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OBJECTIVES FOR REVIEW OF PRESENT AND FUTURE USE OF NONNUTRITIVE SWEETENERS

Upon completion of this paper, the reader will be able to:

1. *list at least two nonnutritive sweeteners that are approved for use by persons with diabetes mellitus;*
2. *counsel patients with IDDM and NIDDM about the safety and recommended intake of nonnutritive sweeteners;*
3. *counsel select groups (particularly children and pregnant and lactating women), about the safety and recommended intake of nonnutritive sweeteners;*
4. *list sweeteners pending approval and potential future sweeteners;*
5. *describe current and potential applications of sweeteners in commercial products and in various methods of food preparation;*
6. *use additional resources to study and evaluate present and future products.*

Review of Present and Future Use of Nonnutritive Sweeteners

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In response to growing consumer demand for better tasting, low-calorie, sugar-free food products, the number of food items containing nonnutritive sweeteners has grown markedly in recent years. In this paper, present sweetener consumption is reviewed; the history, properties, uses, advantages, and safety of approved sweeteners such as saccharin, aspartame, and acesulfame-K are presented, as well as those of sweeteners such as cyclamate, sucralose, and alitame that are awaiting FDA approval; the role of sweeteners in the dietary management of persons with diabetes is discussed; and counseling guidelines for safe consumption are given.

Research has shown that people have an inborn desire for sweet taste. Studies in newborns and adults have demonstrated that the pleasant response to sweet solutions is a reflex, innate reaction rather than a learned response.[1] Since it was first refined some 600 years ago, table sugar (sucrose) has been the sweetener of general use.[2]

The two basic categories of sweeteners are nutritive, or caloric, and nonnutritive, or noncaloric, sweeteners. For the purpose of this paper, the terms *nonnutritive, noncaloric,* and *artificial sweeteners* will be used interchangeably[3] Sucrose and/or corn sweeteners are the most frequently used nutritive sweeteners. Other nutritive sweeteners include fructose and polyols (sorbitol, mannitol, xylitol, and hydrogenated starch hydrolysate). Common nonnutritive sweeteners are aspartame, saccharin, and acesulfame-K. These nonnutritive sweeteners provide alternatives to sucrose.

The United States Department of Agriculture (USDA) reports disappearance, not consumption, figures for sweeteners. USDA reports that, in 1989, about 62 pounds of sugar (beet or corn), 71 pounds of corn sweeteners, and 1 pound of other sweeteners (honey, maple syrup) per capita were delivered to the food supply. This adds up to a total nutritive sweetener usage of about 134 pounds per person.[4]

As disappearance data, these numbers do not account for waste, and for sugars used in fermentation (as in bread baking) or pet food. Recently the Food and Drug Administration (FDA) estimated that the amount of added sweeteners (sugar, corn syrups, and others) that Americans actually consume is

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Table 1. Characteristics of an Ideal Sweetener

- As sweet or sweeter than sucrose
- Pleasant taste with no aftertaste
- Consumer acceptance based on how close its taste is to sugar's
- Colorless
- Odorless
- Readily soluble
- Stable
- Functional
- Economically feasible
- Does not promote dental cavities
- Nontoxic
- Metabolized normally or excreted from body unchanged
- Does not contribute to metabolic abnormalities, such as diabetes

Source: Caloric Control Council.[2]

considerably less than the disappearance rate—about 43 pounds per person, or about 11% of total calories.[4]

Among the many varieties of food additives, artificial sweeteners are forecast to show the fastest growth among all additive categories as a result of changing dietary habits and improved sweetening quality.[5] In 1987, artificial sweeteners accounted for 31% of the $2.45 billion food-additive market. By 1992, artificial sweeteners are expected to make up 36% of an estimated $3.5 billion market.[6] By the early to mid-1990s, per capita consumption of high-intensity sweeteners will likely exceed current levels by as much as 50%.[6] Use of multiple nonnutritive sweeteners will provide consumers and manufacturers with greater choices, allowing manufacturers to use the most appropriate sweetener or combination of sweeteners for a given product. Table 1 lists the components of an ideal sweetener.

