

Sugar Substitutes and Your Health

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Executive Summary¹

- Foods and beverages containing sugar substitutes are widely used in the United States and other countries; they offer attractive dietary options for people who are trying to limit calorie intake and/or reduce the risk of tooth decay.
- Extensive scientific research supports the safety of the five low-calorie sugar substitutes currently approved for use in foods and beverages in the U.S. — acesulfame-K, aspartame, neotame, saccharin, and sucralose.
- In several instances, scientific studies have raised questions about the safety of specific sugar substitutes. Concerns about the possible cancer-causing potential of cyclamate and saccharin, raised during the 1960s and 1970s, respectively, have been resolved. A controversial animal cancer study of aspartame is currently being reviewed by regulatory authorities in the United States and other countries.
- Three sugar substitutes currently used in some other countries — alitame, cyclamate, and stevia — are not approved as food ingredients in the United States. Alitame and cyclamate are under consideration for approval. Stevia may be sold as a dietary supplement, but marketing this product as a food ingredient in the U.S. is illegal.
- A variety of polyols (sugar alcohols) and other bulk sweeteners, including two unusual sugars, trehalose and tagatose, are accepted for use in foods in the U.S. The only significant health issue pertaining to these sugar substitutes, most of which are incompletely digested, is the potential for gastrointestinal discomfort with excessive use.
- The availability of a variety of safe sugar substitutes is a benefit to consumers because it enables food manufacturers to formulate a variety of good-tasting sweet foods and beverages that are safe for the teeth and lower in calorie content than sugar-sweetened foods and beverages.

1. The term sugar substitutes includes both food ingredients with very strong sweetening power that provide zero or very few calories, which are used in very small amounts to sweeten foods, and bulk sweetening agents such as polyols, which can replace both the bulk of sugar and some of its sweetness. This booklet discusses both types of sweeteners, with an emphasis on the safety aspects of the five low-calorie sweeteners currently approved for use in the United States.

Introduction

If you enjoy diet soft drinks or other reduced-calorie or “light” products, you’re in good company. According to a recent survey, 180 million American adults use low-calorie, sugar-free foods and beverages. Despite the popularity of these products, though, some people have concerns or questions about the safety of the sugar substitutes that make the products possible. Misinformation about sugar substitutes abounds, especially on the Internet, and people may have difficulty distinguishing trustworthy sources of information on this topic from less reliable ones.

This report by the American Council on Science and Health summarizes the scientific facts about the safety of sugar substitutes. The principal source of information for this booklet was a technical manuscript entitled “Low-Calorie Sweeteners and Other Sugar Substitutes: A Review of the Safety Issues,” published in the journal *Comprehensive Reviews in Food Science and Food Safety*, by Dr. Manfred Kroger of Pennsylvania State University and Kathleen Meister and Dr. Ruth Kava of the American Council on Science and Health.

Sugar Substitutes that Provide Zero or Negligible Calories

The sugar substitutes discussed in this section of this booklet, which may also be called alternative, artificial, high-intensity, or nonnutritive sweeteners, can replace the sweetness of sugar while providing few or no calories. In addition to the calorie savings, these sugar substitutes have the advantage of not promoting tooth decay, and they are useful in dietary planning for people who are coping with obesity or diabetes. Five sweeteners of this type are currently approved for use in foods and beverages in the United States: *acesulfame-K*, *aspartame*, *neotame*, *saccharin*, and *sucralose* (Table 1). Others, including *alitame*, *cyclamate*, and substances derived from the *stevia* plant, are approved as food ingredients in some other countries but not in the United States. Each of these sugar substitutes is discussed individually below.

With the exception of saccharin, which was in use long before current procedures were adopted in the 1950s, each of the sugar substitutes discussed here had to earn approval as a new food additive in the United States. The Food and Drug Administration (FDA) approves new food additives based on reviews of extensive scientific research on safety. Before a new food additive can go on the market, the company that wishes to sell it must petition the FDA for its

Table 1. Low-Calorie Sugar Substitutes Currently Approved for Use in the United States

Sugar Substitute	Caloric Value (Cal/g)	Date Approved	Regulatory Status	Potency (times sweeter than sucrose) ^a	Brand Names
Acesulfame-K	0	1988	Approved as a food additive; ADI ^b = 15 mg/kg bw/day	200	Sunett, Sweet One
Aspartame	4 ^c	1981	Approved as a food additive; ADI = 50 mg/kg bw/day	180	NutraSweet, Equal, others
Neotame	0	2002	Approved as a food additive; ADI = 18 mg/p/day	7,000	Information not yet available
Saccharin	0	In use for decades prior to the Food Additives Amendment of 1958	Permitted for use under an interim regulation	300	Sweet'n Low, Sweet Twin, Sugar Twin, others
Sucralose	0	1998	Approved as a food additive; ADI = 5 mg/kg/day	600	Splenda

a. Potency varies in different food applications. These values should be regarded as rough estimates.

b. ADI = acceptable daily intake, defined as the estimated amount that a person can safely consume on average every day over a lifetime without risk. The ADI values listed here are those established by the U.S.

