Xylitol, Sweeteners, and Dental Caries

Kiet A. Ly, MD, MPH[1] Peter Milgrom, DDS[2] Marilynn Rothen, BS, RDH[3]

Abstract

The purpose of this report was to provide an overview of xylitol and other polyol sweeteners and dental caries for clinicians and to discuss current applications for dental practice and potential community-based public health interventions. Xylitol, like other polyol sweeteners, is a naturally occurring sugar alcohol. Studies suggest polyols are noncariogenic. Furthermore, studies indicate that xylitol can decrease mutans streptococci levels in plaque and saliva and can reduce dental caries in young children, mothers, and in children via their mothers. Food products containing xylitol are now available and have the potential to be widely accessible to consumers to help control rampant decay. Determining whether products contain adequate xylitol amounts for practical use towards prevention is challenging, however, because xylitol content is not clearly labeled. Sufficient evidence exists to support the use of xylitol to reduce caries. Clinicians and dental associations should push for clear recommendations of efficacious dose and frequency of xylitol use and for clear labeling of xylitol content in products to help consumers choose appropriately. (Pediatr Dent 2006;28:154-163)

KEYWORDS: PREVENTIVE DENTISTRY, DENTAL CARIES, XYLITOL, SWEETENING AGENTS

Xylitol is a sugar substitute with sweetness equal to that of table sugar (sucrose), but with 40% fewer calories.[1] It is a member of the sugar alcohol or polyol family, which includes other common dietary sweeteners such as sorbitol, mannitol, and maltitol. Xylitol is produced commercially from birch trees and other hardwoods containing xylan. More recently, to reduce production cost, commercial xylitol is being produced from corn cobs[2,3] and the waste of sugarcane or other fibers[4-6] using biotechnology. Xylitol can be found in small quantities in fruits and vegetables and is produced as part of human metabolic processes.

Sorbitol, mannitol, and maltitol are also naturally occurring substances found in many trees, plants, and fruits and are produced commercially. They are less sweet than xylitol but are widely used in sugar-free products such as chewing gums, candies, and toothpastes because they are cheaper. Polyol sweeteners are frequently combined together with small amounts of high intensity artificial sweeteners such as saccharin or aspartame to improve the flavor and sweetness of products. The US Food and Drug Administration (FDA) allows "sugar-free" labeling of products sweetened only with sugar alcohols, artificial sweeteners, or a combination of these sweeteners (Table 1).

[1]Dr. Ly is assistant professor and [2]Dr. Milgrom is professor in the Department of Dental Public Health Sciences, the Northwest/Alaska Center to Reduce Oral Health Disparities, and [3]Ms. Rothen is the clinical manager of the Regional Clinical Dental Research Center, University of Washington, Seattle, Wash.
Correspond with Dr. Milgrom at dfrc@u.washington.edu.

Xylitol has been approved by the FDA since the 1960s and is safe for use with children.[7] Similar to many other polyols, it is most commonly used as a sweetener in foods in the United States. There has been, however, a recent explosion of xylitol use in the food, pharmaceuticals, and nutraceuticals industries. Polyols are absorbed slowly by the human gastrointestinal tract. The main side effect associated with most polyol consumption is osmotic diarrhea—which, for xylitol, only occurs when it is consumed in large quantities, 4 to 5 times that needed for the prevention of dental caries.[7,8] Tables 2 and 3 provide lists of commercially available products containing xylitol as well as information on their xylitol content. Note that these lists are not exhaustive. Many products were not included, as an overwhelming majority use xylitol along with other polyols as sweeteners and often do not contain sufficient xylitol to prevent dental caries. Furthermore, most products do not specifically state the xylitol content in the packaging, making it impossible for consumers to make informed decisions about which product to purchase and consume for dental caries prevention.

Sugar alcohols and tooth decay

Sugar alcohols have been shown to be noncariogenic. Consumption does not promote tooth decay.[9] Furthermore, xylitol has been shown to have a protective effect and to reduce tooth decay in part by reducing the levels of *Streptococcus mutans* in plaque and saliva and by reducing the level of lactic acid produced by these bacteria.

Table 1. Properties of Natural Sugars and Sugar Substitutes

	Nutritive value (calories/g)	Cariogenic	"Sugar-free" label (noncariogenic)	Sweetness*
Natural sugars				
Sucrose	4	Yes	No	1.0
Glucose	4	Yes	No	.7
Fructose	4	Yes	No	1.5
Lactose	4	Yes	No	.2
Sugar substitutes				
Sugar alcohols/polyols				
Xylitol	2.4	No	Yes	1.0
Sorbitol	2.6	No	Yes	.6
Mannitol	1.6	No	Yes	.5
Maltitol	2.1	No	Yes	.9
Artificial sweeteners				
Aspartame† (NutriSweet, Equal)	0.0	No	Yes	180
Saccharin (Sweet 'N Low)	0.0	No	Yes	300
Sucralose (SPLENDA)	0.0	No	Yes	600
Acesulfame potassium (Sunett)	0.0	No	Yes	200

*Sucrose (table sugar) is the standard for sweetness comparison and is given the sweetness value of "1."
†Aspartame is technically a nutritive sweetener. Because of its intense sweetness, however, it is used in such small amounts that its nutritive value is negligible.

Table 4 contains an overview of selected clinical studies in which xylitol chewing gum was included in the study design and where the results showed either a reduction in *S mutans* levels in plaque or saliva or a reduction in tooth decay. In some of these studies, xylitol and sorbitol were included, independently or in combinations. Overall results showed that participants in groups consuming 100% xylitol had greater reductions in caries or *S mutans* levels than participants in groups that consumed a combination of xylitol and sorbitol. In turn, the participants in this latter group experienced greater reductions in tooth decay than those in groups that consumed sorbitol alone.