Many people with diabetes are advised to restrict the amount of simple sugars (eg, glucose, sucrose, etc) in their diet.[7] Consequently, foods containing noncaloric sweeteners provide alternative choices to foods containing nutritive sweeteners, making possible increased variety, tolerance to prescribed meal plans and, in some cases, improved psychological well-being. The purpose of this paper is to review presently approved and pending sweeteners and to explore issues regarding product use and safety. Practical suggestions for counselling will also be addressed. A list of resources will be given to further assist the diabetes educator in keeping abreast of upcoming products.

Currently Approved Sweeteners

Saccharin Saccharin, a coal-tar derivative, was synthesized accidentally in 1879 by an American chemist, Constantin Fahlberg, at Johns Hopkins Institute. It is the oldest nonnutritive sweetener in the US food supply. Initially, saccharin was intended to be used as an antiseptic agent in the treatment of urinary tract infections. However, its potential as a sweetening agent was readily apparent, and it soon came to be used as a substitute for sugar in canned vegetables and beverages.[8]

Properties Saccharin is 300 to 400 times as sweet as sucrose. It is stable at physiological pH and temperature. Saccharin is well absorbed in the body and does not accumulate in body tissue. The product is not metabolized in rats, rhesus monkeys, and humans, and is excreted unchanged in the urine and feces. It is not electrophilic and does not bind covalently with DNA in the liver or bladder of rats, nor does it produce other cellular effects considered traditionally to be part of the process of carcinogenesis.[8] Saccharin is known to have a metallic, bitter aftertaste, and is often used with a buffer, such as dextrose, to help eliminate an aftertaste.

Uses Saccharin has a wide range of application in both food and beverages. It also is used in cosmetic products, vitamins, and pharmaceuticals.

Advantages Saccharin has been used for more than 80 years to sweeten foods and beverages without calories and carbohydrates, and for many decades was the only available sweetener in the United States.

Safety In April 1977, the FDA proposed a ban on saccharin because the agency had accumulated sufficient information from chronic bioassay tests to indicate that saccharin may cause urinary bladder cancer in experimental animals. Because of an intense public response against the ban, Congress instituted a moratorium postponing the ban, which continues to be extended; it is currently scheduled to expire May 1, 1992.

Previous GRAS (generally recognized as safe) recommendations (1955) limited saccharin use to 500 mg/day in children and approximately 1,000 mg/day in 70-kg adults. Today's intake is significantly lower, partly because of the availability of other sweeteners.[3] Saccharin can cross the placenta during pregnancy. There is no evidence that saccharin is harmful to the fetus; however, avoiding heavy use during pregnancy would seem prudent.[3] Continued research is needed to identify safe limits for human use.

Aspartame Aspartame, a dipeptide containing phenylalanine and aspartic acid, was discovered accidently by James M. Schlatter, a Searle chemist. It is metabolized as a protein and hydrolyzed in the body to aspartate, phenylalanine, and methanol. Once metabolized to amino acids and methanol, it enters directly into portal circulation. Methanol is further metabolized by the liver into formate and carbon dioxide.

Properties Aspartame is 180 times as sweet as sucrose. The product enhances the flavors of some foods, especially fruit.

Uses Aspartame can be found in carbonated beverages, tabletop sweeteners, fruit juice, and milk beverages. It also can be found in frozen desserts, puddings, and yogurt products. It is not stable to heat, but may be added to products that have completed the cooking process. Its shelf life is 6 months to 1 year.

Advantages Aspartame is low in calories. It has a sweet, clean, and bitterless taste, which extends its application to a wide variety of foods. The chemical does not promote tooth decay.

