

^a Because of legal liability concerns with injectable paraldehyde, the primary manufacturer, Elkins-Sinn, Inc., has discontinued sales of this product. However, according to the 1987 American Druggist Blue Book, paraldehyde for injection is available from Consolidated Midland Corporation.

References

1. Goodman and Gilman's the pharmacological basis of therapeutics. 6th ed. Gilman AG, Goodman LS, Gilman A, eds. New York: Macmillan Publishing Co., Inc.; 1980:368.
2. Martindale: the extra pharmacopeia. 28th ed. Reynolds JEF, Prasad AB, ed. London: The Pharmaceutical Press; 1982:809-10.
3. United States Pharmacopeial Convention, Inc. USP DI: Drug information for the health care provider. 5th ed. Rockville, MD: United States Pharmacopeial Convention, Inc. 1985:938-41.
4. Browne TR. Paraldehyde, chlormethiazole and lidocaine for the treatment of status epilepticus. In: Delgado-Escueta AV, Westerlain CG, Treiman DM et al., ed. Advances in neurology: status epilepticus. New York: Raven Press; 1983; 34:509-13.
5. DeElio FJ, DeJalon PG, Obrader S. Some experimental and clinical observations on the anticonvulsant action of paraldehyde. *J Neurol Neurosurg Psychiatry*. 1949; 12:19-24.
6. Curless RG, Holzman BH, Ramsey RE. Paraldehyde therapy in childhood status epilepticus. *Arch Neurol*. 1983; 40:477-80.
7. Evans RJ. Effect of paraldehyde on disposable syringes and needles. *Lancet*. 1961; 2:1451. Letter.
8. Addy DP, Adesbury P, Winter L. Paraldehyde and plastic syringes. *Br Med J*. 1978; 2:1434. Letter.
9. Fenton-May VI, Lee F. Paraldehyde and plastic. *Br Med J*. 1978; 2:1166. Letter.
10. Anthony RM, Bost RO, Thompson WL et al. Paraldehyde, toluene and methylene chloride analysis by head space gas chromatography. *J Anal Toxicol*. 1978; 2:262-4.
11. Windholz M, ed. The Merck index. 9th ed. Rahway, New Jersey: Merck and Company, Inc.; 1976:911.
12. Moorhatch P, Chiou WL. Interactions between drugs and plastic intravenous fluid bags: leaching of chemicals from bags containing various solvent media. *Am J Hosp Pharm*. 1974; 39:149-52.
13. MacKichan J, Duffner PK, Cohen ME. Adsorption of diazepam to plastic tubing. *N Engl J Med*. 1979; 301:332-3. Letter.
14. Hancock BG, Black CD. Effect of a polyethylene-lined administration set on the availability of diazepam injection. *Am J Hosp Pharm*. 1985; 42:335-9.
15. Johnson CE, Vigoreaux JA. Compatibility of paraldehyde with plastic syringes and needle hubs. *Am J Hosp Pharm*. 1984; 41:306-8.
16. Rubin RJ, Jaeger RJ. Some pharmacologic and toxicologic effects of di-2-ethylhexylphthalate (DEHP) and other plasticizers. *Environ Health Perspect*. 1973; 3:53-9.

Sweetener content of common pediatric oral liquid medications

ELAINE M. HILL, CATHERINE M. FLAITSZ, AND GARY R. FROST

Abstract: The types and concentrations of sweeteners in common prescription liquid and chewable medications for pediatric use were determined by manufacturer survey.

Oral-liquid and chewable antibiotic, antifungal, bronchodilator, antihistamine, anticonvulsant, and miscellaneous products were identified. The manufacturers were asked by telephone the type and amount of sweeteners in their products. Two follow-up letters requested confirmation of the sweetener contents; manufacturers' approval for publication of the information was also requested by mail.

Sweetener information on 160 preparations was obtained. For antibiotics such as ampicillin, amoxicillin, erythromycin ethylsuccinate, and penicillin VK, products from different manufacturers had a wide range of sucrose concentration (18%-80%). Only four antibiotic preparations were sucrose free. The bronchodilators and antihistamines contained either sucrose, sorbitol, or saccharin. The anticonvulsants contained 0%-60% sucrose.

Health-care practitioners who prescribe or dispense oral liquid or chewable prescription drug prod-

ucts should know that products in a given category can vary in type and amount of sweetener.