Food and Drug Administration; ADIs used in other countries may be slightly different. ADI values are usually expressed in milligrams per kilogram of body weight per day (mg/kg bw/day); however, FDA has expressed the ADI for neotame in terms of milligrams per person per day (mg/p/day).

c. Although aspartame provides 4 Cal/g, as many calories as an equivalent weight of protein or carbohydrate, the amount of aspartame used in foods and beverages is so small that its caloric contribution is negligible.

approval. The petition must provide convincing evidence that the new additive performs as intended and is safe, where “safe” means a reasonable certainty of no harm under the intended conditions of use. Demonstrating that an additive is safe is the manufacturer’s responsibility; it is the manufacturer, not the FDA, who conducts and pays for the necessary research.² FDA’s roles are to assess the research results and to make decisions on the submitted petitions; FDA does not decide what substances will be considered as potential food additives, and it does not conduct safety studies. For additives that are likely to be widely used, such as sugar substitutes, the necessary research includes extensive studies in experimental animals, including studies in which high doses of the additive are administered to two species of animals for the greater part of the animals’ lifetime. In many instances, studies in human volunteers are also conducted.

2. Opponents of particular food additives sometimes attempt to cast aspersions on them by pointing out that the studies supporting their safety were conducted by the additives’ manufacturers. But there is nothing scandalous in this. It is inherent in the way the system for food additive approval works. The alternative (having a government agency or independent entity test food additives for safety) may sound good in theory, but it would require research on prospective new products to be paid for with the public’s tax dollars. Under the current system, the company that will benefit financially from the new product pays for the research, and FDA’s stringent review process ensures that the studies were properly performed and interpreted.

It can be difficult for people who are not involved in the testing of food additives to appreciate just how extensive their premarket testing must be. Most safety studies on prospective food additives are never published in the scientific literature because they do not make an important contribution to scientific knowledge. One exception, however, involves the sugar substitute sucralose. Many of the more than 100 studies conducted in support of the safety of this additive were published in a scientific journal in 2000 (see the Suggestions for Further Reading at the end of this report). They provide insight into the quantity and sophistication of the research required before a new food additive can be marketed in the United States.

Low- or Zero-Calorie Sugar Substitutes Currently Approved for Use in the United States

Acesulfame-K

Acesulfame-K, sold under the brand name Sunett, is the most successful sugar substitute that you've probably never heard of. It is inconspicuous because it is almost always used in combination with other sweetening agents. When used in this way, it contributes to creating a sweet taste very close to that of sugar. However, if used alone, it can have a bitter aftertaste that consumers would find undesirable. Acesulfame-K is approximately 200 times as sweet as sugar, and it provides zero calories.

As with all new food additives, acesulfame-K underwent extensive safety testing before regulatory authorities in the U.S. and other countries approved its use. More than 50 studies of various aspects of safety were conducted before the FDA approved acesulfame-K for use in dry foods in 1988, and additional tests were conducted before FDA approved its use in beverages a few years later.

Over the years, concerns have been raised about several aspects of the safety of acesulfame-K. All of these issues have been resolved, as follows:

- Questions were raised about one of the animal experiments, a long-term study in rats, that was conducted during the safety testing of acesulfame-K. It has been claimed that this study was inadequate and that its results might have linked acesulfame-K to an increased risk of cancer. There was indeed a problem with this study; an illness had spread through the rat colony while the study was in progress. Because of this complication, it was necessary for

the researchers to repeat the study. The second study was completed with no problems, and it did not link acesulfame-K to cancer or other harmful effects. It was this second study, not the first, that was used by regulatory authorities in their evaluation of acesulfame-K.

- It has been argued that a breakdown product, acetoacetamide, that may form during storage in beverages sweetened with acesulfame-K could have harmful effects. Regulatory authorities are aware of this breakdown product, and they took its formation into account before approving acesulfame-K for use in beverages. Because the amount of acetoacetamide that could form in beverages is extremely small, far too small to cause adverse health effects, the formation of this substance is not considered to be a cause for concern.
- In the late 1990s, researchers from India reported findings that seemed to indicate that acesulfame-K could cause mutations (genetic changes) in mouse bone marrow cells. However, when the same researchers and others attempted to replicate this finding, they were unable to do so. The later studies showed no evidence of mutations, indicating that the original finding was incorrect.

