Food sugar substitutes: a brief review for dental clinicians

Michael W. Roberts* / J. Timothy Wright**

The frequent ingestion of fermentable sugars such as sucrose, fructose, glucose and maltose is conducive to the development of caries in the teeth of susceptible individuals. Natural and artificial alternatives to these sugars have been and continue to be developed as non/low-caloric sweeteners. The US Food and Drug Administration have approved four non-caloric sweeteners at present. However, there are several other non-caloric sweeteners being commonly used in other countries. A review of these sweeteners is provided with information on a promising new agent that has not yet gained FDA approval.
J Clin Pediatr Dent 27(1): 1-4, 2002

INTRODUCTION

The importance of diet in the development of caries was suspected in antiquity and established in modern times.[1-3] The process has been shown to be multifactorial in nature, but it has been generally accepted that sugars in the diet are a major contributor to the disease.[4] The retention and exposure frequency of fermentable carbohydrates to the teeth is an important consideration when evaluating the cariogenicity of food substances.[5] Fermentable carbohydrates include sugars or cooked starches that can be degraded into acids by the oral bacteria. There is substantial evidence to implicate sugars such as sucrose, glucose, fructose, maltose and all fermentable carbohydrates as principle dietary substances in caries formation.[6-10] Sucrose is the most common sugar added to beverages and food products. Consumption in developed countries is reported to be 40 to 60 kg/person/year,[11] Figure 1.

In recognition of the caries potential of sucrose, investigators have searched for alternative sweeteners. The ideal agent would provide sweetness, but with no unpleasant after-taste, have little or no calories, not be carcinogenic or mutagenic, be economical to produce, and would not be degraded by heat when cooked. Identification of such a product has been challenging. Although several non-nutritive sweetening agents have been marketed in the United States (US), none have possessed all of the preferred properties.

Dentists are often asked questions relative to specific sugars in food and sugar substitutes. The purpose of this brief review is to provide information that can be of value to the practicing dentist when counseling their patients regarding diet and caries prevention.

SWEETENERS

FDA approved sweeteners

The only US Food and Drug Administration (FDA) approved noncaloric sweeteners to date are aspartame, acesulfame potassium, saccharin and sucrolose,[12] Figure 2.

Aspartame

Aspartame, sold under the brand names of Nutrasweet and Equal, is a dipeptide methyl ester, discovered in 1965 and is approximately 200 times sweeter than sucrose.[13] Aspartame was approved in 1981 for limited use as a sweetener in the US, and extended to a larger market in 1983. Aspartame is the most widely used non-cariogenic artificial sweetener. Its primary use is in diet soft drinks, yogurt, puddings, gelatin and snack foods.[14] Aspartame has been shown to have a protective effect against some mycotoxins and is claimed to be safe for use by type 2 diabetics. Mycotoxins are toxic metabolic products of some fungi and can result in mycotoxicosis in humans. Mycotoxins can be found in contaminated cereals and foods obtained from animals, that ingested a mycotoxin contained diet.[15] Oral ingestion of 6mg/kg of aspartame has been reported to reduce the number of sickled cells in the blood of patients with homogenous sickle cell anemia.[16]

The approval of aspartame by the FDA was not without dissenting opinions and there have been concerns raised relative to toxic affects on growth, glucose homeostasis, and liver functions with long term usage.[17-21] People with

* Send all correspondence to Michael W. Roberts, DDS, MScD, Professor and Chair, Department of Pediatric Dentistry, University of North Carolina School of Dentistry, 228 Brauer Hall, CB# 7450, Chapel Hill, NC 27599-7450.

** J. Timothy Wright, DDS, MS Professor, Department of Pediatric Dentistry, University of North Carolina School of Dentistry, 228 Brauer Hall, CB# 7450, Chapel Hill, NC 27599-7450.