Index terms: Amoxicillin; Ampicillin; Antibiotics; Anticonvulsants; Antifungals; Antihistamines; Bronchodilators; Concentration; Data collection; Equivalency, generic; Erythromycin ethylsuccinate; Erythromycins; Formulations; Liquids; Pediatrics; Penicillins; Penicillin V potassium; Saccharin; Sorbitol; Sucrose; Sweetening agents; Tablets

Am J Hosp Pharm. 1988; 41:135-42

Sweetening agents are frequently included in liquid and chewable-tablet drug products. The most common sweetener bases for medications include sucrose, sorbitol, and saccharin. Although

these inactive ingredients are not harmful to most individuals, some children's dietary intake of sweetening agents needs to be limited because of diabetes, gastrointestinal problems, or susceptibil-

ELAINE M. HILL, PHARM.D., is Director of Drug Information, University Hospital, and Assistant Professor, School of Pharmacy, University of Colorado Health Science Center, Denver. CATHERINE M. FLAITSZ, D.D.S., M.S., is Assistant Clinical Professor, Department of Growth and Development, School of Dentistry, University of Colorado Health Science Center. GARY R. FROST, M.S., is Assistant Director of Pharmacy Services, University Hospital, University of Colorado Health Science Center.

Address reprint requests to Dr. Hill at UCHSC Box C-239, 4200 E. 9th Avenue, Denver, CO 80262.

Presented at the 21st Annual ASHP Midyear Clinical Meeting, Las Vegas, NV, December 10, 1986.

Copyright © 1988, American Society of Hospital Pharmacists, Inc. All rights reserved. 0002-9289/88/0101-0135\$02.00.

ity to caries.

Health-care consumers' increased participation in decisions about their care, coupled with inquiries from professionals, has led to manufacturers' voluntary labeling of inactive ingredients in drug products for oral administration.¹ However, to obtain information on specific quantities of the inactive ingredients, the health-care provider or consumer must contact the manufacturer. We surveyed manufacturers for the purpose of compiling a list of the sweetener concentrations in common liquid and chewable prescription drug products intended for pediatric use. Previously published lists of sweetener content are either outdated^{2,3} or limited in scope.⁴

Methods

Data on the most commonly prescribed liquid pediatric medications were obtained from IMS America Ltd., Ambler, Pennsylvania. The preparations were placed into the following categories: antibiotics, antifungal agents, bronchodilators, antihistamines, anticonvulsants, and miscellaneous medications (including ferrous sulfate and cimetidine). Emphasis was placed on medications that were most frequently prescribed or were used for long-term therapy in pediatric patients.

The manufacturers of these pediatric preparations were asked by telephone to provide data on the sweetener content of their products. A follow-up letter was mailed to each manufacturer to confirm the stated sweetener amount; a second letter was mailed if the manufacturer did not respond to the first letter. Manufacturers' permission to publish the information on sweetener content was also requested in a letter. Manufacturers were telephoned in June 1987 for final confirmation of the information.

The following data were collected for each drug product: the type, amount (in grams per 5 mL), and percentage concentration (weight/volume%) of sweetener in liquid preparations and the type and amount of sweetener in chewable tablets.

Results

From November 1985 to January 1986, we contacted 47 companies. Five companies were excluded from follow-up; one generic company declined to contact the individual manufacturers of their products, one company had discontinued the products of interest, and the products of three companies were not included in the final list for other reasons. Of the remaining 42 companies, 13 identified the sweetener bases but did not disclose the amounts contained in their products. The prevailing reason for not disclosing this information was the desire for proprietary secrecy. Thirteen companies made corrections in their information and

three companies reported the sweetener contents but said they had discontinued the products. During our final round of confirmation telephone calls in 1987, two companies did not respond to multiple calls requesting confirmation. Two companies had changed control of the products to other divisions but still provided information on these products. One company had acquired responsibility for the products from another company and could not confirm the exact sweetener amounts. One company had discontinued three antibiotic preparations. Many companies gave us new information that they had not disclosed during the initial period (e.g., saccharin, aspartame, and sorbitol information).

The sweetener content of 150 liquid preparations (Tables 1 and 2) and 10 chewable tablets (Table 3) was obtained from 39 companies. For 43 preparations, the exact amount of sweetener was not published at the manufacturer's request. The telephone numbers of 13 manufacturers that would not allow publication of the exact amount of sweeteners are listed in the table footnotes for practitioners' use.

Antibiotic preparations contained a wide range of sucrose concentrations. The greatest variability was in the ampicillin oral suspension 125 mg/5 mL preparations; sucrose content ranged from 0.9 to 4.0 g/5 mL (18%–80%). Four of these eight preparations also contained saccharin. Sucrose content of ampicillin oral suspension 250 mg/5 mL preparations ranged from 1.8 to 4.0 g/5 mL (36%–80%), and four of these eight preparations also contained saccharin. Similar wide variability exists in amoxicillin, erythromycin ethylsuccinate, and penicillin preparations. Only four of the antibiotic preparations were sucrose free: Augmentin (amoxicillin-clavulanic acid, Beecham) oral suspension and chewable tablets (mannitol and saccharin based); Septra (sulfamethoxazole-trimethoprim, Burroughs Wellcome) oral suspension; and Biocraft's sulfamethoxazole-trimethoprim pediatric suspension (sorbitol and saccharin based).