Recent reevaluations of the scientific evidence on acesulfame-K, including a comprehensive review by the food safety authorities of the European Union in 2000, have reaffirmed its safety. No human health problems associated with the consumption of acesulfame-K have been reported in the scientific literature, despite more than 15 years of extensive use in many countries.

Aspartame

Aspartame was discovered in 1965 and approved by the FDA in 1981. It is widely used in foods and beverages because its taste is very close to that of table sugar. During the first years after approval, when aspartame was sold exclusively by the patent holder, it was known primarily by the brand names NutraSweet and Equal (the latter is the popular table-top sugar substitute sold in blue packets). Since the expiration of the patent in December 1992, aspartame has also been sold under other brand names. Aspartame is approximately 180 times as sweet as sugar.

The aspartame molecule consists of two amino acids — phenylalanine and aspartic acid — linked to methanol (methyl alcohol). The two amino acids in aspartame occur naturally in foods as protein components. Methanol also occurs naturally in foods and is produced by the digestion of other food constituents. Aspartame itself does not occur naturally.

Unlike most other low-calorie sugar substitutes, aspartame is broken down in the human body. Enzymes in the digestive tract break it down into its components (phenylalanine, aspartic acid, and methanol), each of which is then metabolized just as it would be if derived from other dietary sources. Because aspartame is metabolized, it provides as many calories as an equivalent weight of protein or carbohydrate does. However, because aspartame is intensely sweet, the amount used in foods and beverages is so small that its caloric contribution is negligible.

As with all modern food additives, aspartame underwent extensive safety testing prior to approval. Many additional studies have been conducted in the decades since aspartame went on the market. On the basis of this scientific evidence, authorities in numerous countries have approved and repeatedly reapproved the use of aspartame. The most recent reevaluations, including a reassessment of aspartame by authorities in the European Union in 2002, have continued to support its safety.

To scientists, it has always seemed unlikely that the normal use of aspartame could cause adverse health effects. Aspartame breaks down in the digestive tract into ordinary food components, and it accounts for only a small proportion of the total intake of these components. Thus, it is difficult to conceive of a mechanism by which the use of normal amounts of aspartame could cause an adverse effect.

Of course, any substance can be harmful if consumed in a large enough quantity. This is true for the components of aspartame, just as it is true for water, vitamins, and numerous other substances in foods and beverages. However, the amounts of phenylalanine, aspartic acid, and methanol in aspartame-sweetened foods and beverages are small — well below the levels that could cause any harm.

It has been calculated that even a relatively heavy user of aspartame (a person at the 90th percentile of aspartame consumption)³ would increase his or her intake of the two amino acids in aspartame — aspartic acid and phenylalanine — by only one to two percent. Such changes are within the range of variation caused by day-to-day differences in food intake and are clearly not harmful. A 90th-percentile consumer of aspartame-sweetened products would increase his

3. The 90th percentile of aspartame consumption is roughly 3.0 milligrams per kilogram of body weight per day. For a 150-lb adult, this would be about 210 milligrams of aspartame, which is approximately the amount in one 12-oz. can of aspartame-sweetened soft drink plus one packet of aspartame-based table-top sweetener. The acceptable daily intake of aspartame (the estimated amount that a person can safely consume on average every day over a lifetime without risk) is 50 milligrams per kilogram of body weight per day, or about 16 times the 90th percentile intake.

or her daily consumption of methanol by an amount only one twenty-fifth of the maximum tolerable level established by the FDA; a small increase of this sort would not cause harmful effects.

Even when aspartame is consumed in unusually large (but physically possible) amounts, adverse health effects do not occur. Aspartame has been tested in human volunteers in single doses four times the acceptable daily intake (the amount considered safe for daily consumption for a lifetime) and in studies where volunteers consumed aspartame daily at a level 50% higher than the acceptable daily intake for several months. Even at these high doses, the levels of all three of aspartame's components in the volunteers' blood remained within safe ranges, and no adverse effects occurred.

Consumers sometimes worry about the presence of methanol in aspartame because they know that methanol, in large doses, is toxic. Many people do not realize that methanol is a common constituent of foods and beverages and that people routinely consume small amounts of it without ill effect. Methanol is found in many fruits and vegetables. Fruit juices contain substantial amounts of methanol; for example, apple juice has been reported to contain up to 88 milligrams per liter. This is not a reason to avoid apple juice, however. To obtain a fatal dose of methanol from apple juice, an individual would have to consume between 100 and 1000 quarts of the juice at a single sitting — an obviously absurd scenario. All fermented foods and beverages, such as alcoholic beverages and fermented milk products, can be expected to contain methanol as well as other alcohols in trace amounts. Except in the case of unprofessionally distilled alcoholic beverages, however, the amount of methanol in fermented foods and beverages is too low to cause any health damage. The same is true of the small amounts of methanol present in aspartame-sweetened foods or beverages.

