Noncariogenic Sweeteners: Sugar Substitutes for Caries Control

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ABSTRACT
The evidence is clear that the incidence of dental caries is related to the frequency of eating sugar. The use of sugar substitutes is a suggested way of reducing sugar intake. A variety of noncariogenic sweeteners exists, but most have no practical value for caries control because of their technical or safety problems, taste, or cost. Urinary bladder tumorigenic effects have been reported in experimental animals treated with saccharin and cyclamates. Because of concerns for human safety, cyclamates were banned in the U.S., and saccharin use was permitted only by special legislation. The polyalcohols sorbitol and xylitol are important sugar substitutes since they are not efficient substrates for plaque bacteria and therefore produce only minimal plaque pH drop.

Aspartame, with its sugar-like taste, is an excellent low-calorie sweetener now used in over 100 products under the name NutraSweet. Consumption of aspartame by normal humans is safe and does not promote tooth decay. Individuals with a need to control their phenylalanine intake should handle aspartame like any other source of phenylalanine.

INTRODUCTION
It is apparent that sugar has a profound effect on the development of dental decay. A diet high in sugar is undesirable for overweight persons and dangerous for diabetics. No study has shown that sugar consumption improves or even supports health. However, because of its taste, availability, and low cost, it is difficult to exclude sugar from our diets. In Western nations it accounts for one-sixth or more of total caloric intake.¹

The urge to eat sweets is a basic biologic drive. Many animals respond positively to sweet substances. Studies show that human newborns prefer sugar-flavored water over plain water.² Even a 4-month-old fetus responds to alterations in the sweetness of the amniotic fluid by increasing its rate of swallowing.³

The proclivity for sweets is reinforced by the communications media, by peer pressure, and by family food habits. Sweetness is the taste that is strongly identified with affection and reward. It seems unlikely that a fear of dental decay will lead consumers to deny themselves any significant amount of sugar.

The word sugar is generally used to mean refined sucrose, the most common carbohydrate in the diet. Other sugars found in average diets include glucose, fructose, galactose, and maltose. The difference between sucrose and the other sugars is that most of the sucrose consumed is added to foodstuffs, while the others occur predominantly naturally in various foods. Recently, corn syrup (high fructose and high glucose) is being substituted more and more for sucrose in commercial food preparation.

DIET AND DENTAL CARIES
Tooth decay is a food dependent disease. Unequivocal evidence from epidemiological investigations⁴ and experiments with animals⁵,⁶ show that the incidence and prevalence of dental caries are related to the frequency of ingesting fermentable carbohydrates. These studies indicate a close relationship between caries attack rates and the...
frequency of eating various sugars. The relationship of caries to the amount of sugar consumed is more distant.7

A controlled study on adult inmates was conducted at a Swedish asylum in Vipeholm.8 The results demonstrated increased cariogenicity if retentive carbohydrates are consumed frequently between meals. The form and frequency of the carbohydrates were critical factors. Similar observations were made at Hopewood House in Australia.9 Children residing at this institution were fed sugar-restricted diets and developed substantially fewer carious lesions than those who had unrestricted access to sugar-containing items.

Sugar's role in the pathogenesis of dental caries can be further substantiated. For example, low caries rates have been reported in diabetic children, and fructose-intolerant persons are virtually caries-free.10-11 People suffering from these genetic defects learn to avoid eating sugar. Studies on animals point out that the carious process is not stimulated when carbohydrates are eliminated from the diet. Rats receiving a cariogenic diet by gastric intubation remained caries-free, while those receiving sugar orally developed substantial levels of caries.12

Controversy exists over the relative cariogenicity of the different sugars. Although animal13-15 and human experiments16 do suggest that sucrose is more cariogenic than other sugars, the results are not all in agreement and are probably valid only in experimental conditions in which only one sugar was in each diet. A cautious conclusion is that all the common sugars are cariogenic but that sucrose can, in some conditions, be more so than the other sugars.17

DIETARY COUNSELING

Over the years several clinicians have devised techniques and procedures to change dietary practices. Forty years ago, Jay began using a dietary approach to caries control in Michigan.18 He recommended restricting or eliminating dietary carbohydrate intake in caries-susceptible patients and monitoring compliance with Lactobacillus counts. A few years later, Becks implemented a similar diet supervision program in California.19 Few patients, however, were able to maintain the rigid diets they advocated.