The aminophylline preparations, except for the Roxane products, contained saccharin instead of sorbitol or sucrose. The theophylline, oxtriphylline, and combination theophylline preparations contained any of three sweeteners: sucrose, sorbitol, or saccharin.

Of the anticonvulsant preparations, both phenytoin and phenobarbital preparations had fairly low concentrations of sucrose (20% and 13%, respectively). In contrast, the syrup preparations of valproic acid and ethosuximide had very high sucrose concentrations. Only primidone (Mysoline, Ayerst) was sucrose free.

All the ferrous sulfate preparations contained sucrose and saccharin or sorbitol. Cimetidine liquid was sucrose free but contained a large amount of sorbitol.

Table 1.
Sweetener Content of Common Liquid Pediatric Antibiotic and Antifungal Preparations

Drug Product	Manufacturer	Sweetener Concentration in g/5 mL (Percent Concentration in w/v %)		
		Sucrose	Sorbitol	Saccharin
Ampicillin 125 mg/5 mL				
Ampicillin oral suspension	Warner-Chilcott	0.9(18)		0.0045(0.09)
Ampicillin oral suspension	Biocraft	... ^a		... ^a
Ampicillin trihydrate oral suspension	Lederle	2.07(41)		
Ampicillin trihydrate oral suspension	Schein	2.4(48) ^b		... ^c
Omnipen oral suspension	Wyeth	4.0(80)		
Polycillin oral suspension	Bristol	1.7(34) ^b		
Principen oral suspension	Squibb	... ^d		... ^d
Totacillin oral suspension	Beecham	1.64(33)		
Ampicillin 250 mg/5 mL				
Ampicillin oral suspension	Warner-Chilcott	1.8(36)		0.009(0.18)
Ampicillin oral suspension	Biocraft	... ^a		... ^a
Ampicillin trihydrate oral suspension	Lederle	1.91(38)		
Ampicillin trihydrate oral suspension	Schein	2.25(45) ^b		... ^c
Omnipen oral suspension	Wyeth	4.0(80)		
Polycillin oral suspension	Bristol	1.8(36) ^b		
Principen oral suspension	Squibb	... ^d		... ^d
Totacillin oral suspension	Beecham	1.79(36)		
Ampicillin 500 mg/5 mL				
Omnipen pediatric drops	Wyeth	3.5(70)		
Polycillin oral suspension	Bristol	1.5(30) ^b		
Polycillin pediatric drops	Bristol	1.5(30) ^b		
Amoxicillin 125 mg/5 mL				
Amoxil oral suspension	Beecham	1.67(33)		
Amoxicillin oral suspension	Biocraft	... ^a		... ^a
Amoxicillin oral suspension	Schein	2.4(48) ^b		... ^c
Larotid oral suspension	Beecham	1.67(33)		
Polymox oral suspension	Bristol	2.5(50) ^b		
Trimox oral suspension	Squibb	... ^d		
Utimox oral suspension	Warner-Chilcott	0.85(17)		
Wymox oral suspension	Wyeth	2.1(42)		
Amoxicillin 250 mg/5 mL				
Amoxil oral suspension	Beecham	1.84(37)		
Amoxil pediatric drops	Beecham	2.03(41)		
Amoxicillin oral suspension	Biocraft	... ^a		... ^a
Amoxicillin oral suspension	Schein	2.25(45) ^b		... ^c
Larotid oral suspension	Beecham	1.84(37)		
Polymox oral suspension	Bristol	2.4(48) ^b		
Polymox pediatric drops	Bristol	2.5(50) ^b		
Trimox oral suspension	Squibb	... ^d		
Utimox oral suspension	Warner-Chilcott	1.7(34)		
Wymox oral suspension	Wyeth	1.9(38)		
Amoxicillin-Clavulanic Acid Combination				
Augmentin oral suspension				
125 mg/5 mL ^e	Beecham			0.0325(0.65)
250 mg/5 mL ^f	Beecham			0.0325(0.65)
Cefaclor				
Cecor oral suspension				
125 mg/5 mL	Lilly	2.9(58)		
250 mg/5 mL	Lilly	2.8(56)		
Cefadroxil 250 mg/5 mL				
Ultracel oral suspension	Bristol	2.1(42) ^b		
Cephalexin 125 mg/5 mL				
Cephalexin oral suspension	Biocraft	... ^a		
Keflex oral suspension	Dista	3.1(62)		
Cephalexin 250 mg/5 mL				
Cephalexin oral suspension	Biocraft	... ^a		
Keflex oral suspension	Dista	2.9(58)		

Continued

Reports Pediatric oral liquid medications

Table 1 (continued)