Foods and beverages that contain aspartame must carry a label statement indicating that the product contains phenylalanine. This statement is for the benefit of individuals with the disease phenylketonuria, who must strictly limit their intake of this amino acid.

Phenylketonuria is a rare disease, affecting approximately one in 15,000 people, that results from a hereditary lack of an enzyme necessary for the normal metabolism of phenylalanine. Unless the disorder is detected in early infancy and treated with a phenylalanine-restricted diet, it results in mental retardation and other severe, permanent effects. Newborn infants in the U.S. and many other countries are screened for phenylketonuria at birth. Because of screening and effective treatment, substantial numbers of people with phenylketonuria are living near-normal lives except for the need for dietary restriction.

The phenylalanine notice on aspartame-sweetened products is not relevant to the general public; it is meant only for people with phenylketonuria. It is much like the statements provided on food labels for the benefit of people with food allergies (e.g., “contains wheat and soy”). Such label statements are intended only for people with a specific problem; they do not imply that consumers in general need to avoid the food.

Aspartame is unstable if subjected to prolonged heating and therefore cannot be used in baking or cooking (unless added at the end of the cooking process). Aspartame also decomposes in liquids during prolonged storage (this is why diet soft drinks have a shelf life about half that of regular soft drinks). When aspartame decomposes, the breakdown products include its three components (the two amino acids and methanol), as well as the diketopiperazine derivative of aspartame, which has been tested for safety and is not regarded as hazardous. The relative instability of aspartame is a quality issue, not a safety issue. For example, if you drink a can of diet soft drink that has been left too long in a hot car, causing some of the aspartame in the beverage to break down, it will not make you sick. However, you may notice a deterioration in the quality of the beverage.

Despite the extensive evidence supporting the safety of aspartame and the very low likelihood that a substance of aspartame’s composition could cause adverse health effects, claims of such effects abound, especially on the Internet. Anyone who enters the term “aspartame” into an Internet search engine will find thousands of references to this substance, including hundreds of Web sites filled with anecdotal reports supposedly linking aspartame with a wide variety of effects — including neurological and behavior problems, multiple sclerosis, systemic lupus erythematosus, fibromyalgia, chronic fatigue syndrome, Alzheimer’s disease, birth defects, and even the health problems experienced by some Gulf War veterans. The scientific evidence does not support any of these alleged associations. A lack of scientific support, however, does not prevent misinformation from being repeated, over and over, on the Internet.

It is important to realize that anyone can publish *anything* on a Web site — including speculation, misconceptions, and unsupported allegations — and that in cyberspace, myths and rumors never die. People who use the Internet as a source of information on health-related issues would be well advised to visit the sites of trusted organizations or government agencies and search the collections of documents posted there rather than searching the Internet as a whole. Further advice on using the Internet as a health information source is given at the end of this report.

There is only one unresolved issue concerning aspartame's safety at the present time. In 2005, a group of Italian researchers reported that a study they had conducted had linked aspartame exposure to an increased risk of cancer in rats. The study was performed using methodology that differs from the standard, well-verified techniques for evaluating the cancer-causing potential of substances in experimental animals, and its findings conflict with those of studies conducted using officially recognized methodology. In addition, the researchers did not follow the customary procedure of allowing a second group of scientists to examine all of the samples of the animals' tissues that had been prepared for microscopic study. Moreover, the research was conducted at a laboratory whose previous work has been criticized as "unreliable" by the FDA. Nevertheless, as is prudent, regulatory authorities in the United States and other countries are carefully reviewing the data from the new study to determine whether the findings are indicative of any real cause for concern about aspartame.

Neotame

Neotame is the newest of the low-calorie sugar substitutes. It was approved in 2002 and has not yet appeared in commercial products in the United States. Like aspartame, neotame contains the amino acids phenylalanine and aspartic acid. The two amino acids, however, are combined in a way that is different from that in aspartame, giving neotame different properties. Neotame is extraordinarily sweet, with a sweetness potency at least 7,000 times that of sugar and at least 30 times that of aspartame. Unlike aspartame, neotame is heat stable and therefore can be used in cooking and baking.

Although neotame is chemically similar to aspartame, it is not the same substance. Therefore, neotame had to be comprehensively tested for safety, just as any other new food additive would, before it was approved by the FDA. The scientific evidence submitted to FDA by neotame's manufacturer in support of its safety included the results of more than 110 scientific studies, including tests in both experimental animals and human volunteers. This is typical of the amount of research that is necessary before a new food additive can be marketed.