This suggests that, although polyol sweeteners used in combination can reduce caries, the amount of xylitol in the combination determines the degree of reduction observed. The presence of other polyol sweeteners may enhance, but does not reduce, xylitol's effectiveness. Furthermore, the consumption of greater amounts of xylitol per day has been associated with a larger reduction in tooth decay. Xylitol consumption of less than 5 g per day, however, has often been found to be no more effective than consumption of sorbitol alone (Table 4).

There also appears to be a ceiling effect for xylitol. In an intensive xylitol chewing gum treatment study where a maximum of 14 g per day of xylitol was consumed, the study reported a reduction in DMFS score. This reduction, however, was not significantly different from that of the group that consumed 10 g per day.[10] Two retrospective studies have reported that increasing the frequency of xylitol use is associated with greater reduction in caries and suggested that a frequency of less than 3 times per day may not be effective.[11,12]

Xylitol and mutans streptococci

Microorganisms do not readily metabolize xylitol into energy sources, and its consumption has a minimal effect on plaque pH.[13] Xylitol, however, is absorbed and accumulates intracellularly in *S mutans*. Xylitol competes with sucrose for its cell-wall transporter and its intracellular metabolic processes. Unlike the metabolism of sucrose, which produces energy and promotes bacterial growth, *S mutans* expends energy to break down the accumulated xylitol without yielding energy in return. Furthermore, the energy-producing intermediates are consumed and not reproduced by xylitol metabolism.[14] This has been demonstrated in vitro and may contribute to a reduction of *S mutans* levels in plaque and saliva and a reduction in acid production among those consuming xylitol.[15]

In addition, xylitol has a number of other effects on *S mutans* that may account for some of its clinical effects in caries reduction. Short-term consumption of xylitol is associated with decreased *S mutans* levels in both saliva and plaque.[15] Long-term habitual consumption of xylitol appears to have a selective effect on *S mutans* strains. This results in selection for populations that are less virulent and less capable of adhering to tooth surfaces and, thus, are shed more easily from plaque into saliva.[16] This effect may not only be important to the individual's decay experience,

Table 2. Xylitol-containing Gums and Mints Available in US Markets, Their Xylitol Content, Preventive Potential, and Approximate Cost*

Products†	Xylitol per piece (g) [total polyols (g)]	Pieces for 6 (10) g/d	Preventive Potential‡	Approximate Cost/10 pieces
Gums				
Epic–xylitol gum (various flavors)	1.05	6 (10)	Yes	$0.70–$1.00 online
Clen-Dent/Xponent gum (various flavors)	0.67	10 (15)	Yes	$1.60–$1.70 retail
Fennobon Oy "XyliMax Gum"	0.86	7 (12)	Yes	$0.80–$1.00 online
Hershey "Carefree Koolerz Gum" (various flavors)	1.50	4 (7)	Yes	$0.95–$1.50 retail
Lotte–xylitol gum (various flavors)	0.65	9 (15)	Yes	$0.70–$0.80 online
Omnii "Theragum"	0.70	9 (14)	Yes	$1.25–$1.50 online
Spry Xylitol gum (various flavors)	0.72	8 (14)	Yes	$0.70–$0.90 online
Tundra Trading "XyliChew Gum"	0.80	8 (13)	Yes	$1.50–$1.65 retail
Vitamin Research "Unique Sweet Gum"	0.72	9 (14)	Yes	$1.00 online
WellDent "Xylitol Gum"	0.70	9 (14)	Yes	$0.90–$1.00 online
Altoids Sugar-Free Chewing Gum	First of 3 polyols (1.0)	NC§	Maybe	$0.90–$1.00 retail
B-FRESH Gums (various flavors)	First of 2 polyols (1.0)	NC	Maybe	$0.70 online
Starbucks "After Coffee Gum" Peppermint	First of 2 polyols (1.0)	NC	Maybe	$1.00 retail
Arm & Hammer "Dental Care Baking Soda Gum"	Second of 3 polyols (1.0)	NC	No	$0.80–$1.00 retail
Arm & Hammer "Advance White Icy Mint Gum"	Second of 3 polyols (1.0)	NC	No	$1.00–$1.30 retail
Biotene "Dental Gum" and "Dry Mouth Gum"	Second of 2 polyols (1.0)	NC	No	$1.00–$1.40 retail
Eco-Dent "Between Dental Gum" (various flavors)	0.35	17 (29)	No	$1.05–$1.40 online
Warner-Lambert "Trident Gum with Xylitol"	Second of 3 polyols (1.0)	NC	No	$0.60–$0.70 retail
Warner-Lambert "Trident for Kids Gum"	Third of 3 polyols (1.0)	NC	No	$1.20–$1.40 retail
Wrigley "Orbit Sugar-Free Gum"	Third of 3 polyols (1.0)	NC	No	$0.45 REI online
Ford Gum "Xtreme Xylitol Gums"	NC	NC	NC	$0.65–$0.85 online
Wrigley "Everest Mint Gum"	NC	NC	NC	$0.45 REI online
Mints				
Clen-Dent/Xponent "Mints"	0.67	9 (15)	Yes	$0.62–$0.70 online
Epic "Xylitol Mints"0.50	0.50	12 (20)	Maybe	$0.35–$0.50 online
Omnii "Theramints"	0.50	12 (20)	Maybe	$0.45 online
Spry "Mints"	0.50	12 (20)	Maybe	$0.38–$0.49 online
Tundra Trading "XyliChew Mints"	0.55	11 (18)	Maybe	$0.35–$0.50 retail
VitaDent "Mints"/"Unique Sweet Mints"	0.50	12 (20)	Maybe	$0.62–$0.65 online
WellDent "Xylitol Mints"	0.55	11 (18)	Maybe	$0.38 online
Smint "Mints"	<0.20	30 (50)	No	$0.35–$0.40 retail
Brown & Haley "Zingos Caffeinated Peppermints"	Second of 2 polyols	NC	No	$0.40–$0.50 retail
Oxyfresh "Breath Mints"	Second of 2 polyols	NC	No	$0.35–$0.40 online
Starbucks "After Coffee Mints"	Second of 2 polyols	NC	No	$0.20 Starbucks
Tic Tac "Silvers"	NC	NC	No	$0.35–$0.40 online
Xleardent "Mints"	NC	NC	No	$0.20 Starbucks