Drug Product	Manufacturer	Sweetener Concentration in g/5 mL (Percent Concentration in w/v%)		
		Sucrose	Sorbitol	Saccharin
<i>Cephalexin 500 mg/5 mL</i> Keflex pediatric drops	Dista	3.1(62)		
<i>Cephadrine 125 mg/5 mL</i> Anspor oral suspension Velosef oral suspension	Smith Kline & French Squibb	3.1(62) ... ^d		
<i>Cephadrine 250 mg/5 mL</i> Anspor oral suspension Velosef oral suspension	Smith Kline & French Squibb	2.9(58) ... ^d		
<i>Dicloxacillin 62.5 mg/5 mL</i> Dynapen oral suspension Pathocil oral suspension	Bristol Wyeth	2.3(46) ^b 3.1(62)		... ^c ... ^c
<i>Erythromycin Ethylsuccinate 200 mg/5 mL</i> E.E.S. drops E.E.S. granules E.E.S. 200 liquid E-Mycin E liquid Erythromycin ethylsuccinate oral suspension Pediaamycin drops Pediaamycin liquid Pediaamycin oral suspension Wyamycin E liquid	Abbott Abbott Abbott Upjohn Lederle Ross Ross Ross Wyeth	... ^g ... ^g ... ^g ... ^h 2.25(45) ... ⁱ ... ⁱ ... ⁱ 3.25(65)	... ^h	0.02(0.4)
<i>Erythromycin Ethylsuccinate 400 mg/5 mL</i> E.E.S. 400 liquid E-Mycin E liquid Eryped oral suspension Erythromycin ethylsuccinate oral suspension Pediaamycin 400 Wyamycin E liquid	Abbott Upjohn Abbott Lederle Ross Wyeth	... ^g ... ^h ... ^g 2.25(45) ... ⁱ 3.25(65)	... ^h	0.03(0.6)
<i>Erythromycin Estolate 125 mg/5 mL</i> Erythromycin estolate oral suspension Ilosone liquid	Lederle Dista	2.25(45) 1.85(37)		
<i>Erythromycin Estolate 250 mg/5 mL</i> Erythromycin estolate oral suspension Ilosone liquid	Lederle Dista	2.25(45) 1.8(36)		0.0025(0.05)
<i>Erythromycin Estolate 500 mg/5 mL</i> Ilosone ready-mixed drops	Dista	1.8(36)		
<i>Erythromycin Ethylsuccinate 200 mg-Sulfisoxazole 600 mg Combination</i> Pediazole oral suspension	Ross	... ⁱ		
<i>Oxacillin 250 mg/5 mL</i> Oxacillin oral solution Oxacillin sodium oral solution Prostaphlin oral solution	Biocraft Schein Bristol	... ^a 2.25(45) ^b 2.3(46) ^b		... ^a ... ^c ... ^c
<i>Penicillin G</i> Pentids oral syrup 125 mg/5 mL Pentids oral syrup 250 mg/5 mL	Squibb Squibb	... ^d ... ^d		... ^d ... ^d
<i>Penicillin VK 125 mg/5 mL</i> Beepen-VK oral solution Betapen-VK oral solution Ledericillin VK oral solution Penapar VK oral solution ⁱ Penicillin VK oral suspension Penicillin V potassium solution Pen-Vee K oral solution V-Cillin oral solution Veetids oral solution	Beecham Bristol Lederle Warner-Chilcott Schein Biocraft Wyeth Lilly Squibb	2.87(57) 2.8(56) ^b 3.5(70) 2.5(50) 2.2(44) ^b ... ^a 2.5(50) 2.9(58) ... ^d		0.005(0.1) ... ^c 0.0134(0.27) 0.0125(0.25) ... ^c ... ^a ... ^c ... ^d
<i>Penicillin VK 250 mg/5 mL</i> Beepen-VK oral solution Betapen-VK oral solution Ledericillin VK oral solution Penapar VK oral solution ⁱ	Beecham Bristol Lederle Warner-Chilcott	3.18(64) 2.8(56) ^b 3.5(70) 2.5(50)		0.005(0.1) ... ^c 0.027(0.53) 0.0175(0.35)

Continued

Table 1 (continued)

