International Food Information Council

STEVIA SWEETENERS

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WHAT ARE STEVIA SWEETENERS?

Stevia sweeteners are no-calorie sweeteners that can be used to lower one's intake of added sugars while still providing satisfaction from enjoying the taste of something sweet. While some types of sweeteners in this category are considered low-calorie (e.g., aspartame) and others are no-calorie (e.g., stevia sweeteners, monk fruit sweeteners, and sucralose), collectively they are often referred to as sugar substitutes, high-intensity sweeteners, nonnutritive sweeteners or low-calorie sweeteners.

Like other no-calorie sweeteners, stevia sweeteners are intensely sweet. Stevia sweeteners range from being 200-350 times sweeter than sugar, and as such only small amounts of stevia sweeteners are needed to match the sweetness provided by sugar. Stevia sweeteners can be used by food and beverage manufacturers as an ingredient in beverages (such as diet sodas, light or low-sugar juices and flavored waters), canned fruits, condiments, dairy products (such as ice cream, flavored milk and yogurt) and other foods (such as baked goods, cereals, chocolate and other confections) and syrups. Because they are stable at high temperatures, stevia sweeteners can be used in baked goods. However, a recipe that uses stevia sweeteners in place of sugar may turn out slightly different because, in addition to sweetness, sugar plays several roles related to volume and texture in recipes but varies based on the type of recipe.

Stevia sweeteners are also used in several tabletop sweeteners, such as Truvia®, Pure Via®, Stevia Extract in the Raw®, SPLENDA® Naturals Stevia Sweetener, SweetLeaf® and Enliten®, as well as other retail products sold under store-brand names.

HOW ARE STEVIA SWEETENERS PRODUCED?

Stevia sweeteners are derived from the leaves of the Stevia rebaudiana (Bertoni) plant, an herbal shrub native to South America. The stevia plant

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has been used for food and medicinal purposes for hundreds of years, and its leaves and crude extracts have been sold as a dietary supplement. Stevia sweeteners are made by extracting steviol glycosides from the leaves of the stevia plant and purifying them to remove some of the bitter attributes found in the crude extract. Steviol glycosides all have a common basic backbone called *steviol*. They include compounds like stevioside and many different forms of rebaudiosides, the most common of which is rebaudioside A (or reb A).[1] Some steviol glycosides are also made through processes called bioconversion and fermentation, which allow better tasting and less bitter rebaudiosides, such as reb M, to be produced on a larger scale.

WHAT HAPPENS TO STEVIA SWEETENERS AFTER CONSUMPTION?

Steviol glycosides are not absorbed in the upper gastrointestinal tract and therefore do not contribute to any calories or impact blood glucose levels. When they reach the colon, gut microbes cleave off the glucose molecules and use them as an energy source. The remaining steviol backbone is then absorbed via the portal vein, metabolized by the liver and excreted in urine.[1,2]

ARE STEVIA SWEETENERS SAFE TO CONSUME?

YES. High-purity steviol glycosides are Generally Recognized As Safe (GRAS), a regulatory review process category used by the U.S. Food and Drug Administration (FDA). GRAS requires expert consensus that a food ingredient is safe for its intended use. In 2008, the FDA made its first GRAS determination on a stevia sweetener, rebaudioside A, purified from *Stevia rebaudiana* (Bertoni). Whole stevia leaves and crude stevia leaf extracts are not approved food additives because there is not enough toxicological information available, according to the FDA.[3] However, the use of stevia leaves and crude stevia leaf extracts in dietary supplements are not subject to FDA food additive regulations.

Leading global health authorities such as the European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) have concluded that high-purity steviol glycosides are safe for consumption within the acceptable daily intake (ADI) level.[4,5,6] The safety of stevia sweeteners has also been confirmed by Japan's Ministry

WHAT IS AN ADI?