When a person consumes neotame, most of it is broken down into a derivative and methanol, both of which are rapidly excreted from the body through either the digestive tract or the urinary tract. Because the amount of neotame used to sweeten a food or beverage is extremely small, the exposure to methanol from neotame is also extremely small in comparison to methanol exposure from other sources. The amount of methanol in a glass of fruit juice is about 100 times that in a glass of a neotame-sweetened soft drink.

Although neotame contains phenylalanine, products sweetened with neotame will not be required to bear a warning notice for people with phenylketonuria, in the way that aspartame-sweetened products do. The amount of phenylalanine in a neotame-sweetened product is so small that it is insignificant, even for people who must limit their phenylalanine intake. The FDA has calculated that the amount of phenylalanine that would be consumed by a person in the 90th percentile of predicted consumption for neotame is only about 0.4 percent of the amount that a child with phenylketonuria is permitted to consume daily. Thus, the effect of consumption of neotame-sweetened products on total phenylalanine intake is negligible.

Neotame is likely to receive increased public attention once products containing it begin to appear on the market. Consumers should be aware that neotame is a safe, well-tested food ingredient.

Saccharin

Saccharin, the oldest low-calorie sugar substitute, was discovered in 1878. It is 300 times sweeter than sugar and provides no calories. In the first half of the twentieth century, saccharin was popular as a sugar substitute in the diets of people with diabetes and other medical conditions. It was also used extensively as a replacement for strictly rationed sugar in Europe during both World Wars. Between 1970 and 1981, saccharin was the only low-calorie sugar substitute available in the United States. Saccharin is still widely used today, often in combination with other sugar substitutes, and owes much of its popularity to its low cost. Although saccharin can have a bitter aftertaste when used alone, it works well in blends with other sugar substitutes. Saccharin is perhaps most familiar to U.S. consumers as the sugar substitute sold in pink packets, under the brand name Sweet'n Low.

During the 1970s, concerns were raised about whether saccharin might be capable of causing human cancer. In several studies in which a particular chemical form of saccharin, sodium saccharin, was administered to rats in extremely large doses for a lifetime, the male rats had an increased rate of bladder cancer. In 1977, on the basis of this evidence, the FDA attempted to ban saccharin. This decision met with an extremely negative reaction from the American public because saccharin was the only low-calorie sugar substitute on the market at that time, and banning it would have meant that diet soft drinks and other sweet low-calorie products would become unavailable. Acting in response to a massive public mandate, Congress passed a law that imposed a moratorium on the proposed FDA action, and saccharin was never banned, although a warning label was required on saccharin-sweetened products.

Since the 1970s, scientific research has shown that saccharin is not a cancer hazard in humans. Researchers have learned that the mechanism by which sodium saccharin causes bladder cancer in rats is not applicable to people. In rats fed high doses of sodium saccharin, crystals form in the urine. These crystals damage bladder tissues, leading to the proliferation of new cells, which increases the risk of cancer. This phenomenon does not occur in humans, whose bladder physiology is quite different from that of rats. Moreover, the effect in rats is not even attributable to saccharin per se — it is caused by the sodium component of sodium saccharin, not the saccharin component. Researchers have been able to produce bladder tumors in male rats by feeding them very high doses of other sodium compounds, too — including sodium chloride (table salt) and sodium ascorbate (one of the chemical forms of vitamin C) — neither of which poses a bladder cancer risk in humans.

The relationship between saccharin and bladder cancer has been evaluated in epidemiological studies (studies of the occurrence of disease in human populations), most of which used the case-control design (i.e., people diagnosed with bladder cancer were compared with people of the same age and sex who did not have the disease to see how their past experiences, including exposure to saccharin, differed). The combined evidence from the many case-control studies indicates that no detectable association exists between saccharin consumption and the risk of bladder cancer in humans.

Because the animal evidence indicates that the mechanism by which saccharin causes cancer in rats is not relevant to humans and because the human evidence does not demonstrate any cancer hazard from the use of saccharin, regulatory agencies and international organizations have removed saccharin from their lists of probable human carcinogens, and the requirement for a warning label on saccharin-sweetened products has been discontinued. There are no unresolved safety issues pertaining to saccharin at the present time. Saccharin is currently permitted for use in the U.S. under an interim regulation that specifies the amounts of saccharin permitted in beverages, processed foods, and table-top sweeteners and requires that the product label must state saccharin in the ingredient declaration and specify the amount used.

Sucralose

Sucralose was discovered in 1976 and approved for use in the United States in 1998. It is made from sucrose (table sugar) by a process that substitutes three chlorine atoms for three hydrogen-oxygen (hydroxyl) groups on the sucrose molecule. Although sucralose is made from sugar, the human body does not recognize it as a sugar and does not obtain energy by breaking it down; in fact, almost all of it is excreted from the body unchanged. Sucralose is about 600

times sweeter than sugar, and it is heat-stable. Like the other low-calorie sugar substitutes, it does not promote tooth decay. It is sold in the U.S. under the brand name Splenda and is perhaps most familiar to U.S. consumers as the sugar substitute that comes in yellow packets.