Drug Product	Manufacturer	Sweetener Concentration in g/5 mL (Percent Concentration in w/v %)		
		Sucrose	Sorbitol	Saccharin
Penicillin VK oral suspension	Schein	2.0(40) ^b		... ^c
Penicillin V potassium solution	Biocraft	... ^a		... ^a
Pen-Vee K oral solution	Wyeth	3.3(66)		... ^c
V-Cillin oral solution	Lilly	3.2(64)		0.033(0.66)
Veetids oral solution	Squibb	... ^d		... ^d
<i>Sulfisoxazole 500 mg/5 mL</i>				
Gantrisin syrup	Roche	3.5(70)		
Gantrisin pediatric suspension	Roche	2.7(54)		
<i>Sulfamethoxazole 500 mg/5 mL</i>				
Gantanol suspension	Roche	2.5(50)		0.0125(0.25)
<i>Sulfamethoxazole 200 mg-Trimethoprim 40 mg/5 mL Combination</i>				
Bactrim pediatric suspension	Roche	2.5(50)	0.35(7)	0.005(0.1)
Bactrim suspension	Roche	2.5(50)	0.35(7)	0.005(0.1)
Septra suspension	Burroughs Wellcome		... ^k	... ^k
Sulfamethoxazole & trimethoprim pediatric suspension	Biocraft		... ^a	... ^a
Sulfamethoxazole & trimethoprim pediatric suspension	Lederle	2.8(56)	0.5(10)	0.005(0.1)
<i>Nystatin 500,000 Units/5 mL</i>				
Mycostatin oral suspension	Squibb	2.5(50) ^l		... ^d
Nilstat oral suspension	Lederle	3.05(61)		
Nystex oral suspension	Savage	2.5(50) ^l		

^a For exact amounts of sweeteners, call Biocraft at 201-796-3434.^b Not confirmed in 1987.^c Amount not disclosed by manufacturer.^d For exact amounts of sweeteners, call Squibb at 609-921-4006.^e Also contains mannitol 0.51 g/5 mL (10.2% w/v).^f Also contains mannitol 0.63 g/5 mL (12.6% w/v).^g For exact amount of sweetener, call Abbott Scientific Affairs at 312-937-7302.^h For exact amount of sweeteners, call Upjohn at 616-323-6615.ⁱ For exact amount of sweetener, call Ross at 614-227-3333.^j Also contains aspartame 0.008 g/5 mL (0.16% w/v).^k For the exact amounts of sweeteners, call Burroughs Wellcome at 919-248-3000.^l Source: Physicians' Desk Reference, 41st ed. Oradell, NJ: Medical Company Economics, Inc.; 1987.Table 2.
Sweetener Content of Common Liquid Pediatric Respiratory, Anticonvulsant, and Miscellaneous Agents

Drug Product	Manufacturer	Sweetener Concentration in g/5 mL (Percent Concentration in w/v %)		
		Sucrose	Sorbitol	Saccharin
<i>Aminophylline 105 mg/5 mL</i>				
Aminophylline oral liquid	Barre-National			... ^a
Aminophylline oral liquid	Roxane		1.0(20)	0.0075(0.15)
Aminophylline oral liquid	Schein			... ^b
Somophyllin oral liquid	Fisons			... ^c
Somophyllin-DF oral liquid	Fisons			... ^c
<i>Diphenhydramine 12.5 mg/5 mL</i>				
Benadryl elixir	Parke-Davis	1.5(30)		
Benylin cough syrup ^d	Parke-Davis	3.0(60)		0.0185(0.37)
Diphenhydramine hydrochloride cough syrup	Lederle	3.84(77)		
Diphenhydramine Hydrochloride Elixir, USP	Lederle	1.5(30)		
Diphenhydramine Hydrochloride Elixir, USP	Roxane	1.5(30)		
<i>Hydroxyzine Hydrochloride 10 mg/5 mL</i>				
Atarax syrup	Roerig	5.9(108)		
Hydroxyzine hydrochloride syrup	Schein	0.6(12) ^e		
<i>Hydroxyzine Pamoate 25 mg/5 mL</i>				
Vistaril oral suspension	Pfizer		... ^f	
<i>Hydroxyzine 2.5 mg-Ephedrine 6.25 mg-Theophylline 32.5 mg/5 mL Combination</i>				
Marax DF syrup	Roerig	5.0(100)		
<i>Metaproterenol 10 mg/5 mL</i>				
Alupent syrup	Boehringer Ingelheim		1.4(28)	0.0035(0.07)
Metaprel syrup	Sandoz		... ^g	... ^g

Continued

Reports Pediatric oral liquid medications

Table 2 (continued)

Sweetener Content of Common Liquid Pediatric Antibiotic and Antifungal Preparations