Voice: (919) 966-2739
Fax: (919) 966-7992
E-mail: Mike_Roberts@dentistry.unc.edu

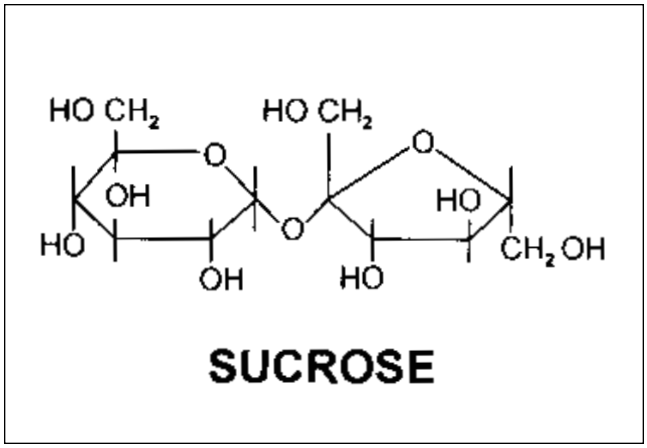

Figure 1. Chemical structure of sucrose

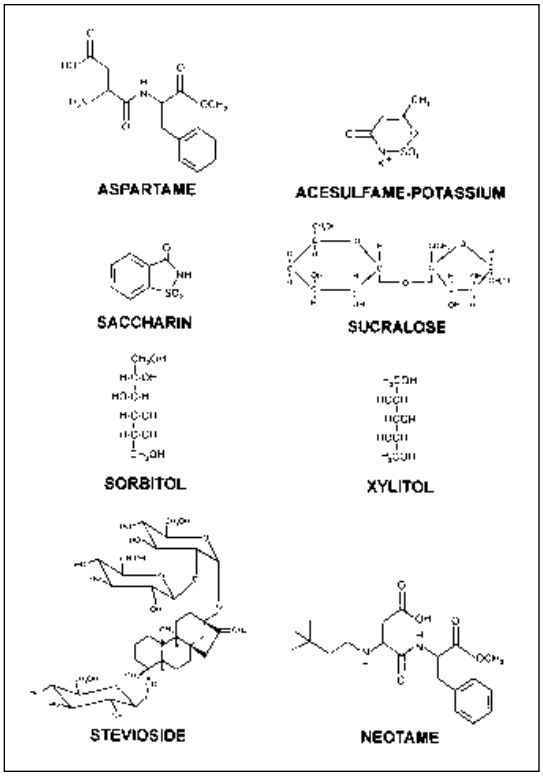

Figure 2. Chemical structure of non-caloric sweeteners

phenylketonuria should avoid aspartame as they cannot metabolize phenylalanine, a component of aspartame.

Acesulfame potassium

Acesulfame potassium, a non-nutritive product, was approved by the FDA in 1988 for use as a sweetener in dry food products. In 1994 yogurt, refrigerated desserts, syrups and baked goods were added to the approved list. The use of acesulfame potassium is approved for use in foods, beverages, cosmetics and pharmaceutical in more that 30 countries. Although considered safe for consumption by humans there have been some health issues raised relative to dose-dependent cytogenetic toxicity.[14,22]

Saccharin

Saccharin is 200 to 500 times sweeter than sucrose and is the oldest of the artificial sweeteners used in the United States. It is non-cariogenic and non-caloric and is available in liquid and tablet form as a table-top sweetener but has a slightly bitter after-taste. In 1970 saccharin was identified as a potential bladder carcinogen. A warning label is required on all food products in the US that contain saccharin.[14]

Sucrolose

Sucrolose is a non-nutritive, non-caloric trichiorinated derivative of sucrose. It is not metabolized by the body and it has been shown to be non-cariogenic.[23] Sucrolose is widely used throughout the world in many food products such as such as tea and coffee sweetener, carbonated and non-carbonated beverages, baked goods, chewing gum and frozen desserts. No health concerns have been reported with sucrolose.[24,25]

Other sweetner agents

Sorbitol

Sorbitol is a sugar alcohol that occurs naturally in many fruits and berries. It is produced commercially from glucose, but is expensive to manufacture. Sorbitol is often used as a "bulk" sweetener in a variety of food substances such as chewing gum, chocolates, and confectioneries. It is half as sweet as sucrose and is considered non-cariogenic, although in solution it can be fermented slowly by mutans streptococci. Sorbitol has been shown to be cariogenic with prolonged use by patients with reduced salivary gland function.[26] Sorbitol is not easily metabolized or absorbed from the gastrointestinal tract and can cause diarrhea if ingested in large quantities.