As is true for all new food additives introduced in recent decades, sucralose underwent extensive safety testing in both experimental animals and human volunteers before it was approved in the United States and other countries. Sucralose is considered safe for all segments of the population, including people with chronic health problems such as diabetes.

In the years since sucralose was approved, some popular products have been reformulated to contain it, often with considerable publicity. During this time, concerns about the safety of sucralose have been raised on various Internet sites, especially those that also express concerns about aspartame. Most of these concerns seem to be based on a general distrust of synthetic food ingredients or a specific unease about any substance that contains chlorine, which is also a component of some pesticides. However, the presence of chlorine in the sucralose molecule is not a cause for concern. Many commonly consumed substances, including table salt (sodium chloride), contain chlorine; the presence of this element in a compound does not indicate that the compound is toxic. Sucralose is a safe, well-tested food additive. There are no unresolved scientific concerns about its use.

Other Low-Calorie Sugar Substitutes

The five low-calorie sugar substitutes described in detail above are the only ones currently approved in the United States. Several other compounds are in use in other countries, however.

One of these is *alitame*. Like aspartame and neotame, alitame is a sugar substitute made from amino acids. Like neotame, it is a very powerful sweetening agent; alitame is 2,000 times sweeter than sugar. Alitame has been approved in Mexico, Colombia, China, Australia, and New Zealand. In the United States, a petition for the approval of alitame as a food additive has been submitted to the FDA. As of March 2006, this petition was being “held in abeyance,” according to the FDA Web site. “Held in abeyance” indicates that FDA needs additional data in order to evaluate a substance and has deferred its evaluation until the data are submitted. Thus, there appears to be some scientific issue delaying the approval of this sugar substitute in the United States.

Cyclamate is in use in about 50 countries. Cyclamate is not a new product; it was discovered in 1937 and was used as a sugar substitute in the U.S. in the 1950s and 1960s, primarily in a very successful blend with saccharin. In 1970, however, cyclamate was banned in the U.S. in response to an animal experiment that seemed to indicate that it could cause bladder cancer. Later, extensive further studies in several animal species did not show any link between cyclamate and cancer. Thus, on the basis of the complete body of evidence, scientists have concluded that cyclamate is not a cancer-causing agent. The manufacturer of cyclamate has submitted a petition for its reapproval in the United States. This petition, like the one for alitame, is currently being “held in abeyance” (as of March 2006) while additional scientific data are developed.

Indigenous peoples of South America have used the leaves of the *stevia* plant, a shrub that grows wild in Brazil and Paraguay, as a sweetener for centuries. Stevia leaves contain at least ten sweet components, the most important of which are stevioside and rebaudioside A. An extract of stevia containing these components has been used as a food ingredient in Japan for more than 30 years and more recently in other countries including China, Russia, and Korea. Stevia is not approved as a food ingredient in the United States. However, it is sold as a “dietary supplement.” According to the provisions of the Dietary Supplement Health and Education Act (DSHEA), which was passed in 1994, dietary supplements do not need FDA approval before they are marketed, in the way that new food additives or drugs do. Dietary supplements that contain stevia cannot legally be promoted as sugar substitutes in the U.S., and stevia cannot be used as an ingredient in foods. The sale of the supplements is legal, however.

Some proponents of stevia contend that its safety has been adequately demonstrated by its history of apparently safe use in other parts of the world. In addition, they argue that a natural product such as stevia need not be subjected to the same type of scientific evaluation required for synthetic food additives. However, the mere fact that a substance is “natural” does not mean that it is necessarily safe. Many natural plant components are toxic. And while a long history of use does indicate that a substance is free from severe, immediate toxic effects, it does not guarantee that the substance is entirely safe. Rare adverse effects, delayed effects, or effects that occur only with long-term use may not be identified without systematic scientific testing. There are, in fact, some safety concerns about stevia. Animal experiments have raised the possibility that stevia extract may have harmful effects on the male reproductive system; it is uncertain what components of the extract are responsible. Whether the results of these experiments are applicable to humans is unclear.

It is often claimed that the FDA is unfairly persecuting stevia by not allowing the product to be sold as a food additive. This claim reflects a misunderstanding of how the food additive approval system works. FDA does not, on its own initiative, make decisions to permit new ingredients in the food supply. It only acts in response to petitions submitted to it. For stevia to be approved as a food additive, someone would have to submit a petition to FDA that provides adequate evidence of its safety.⁴ This has not happened.