*Cost varies based on retail, convenience stores, and Internet vendors. Stated cost based on a few Seattle retailers or Internet vendors.
†Product list is not exhaustive. Xylitol market is rapidly changing and new xylitol containing products appear frequently.
‡"Yes," "no," or "maybe" are based on the potential a person is willing to consume 2 to 3 pieces, 3 to 5 times per day to meet the effective dose range of 6 to 10 g per day. Products with a potential for effectiveness, but for which xylitol dose is either unknown or required consumption, is >10 pieces/day to provide 6 g of xylitol are assigned "maybe."
§N/C=not certain. Information cannot be derived from Internet vendor or market packaging, or authors unsuccessful in obtaining information from vendors' information representatives.

Table 3. Xylitol-containing Diet, Oral Hygiene, and Health Care Products Available in US Markets and Their Xylitol Content

Products*	Xylitol content	Cost/unit†	Availability
Energy bars and food			
Buddha Bars	4-5 g/bar	$3.00/bar	Online
E Enterprises–"E Bar"	14 g/bar	$2.00/bar	Online
Fran Gare's "Decadent Desserts" Mix (various types)	15-25 g/30 g serving	$7.00/canister	Online
Jay Robb Enterprise "Jaybar"	13 g/bar	$3.00/bar	Online
Kraft Jell-O Pudding Sugar Free Chocolate	7 g/serving	$0.65/serving unit	Retail
Nature's Hollow–Sugar Free Jam (various flavors)	4.5 g/20 g serving	$6.00/10 oz	Online
Nature's Hollow–Sugar Free Syrup (various flavors)	2.5 g/40 ml serving (7%)	$5.40/8.5 oz	Online
Nature's Hollow–Sugar Free Ketchup	.8 g/20 g serving (4%)	$5.50/10 oz	Online
Nature's Hollow–Sugar Free Honey	1.2 g/20 g serving (8%)	$5.50/10 oz	Online
Biochem "Ultimate LoCarb 2" bars	Second of 2 polyols	$2.00/bar	Retail and online
Richardson Labs "Carb Solutions" Creamy Chocolate	Third of 3 polyols (13 g)	$1.50/bar	Retail and online
Oral hygiene			
Biotene "Dry Mouth Toothpaste" (±Calcium)	10%	$6.00-$7.00/4.5oz	Retail and online
Crest "Multicare Cool Mint Toothpaste"	10%	$3.50-$4.50/8 oz	Retail and online
Epic Toothpaste (fluoride free)	25% (no fluoride)	$4.50-$5.00/4.9 oz	Online
Epic Toothpaste with fluoride	35%	$7.00-$8.00/4.9 oz	Online
Squigle "Enamel Saver Toothpaste"	36% (.24% sodium fluoride)	$7.25-$8.00/4 oz	Online
Topex Toothpaste "Take Home Care," "White Care"	10% (1.1% sodium fluoride)	$4.50-$5.50/2 oz	Dental office and online
Rembrandt Toothpaste "For Canker Sore"	Only sweetener (fourth ingredient)	$6.50-$7.50/3 oz	Retail and online
Spry Toothpaste "MaxXylitol and Aloe"	N/C‡ only polyol (no fluoride)	$4.50-$5.00/4 oz	Online
Tom's of Maine "Baking Soda" Toothpaste line	N/C (varies in ingredient list)	$3.50-$4.50/6 oz	Retail and online
Tom's of Maine "Natural Toothpaste" line	N/C (varies in ingredient list)	$3.50-$4.50/6 oz	Retail and online
Tom's of Maine "Sensitive Toothpaste" line	N/C (varies in ingredient list)	$3.50-$4.50/6 oz	Retail and online
XyliWhite Toothpaste (fluoride free)	25% (no fluoride)	$3.50/6.4 oz	Online
Biotene "First Teeth" Infant Toothpaste	First of 2 polyols	$5.00-$6.00/1.4 oz	Retail and online
Gerber "Tooth and Gum Cleanser"	Second of 2 polyols (sixth ingredient)	$5.00-$5.50/1.4 oz	Retail and online
Spry Infant "Tooth Gel"	N/C only polyol (no fluoride)	$4.50-$5.50/2 oz	Online
Biotene "Oral Balance" Dry mouth gel	Second of 2 polyols	$5.00-$6.00/1.5 oz	Retail and online
Biotene "Mouthwash"	First of 2 polyols	$6.00-$7.00/16 oz	Retail and online
Epic "Oral Rinse"	25%	$7.50-$8.50/16 oz	Online
Oxyfresh "Mouthrinse"	Only sugar (second ingredient)	$9.00-$10.00/16 oz	Online
Rembrandt "Dazzling Breathdrops"	Only sugar (second ingredient)	$1.00-$1.50/.22 oz	Retail and online
Spry "Oral Rinse"	First of 2 polyols (no fluoride)	$5.00-$5.50/16 oz	Online
Tom's of Maine "Natural Mouthwash" line	N/C (varies in ingredient list)	$4.00-$6.00/16 oz	Retail and online