The acceptable daily intake, or ADI, is the average daily intake over a lifetime that is expected to be safe for human consumption based on significant research.[9] It is derived by determining the no-observed-adverse-effect-level, or NOAEL, which is the highest intake level found to have no adverse effects in lifetime studies in animal models, divided by 100.[10] Setting the ADI 100 times lower than the upper level found to have no adverse effects in toxicology studies adds a margin of safety that helps to ensure that human intakes will be safe.

WHAT IS GRAS?

Food ingredients permitted for use in the U.S. fall into one of two categories: food additives (which require review prior to approval from the FDA) or Generally Recognized as Safe (GRAS) ingredients. Whether GRAS or a food additive, food ingredients must be safe and must meet the same high food safety standards. To be considered GRAS, an ingredient must meet one of the following two conditions:

> A history of safe use has been established and a significant number of people consumed the ingredient prior to the enactment of the Food Drug and Cosmetic Act of 1958; or

> Scientific data and information about the safety and use of the ingredient are widely known and publicly available in scientific articles, position papers, etc., with consensus among scientific experts that the ingredient is safe for its intended use.

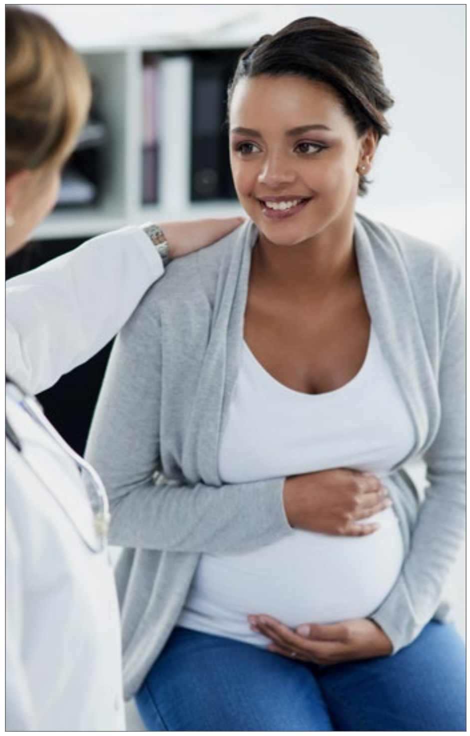
of Health, Labour and Welfare; Food Standards Australia New Zealand; and Health Canada. Based on the conclusions of these global authorities, stevia sweeteners are currently permitted for use in more than 60 countries. For more on the FDA GRAS process, see the **"What is GRAS?"** sidebar on page 2.

Because all steviol glycosides are metabolized to one common end product, steviol, the JECFA has established a group ADI for stevia sweeteners of four milligrams (mg) per kilogram (kg) of body weight per day of steviol equivalents. This is equivalent to 12 mg/kg of body weight per day of rebaudioside A and 10 mg/kg of body weight per day of stevioside. The FDA refers to the ADI established by the JECFA for certain high-purity steviol glycosides purified from the leaves of *Stevia rebaudiana* (Bertoni).

The ADI represents an amount 100 times less than the quantity of stevia sweeteners found to achieve a no-observed-adverse-effect-level (NOAEL) in toxicology studies. The ADI is a conservative number that the vast majority of people will not reach. While information on the amount of stevia sweeteners people consume is limited in the U.S., estimates of daily intake are below the ADI.[8,70] Globally, intake of stevia sweeteners also remains well below the ADI. A 2018 scientific review found that studies conducted since 2008 raise no concerns for exceeding the ADI of the major low- and no-calorie sweeteners—including stevia sweeteners—in the general population.[8] For more on how ADIs are set, see the **"What Is an ADI?"** sidebar on page 2.

CAN CHILDREN CONSUME STEVIA SWEETENERS?

YES. Stevia metabolism is the same in healthy children as it is in healthy adults.[11] As such, the FDA and JECFA have concluded that high-purity stevia



sweeteners are safe for children to consume within the ADI.