Xylitol

Xylitol was discovered in wood chips in 1890 and in wheat and oat straw in 1891.[28] It is a non-fermentable, pleasant tasting, non-cariogenic polyol derived from pentose sugar xylose and is relatively expensive to manufacture.[29] Xylitol is as sweet as sucrose and was approved as safe for use in humans in 1986. It is used primarily in chewing gum and possesses approximately the same sweetness potency as sucrose. Studies have suggested that the regular use of xylitol containing chewing gum reduces the amount of dental plaque as well as increase saliva flow. A significant reduction in caries incidence has been reported in caries active age-groups when xylitol containing gum was chewed regularly.[30,31] Recently, xylitol has been credited in reducing the transmission of cariogenic bacteria from mother to infant and has been shown to have bacteriocidal qualities.[32-34] The FDA has not yet approved additional uses

of xylitol as a sweetener. However, numerous European studies have established the safety for human consumption. An additional reported benefit of chewing gum containing xylitol is reduced ear infection in young children at day-care centers.[35]

Stevia

Stevia is a natural occurring, heat stable sweetener, which is extracted from *Stevia rebaudiana* Bertoni, a member of the chrysanthemum family.[36] The active ingredient, stevioside, is a white crystalline material that contains three glucose molecules and steviol, a ditepenic carboxylic alcohol, Figure 2. Its sweetness potency is 100 to 300 times greater than sucrose. Stevia is calorie-free, non-cariogenic and has been used by the indigenous peoples of Paraguay for centuries as a sweetener.[37,38] It is widely used commercially in Brazil and Japan, and to a lesser extent in China, Germany, Malaysia and Israel, for more than 20 years as a sweetener in many food categories.[12] In 1995, the FDA approved the importation and use of stevia as *dietary supplement,* but not as a sweetener. The argument to include stevia as a *food additive* has become deeply politicized in the US. Commercial companies have been discouraged in fronting the necessary expenses to challenge the FDA on this approval distinction since stevia is a herb and not a patentable pharmaceutical product.[39]

A weak estrogenic effect, similar to that associated with *soy* beans, has been reported with the chronic ingestion of an aqueous extract of *Stevia rebaudiana* Bertoni. It has been suggested that this could act as a weak male contraceptive agent.[40] This affect was not found when the sweetening agent, stevioside, was extracted from the whole leaves and tested.[41] Stevia has been shown to be safe for use by diabetics and it has a mild antihypertensive quality in humans.[42,43] It has not been found to be mutagenic.[44]

Neotame

Neotame is a new product being developed commercially by the NutraSweet Company, a subsidiary of Mansanto Chemical-Mt. Prospect, IL. It is very similar in chemical structure to aspartame, Figure 2. Neotame is a highly intensity sweetener reported to have a clean taste with no unpleasant characteristics. It has sweetness potency 6000 to 9000 greater than sucrose and is reported to be heat stable in baking applications. Similar to other sweeteners the potency of neotame may vary depending upon the food or how it is used.[45] Neotame is reported to be functional and stable in carbonated soft drinks, powdered soft drinks, yellow cake, yogurt and hot-packed still drinks.[46]

Neotame has been submitted to the FDA for consideration as a new sweetener in several food categories. However, it has not yet been approved.[47]

DISCUSSION

The dentist often has the opportunity to provide advice regarding the importance of diet and the role of sugars in caries formation. As such, the dentist must have a familiarization with alternatives to sugar and the types of food products that are available with substitute sweetening agents.

It is difficult to avoid sugar in the diet as it is an added ingredient to enhance the taste of many processed foods. However, reducing the amount and exposure to sugar in the diet of humans, especially children, is an important consideration in preventing caries.[48] Non-cariogenic sweeteners offer an alternative to sugar if used in moderation. The identification of new safe, palatable, heat stable, non- or low-caloric sweetener substitutes for the more cariogenic sugars such as sucrose, glucose, fructose and maltose continue to be actively sought for use in the food industry.