Table 3 continued

Health care	Xylitol content	Cost/unit†	Availability
Bayer "Flintstone Vitamins—Complete"	N/C	$15.00-$17.00/150 tablets	Retail and online
Bayer "One a Day Kids Vitamins—Complete"	N/C	$5.00-$8.50/50 tablets	Retail and online
Sundown "Spiderman Complete Vitamins"	N/C	$7.00-$8.00/60 tablets	Retail and online
Micro Spray "Vitamin Sprays"	N/C (2nd ingredient)	$13.00-$20.00/9 ml	Online
B&T "Echina Spray"	N/C	$6.00-$10.00/0.68 oz	Online
Dr. Ray's Products "Spiffies Dental Wipes"	N/C (2nd ingredient)	$5.50-$9.00/48 wipes	Online
Nicorette "Gum"—Mint	N/C (last ingredient)	$27.00-$33.00/40 pieces	Retail and online
Xlear "Nasal Wash"	N/C (2nd ingredient)	$13.00-$14.00/1.5 oz	Retail and online
Xylifloss "Pocket Dental Flosser"	N/C	$4.00/250 uses	Retail and online

*Product list is not exhaustive. Xylitol market is rapidly changing, and new xylitol-containing products appear frequently. Aside from toothpaste, most products have not been studied or published in peer-reviewed journals; thus, the potential impact on caries reduction is not known.

†Cost varies based on retail and convenient stores. Stated cost based on a few Seattle area retailers.

‡N/C=not certain. Information cannot be derived from market packaging and authors unsuccessful in obtaining information from company information representative.

but may also influence the transmission of *S mutans* from mothers who consume xylitol to their children.

Xylitol dose and frequency for effectiveness

Dosing and frequency guidelines for xylitol have not been fully developed. This is because there have been no prospective studies designed to determine the minimum effective amount and frequency of xylitol use and to specifically determine the dose-response and frequency-response relationship of xylitol and *S mutans* or dental caries.

Researchers at the University of Washington, Seattle, Wash, conducted a series of studies with adults chewing xylitol gum to clarify the relationship of dose and frequency of use of xylitol to the reductions of mutans streptococci (MS) levels in plaque and saliva. In the initial study, participants were randomly assigned to 1 of 4 groups and chewed 12 pellets of xylitol and/or control (sorbitol) gums evenly divided into four doses per day and giving varying amounts of xylitol per group. The study concluded that MS levels were reduced with increasing doses of xylitol, with the effect leveling off between 6.88 g per day and 10.32 g per day. Although the smallest dose in the study, 3.44 g per day, showed a reduction, the difference was not statistically significant.[17]

In a second study, participants consumed 10.32 g per day of xylitol divided into 2, 3, or 4 administrations per day. The results demonstrated a linear response where increasing frequency of use is associated with decreasing levels of MS in plaque and saliva. Although a reduction was observed with xylitol use of 2 times per day and the reduction was consistent with the linear line model, however, the difference was not statistically significant when compared to the sorbitol control (unpublished data). Thus, xylitol consumed twice a day was not effective in reducing MS.

These results confirm previous suggestions regarding dose and frequency. A range of 6 to10 g divided into at least 3 consumption periods per day is necessary for xylitol to be effective with chewing gum as the delivery system. Future studies in this series will evaluate the effectiveness of other xylitol-containing snack food to xylitol chewing gum in both adults and children.

Clinical applications

The use of polyols as sweeteners in foods and beverages to not promote tooth decay is widespread. Sorbitol, mannitol, and/or maltitol are most frequently used. Nevertheless, evidence supporting the role of xylitol in reducing MS in plaque and saliva and in reducing the incidence of tooth decay is influencing the market; xylitol is appearing in consumer products rapidly, sometimes purely as a sweetener while at other times it is included to provide therapeutic levels. These xylitol-containing products, when used at efficacious levels by consumers and particularly if used in well-planned dental public health programs for children at high caries risk, may help significantly reduce tooth decay beyond the results from currently applied strategies.

Children at high risk for caries

There are few well-studied strategies available to clinicians to prevent and control the high rates of caries in the primary dentition.[18] In the absence of water fluoridation, fluoridated toothpaste and topical fluorides are the primary preventive tools for clinicians. For children in mixed dentition, sealants are added to the regimen. Effective strategies to reduce risk by modifying children's diets are not readily applicable to dental practice, nor are they typically effective without significant effort. As such, the use of xylitol is particularly attractive because its action is not dependent upon reducing the amount of other sugars in the diet. Thus, a clinician can recommend adding xylitol to the diet without asking patients to make additional alterations to their dietary patterns. Xylitol-containing products have the potential to improve success in controlling rampant decay in the primary dentition.

A number of studies conducted among schoolchildren of various ages have shown that consumption of gum containing xylitol reduces the extent of dental caries (Table 4). One study conducted among schoolchildren in Belize with very high rates of tooth decay showed that consumption of xylitol gum was associated with arrest of carious lesions. The number of lesions that rehardened ranged from 9% to 27% in all groups.[19] This study is important because the children continued to consume very high levels of sucrose in their everyday diet. A recent study of 3- to 6-year-olds compared xylitol chewing gum and tooth-brushing using a fluoridated toothpaste (.05% NaF). The children brushed once after lunch or chewed xylitol gum 3 times each day during daycare hours. All children brushed as they normally would at home. The study found that the xylitol gum group had better oral health status than the group that brushed.[20] Another study in Europe showed that the DMFS increment among groups of fifth graders who consumed xylitol chewing gum either for 2 or 3 years were no different than the group that received sealants at the end of the 5-year study period.[21] A major limitation in extending these results to the United States, however, is that chewing gum is not considered safe for very small children and is actively discouraged in daycare and schools because of choking risk.

Other xylitol-containing products have been studied. A field trial of the use of xylitol-containing candy among 10-year-old schoolchildren in Estonia showed a 33% to 59% tooth decay reduction in the groups using xylitol candy and a 54% tooth decay reduction in the group using xylitol gum relative to the control group.[22] This suggests that candy may be as effective as chewing gum as a vehicle for the delivery of xylitol in caries prevention.