Stevia sweeteners can add sweetness to a child's foods and beverages without contributing to calories consumed or added sugars intake. Stevia sweeteners are not cariogenic, so they do not increase the risk of dental caries.[5] With a focus on reducing consumption of added sugars in recent decades, the number of food and beverage products containing low-calorie sweeteners has increased. While observational research among children and adults has shown an increase in the percentage of people reporting daily consumption of products containing low-calorie sweeteners,[12] current intake of low-calorie sweeteners is considered to be well within acceptable levels.[8] One modeling study estimated intakes of stevia sweeteners in children with type 1 diabetes, who may be at a higher risk of exceeding the ADI due to a need to reduce consumption of added sugars.[13] The researchers concluded that there is little chance for children with type 1 diabetes to exceed the ADI for stevia sweeteners.

The American Heart Association (AHA) advises against children regularly consuming beverages containing low-calorie sweeteners, instead recommending water and other unsweetened beverages such as plain milk.[14] One of the notable exceptions in the 2018 AHA science advisory is made for children with diabetes, whose blood glucose management may be benefitted by consuming low-calorie-sweetened beverages in place of sugar-sweetened varieties. Citing an absence of data, the 2019 policy statement from the American Academy of Pediatrics (AAP) does not provide advice on children under two years of age consuming foods or beverages that contain low-calorie sweeteners.[15] The 2019 AAP policy statement does, however, acknowledge potential benefits of low-calorie sweeteners for children by reducing calorie intake (especially among children with obesity), incidence of dental caries and glycemic response among children with type 1 and type 2 diabetes. The 2020—2025 Dietary Guidelines for Americans (DGA) do not recommend the consumption of low-calorie sweeteners or added sugars by children younger than two years of age.[16] This DGA recommendation is not related to body weight, diabetes or the safety of added sugars or low-calorie sweeteners, but is instead intended to avoid infants and toddlers developing a preference for overly sweet foods during this formative phase.

CAN PREGNANT AND BREASTFEEDING WOMEN CONSUME STEVIA SWEETENERS?

YES. While no published research has examined possible effects of purified steviol glycosides on pregnant and lactating women, several landmark studies in animals have demonstrated no adverse reproductive or developmental effects on mothers or their offspring, even when animals were exposed to levels more than 100 times the ADI, every day, over long periods of time.[17,18] After reviewing the safety evidence, regulatory agencies like the EFSA, FDA and JECFA have determined that stevia sweeteners are safe for the general population, including pregnant and breastfeeding women, when consumed within the limits of the ADI. All women who are pregnant or nursing need the necessary nutrients and calories for their baby's optimal growth and development, while taking care not to exceed their needs.

CAN PEOPLE WITH DIABETES CONSUME STEVIA SWEETENERS?

YES. Foods and beverages made with stevia sweeteners are frequently recommended to people with diabetes as an alternative to sugar-sweetened foods and beverages and as a way to help these individuals satisfy their desire for sweet taste while managing carbohydrate intake. Extensive research shows that stevia sweeteners do not raise blood glucose levels or otherwise affect blood glucose management in humans.[19–23] Recent consensus statements by experts in nutrition, medicine, physical activity and public health cite the neutral effects of low-calorie sweeteners on hemoglobin A1C, fasting and post-prandial glucose, and insulin levels and conclude that the use of low-calorie sweeteners in diabetes self-care may contribute to better glycemic management.[24–26]

Global health professional organizations have published their own conclusions on the safety and role of low-calorie sweeteners for people with diabetes. The 2021 American Diabetes Association Standards of Medical Care in Diabetes state that, "For some people with diabetes who are accustomed to regularly consuming sugar-sweetened products, nonnutritive sweeteners

(containing few or no calories) may be an acceptable substitute for nutritive sweeteners (those containing calories, such as sugar, honey, and agave syrup) when consumed in moderation. Use of nonnutritive sweeteners does not appear to have a significant effect on glycemic management, but they can reduce overall calorie and carbohydrate intake, as long as individuals are not compensating with additional calories from other food sources." [27] Similar statements addressing the safety and potential use of low- and no-calorie sweeteners such as stevia sweeteners for people with diabetes are supported by Diabetes Canada and Diabetes UK.[28,29]

Despite these conclusions, some studies raise questions about low-calorie sweeteners and blood glucose management. Some observational studies have demonstrated an association between low-calorie sweetener consumption and risk for type 2 diabetes,[30,31] however, observational studies do not prove cause and effect. Conclusions from observational study designs are at risk for reverse causality and confounding. For instance, many studies do not adjust for obesity status, a direct contributor to developing prediabetes and type 2 diabetes. Given that individuals with overweight and obesity tend to consume more low-calorie-sweetened beverages as compared with lean individuals,[32] this is a critical omission.