Safety The metabolites of aspartame, phenyalanine, aspartate, and methanol are naturally occurring in foods. The most visible contraindication for use of the sweetener is in the patient with phenylketonuria because blood levels of phenylalanine can become elevated with use of aspartame. Other safety issues include possible alterations of neurotransmitter activity and ocular toxic effects. The safety of long-term large doses of aspartame has been investigated by Leon et al.[8] These data show no significant effect of methanol metabolism on healthy adults. Other studies, using aspartame in abusive doses of 200 mg/kg of body weight, failed to show any

significant clinical or biochemical changes.[3,10]

The Centers for Disease Control (CDC) is responsible for reviewing all consumer issues pertaining to use of aspartame. In 1983, the CDC reviewed 517 health concerns. Those noted were: sinus congestion, constipation, gastroenteritis, severe diarrhea, itching, missed menstrual periods and, most noted, headaches.[11,12] A double-blind study was undertaken at Duke University to assess the effect of aspartame on blood glucose control. This study found that adverse reactions were no more common in the group taking the aspartame than in the group taking the placebo.[13]

The Food and Drug Administration's acceptable daily intake (ADI) for aspartame is limited to 50 mg/kg of body weight in adults. It is conceivable that young children, because of their small body weight, may easily exceed this advisable intake level. There is no experimental evidence that suggests, at intake levels of at least three times the 99th percentile of the projected daily intake of aspartame (3×34 mg/kg = 102 mg/kg), risk to the fetus from the metabolites of aspartame.[14] Aspartame appears to be safe in lactating women at levels recommended for healthy adults.[15] However, further studies have been recommended to address the safety of aspartame use in children and in pregnant and lactating women.[9,10]

Acesulfame Potassium Acesulfame potassium, or acesulfame-K, was discovered in 1967 in Frankfurt, West Germany. Hoechst developed the product, which it markets under the brand name Sunett outside the United States. The sweetener was petitioned for FDA review in 1982 and underwent 6 years of testing before its approval in 1988. Hoechst Celanese of Somerville, NJ, introduced the sweetener into the US market in 1989 under the brand name Sunette.

Properties Acesulfame-K is a derivative of acetoacetic acid. It is a white, odorless, crystalline product 200 times sweeter than sucrose based on a comparison with a 3% aqueous solution of sucrose. The sweetener is water soluble and stable at normal temperatures of up to 400° F (225° C) and moderate pH. It is described as having a "clean, quick, perceptible sweet taste that does not linger."[11] A slight aftertaste may be noted in certain products when the sweetener is used alone at high concentrations. In one study, however, participants found it to have a somewhat bitter taste reminiscent of saccharin.[16]

Uses The FDA approved the use of acesulfame-K as an ingredient in chewing gum, powdered beverages, gelatins and puddings, instant coffees, and nondairy lighteners. It has also been approved for use as a tabletop sugar substitute in packets or tablets. The company will likely seek approval for Sunette's use in baked goods and in liquids, such as soft drinks.

Advantages The sweetener is the only one of the three approved that is not required to carry a health statement on its label. Its stability in heat makes it, unlike aspartame, suitable for use in baked goods. Animal experiments suggest that acesulfame may decrease the incidence of dental caries caused by natural sugars.[17] The product is synergistic with other low-calorie sweeteners. For example, when combined in one-to-one proportion with aspartame, the mixture can be four to six times as sweet, depending on the application.

Safety The ADI established by the FDA is 0 to 15 mg/kg of body weight. For a 60-kg person, this is the equivalent of 180 g of sugar. The World Health Organization (WHO) established an ADI of 0 to 9 mg of acesulfame-K per kilogram of body weight.

Acesulfame-K's structural resemblance to saccharin, which in large doses increases the incidence of bladder cancer in male rats, raises the question of carcinogenicity.[18] In addition, the Center for Science in the Public Interest (CSPI), a Washington-based nonprofit organization, stated that acesulfame-K causes cancer and should not have been approved by the FDA. The group reported that its review of Hoescht's data revealed that acesulfame-K caused lung tumors in male and female rats, mammary gland tumors in rats, and high cholesterol levels in diabetic rats.[18] The FDA stated that its detailed analysis of all the data showed that tumors found were typical of what could be expected and were not caused by feeding with acesulfame potassium.[18] One study found acesulfame-K in large doses potentiated glucose-induced insulin secretion in rats, although it was not found to cause hypoglycemia.[19]

Future Sweeteners

Cyclamates Cyclamate was discovered in 1937. It is an organic acid derivative and is usually found in foods as sodium cyclamate or calcium cyclamate. The FDA, which approved cyclamate in 1949, banned its use in 1970 because of evidence suggesting that it caused bladder tumors in rats.[11]

Properties Only 30 times as sweet as sucrose, cyclamate has the least sweetening effect of all artificial sweeteners. The product is soluble, stable in heat and cold, and has a long shelf life. Cyclamate has almost no aftertaste.