At the University of Washington, researchers have produced and field tested xylitol-containing popsicles, gummy bears, puddings, macaroons, and sorbet.[23] They have shown that children will readily accept such foods when offered as part of the daily diet and that they suffer no side effects from their use. Food producers are available to develop these snacks, but considerable work is needed to produce commercially viable products that will be accepted. In the future, these xylitol snack foods need to be tested with children to establish their effectiveness at preventing decay because certain foods are better than others at delivering and releasing xylitol in the oral cavity.

Xylitol is also found in several toothpaste formulations (see Table 3). Several studies have evaluated toothpaste formulations with 10% xylitol. A study conducted in Costa Rica involving 2,630 children between 8 and 10 years old compared sodium fluoride toothpaste with and without 10% xylitol. After 3 years of twice daily brushing, the children using the xylitol toothpaste showed a 12% reduction in decayed/filled surfaces (DFS) and 11% reduction in decayed/filled buccal and lingual surfaces (DFS-BL) compared to the fluoride-only toothpaste.[24] In a more recent study, the same author conducted a 30-month study to evaluate long-term tooth decay increment among 3,394 public school children 7 to 12 years old who used fluoride toothpaste with or without 10% xylitol. The DFS and DFT increments for the 10% xylitol group were 1.30 and .69, respectively, compared to fluoride-only group scores of 1.51 and .81.[25] A study conducted in Sweden among 155 students (average age=25 years) with high MS levels compared 3 fluoride toothpaste formulations, Colgate Total with or without triclosan (control) or with triclosan plus 10% xylitol (Colgate Oral Pharmaceuticals, Canton, Mass). After 6 months of twice daily brushing, only the 10% xylitol toothpaste group demonstrated a significant reduction of MS in plaque (9-fold reduction) and saliva (8-fold reduction).[26] Fluoride toothpaste with xylitol can be recommended as a substitute for regular fluoride toothpaste, and other xylitol products can be recommended concurrently with fluoridate toothpaste, topical fluorides, and sealants. Xylitol and fluoride can be used simultaneously, as they have different mechanisms of action and a potentially synergistic effect.

According to available data, there is no xylitol product commercially available in the United States that is suitable for toddlers and preschool children too young to chew gum. An ongoing study of adults at the University of Washington is comparing xylitol delivered via gum to xylitol delivered via a snack food for young children at the effective doses and frequencies. Syrups have also been developed for evaluation. In older children, chewing gum, mints, or lozenges with xylitol can be recommended. It should be recognized, however, that most products available at local retail stores are not optimizing xylitol for the caries preventive effects and are likely to have minimal, if any, caries prevention impact.

Pregnant women and new mothers

A combination of good dental care, instruction to improve oral hygiene, and chlorhexidine gels and fluoridated toothpastes leads to reductions in maternal *S mutans* levels and reduction in the extent of transmission to the child.[27] Hildebrandt and colleagues showed that the use of commercially available chlorhexidine rinses for 2 weeks—followed by the daily use of xylitol gum (2 pellets containing 1.7g xylitol) in high-caries-rate adults with recent restorations—led to major reductions in *S mutans*.[28] A clinical trial conducted in Finland comparing the effects of strategies to modify the maternal transmission of *S mutans* to infants demonstrated that xylitol had the greatest effect.[29] The mothers, all of whom had high *S mutans* levels at the beginning of the study, were treated with either chlorhexidine varnish, fluoride varnish, or 100% xylitol gum chewed at least 2 to 3 times per day for 18 to 21 months. The children were not treated.

The children of mothers treated with xylitol had the lowest levels of *S mutans* levels during the intervention period (treatment continued until the child was 2 years old) and during followup.[30] The percentage of colonization with *S mutans* in the children in the xylitol group at 2 years old was 10%, compared to 29% in the chlorhexidine group and

Table 4. Summary of Selected Clinical Trials that Included the Use of Xylitol Chewing Gum and that Reported a Reduction in Streptococcus mutans, in Mutans streptococci, or in Caries