Today, most dental offices that incorporate dietary programs in their preventive practices emphasize a limit on the intake of sugar-containing foods, especially between meals;19 however, few people are sufficiently motivated by dental health considerations to voluntarily forego the pleasure of eating and drinking sweet substances. Herein lies the importance of sugar substitutes in aiding dental health, enabling sugar intake to be reduced without hardship, and shifting part of the responsibility for improving dental health away from the consumer and onto the food manufacturer.20

SUGAR SUBSTITUTES

The search for a sugar substitute was originally a response to the needs of diabetic patients, but replacing sugar is difficult. It involves economic and industrial considerations, palatability, and consistency, as well as health and safety factors. There are several sugar substitutes now being used in place of sucrose. This paper gives information on the status of the most common sugar substitutes. These are saccharin, cyclamates, sorbitol, xylitol, and aspartame.

Saccharin

Saccharin is an organic compound chemically identified as 0-sulfobenzimide. Discovered a century ago, saccharin was first used as an antiseptic or food preservative and later as a sweetening agent for diabetics.21 Saccharin has a reported sweetness 300 times that of sucrose.22 It evokes a sweet sensation at dilutions of 1 to 100,000. Increased concentration does not enhance its sweetness and it tends to taste better at concentrations in excess of 1 to 1,000.21

Saccharin has a short-lasting sweetness, which is followed by a slight aftertaste. People who are sensitive to this aftertaste note that it is bitter or metallic.23 Saccharin has no caloric value and because it is readily soluble, it is used mainly in its sodium form. Saccharin is compatible with most food and drug ingredients, is stable in aqueous solution and under most conditions of food preparation and processing.

Saccharin is manufactured from petroleum derivatives and is only 3% as costly as sucrose at equivalent sweetness.24 About 70% of the total amount used in the U.S. has been used in diet soft drinks, 13% in dietetic foods, 12% in products sold at retail for table use, and the remaining 5% in miscellaneous products such as toothpastes, mouthwashes, cosmetics, and medicinal preparations. Saccharin is excreted unchanged, with little evidence of metabolism to other products. Seventy to ninety percent is excreted in the urine.

Since saccharin was introduced commercially around 1900, its safety has been questioned repeatedly. Studies linking saccharin to bladder cancer in male rats began to appear in the 1970s.25-30 In 1977 the Food and Drug Administration (FDA) proposed a saccharin ban.31 However, every two years, Congress has voted to extend a moratorium on the ban and recent major studies have failed to confirm a link between saccharin and cancer.32

The consensus among scientists involved in evaluating the conflicting reports concerning saccharin use is the following: Any use of saccharin by non diabetic children or pregnant women, heavy use by young women of child-bearing age, and excessive use by anyone is ill-advised.33 Saccharin may be noncariogenic (or even cariostatic). Growth of S. mutans is inhibited by saccharin.34,35 The addition of saccharin to a cariogenic diet reduces the incidence of caries in rats.36 No controlled clinical studies on caries-inhibitory effects on human caries are available.

Cyclamate

Cyclamates are cyclic organic compounds chemically known as N-cyclohexylsulphamic acid. Discovered in 1937, cycla-
Sorbitol

Sorbitol is an alcohol derivative of glucose and is classified as a polyhydric alcohol. First isolated in 1872, sorbitol is found naturally in many types of fruits and berries, and in seaweeds and algae. Normally it is formed by hydrolysis of glucose. Sorbitol, having a relative sweetness of about half that of sucrose, is usually supplemented by noncaloric sweeteners, especially saccharin. It is not broken down by cooking temperatures and no carmelization occurs when it is used in food preparation.

Sorbitol is relatively inexpensive. It is frequently an ingredient of sugarless gum in concentrations of 20%-50% with mannitol, another sugar alcohol used in the same concentration. Many commercial candies sweetened with sugar also contain up to 10% sorbitol as a moistening or texturizing agent. Some sugarless gums and candies are sweetened entirely by sorbitol and synthetic sweeteners. Sorbitol as a 70% solution is added as a humectant in paste-type dentifrice formulations. World production of sorbitol was about 250,000 tons per year in the beginning of the 1970s and has increased considerably since then. About one-third is used in foods. This amount is negligible compared to sugar consumption and production.