Drug Product	Manufacturer	Sweetener Concentration in g/5 mL (Percent Concentration in w/v %)		
		Sucrose	Sorbitol	Saccharin
Oxtriphylline				
Choledyl elixir 100 mg/5 mL	Parke-Davis	1.0(20)	0.965(19.3)	
Choledyl pediatric syrup 50 mg/5 mL ^a	Parke-Davis		0.525(10.5)	0.006(0.12)
Theophylline 80 mg/15 mL				
Aquaphyllin syrup	Ferndale	...		
Elixophyllin elixir	Forest			0.005(0.1)
Slo-Phyllin 80 mg syrup	Rorer		2.02(40)	...
Theoclear-80 syrup	Central Pharmaceuticals		1.3(26)	0.01(0.2)
Theolair liquid	Riker	2.4(48)	0.75(15)	...
Theophylline elixir	Barre-National			...
Theophylline oral solution	Roxane		3.25(65)	0.0037(0.075)
Theostat 80 syrup	Laser	2.4(48) ^e		
Theophylline 150 mg/5 mL				
Accurbron liquid ^k	Merrell Dow		0.40(8)	...
Aerolate liquid	Fleming		1.19(24)	
Synophylate elixir	Central Pharmaceuticals	1.25(25)		0.004(0.08)
Theon syrup	Bock		...	...
Theophylline-Guaifenesin Combinations				
Elixophyllin GG	Forest		2.3(46)	
Quibron	Mead Johnson	2.75(55)	0.208(4.2)	
Slo-Phyllin GG syrup	Rorer		0.62(12.4)	...
Synophylate GG syrup	Central Pharmaceuticals	1.0(20)	1.05(21)	0.0067(0.13)
Theolair-Plus liquid	Riker	2.5(50)		
Theophylline-Ephedrine-Phenobarbital Combinations				
Tedral elixir	Parke-Davis		0.42(8.4)	0.010(0.2)
Tedral suspension ^m	Parke-Davis			0.018(0.36)
Ethosuximide 250 mg/5 mL				
Zarontin syrup	Parke-Davis	3.0(60)		0.0075(0.15)
Phenobarbital 20 mg/5 mL				
Phenobarbital Elixir, USP	Lilly	0.64(13)		
Phenobarbital Elixir, USP	Roxane	0.64(13)		
Phenobarbital #2 liquid	Pharmaceutical Associates	0.65(13)		
Phenobarbital 15 mg/5 mL				
Phenobarbital liquid	Pharmaceutical Associates	0.65(13)		
Phenytoin				
Dilantin-30 suspension 30 mg/5 mL	Parke-Davis	1.0(20)		
Dilantin-125 suspension 125 mg/5 mL	Parke-Davis	1.0(20)		
Primidone 250 mg/5 mL				
Mysoline suspension	Ayerst			0.00375(0.075)
Valproic Acid 250 mg/5 mL				
Depakene syrup	Abbott	...	...	
Ferrous Sulfate				
Feosol elixir 220 mg/5 mL ^o	Smith-Kline & French	0.822(16.4)		...
Fer-In-Sol drops 75 mg/0.6 mL	Mead Johnson	1.9(38)	1.6(32)	
Fer-In-Sol syrup 90 mg/5 mL	Mead Johnson	3.0(60)	.35(7)	
Ferrous sulfate elixir 220 mg/5 mL	Lederle	1.8(36)		0.0024(0.048)
Ferrous sulfate liquid 300 mg/5 mL	Roxane	2.0(40)		0.00125(0.025)
Cimetidine 300 mg/5 mL				
Tagamet liquid	Smith-Kline & French		2.8(56)	0.02(0.4)

^a For exact amount of sweetener, call Barre-National at 301-298-1000.

^b For exact amount of sweetener, call Schein at 516-621-4300.

^c For exact amount of sweetener, call Fisons at 617-275-1000.

^d Also contains liquid glucose 1.2 g/5 mL (24% w/v).

^e Not confirmed in 1987.

^f For exact amount of sweetener, call Pfizer at 212-573-2422.

^g For exact amounts of sweeteners, call Sandoz at 201-386-7764.

^h Also contains invert sugar 4.0 g/5 mL (80% w/v); invert sugar contains 40%-50% sucrose and 50%-60% fructose and glucose.

ⁱ For exact amount of sweetener, call Ferndale at 313-548-0900.

^j Amount not disclosed by manufacturer.

^k Also contains invert sugar 2.3 g/5 mL (46% w/v).

^l For exact amounts of sweeteners, call Bock at 314-343-0994.

^m Also contains invert sugar 4.8 g/5 mL (96% w/v).

ⁿ For exact amounts of sweeteners, call Abbott Scientific Affairs at 312-937-7302.

^o Also contains glucose 0.275 g/5 mL (5.5% w/v).

