.
14. Suleiman MS, Najib NM, Abdelhameed ME. Stability of diltiazem hydrochloride in aqueous sugar solutions. J Clin Pharm Ther. 1988; 13:417-22.
15. Mazzo DJ, Obetz CL, Shuster J. Diltiazem hydrochloride. In: Florey K, ed. Analytical profiles of drug substances and excipients. Vol. 23. Washington, DC: American Pharmaceutical Association; 1994:53-98.
16. Extemporaneous oral liquid dosage preparations. Toronto, Ontario: Canadian Society of Hospital Pharmacists; 1988:13.
17. Dipyridamole. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health-System Pharmacists, Bethesda MD, 1996, pp 1343-1344.
18. Flecainide Acetate. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health-System Pharmacists, Bethesda MD, 1996, pp 1167-1175.
19. Wiest DB, Garner SS, Pagacz LR et al. Stability of flecainide acetate in an extemporaneously compounded oral suspension. Am J Hosp Pharm. 1992; 49:1467-70.
20. Labetalol. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health- System Pharmacists, Bethesda MD, 1996, pp 1297-1304.
21. Nahata MC. Stability of labetalol in distilled water, simple syrup and three fruit juices. DICP Ann Pharmacother. 1991; 25:465-9.
22. Woods D. Formulations in pharmacy practice health care. Dunedin, New Zealand: University of Otago; 1993:54.
23. Yuen PC, Taddei CR, Wyka BE et al. Compatibility and stability of labetalol hydrochloride in commonly used intravenous solutions. Am J Hosp Pharm. 1983; 40:1007-9.
24. Metoprolol. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health- System Pharmacists, Bethesda MD, 1996, pp 1181-1187.
25. Peterson GM, Meaney MF, Reid CA et al. Stability of extemporaneously prepared mixtures of metoprolol and spironolactone. Aust J Hosp Pharm. 1989; 19:344-6.
26. Luch JR. Metoprolol tartrate. In: Florey K, ed. Analytical profiles of drug substances. Vol. 12. New York: Academic Press; 1983:325-56.
27. Verapamil Hydrochloride. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health-System Pharmacists, Bethesda MD, 1996, pp 1228-1235.
28. Chang ZL. Verapamil. In: Florey K, ed. Analytical profiles of drug substances. Vol. 17. New York: Academic Press; 1988:643-74.
29. Spironolactone. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health-System Pharmacists, Bethesda MD, 1996, pp 1931-1934.
30. Nahata MC, Morosco RS, Hipple TF. Stability of spironolactone in an extemporaneously prepared suspension at two temperatures. Ann Pharmnacother. 1993; 27:1198-9.
31. Pramar Y, Das Gupta V, Bethea C. Development of a stable oral liquid dosage form of spironolactone. J Clin Pharm Ther. 1992; 17:245-8.
32. Mathur LK, Wickman A. Stability of extemporaneously compounded spironolactone suspensions. Am J Hosp Pharm. 1989; 46:2040-2.
33. Prammar Y, Jgupta VD. Preformulation studies of spironolactone: effect of pH, two buffer species, ionic strength, and temperature on stability. J Pharm Sci. 1991;80:551-3.
34. Hydrochlorothiazide. AHFS-96 Drug Information, McEvoy GK, Ed., American Society of Health-System Pharmacists, Bethesda MD, 1996, pp 1899-1901.
35. Deppeler HP. Hydrochlorothiazide. In: Florey K, ed. Analytical profiles of drug substances. Vol. 10. New York: Academic Press; 1981:405-41.

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