Uses and Advantages Cyclamate was used as a tabletop sweetener in beverages and other low-calorie foods. It has also been used in baked products.

Safety The controversy surrounding cyclamate metabolism relates to cyclohexylamine, a metabolite detected in the urine of animals and humans following cyclamate administration. Cyclohexylamine is considered more toxic than cyclamate. Cyclohexylamine has been shown to produce testicular atrophy in experimental animals.[20] Early studies indicated that the sweetener was excreted without undergoing metabolism. In a chronic administration study conducted by Kojima and Ichibayase in 1966, cyclohexylamine was detected in dog and human urine.[21]

Abbott Laboratories petitioned the FDA to reapprove cyclamate in 1984. The National Research Council reviewed the cyclamate studies and concluded that the evidence did not indicate that cyclamates, by themselves, were carcinogenic or that the metabolites were carcinogenic. They did recommend that further studies be undertaken to determine: (1) the risk of cancer with heavy or long-term users; (2) the cocarcinogenetic effect of cyclamate with saccharin or other sweeteners; (3) the possible mammalian-cell DNA damage and gene mutation; and (4) the possible relation to testicular atrophy.[3]

The National Academy of Sciences Committee on the Evaluation of Cyclamate for Carcinogenicity stated that cyclamate may be a cocarcinogen or "cancer promoter." That is, cyclamate by itself is not carcinogenic but may enhance the cancer-causing activity of other substances.[13] The FDA has no policy to address the cocarcinogenicity issue; therefore, it may be some time before a decision is reached to reinstate cyclamate as a sweetener.

Aspartame Encapsulate In 1987, the Monsanto Company petitioned the FDA to use encapsulated aspartame in baked products.[22] The encapsulated aspartame, like aspartame, is 180 times sweeter than sucrose. It is made by coating the sweetener aspartame with a water-resistant polymer and then a layer of fat. The outer fat layer acts as a moisture barrier in the early stages of mixing and baking. After the fat layer melts during baking, the polymer layer hydrates, releasing aspartame from the core. The encapsulated aspartame remains unchanged. It can be used to replace sugar in baked goods, but is limited in that other fillers or food production methods are still necessary to add volume.

Alitame The Pfizer Company manufactures alitame.[23] The company filed a petition for approval with the FDA in 1986, but approval is still pending. Alitame is a protein consisting of the amino acids L-aspartic, D-alanine, and a new amine (2,2,4,4-tetramethylthietanyl amine). It is metabolized with little change. Because alitame is 2,000 times sweeter than sucrose, very little is needed; therefore, the calories it contributes are minimal.

Properties Alitame has a clean, sweet taste with no unpleasant aftertaste. When combined with other sweeteners, it has a synergistic sweetening effect. The disadvantage of alitame is that in acidic solutions at high temperatures it may omit an "off" flavor.

Uses A broad range of food products, including beverages, sweet baked goods, and confections, have been listed in the petition for use. The cooking quality of alitame should be excellent because it is stable at high temperatures.

Advantages Alitame is such a high-intensity sweetener that low use levels should result in low human intake.

Safety No safety issues have been raised to date. FDA approval is still pending.

Sucralose Sucralose is the generic name for a new noncaloric sweetener derived from sucrose. It has been developed jointly under an agreement between McNeil Specialty Products, Inc, a subsidiary of Johnson & Johnson, and Britain's Tate & Lyle PLC.[24] McNeil filed a food additive petition with the FDA in 1987.