General Issues Pertaining to Low-Calorie Sugar Substitutes

Choice of Sugar Substitutes. Food manufacturers choose among the available sugar substitutes based on taste considerations, stability, and cost. In some instances, blends of sugar substitutes are used. The use of blends has a long history; a cyclamate/saccharin blend was widely used in diet soft drinks in the 1960s, aspartame/saccharin blends are commonly used in fountain soft drinks in the U.S. today, and aspartame/acesulfame-K blends are currently used in many foods and beverages. Blends may have taste or cost advantages over individual sugar substitutes. There are no health-related reasons for choosing one sugar substitute over the others; all are safe, well-tested products.

Acceptable Levels of Consumption. Estimated intakes of all the low-calorie sugar substitutes currently approved in the U.S. are well within the ranges that are considered acceptable. Therefore, people do not need to limit their intake of products made with these ingredients for reasons pertaining to the sugar substitutes themselves. However, since many of the products that contain sugar substitutes are foods of minimal nutritional value (e.g., carbonated beverages), people who are trying to eat healthfully may find it necessary to limit consumption of these foods to avoid displacement of more nutritious foods from the diet. This issue is especially important for children and adolescents, among whom displacement of milk by other beverages is a concern.

The use of low-calorie sugar substitutes could improve dietary quality if consumers use calorie savings for the consumption of more nutritious foods. For

4. For some food ingredients, an alternative route to approval called GRAS notification is possible. In this instance, the sponsor of the food ingredient notifies FDA that it believes a substance to be generally recognized as safe (GRAS) and provides both technical evidence of its safety and evidence that a consensus exists among qualified experts as to the safety of the substance under the conditions of its intended use. FDA then reviews the notification and decides whether or not to object to it. In this procedure, as with the food additive approval procedure described above, the manufacturer of the proposed food ingredient must take the initiative. In both instances, FDA merely reviews evidence submitted to it; the agency does not choose which substances to evaluate.

example, if a person drinks a zero-calorie diet soft drink rather than a 150-calorie regular soft drink, this provides the opportunity to include 150 calories from a more nutritious food in the diet. Some people may indeed be using reduced-calorie foods and beverages this way. A recent analysis of data from two national diet surveys indicates that American adults who use reduced-sugar products have better diets and higher vitamin and mineral intakes than those who use the full-sugar versions of the same foods and beverages.

Effect on Weight Control. The effect of low-calorie sugar substitutes on weight control has been a subject of controversy. It has been claimed that the use of these products could hamper weight loss efforts by promoting increased food intake. However, the overall scientific evidence does not support this concern.

The idea that sugar substitutes might promote weight gain originated with a 1986 British study in which self-rated appetite was found to be higher in people who drank aspartame-sweetened water as compared to those who drank plain water. In several other studies, however, consumption of aspartame or other sugar substitutes did not lead to increases in self-rated appetite. In addition, several studies have assessed the effect of sugar substitute consumption on actual food intake, and none has shown an increase.

The use of sugar substitutes may be helpful for individuals who are trying to control their weight by providing palatable low-calorie food choices. A study from Harvard Medical School supports this idea. The study involved overweight women who participated in a four-month multidisciplinary weight-reduction program. The women were divided into two groups; one group was encouraged to consume aspartame-sweetened products, while the other group was asked to avoid them. The two groups of women lost similar amounts of weight during the program. However, during the three years after the program ended, the women in the aspartame group were more successful than those in the other group in maintaining their weight loss.

Other Types of Sugar Substitutes

The sugar substitutes discussed earlier in this booklet substitute only for the sweetness of sugar, not its physical bulk. When bulk is important, for example in chewing gums, candies, ice cream, baked goods, and fruit spreads, other types of sugar substitutes, such as sugar alcohols (polyols), may be used. Polyols usually replace sugar on a one-to-one basis (that is, one ounce of polyol substitutes for one ounce of sugar). Since some polyols are not as sweet as sugar, a low-calorie sugar substitute may also be included in the product to pro-

vide additional sweetness. Polyols used in foods in the U.S. include *sorbitol*, *mannitol*, *xylitol*, *isomalt*, *erythritol*, *lactitol*, *maltitol*, *hydrogenated starch hydrolysates*, and *hydrogenated glucose syrups*.

Polyols and other bulk sugar substitutes have three potential advantages over sugar as food ingredients:

- Unlike sugars, they do not promote tooth decay. The bacteria in dental plaque, which produce substantial amounts of decay-promoting acid from sugars and starches, produce little or no acid from polyols. In the United States, FDA allows a health claim on foods made with polyols stating that the food does not promote tooth decay, provided that the food also meets other requirements (such as not containing decay-promoting sugars). Label claims of this type are often found on sugarless chewing gums made with polyols.
- Polyols produce a lower glycemic response (i.e., a lower rise in blood sugar levels after consumption) than most sugars and starches do. Thus, their use may have advantages for people with diabetes.
- Polyols are lower in calories than sugar is — usually by about half — because they are incompletely digested.