CAN STEVIA HELP WITH WEIGHT LOSS OR WEIGHT MAINTENANCE?

Substituting foods and beverages sweetened with stevia sweeteners for their full-sugar counterparts can play a role in weight loss and/or weight management. The National Weight Control Registry (NWCR) is the largest longitudinal study of successful weight loss maintainers who have lost at least 30 pounds and kept if off for more than one year. In an online survey of 434 NWCR members, over 50 percent reported that they regularly consumed low-calorie beverages; 78 percent of these members reported that doing so helped control their calorie intake.[33]

Conclusions from observational research studying the impact of low-calorie sweeteners on body weight often conflict with data from randomized controlled trials. Some observational studies have reported an association between use of low-calorie sweeteners and increased body weight and waist circumference in adults.[34] A systematic review and meta-analysis of observational studies published in 2017 found that consumption of low-calorie sweeteners was also associated with increases in body mass index (BMI) and higher incidence of obesity and cardiometabolic disease in adults.[35] In children and adolescents, observational studies have shown an association between consumption of low-calorie-sweetened beverages and increased body weight, while evidence from randomized trials have not.[36] Other recent systematic reviews and meta-analyses have concluded that findings from observational studies showed no association between low-calorie sweetener intake and body weight and a small positive association with higher BMI.[37–39]

While observational studies can be important for generating hypotheses, it is important to note that they have limitations. By their nature, observational studies cannot prove cause and effect. Instead, observational studies examine the association between an exposure (such as reported stevia sweetener intake) and an outcome (such as body weight or a health condition). Associations found in observational studies can be confounded by various factors and/or may be the result of reverse causality. A common example of this is a person changing their food and beverage choices after being diagnosed with a health condition: The disease led to them making these changes; the changes they made did not lead to the disease.

Additionally, observational studies are not randomized, so they cannot control for all of the other exposures or factors that may be causing or influencing results. For example, one hypothesis is that people may compensate for "calorie-free" choices by eating or drinking more calories in other food choices or future meals.[40,41] Think of a person who may justify ordering dessert at a restaurant because they had a diet soda with their meal: The extra calories from the dessert will likely be greater than the calories saved by ordering the diet beverage. These additional calories may contribute to weight gain or prevent further weight loss. This behavior is called the "licensing effect" or "self-licensing," in which an individual justifies giving in to indulgences by finding reasons to make a behavior that is inconsistent with their goals more acceptable.[42] Although it may occur in some instances, there is little evidence from scientific studies that people consistently and consciously overconsume calories as a result of consuming low-calorie sweeteners or foods and beverages that contain them.[43]

It has also been suggested that people who already have overweight or obesity may begin to choose low-calorie-sweetened foods and beverages as one method for losing weight.[44–47] This makes it difficult to assume that the use of low-calorie sweeteners can be the cause of weight gain, since reverse causality may be a factor. A 2019 systematic review and meta-analysis funded by the World Health Organization recommended cautiously interpreting results from observational studies on low-calorie sweeteners and health outcomes, while concentrating on plausible confounding and reverse causality.[39]

Data from randomized clinical trials, considered to be the gold standard for assessing causal effects, support that substituting low-calorie sweetener options for regular-calorie versions leads to modest weight loss.[37–39, 48–51] Some research that has been conducted on stevia sweeteners has shown potential weight-management benefits. A 2020 randomized controlled trial of two groups of healthy, normal-weight, non-habitual adult consumers of nonnutritive sweeteners tested the effects of daily consumption of stevia sweeteners for 12 weeks.[52] One group was instructed to add drops of stevia sweetener to their typical drinks. The other group was not provided stevia or instructions for its use. After weeks six and 12, individuals in the stevia group maintained their body weight, whereas individuals in the control group showed a significant increase in body weight.