Sorbitol is as caloric as sucrose. It has no known toxic effects, although ingestion of more than 35g-40g may cause osmotic diarrhea. For this reason, WHO recommends that the daily intake of sorbitol be limited to 150mg/kg. Seventy to ninety percent of ingested sorbitol is absorbed and metabolized to glucose in the body. Orally administered, sorbitol is used efficiently by the liver. Diabetics tolerate dietary sorbitol with no change in blood glucose level or glycosuria.

Most strains of the caries-inducing S. mutans will ferment sorbitol to give a final pH below 5.0. The loss of tooth mineral during caries formation is caused by the formation of bacterial acids which lower the pH of the plaque fluid to the point where the hydroxyapatite mineral of enamel dissolves. At pH values in the range from 5 to 6, with an average of 5.6, the plaque fluid no longer has a saturation index with respect to calcium and phosphate ions, thereby permitting hydroxyapatite to dissolve.

Sorbitol is not readily fermented by other oral microorganisms and when mixed oral flora from plaque or saliva are

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incubated with sorbitol, fermentation occurs very slowly.\textsuperscript{53} The application of sorbitol to dental plaque in situ or in vitro results in little alteration in the plaque pH, whereas most sugars cause a dramatic and rapid drop in the plaque pH.\textsuperscript{54} Apparently, sorbitol does not appreciably decrease plaque pH because the rate of sorbitol fermentation by \textit{S. mutans} is much slower than that of other fermentable mono- and disaccharides. This allows salivary buffers to neutralize acid end products as they are formed.\textsuperscript{55} Prolonged ingestion of sorbitol by monkeys or humans does not lead to the development of a flora with enhanced ability to ferment sorbitol.\textsuperscript{56,57} All the evidence indicates that sorbitol has negligible caries activity in animals and humans.

\textbf{Xylitol}

Xylitol, a pentose alcohol, has been known chemically at least since the 1890s. Virtually all plant materials appear to contain xylitol. The richest natural resources seem to be plums, strawberries, raspberries, cauliflower, and endive. Commercially, xylitol has mainly been produced by hydrogenation of D-xylose obtained from prehydrolysis of various xylan-containing plant materials (birchwood, cottonseed hulls, and coconut shells). Present world production of xylitol is estimated at several hundred tons per year.\textsuperscript{48} Xylitol costs about ten times as much as sucrose. Xylitol was first used in parenteral nutrition. Because it is largely metabolized independent of insulin, it was subsequently used as a sweetener in diets for diabetics. Its high endothermic heat of solution gives xylitol a pleasing, cool taste. Many of its properties, such as sweetness, appearance, and caloric density, are the same as sucrose.\textsuperscript{58} It is well suited to various food-manufacturing processes and can be substituted for sucrose in most cooked foods, for which it provides similar bulk and textural qualities. Xylitol has been used in chewing gum, candies, fruit lozenges, and dentifrices.

Xylitol appears to be safe for consumption.\textsuperscript{59} In Turku, Finland, biochemical investigations of its potential toxic effects were conducted and none were found.\textsuperscript{16} Recently, its use was questioned when an increased incidence of bladder stones and tumors was observed in mice fed large amounts of xylitol.\textsuperscript{60} Because of this, some chewing gums containing this sweetener were voluntarily withdrawn from the market by their manufacturers. Xylitol is a normal intermediary in human metabolism. Oral administration is followed by efficient uptake by the liver. In some unadapted subjects, enteral xylitol may cause transient osmotic diarrhea in dosages of 0.5 g (kg/day). Most unadapted adults can consume 30-60 g per day and not experience the laxative effect. In some cases, adaptation to doses of 200-400 g daily has been reported.\textsuperscript{61}

The dental health effects of xylitol have been studied extensively in man and in animals.\textsuperscript{16,62,63} Xylitol is not fermented nor utilized by microorganisms closely associated with dental caries formation.\textsuperscript{21} Results of a two-year clinical study conducted in Finland showed that xylitol is nontoxicogenic in humans.\textsuperscript{61} Studies conducted in humans and animals indicate that xylitol may possess cariostatic properties; however, this has not been confirmed.\textsuperscript{63} Prolonged use of xylitol in the absence of other sugars leads to remineralization of incipient carious lesions.