Incomplete digestion, however, is a mixed blessing. Although it helps with calorie reduction, it can also lead to gastrointestinal effects such as looser stools and gas production (flatulence). These effects are similar to those associated with foods that contain carbohydrates of low digestibility, such as bran cereals. Gastrointestinal effects of polyols increase with the amount consumed, and some people are more sensitive than others to these effects. In the United States, some products containing substantial amounts of polyols are required to carry a label notice stating that “excess consumption may have a laxative effect.”

Two new sugar substitutes that are functionally similar to polyols, *trehalose* and *tagatose*, have recently come onto the market. These substances are actually sugars, but their properties are more similar to those of sugar alcohols than those of table sugar. Tagatose is used in foods much as the polyols are. Although it is a sugar, it does not promote tooth decay, and products sweetened with it are permitted to carry a “does not cause tooth decay” label claim. Trehalose is used in foods primarily because it helps to stabilize them during freezing or dehydration, rather than as a sweetening agent. Both trehalose and tagatose have been evaluated for safety and accepted as “generally recognized as safe” (GRAS).

Conclusions

Extensive scientific research supports the safety of the five low-calorie sugar substitutes currently approved for use in foods in the U.S. (acesulfame-K, aspartame, neotame, saccharin, and sucralose). The polyols and similar substances used as bulk sugar substitutes in the U.S. are also safe, but consumers need to be aware of their presence in food products so that they can limit their intake sufficiently to avoid gastrointestinal discomfort. The availability of a variety of safe sugar substitutes is of benefit to consumers because it enables food manufacturers to formulate a variety of good-tasting sweet foods and beverages that are safe for the teeth and lower in calorie content than sugar-sweetened foods.

The proliferation of myths and misinformation on the Internet about the safety of sugar substitutes should serve as a reminder that all sources of health-related information are not created equal. Distinguishing between reliable and unreliable information sources on the World Wide Web can be challenging. Simply entering a topic into an Internet search engine is not the best way to obtain science-based advice.

A better approach is to visit trustworthy health-related Web sites, such as the National Library of Medicine site (<http://www.nlm.nih.gov/medlineplus/>), the U.S. government's health clearinghouse site (<http://www.healthfinder.gov/>), the sites of government agencies such as the Food and Drug Administration (www.fda.gov) or the U.S. Department of Agriculture (www.usda.gov), or the sites of trusted professional organizations or voluntary groups such as the American Dietetic Association (www.eatright.org), the American Heart Association (www.americanheart.org), or the American Cancer Society (www.cancer.org), and then search within the collections of documents at these sites for information on a specific topic.

In instances where something sounds too good — or too horrible — to be true, it's also a good idea to see whether the topic in question is discussed on the Urban Legends Reference Pages (www.snopes.com) and/or Quackwatch (www.quackwatch.com). Both sites are reliable, and they are frequently updated with new information about various health myths and misinformation.

Sources for Further Reading

A good basic source of information on all types of sugar substitutes is an article by John Henkel called “Sugar Substitutes: Americans Opt for Sweetness and Lite,” published in the Food and Drug Administration’s magazine *FDA Consumer* in 1999 and updated in some respects in 2006 (its discussion of neotame is still outdated, however). It is available on the FDA Web site at www.cfsan.fda.gov/~dms/fdsugar.html

The American Dietetic Association publishes and regularly updates a position paper on the use of nutritive and nonnutritive sweeteners. The current version, updated in 2004, is available online at www.eatright.org/cps/rde/xchg/ada/hs.xsl/advocacy_adap0598_ENU_HTML.htm

The Association also has an informative fact sheet about aspartame, which you can find at www.eatright.org/cps/rde/xchg/SID-5303FFEA-32E724A8/ada/hs.xsl/nutrition_1030_ENU_HTML.htm

The International Food Information Council has a brief but informative summary of information on sugars and sugar substitutes on its Web site at ific.org/nutrition/sugars/index.cfm

The National Cancer Institute has a fact sheet about sugar substitutes and cancer, with a link to additional information on the cancer testing of saccharin, on its Web site at www.cancer.gov/cancertopics/factsheet/Risk/artificial-sweeteners.

Readers who are interested in finding out about the research necessary before a new food additive can be approved may wish to browse supplement 2 of volume 38 of the journal *Food and Chemical Toxicology*, published in 2000. This 129-page report, devoted entirely to the safety testing of sucralose, can be found in many university libraries.

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