Table 3.
Sweetener Content of Common Chewable Pediatric Medications

Drug Product	Manufacturer	Sweetener (mg/tablet)		
		Sucrose	Mannitol	Saccharin
<i>Antibiotics</i>				
Amoxil (amoxicillin) chewable tablet 125 mg	Beecham	96.6	76	0.45
Amoxil (amoxicillin) chewable tablet 250 mg	Beecham	193.3	152	0.9
Augmentin (amoxicillin-clavulanic acid) chewable tablet 125 mg	Beecham		171	1.0
Augmentin (amoxicillin-clavulanic acid) chewable tablet 250 mg	Beecham		341	2.0
E.E.S. (erythromycin ethylsuccinate) 200 mg chewable tablet	Abbott	... ^a		
Ilosone (erythromycin estolate) chewable tablet 125 mg	Dista	25	292	4.0
Ilosone (erythromycin estolate) chewable tablet 250 mg	Dista	50	585	8.0
<i>Antifungal Agents</i>				
Clotrimazole 10 mg Troches ^b	Miles	903.5		
<i>Anticonvulsants</i>				
Dilantin (phenytoin) Infatab 50 mg	Parke-Davis	463		1.2
Tegretol (carbamazepine) chewable tablet 100 mg	Geigy	249.95		

^a For exact amount of sucrose, call Abbott Laboratories at 312-937-7302.

^b Not chewable.

The chewable tablet preparations contained sucrose, mannitol, or saccharin. Only Augmentin chewable tablets were sucrose free.

Discussion

The dental literature indicates that a 10% sucrose solution may contribute to dental caries.^{5,6} Ingested fermentable sugars are metabolized by oral bacteria to an acid end-product. The decrease in oral pH causes ionic dissolution of the enamel and could initiate caries.⁶ The frequency of administration, the chronicity of intake, and the pH of the sucrose solution are factors that contribute to caries susceptibility in individuals.^{3,5} A study by Roberts and Roberts⁷ demonstrated significantly more caries and gingivitis in children receiving sucrose-based medications for at least six months than in children not receiving chronic medication.

Sucrose intake is of particular concern in diabetic and hyperactive children. Bosso and Pearson² described the caloric imbalance that may occur in diabetic patients who take many drug products with high sucrose concentrations. High sucrose concentrations in drug products may affect behavior in susceptible children, although this relationship is controversial.^{8,9}

Sorbitol may be an appropriate substitute sweetener for children whose sucrose intake needs to be restricted, such as children with diabetes or a high dental caries rate. However, sorbitol also has the potential to cause adverse effects. Pediatric patients susceptible to the cathartic or emetic effects of sorbitol should not be given sorbitol-based theophylline preparations.^{10,11} Differentiating the adverse effects of theophylline, specifically, theophylline toxicity (nausea, vomiting, and diarrhea), from those of sorbitol can be a problem.

Saccharin is frequently used alone or in combi-

nation with other sweetening agents in these medications. Saccharin is an acceptable substitute for children whose sucrose ingestion must be restricted because of diabetes, obesity, or dental caries susceptibility. It is recommended that the daily intake of saccharin be limited to 1 g because of carcinogenic risk.¹² The maximum amount of saccharin in any of the preparations evaluated was 33 mg/5 mL, demonstrating very low potential daily intake from the medications.

The list demonstrates that health-care practitioners can make choices to benefit consumers. Although this list of medications is not a complete representation of all the preparations available in any class studied, it does give a fair representation of the variety of sucrose concentrations and sweetener bases. We had difficulty in obtaining this proprietary information from the many pharmaceutical companies. It would be useful for this product information to be supplied in one standardized source that is routinely updated, as is done in Australia.¹³

This list does not take into account the palatability of the medications. A benefit-to-risk ratio must be realized when a medication with low sucrose or sorbitol concentration is chosen. The palatability of a product is often important to ensure compliance with a therapeutic regimen. The benefit from low sugar or sorbitol content, therefore, becomes secondary to the potential adverse effects of a missed antibiotic, respiratory medication, or anti-convulsant dose.

Conclusion

The sweetener content of common pediatric liquid and chewable medications varies widely. Health-care providers should know that sucrose concentrations within a group of drug products

vary and that a variety of sweetener bases may be available in a class of drugs. This information is useful for health-care practitioners prescribing or dispensing these medications for consumers who need to restrict intake of these sweeteners.

References

1. Department of Health and Human Services, Food and Drug Administration. Inactive ingredients listed in labeling. *FDA Drug Bull.* 1985; 15:34-44.
2. Bosso JA, Pearson RE. Sugar content of selected liquid medications. *Diabetes.* 1973; 22:776-84.
3. Shannon IL, Edmonds EJ. The physician's role in reducing patient exposure to sucrose. *Tex Med.* 1966; 73:52-8.
4. Schneiweiss F. Sweetener content of fluoride-containing pediatric vitamin preparations. *Am J Hosp Pharm.* 1980; 37:1048.
5. Lokken P, Birkeland JM, Sannes E. pH changes in dental plaque caused by sweetened, iron-containing liquid medicine. *Scand J Dent Res.* 1975; 83:279-83.
6. Feigal RJ, Jensen ME, Mensing CA. Dental caries potential of liquid medications. *Pediatrics.* 1981; 98:416-9.
7. Roberts IF, Roberts GJ. Relation between medicines sweetened with sucrose and dental disease. *Br Med J.* 1979; 2:14-6.
8. Wolraich M, Milich R, Stumbo P et. al. Effects of sucrose ingestion on the behavior of hyperactive boys. *J Pediatr.* 1985; 106:675-82.
9. Prinz RJ, Roberts WA, Hantman E. Dietary correlates of hyperactivity behavior in children. *J Consult Clin Psychol.* 1980; 48:760-9.
10. Gryboski JD. Diarrhea from dietetic candies. *N Engl J Med.* 1966; 275:718.
11. Hyams JS. Chronic abdominal pain caused by sorbitol malabsorption. *J Pediatr.* 1982; 100:772-3.
12. Martindale: The extra pharmacopoeia. 28th ed. Reynolds JE, Prasad AB, eds. London: The Pharmaceutical Press; 1982.
13. Plumridge RJ. The sugar content of liquid pharmaceuticals in Australia. 4th ed. Dandenong, Victoria: Beecham Research Laboratories; 1985.