Study	Population	Consumption frequency	Xylitol doses (g/d)	Conclusion
24 mos; 3 groups: xylitol, fructose, and sucrose	Adults (n=125); age=27 ys (avg)	1 piece, 4.5 x/d on avg (range=3–7)	6–7	Reduction in caries increment rate[34]
4 wks chewing, then 4 wks not chewing; 3 groups: xylitol, fructose, sorbitol/mannitol	Children (n=80) (pedodontic clinic)	2 pieces, 5 x/d	5-7	Reduction in unstimulated saliva and plaque S mutans levels[35]
24 mos; 3 groups: xylitol 15%, xylitol 65%, no gum	Children (n=433); age=8-9 ys	1 piece, 3 x/d School days only	15%=0.8 65%=3.4	Lower DMFS increment of decay in both active groups[36]
24 mos; retrospective study categorized original cohort into 3 chewing frequencies	Children (n=212); age=11-12 ys	1 piece, 3 x/d	10.5 (3.5 g/piece)	Lower DMFS increment with frequency of >3 x/d groups[11]
32 mos; 2 groups, xylitol, no xylitol snack foods	Children (n=468); age=6-12	Combination of xylitol snack foods daily	20 (combine maximum)	Lower DMFS increment than no xylitol controls[37]
24 mos; 2 groups: xylitol gum vs no gum	Children (n=212); Age=11-12 ys	1 piece, 3 x/d	10.5 (3.5 g/piece)	Lower DMFS increment vs controls[38]
12 mos: retrospective study categorized original cohort into chewing frequencies	Young adults (n=100); age=22 ys (avg)	1 piece, 4.5 x/d on average (range=3–7)	6–7	Greater reduction in caries incidence with increased frequency of use[12]
25 days chewing crossover; 4 groups r: 3 xylitol groups, 1 sorbitol	Adult (n=20); age=25.5 ys (avg)	1 piece, 12 x/d	13.4, 6.7, 3.36	Higher xylitol level associated with lower S mutans levels in plaque and saliva; xylitol 3.36 g same as controls[39]
24 mos; 6 groups: 3 xylitol, 2 sorbitol, 1 no gum	Children (n=510); age=6 ys, 10 schools with 3 no gum chewing	1 stick or 2 pellets, 5 x/school days and nonschool days	x/s*=7.11, x/s=9.68 Xylitol stick=10.42 Xylitol pelet=10.67	Reduction in caries rate among groups chewing gums; 100% XylPellet most effective[40]
40 mos; 9 groups: 6 xylitol, 1 sorbitol, 1 sucrose, 1 no gum control	Children (n=1,227); age=10 ys	3-5 x/school days and nonschool day	7.11—x/s mixed 3 x/d 9.68—x/s mixed 5 x/d 6.25—xylitol stick 3 x/d 10.42—xylitol stick 5 x/d 6.40—xylitol pellet 3 x/d 10.67—xylitol pellet 5x/d	Reduction in caries increment among gum groups except sucrose; 100% xylitol pellet most effective[19] Saliva S mutans not increase with age among 100% Xylitol Pellet groups as did other groups[41]
16 mos; intensive treatment 1 group (high-risk participants)	Children (n=109); age=13.5 ys(mean)	7 x/d	14 (max)	Reduction in caries onset rate and in DMFS score[10]
60 mos; 3 groups: 2-year or 3-year xylitol, sealants	14 classrooms of fifth graders	2 pieces, 3 x/d (Xylifresh) school days	5	No difference in DMFS increment between sealant and xylitol groups[21]
32 mos; 2 groups: xylitol, brushing	Children (n=921); 11 daycare centers	1 pieces, 3 x/d (Xylifresh) daycare hours	2.5 g/d	No difference in dfm between xylitol and brushing[20]
3 mos; 3 groups: xylitol 55%, xylitol 100%, no gum	Children (n=91); age=10-12 ys	2 pieces, 3 x/d school days only	55%=5.76 g/d 100%=11.88g/d	Reduction in saliva and plaque S mutans counts in both treatment groups[42]

*x/s is a gum that contains both xylitol and sorbitol.

49% in the fluoride group. These children were followed up most recently at 6 years old and were found to still have the lowest *S mutans* levels—52% were colonized in the xylitol group compared to 86% and 84% in the chlorhexidine and fluoride groups, respectively.[31] Children of mothers treated with xylitol also had the lowest rates of decay. Follow-up at 5 years of age found that dentinal caries among children in the xylitol group was reduced by 70%, compared to children

in the fluoride or chlorhexidine groups.[29] These studies have been conducted only in settings in which child rearing is done primarily by the mother and in which mother-to-child transmission is presumed. No studies have been completed in communities where child rearing is shared among greater numbers of people.

Whether used alone or in combination with other antimicrobial therapies such as chlorhexidine, xylitol has an important role in the prevention of dental decay among children born to mothers with high *S mutans* levels. This is not only because of its effects on *S mutans* levels and bacterial properties during the period of consumption, but also because its beneficial effect on decay reduction in these children appears to persist far beyond the period of consumption.[30] Both chlorhexidine and xylitol may be used safely by pregnant women and nursing mothers.[32,33] Currently available data suggest that twice daily use of chlorhexidine gluconate rinse (.12%) for 2 weeks, followed by 6 to 10 g of xylitol via chewing gum per day chewed for 5 minutes each time, should lead to a major reduction in the mother's MS levels and tooth decay. This regimen should also benefit the child. In very high-risk individuals, follow-up periods of chlorhexidine use may be beneficial.

Deciphering xylitol product ingredients list for efficacy potential

Food products containing xylitol, including chewing gums and mints, are currently available in retail stores, through specialized manufacturers, and online (Tables 2 and 3). The number and types of products have been proliferating at a rapid rate. There are now, for example, xylitol-containing flavored towelettes for cleaning infants' and toddlers' teeth and gums. The challenge is for clinicians to recommend products that have been shown to be effective and deliver the recommended 6 to 10 g per day. This requires a basic understanding of sugar substitutes and clear product labeling. Gums, mints, and other products labeled "sugar-free" or "does not promote tooth decay" may contain 3 or 4 sweeteners including artificial intense sweeteners with the total of the sugar alcohols (polyols) listed by percent or weight in grams. Xylitol may not be the first sugar alcohol listed, though the packaging may highlight its presence for marketing purposes. The amount of an ingredient in a product decreases with the order in which it appears. Furthermore, often the first several ingredients make up the bulk of the product.

Take a hypothetical gum for which the nutritional information indicates that one piece weighs 2 g and lists sugar alcohols to be 1 g. The ingredients list shows that xylitol is the second of 3 sugar alcohols listed and is the sixth ingredient in the list. Therefore, the exact amount of xylitol in the product is unknown, but being the sixth ingredient indicates that a small proportion of the gum weight is xylitol. Being the second sugar alcohol indicates that xylitol does not make up the bulk of the sugar in the gum. Consequently, only a small proportion, likely between 0.1 to 0.3 g, of the 1 g of sugar alcohols in the gum is xylitol. Thus, chewing this gum would unlikely yield a caries-preventive benefit. Manufacturers who indicate that their product is sweetened with 100% xylitol, who list xylitol as the first ingredient, or who indicate the number of grams of xylitol per piece facilitate professional evaluation and consumer knowledge.