REFERENCES

1. Jensen ME. Diet and dental caries. Dent Clin North Am 43: 615-633, 1999.
2. Gustfsson BE, Wuensel CE, Lanke LS, et al. The Vipeholm dental caries study. The effect of different levels of carbohydrate intake on caries activity in 436 individuals observed for 5 years. Acta Odontol Scand 11: 232-364, 1954.
3. Sheinin A, Makinen KK. Turku sugar studies: an overview. Acta Odontol Scand 34: 405-408, 1976.
4. Harel-Raviv N, Laskaris H, Chu KS. Dental caries and sugar consumption into the 21st century. Am J Dent 9: 184-190, 1996.
5. Holt RD. Foods and drinks at 4 daily time intervals in a group of young children. Br Dent J 170: 137-143, 1991.
6. Rugg-Gunn AJ. Diet and dental caries. In The Prevention of dental diseases, 2nd Ed. J.J. Murray Ed, Oxford, Oxford University Press, pp 4-114, 1989.
7. Scheinin A, Makinen KK. Turku sugar studies I-XXI. Acta Odontol Scand 33 (Suppl 70): 1-349, 1975.
8. Koulourides T, Bodden R, Keller S, et al: Cariogenicity of nine sugars tested with an intraoral device in man. Caries Res 10: 427-441, 1976.
9. Kandelman D. Sugar, alternative sweeteners and meal frequency in relation to caries prevention: new perspectives. Br J Nutr, 77 (Suppl 1): S121-128, 1997.
10. Sreebny L. Sugar and human dental caries. World Rev Nutr Diet 40: 19-65, 1982.
11. Burt BA. Relative consumption of sucrose and other sugars: has it been a factor in reduced caries experience? Caries Res 27 (Suppl 1): 56-63, 1993.
12. Nabors LO, Gelardi RC. Alternative sweeteners. 2 Ed. New York, Marcel Dekker, Inc., pp 1-450, 1991.
13. Walters DE, Prakash I, Desal N. Active conformations of neotame and other high-potency sweeteners. J Med Chem 43: 1243-1245, 2000.
14. Kingborn AD, Kaneda N, Baek N-I, et al. Noncariogenic intense natural sweeteners. Med Res Rev 18: 347-360, 1998.
15. Galvano F, Piva A, Ritieni AL, et al. Dietary strategies to counteract the effects of mycotoxins: a review. J Food Prot 64: 120-131, 2001.
16. Manion CV, Howard J, Ogle B, et al. Aspartame effect in sickle cell anemia. Clin Pharmacol Ther 69: 346-355, 2001.
17. Goerss AL, Wagner GC, Hill WL. Acute effects of aspartame on aggression and neurochemistry of rats. Life Sc 67: 1325-1329, 2000.
18. Stoddard M. Deadly deception: story of aspartame. Dallas, Oderlwald Press (http://web2.airmai1.net/net/marystod/), pp 1-250, 1998.
19. Wurtman R. Neurochemical changes following high-dose aspartase with dietary carbohydrates. New Engl J Med 389: 429-430, 1983.