Properties Sucralose is 600 times sweeter than sucrose. It does not break down in the body and yields no calories. The product has a "high quality" of sweetness, good water solubility, and an excellent stability in a wide range of processed foods and beverages. Like sugar, sucralose will hydrolyze in solution, but only over an extended period of time under extreme conditions of acidity and temperature. These properties make the sweetener acceptable for use in baked goods.

Uses and Advantages Sucralose can be used in a broad array of products, including tabletop sweeteners, carbonated and noncarbonated beverages, baked goods, chewing gums, dry-mix products, processed fruit and fruit spread, milk products, frozen desserts, and salad dressings. It does not promote tooth decay.

Safety FDA approval is still pending. According to the manufacturer, extensive studies have been conducted to support the safety of sucralose. Applications for approval are also pending in other countries, including Canada and the United Kingdom.

L-sugars L-sugars (left-handed sugars) are the optical isomers of common sugars. Chemically identical to their right-handed counterpart, it is thought that L-sugars are not metabolized since the body does not recognize them. The product could prove to be one of the best sweeteners because of its bulking and browning properties, which are similar to those in sucrose.[6] Biospherics/Montedison is continuing to develop a product named Lev-o-cal.[6] L-sugars have not been approved for use in any country nor has a petition been filed with the FDA.

Stevioside Stevioside comes from the leaves of the stevia, a shrub native to South America and now grown in other subtropical regions, including Asia and California. The plant provides two main sweetening derivatives—stevioside and rebaudioside-A. Stevioside composes 60% to 70% of the plant's yield.

Properties and Uses Stevia derivatives are 200 to 400 times sweeter than sugar. Stevioside is considered to be a high intensity, noncaloric sweetener and is stable enough to be used in both food and beverages. It alters the taste of food and beverages, leaving a very strong aftertaste compared with other products. Countries that already use stevia derivatives in food and beverages include Japan, Brazil, and Israel. Japan, the only significant stevia importer, initially obtained supplies from Paraguay and Brazil, but more recently has been importing stevia from mainland China, Thailand, and Taiwan.

Some Paraguayan researchers are concerned that stevia and its derivatives may cause infertility in women. Other researchers in Paraguay feel the evidence is not strong enough to draw such conclusions.[25] Japanese health authorities are not concerned by safety issues regarding stevia sweeteners.[25] They reason that the sweeteners are naturally occurring and, therefore, safe. In the United States, stevia producers are cautious about incurring the huge test costs that an FDA application would entail.[25]

Table 2. Approximate Sweetener Content of Selected Foods (in Milligrams per Serving)

Aspartame*	
Equal packet	35
Carbonated beverage (12 oz)	180
Powdered drink mix, diluted (8 oz)	80–120
Gelatin (1/2 cup)	95
Pudding (1/2 cup)	55
Yogurt (8 oz)	125
Hot cocoa mix, diluted (8 oz)	50
Cereal (1 cup)	50
Chewing gum (1 stick)	1
Saccharin†	
Sweet 'N Low packet	40
Carbonated beverage (12 oz)	150
Acesulfame-K‡	
Sunette packet	50

Sources: * NutraSweet Center, Deerfield, Ill.
† Cumberland Packing Corp, Brooklyn, NY.
‡ Hoechst Celanese Corp, Somerville, NJ.

Counseling Persons With Diabetes

To avoid aggravating hyperglycemia, persons with diabetes are advised to limit the amount of sucrose in their diet. This has led to a need for sweetened food that does not affect blood glucose control. The diabetes educator can use the following guidelines for use of nonnutritive sweeteners to counsel persons with diabetes.

1. Both caloric (fructose, sorbitol, etc) and noncaloric (aspartame and saccharin) alternative sweeteners are acceptable in the management of diabetes.
2. The use of refined sugars is contingent upon metabolic control and body weight.
3. A multiple-sweetener approach is recommended so only small amounts of any one sweetener are consumed. (See Tables 2 and 3 for the sweetener content of selected foods.)
4. When counseling parents of young children, remind them that the child's lower body weight, compared with an adult's, should be taken into consideration and that the child's intake level of sweeteners should not exceed acceptable or recommended levels. (Table 4 gives the acceptable daily intake [ADI] or generally recognized as safe [GRAS] levels of approved sweeteners.)
5. If a sweetener is used during pregnancy, limited amounts of aspartame is the sweetener of choice because it theoretically is metabolized by the body like other amino acids, while saccharin is known to cross the placenta.
6. Because nutritional well-being is important, educators should ensure that products with nonnutritive sweeteners provide some nutritional value whenever possible (eg, encouraging the use of sugar-free hot cocoa if a person does not drink milk).