Due to their size, mints often contain insignificant amounts of xylitol. Specialized manufacturers aimed at the dental market, however, produce a suite of products—including gum, mints, toothpaste, and mouth rinses—with therapeutic levels of xylitol. Several toothpaste manufacturer representatives have indicated to the authors that selected products in their line contain at least a 10% level of xylitol (see Table 3). Not all manufacturers of toothpaste with xylitol listed in their ingredients were forthcoming with this proprietary information when the authors questioned them. Almost no research has been done on mouth rinses containing xylitol. There is no scientific evidence available on which to base any recommendation on the value of xylitol-containing towelettes, nasal sprays, or xylitol-sweetened children's vitamins.

Another consideration in recommending daily xylitol consumption for patients is cost and adherence. In xylitol studies to date, the vehicle (gum, candies, toothpaste) has been provided to subjects and use has been closely monitored. A daily xylitol chewing gum habit may cost $30 per month depending on the market in which the product is purchased. There is at least one gum aimed at children available in most retail stores that contains significant amounts of xylitol for dental caries benefit (see Table 2). Retail store gums are typically less costly than those produced by specialty Internet vendors or products positioned as dental gum providing therapeutic benefits. Additionally, xylitol gum and mints are very popular in Asian countries, and these products can frequently be found in Asian retail stores in the United States. As the products are not often labeled in English, however, determining the amount of xylitol they contain may be challenging.

Conclusions

The list of snack foods and dietary products containing xylitol is rapidly expanding. The overwhelming majority of studies showed the protective effect of xylitol on tooth decay. In the face of the continuing high rate of caries in some populations in the presence of current dental caries prevention modalities, xylitol offers a potent tool that can have a significant impact. The evidence is sufficient for clinicians to consider including xylitol-containing products in their clinical armamentarium for the prevention of tooth decay in high-risk populations. Clinicians, consumers, and dental pubic health agencies should advocate for:

1. clear labeling of the xylitol content in products to help consumers make well-informed decisions when using these products for the prevention of tooth decay; and
2. clear recommendations of efficacious dose and frequency of xylitol use.

Prospective studies at the University of Washington confirmed previous observations and retrospective studies and provide adequate evidence that:

1. the effective daily xylitol dose range is 6 to 10 g;
2. the effective frequency of consumption is 3 to 5 times per day; and
3. the effectiveness is greater at higher frequency of consumption as well as with a higher dose of xylitol.

There appears to be a ceiling effect, however, where effectiveness is not enhanced for xylitol dose beyond 10 g per day.

Xylitol's favorable side-effect profile, its benefits as a sugar substitute in other areas of health, and its potential to be widely acceptable to the general population add to its utility and applicability. Demand by consumers and dental professionals for less expensive xylitol-containing products should make it more accessible. Development of products and public health programs for delivering xylitol products routinely to high risk preschool populations should be seriously debated and implemented.

Acknowledgments

Work cited in this paper was supported in part by grants no. 1 P50 DE14254 and no. T32 DE07132 from the National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Md, and grant no. R40MC03622 from the Maternal and Child Health Bureau, Health Resources Services Administration, Rockville, Md.

References

1. Lindley MG, Birch GG, Khan R. Sweetness of sucrose and xylitol. Structural considerations. J Sci Food Agric 1976;27:140-144.
2. Tada K, Horiuchi J, Kanno T, Kobayashi M. Microbial xylitol production from corn cobs using Candida magnoliae. J Biosci Bioeng 2004;98:228-230.
3. Latif F, Rajoka MI. Production of ethanol and xylitol from corn cobs by yeasts. Bioresour Technol 2001;77:57-63.
4. Buhner J, Agblevor FA. Effect of detoxification of dilute-acid corn fiber hydrolysate on xylitol production. Appl Biochem Biotechnol 2004;119:13-30.
5. Dominguez JM, Gong CS, Tsao GT. Pretreatment of sugar cane bagasse hemicellulose hydrolysate for xylitol production by yeast. Appl Biochem Biotechnol 1996;57-58:49-56.
6. Santos JC, Pinto IR, Carvalho W, Mancilha IM, Felipe MG, Silva SS. Sugarcane bagasse as raw material and immobilization support for xylitol production. Appl Biochem Biotechnol 2005;121-124:673-683.
7. Forster H, Quadbeck R, Gottstein U. Metabolic tolerance to high doses of oral xylitol in human volunteers not previously adapted to xylitol. Int J Vitam Nutr Res 1982;22(suppl):67-88.
8. Akerblom HK, Koivukangas T, Puukka R, Mononen M. The tolerance of increasing amounts of dietary xylitol in children. Int J Vitam Nutr Res 1982;22(suppl):53-66.
9. Hayes C. The effect of noncariogenic sweeteners on the prevention of dental caries: A review of the evidence. J Dent Educ 2001;65:1106-1109.
10. Makinen KK, Hujoel PP, Bennett CA, Isokangas P, Isotupa K, Pape HR, Jr, et al. A descriptive report of the effects of a 16-month xylitol chewing-gum programme subsequent to a 40-month sucrose gum programme. Caries Res 1998;32:107-112.
11. Isokangas P. Xylitol chewing gum in caries prevention. A longitudinal study on Finnish school children. Proc Finn Dent Soc 1987;83(suppl 1):1-117.
12. Rekola M. Correlation between caries incidence and frequency of chewing gum sweetened with sucrose or xylitol. Proc Finn Dent Soc 1989;85:21-24.
13. Edgar WM. Sugar substitutes, chewing gum and dental caries—a review. Br Dent J 1998;184:29-32.
14. Trahan L, Bareil M, Gauthier L, Vadeboncoeur C. Transport and phosphorylation of xylitol by a fructose phosphotransferase system in Streptococcus mutans. Caries Res 1985;19:53-63.
15. Trahan L. Xylitol: a review of its action on mutans streptococci and dental plaque—its clinical significance. Int Dent J 1995;45(suppl 1):77-92.
16. Trahan L, Soderling E, Drean MF, Chevrier MC, Isokangas P. Effect of xylitol consumption on the plaque-saliva distribution of mutans streptococci and the occurrence and long-term survival of xylitol-resistant strains. J Dent Res 1992;71:1785-1791.
17. Milgrom P, Ly K, Roberts M, Rothen M, Mueller G. Mutans streptococci dose response to xylitol chewing gum. J Dent Res 2006;85:177-181.
18. Weinstein P, Harrison R, Benton T. Motivating parents to prevent caries in their young children: One-year findings. J Am Dent Assoc 2004;135:731-738.
19. Makinen KK, Bennett CA, Hujoel PP, Isokangas PJ, Isotupa KP, Pape HR, Jr, et al. Xylitol chewing gums and caries rates: A 40-month cohort study. J Dent Res 1995;74:1904-1913.
20. Kovari H, Pienihakkinen K, Alanen P. Use of xylitol chewing gum in daycare centers: A follow-up study in Savonlinna, Finland. Acta Odontol Scand 2003;61:367-370.
21. Alanen P, Holsti ML, Pienihakkinen K. Sealants and xylitol chewing gum are equal in caries prevention. Acta Odontol Scand 2000;58:279-284.
22. Alanen P, Isokangas P, Gutmann K. Xylitol candies in caries prevention: Results of a field study in Estonian children. Community Dent Oral Epidemiol 2000;28:218-224.
23. Lam M, Riedy CA, Coldwell SE, Milgrom P, Craig R. Children's acceptance of xylitol-based foods. Community Dent Oral Epidemiol 2000;28:97-101.
24. Sintes JL, Escalante C, Stewart B, McCool JJ, Garcia L, Volpe AR, et al. Enhanced anticaries efficacy of a 0.243% sodium fluoride/10% xylitol/silica dentifrice: 3-year clinical results. Am J Dent 1995;8:231-235.
25. Sintes JL, Elias-Boneta A, Stewart B, Volpe AR, Lovett J. Anticaries efficacy of a sodium monofluorophosphate dentifrice containing xylitol in a dicalcium phosphate dihydrate base. A 30-month caries clinical study in Costa Rica. Am J Dent 2002;15:215-219.