\textbf{Aspartame}

Aspartame, a dipeptide, was discovered accidentally in the laboratories of G.D. Searle in 1965. Although the components of aspartame are widely distributed in the food supply, the particular combination of amino acids and a methyl ester do not occur naturally, so it has both natural and synthetic characteristics. Aspartame has a sugar-like taste and a potency 120 to 280 times that of table sugar depending upon the food system in which it is used.\textsuperscript{64} It has no undesirable aftertaste and like sugar, provides approximately 4 calories per gram; however, if it is used as a sweetener in place of sugar, the amount needed to yield equivalent sweetness will provide only 100 of the calories of sugar. Aspartame functions as a flavor enhancer and flavor extender, and under the trade name NutraSweet, is now being used in over 100 products, including soft drinks, chewing gum, presweetened cereal, and cocoa mixes. It is also available in tabletop form (Equal) for home use.

Aspartame has limited stability in solution, especially in non-acid conditions, and it loses its sweetness at temperatures used for cooking. Aspartame also does not provide the bulk and structure of sucrose.\textsuperscript{65} Its biggest drawback is that it is about 20 times more expensive than saccharin.

Aspartame has been described as one of the most thoroughly tested and studied additives approved by the FDA. Over 100 safety studies were conducted prior to approval. These include metabolism, pharmacology, toxicology, teratology, mutagenicity, and clinical studies. Aspartame was approved briefly in 1974.\textsuperscript{65} The FDA quickly withdrew its approval because one study by Searle suggested that aspartame might cause brain damage.\textsuperscript{66} Questions about its safety and the validity of Searle's research on the product since have been adequately answered, and in 1981, aspartame received approval for use in dry form.\textsuperscript{67} In 1983, approval was granted for aspartame's use in carbonated beverages.\textsuperscript{68} In approving its use in carbonated beverages, the FDA commissioner concluded that the maximum projected consumption of aspartame from foods and beverages by normal children and adults was far below any level even suspected of being toxic.\textsuperscript{69}

Aspartame appears safe for lactating women and is well tolerated by persons with diabetes.\textsuperscript{70-71} In addition, aspartame ingestion is not associated with serious adverse health effects.\textsuperscript{72} Recently, the Centers for Disease Control, at the request of the FDA, evaluated complaints the FDA had received from consumers with respect to consumption of products containing aspartame. Following interviews with 517 complainants, the Centers for Disease Control reported "although some individuals may have an unusual sensitivity to aspartame products, the data obtained do not provide..."
evidence for the existence of serious, widespread, adverse health consequences attendant to the use of aspartame."

Aspartame is metabolized as its three subcomponents, aspartic acid, phenylalanine, and methanol, which are normal dietary constituents. Individuals with phenylketonuria (PKU) must consider the phenylalanine content of aspartame. Phenylketonuria is a hereditary disease characterized by the inability to properly metabolize phenylalanine, an essential amino acid found in protein foods. In the U.S. this condition occurs in approximately 1 to 16,000 live births and if not treated can lead to irreversible mental retardation. Damage can be avoided by early diagnosis and rigid adherence to a phenylalanine-free diet.

Since aspartame is not a carbohydrate, it does not promote tooth decay. The American Dental Association has issued a statement supporting the approval of aspartame. A study conducted by the National Institute of Dental Research determined that aspartame was noncariogenic in laboratory animals. Of course some products sweetened with NutraSweet may also contain other ingredients that could cause cavities.

CONCLUSION

Patients will reduce their risk of dental caries if they consume soft drinks, bakery products, and other sweet between-meal snacks made with noncariogenic sweeteners instead of items made with sugar. Due to cost, taste, technical, and safety reasons, current sugar substitutes do not have equal application to all products.

Cyclamates were banned in 1970 because they were found to cause bladder cancer in rats. Saccharin has a metallic aftertaste, and products containing saccharin are required by law to carry warning labels stating that saccharin has been shown to cause cancer in laboratory animals. Sugarless gums and candies are available in which sugar has been completely replaced by sorbitol. These sugarless gums could cause cavities.

When aspartame replaces sugar, it provides a dental health advantage.

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