Table 3. Sugar Substitutes and Equivalents

Sugar	Equal	Sweet 'N Low	Sweet One*
2 tsp	1 packet	1/5 tsp	1 packet
1 Tbs	1 1/2 packets	1/3 tsp	1 1/4 packets
1/4 cup	6 packets	3 packets	3 packets
1/3 cup	8 packets	4 packets	4 packets
1/2 cup	12 packets	6 packets (1 Tbs)	6 packets
2/3 cup	16 packets		
3/4 cup	18 packets	1 1/2 Tbs	
1 cup	24 packets	12 packets (2 Tbs)	12 packets

* For best results, substitute half the sugar called for with the equivalent amount of Sweet One.

Conclusion

Diabetes educators must keep abreast of the most current

Table 4. Sweetener Fact Sheet

Sweetener	Sweetness*	AID or GRAS†	FDA Status	Manufacturer	Limitations
Saccharin	300X	500 mg/day/child 1000 mg/day/adult	moratorium extended to 1992	Cumberland Packing Corp	Safety issues
Aspartame	180X	50 mg/kg body weight	Approved 1981	Monsanto	Heat sensitive; PKU safety issue
Acesulfame-K	200X	15 mg/kg body weight	Approved 1988	Hoechst Celanese Corp	Safety issues
Cyclamate	30X	N/A‡	Resubmitted 1980, pending	Abbott Labs	Safety issues
Encapsulated aspartame	180X	N/A	Submitted 1986, pending	Monsanto	Needs bulking agent
Alitame	2,000X	N/A	Submitted 1986, pending	Pfizer, Inc	May omit "off" flavor in acidic solution with high temperature
Sucralose	600X	N/A	Submitted 1987, pending	Johnson & Johnson McNeil Specialty Products, Inc	N/A
L-Sugars	Same	N/A	Toxicology testing to be finished 1990; nothing filed	Biospherics/ Montedison	Needs bulking agent
Stevioside	200–400X	N/A	Nothing filed	N/A	Possible infertility in women

* Compared with sucrose.
† ADI = acceptable daily intake; GRAS = generally recognized as safe.
‡ N/A = not available.

Table 5. Sources of Information on Nonnutritive Sweeteners

American Council on Science and Health
1995 Broadway
New York, NY 10023
Tel: 212/362-7044

American Dietetic Association
216 West Jackson Blvd, Suite 800
Chicago, IL 60606
Tel: 312/899-0040

Calorie Control Council
5775 Peachtree-Dunwoody Road, Suite 500-D
Atlanta, GA 30342
Tel: 404/252-3663

Cumberland Packing Corporation
Department HHR
60 Flushing Avenue
Brooklyn, NY 11205
Tel: 718/858-4200

Food and Drug Administration
Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857
Tel: 301/443-1544

The NutraSweet Company
Consumer Affairs Department
1751 Lake Cook Road
Deerfield, IL 60015
Tel: 1-800/321-7254 or 708/940-9800

Sugar Association
1101 15th Street NW, Suite 600
Washington, DC 20005
Tel: 202/785-1122

information on the use and safety of sweeteners. Table 5 lists resources that health care professionals can use to obtain accurate information about sweeteners. This information will enable clients to make conscious food selections and to select alternatives, if necessary.

Manufacturers should be encouraged to include better labeling to inform consumers about the sweeteners contained in foods. Ideally, food labels should list the specific sweetener and the amount, in milligrams, contained in each serving. Finally, further research is needed to identify the risks and long-term effects of sweetener use in children and in pregnant and lactating women, and the effect of sweeteners on metabolism, particularly the metabolism of individuals with diabetes.

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