26. Jannesson L, Renvert S, Kjellsdotter P, Gaffar A, Nabi N, Birkhed D. Effect of a triclosan-containing toothpaste supplemented with 10% xylitol on mutans streptococci in saliva and dental plaque. A 6-month clinical study. Caries Res 2002;36:36-39.
27. Kohler B, Bratthall D, Krasse B. Preventive measures in mothers influence the establishment of the bacterium Streptococcus mutans in their infants. Arch Oral Biol 1983;28:225-231.
28. Hildebrandt GH, Sparks BS. Maintaining mutans streptococci suppression with xylitol chewing gum. J Am Dent Assoc 2000;131:909-916.
29. Isokangas P, Soderling E, Pienihakkinen K, Alanen P. Occurrence of dental decay in children after maternal consumption of xylitol chewing gum: A follow-up from 0 to 5 years of age. J Dent Res 2000;79:1885-1889.
30. Soderling E, Isokangas P, Pienihakkinen K, Tenovuo J, Alanen P. Influence of maternal xylitol consumption on mother-child transmission of mutans streptococci: 6-year follow-up. Caries Res 2001;35:173-177.
31. Soderling E, Isokangas P, Pienihakkinen K, Tenovuo J. Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants. J Dent Res 2000;79:882-887.
32. Brambilla E, Felloni A, Gagliani M, Malerba A, Garcia-Godoy F, Strohmenger L. Caries prevention during pregnancy: results of a 30-month study. J Am Dent Assoc 1998;129:871-877.
33. Wang YM, van Eys J. Nutritional significance of fructose and sugar alcohols. Annu Rev Nutr 1981;1:437-475.
34. Scheinin A, Makinen KK, Ylitalo K. Turku sugar studies. V. Final report on the effect of sucrose, fructose, and xylitol diets on the caries incidence in man. Acta Odontol Scand 1976;34:179-216.
35. Loesche WJ, Grossman NS, Earnest R, Corpron R. The effect of chewing xylitol gum on the plaque and saliva levels of Streptococcus mutans. J Am Dent Assoc 1984;108:587-592.
36. Kandelman D, Gagnon G. A 24-month clinical study of the incidence and progression of dental caries in relation to consumption of chewing gum containing xylitol in school preventive programs. J Dent Res 1990;69:1771-1775.
37. Kandelman D, Bar A, Hefti A. Collaborative WHO xylitol field study in French Polynesia. I. Baseline prevalence and 32-month caries increment. Caries Res 1988;22:55-62.
38. Isokangas P, Alanen P, Tiekso J, Makinen KK. Xylitol chewing gum in caries prevention: A field study in children. J Am Dent Assoc 1988;117:315-320.
39. Wennerholm K, Arends J, Birkhed D, Ruben J, Emilson CG, Dijkman AG. Effect of xylitol and sorbitol in chewing gums on mutans streptococci, plaque pH, and mineral loss of enamel. Caries Res 1994;28:48-54.
40. Makinen KK, Hujoel PP, Bennett CA, Isotupa KP, Makinen PL, Allen P. Polyol chewing gums and caries rates in primary dentition: A 24-month cohort study. Caries Res 1996;30:408-417.
41. Makinen KK, Chen CY, Makinen PL, Bennett CA, Isokangas PJ, Isotupa KP, et al. Properties of whole saliva and dental plaque in relation to 40-month consumption of chewing gums containing xylitol, sorbitol, or sucrose. Caries Res 1996;30:180-188.
42. Thaweboon S, Thaweboon B, Soo-Ampon S. The effect of xylitol chewing gum on mutans streptococci in saliva and dental plaque. Southeast Asian J Trop Med Public Health 2004;35:1024-1027.