20. Wurtman RJ. Aspartame: possible effect on seizure susceptibility. Lancet 2: 1060, 1985.
21. Olney JW, Faber NB, Spitznagel E, et al. Increasing brain tumor rates: is there a link to aspartame. J Neuropatho Exp Neurol 55: 1115-1123, 1996.
22. Mukherjee A, Chakrabarti J. *In vivo* cytogenetic studies on mice exposed to acesulfame-K, a non-nutritive sweetener. Food Chem Toxicol 35: 1177-1179, 1997.
23. Steinberg L. Effect of sucralose in coffee on plaque pH in human subjects. Caries Res 30: 138-142, 1996.
24. Federal Register 63: 16417, April 3, 1998.
25. Grice HC, Goldsmith LA. Sucralose-an overview of the toxicity data. Food Chem Toxicol 38 (Suppl 2): S1-S6, 2000.
26. Wennerhoim K, Arends J, Birkhed D, et al. Effect of xylitol and sorbitol in chewing-gums on mutans streptococci, plaque pH and mineral loss of enamel. Caries Res 28: 48-54, 1994.
27. Weil A. Natural health, Natural medicine, Boston-New York, Houghton Mifflin Company, p 50, 1995.
28. Bertrand MG. Recherchescur quelques derives du xylose. Bull Soc Chim Paris 5: 554-557, 1891.
29. Fischer E, Stahel R. Zur kenntnis der xylose. Ber Dtsch Chem Ges 24: 528-539, 1891.
30. Isokangas P, Alanen P, Tiekso J et al. Xylitol chewing gum in caries prevention: a field study in children. J A D A 117: 315—320, 1988.
31. Makinen KK, Bennett CA, Hujoel PP, et al. Xylitol chewing gum and caries rate: a 40 month cohort study. J Dent Res 74: 1904-13, 1995.
32. Makinen KK, Makinen PL, Paper HR, et al. Conclusion and review of the Michigan xylitol program (1986-1995) for the prevention of dental caries. Int Dent J 46: 22-34, 1996.
33. Makinen KK. The rocky road of xylitol to its clinical application. J Dent Res 79: 1352-1355, 2000.
34. Makinen KK, Isotupa KP, Kivilompolo T, et al. Comparison of erythritol and xylitol saliva stimulants in the control of dental plaque and mutans streptococci. Caries Res 35: 129-135, 2001.
35. Uhari N, Kontiokari T, Koskela H, et al. Xylitol chewing gum in prevention of acute otitis media: double blind randomized trial. Brit Med J 313: 1180-1184, 1996.
36. Cardello HMAB, Da Silva MAPA, Damaslo MI!. Measurement of the relative sweetness of stevia extract, aspartame and cyclamate/saccharin blend *as* compared to sucrose at different concentrations. Plant Foods Hum Nutr 54: 119-130, 1999.
37. Elkins R. Stevia: nature's sweetener. Pleasant Grove, UT: Woodland Publishing, pp 7-10, 1997.
38. Das S, Das AX, Murphy RA, et al. Evaluation of the cariogenic potential of the intense natural sweeteners stevioside and rebaudioside A. Caries Res 26: 363-366, 1992.
39. Bonvie L, Bonvie B, Gates D. The stevia story. Atlanta, Body Ecology, BED publications, p 5, 1997.
40. Melis J. Effects of chronic administration of *Stevia rebaucliana* on fertility of rats. J Ethnopharmacol 67: 157-161, 1999.
41. Suttajit N, Vinitketkaumnuen U, Meevatee U, et al. Mutagenicity and human chromosomal effect of stevioside, a sweetener from *Stevia rebaucliana* Bertoni. Environ Health Perspect Suppl 101(Suppl 3): 53-56, 1993.
42. Chan P, Tomlinson B, Chen Y-J, et al. A double-blind placebo-controlled study of the effectiveness and tolerability of oral stevioside in human hypertension. Br J Clin Pharmacol 50: 215-220, 2000.
43. Boeckh EMA, Humboldt G. Efeitos cardiocirculatoris do extrato aquoso total de s. rebaudiana en individuos normais e do esteviosideo em ratos. Ciencia e Cultura 32: 208-291, 1981
44. Matsui M, Matsui K, Kawasaki Y et al. Evaluation of the genotoxicity of stevioside and steviol using invitro and one *in vivo* mutagenic assays. Mutagenesis 11: 573-579, 1996.
45. Prakash I, Bishay IE, Desai N, et al. Modifying the temporal profile of the high-potency sweetener neotame. J Agric Food Chem 49: 786-789, 2001.
46. Witt J. Discovery and development of neotame. World Rev Nutr Diet 85: 52-57, 1999.
47. Garbow JR, Likos JJ, Schroeder SA. Structure, dynamics, and stability of β-cyclodextrin inclusion complexes of aspartame and neotame. J Agric Food Chem 49: 2053-2060, 2001.
48. Moynihan PJ. Update on the nomenclature of carbohydrates and their dental effects. J Dent 26: 209-218, 1998.