Compatibility of verapamil hydrochloride with penicillin admixtures during simulated Y-site injection

DENNIS F. THOMPSON, M. LOU STILES, LOYD V. ALLEN, JR., AND YU-HSING TU

Abstract. The compatibility of verapamil hydrochloride during simulated Y-site injection with i.v. admixtures containing 11 different penicillins was studied.

Admixtures of penicillin G potassium (62.5 mg/mL), nafcillin sodium (40 mg/mL), oxacillin sodium (40 mg/mL), ampicillin sodium (40 mg/mL), carbenicillin disodium (40 mg/mL), methicillin sodium (40 mg/mL), ticarcillin sodium (40 mg/mL), azlocillin sodium (40 mg/mL), mezlocillin sodium (40 mg/mL), piperacillin sodium (40 mg/mL), and amdinocillin (20 mg/mL) were prepared in both 5% dextrose injection and 0.9% sodium chloride injection in minibags. Verapamil hydrochloride injection 4 mL (10 mg) was then added to each admixture, and the admixtures were examined macroscopically and microscopically

for precipitate immediately and at 15 minutes and 24 hours after mixing. To simulate Y-site injection of verapamil, verapamil hydrochloride injection 1 mL (2.5 mg) was added to 1 mL of each penicillin admixture in a test tube. For admixtures in which precipitates formed, the pH was recorded before and after verapamil was added to the admixtures. Loss of verapamil hydrochloride when mixed with the penicillin admixtures was determined using reverse-phase high-performance liquid chromatography.

Addition of verapamil hydrochloride to admixtures containing nafcillin sodium, oxacillin sodium, ampicillin sodium, and mezlocillin sodium resulted in substantial loss of verapamil hydrochloride. The results for the Y-site injection study showed visible precipitation with

the same penicillin admixtures.

Because a precipitate formed when verapamil hydrochloride was added to nafcillin sodium, oxacillin sodium, ampicillin sodium, or mezlocillin sodium in the diluents studied, we recommended that verapamil hydrochloride be administered separately or that the i.v. tubing be flushed thoroughly before and after this drug is administered through a Y-injection site with these penicillin admixtures.

Index terms: Additives; Ampicillin sodium; Cardiac drugs; Dextrose; Drug administration routes; Incompatibilities; Injections; Mezlocillin sodium; Nafcillin sodium; Oxacillin sodium; Penicillins; Precipitation; Sodium chloride; Stability; Storage; Verapamil hydrochloride *Am J Hosp Pharm.* 1988; 45:142-5

DENNIS F. THOMPSON, PHARM.D., is Director, Drug Information Service, State of Oklahoma Teaching Hospitals, Oklahoma City, OK, and Clinical Associate Professor, College of Pharmacy, University of Oklahoma Health Sciences Center (UOHSC), Oklahoma City. M. LOU STILES, M.S., is Associate Professor of Pharmaceutics, and Director, Formulations Service, College of Pharmacy, UOHSC. LOYD V. ALLEN, JR., PH.D., is Professor and Head, Department of Pharmaceutics, and Director, Drug Analysis Laboratory, College of Pharmacy, UOHSC. YU-HSING TU, PH.D., is Postdoctoral Research Fellow, Department of Pharmaceutics, College of Pharmacy, UOHSC.

Address reprint requests to Dr. Thompson at the Drug Information Service, University of Oklahoma Health Sciences Center, 1000 Stanton L. Young Boulevard, Oklahoma City, OK 73190.

The assistance of Knoll Pharmaceuticals in providing the pure sample of verapamil hydrochloride is acknowledged.

Presented at the 21st Annual ASHP Midyear Clinical Meeting, Las Vegas, Nevada, December 10, 1986.

Copyright © 1988, American Society of Hospital Pharmacists, Inc. All rights reserved. 0002-9289/88/0101-0142\$01.00.