Most of the scientific research examining the relationship between low-calorie sweetener intake and body weight assesses various types of low- and no-calorie sweeteners, including blends. In a 2016 randomized clinical trial, over 300 participants were assigned to consume either water or low-calorie-sweetened beverages for one year as part of a program that included 12 weeks of weight loss followed by 40 weeks of weight-maintenance interventions. Those who were assigned to the low-calorie-sweetened beverage group lost 6.21 kg on average as compared with those in the water group, who lost 2.45 kg.[53]

While a few systematic reviews have concluded that low-calorie sweetener consumption does not lead to appreciable weight loss or weight gain, such findings appear to be the result of how the studies are compared.[35] As stated by Mela, et al.,[47] some study designs allow for the analysis of outcomes between caloric and non-caloric alternatives,[38,51] while others do not.[35]

A 2020 systematic review and meta-analyses of intervention studies concluded that low-calorie sweetener consumption can help reduce body weight by decreasing overall caloric intake.[51] Researchers examined 88 sustained intervention studies that included objective measurements of body weight and BMI and the use of relevant comparators. Compared with sugar consumption, low-calorie sweetener consumption reduced body weight, BMI and total calorie intake. When comparing consumption of low-calorie sweeteners with the intake of water or nothing, there was also no difference in body weight, BMI or total calorie intake. Additionally, no effect was found between taking low-calorie sweetener capsules versus placebo capsules, indicating that the effect of low-calorie sweetener intake on energy balance is through calorie displacement.

The Scientific Report of the 2020 Dietary Guidelines Advisory Committee (DGAC) included a systematic review of 37 studies (six of which were randomized controlled trials) published between January 2000 and June 2019 on the role of low- and no-calorie-sweetened beverages on adiposity. The DGAC report concluded that low- and no-calorie sweeteners should be considered an option for managing body weight.[54]

It is important to note that losing and maintaining body weight requires multiple simultaneous approaches. Making a single change, such as substituting low-calorie-sweetened options for full-calorie, sugar-containing products is just one approach. Lifestyle and behavioral practices like eating healthfully, exercising regularly, getting enough sleep, and maintaining social support networks are all important factors in achieving weight loss and weight-maintenance goals.

STEVIA SWEETENERS AT A GLANCE

SCIENTIFIC NAME: *Stevia rebaudiana* Bertoni

BRAND NAME: Truvia®, Pure Via®, Stevia Extract in the Raw®, SPLENDA® Naturals Stevia Sweetener, SweetLeaf®, Enliten®

FDA STATUS: Generally Recognized as Safe (GRAS) in 2008 for use in foods and beverages

CAN STEVIA SWEETENERS MAKE ME HUNGRIER?

Highly palatable foods activate brain regions of reward and pleasure. This positive association has been hypothesized to enhance appetite, and, if left unchecked, the resulting increase in food intake may contribute to overweight and obesity.[55] Low-calorie sweeteners can also lead to a stimulation of reward pathways by activating sweet taste receptors, but they are not a source of calories.

Some have expressed concern that activating reward pathways without delivering sugar to the body may have unintended consequences. Some animal studies have demonstrated changes in food intake and appetite-related hormones after consuming low-calorie sweeteners.[34,48] And yet, similar effects have not been seen in humans. To date, there is no strong evidence that low- and no-calorie sweeteners, including stevia sweeteners, enhance appetite or cravings in humans,[26,43] and some randomized trials have demonstrated the opposite effect—including a decrease in hunger[52] and reduced dessert intake among those who drank low-calorie-sweetened beverages compared with those who drank water.[55] Others have shown no effect of stevia sweeteners on satiety[57,58] as well as a reduction in overall daily calorie intake compared with a full-sugar control,[57] results that can be attributed to the lower calorie content of the stevia sweetener intervention and the fact that participants did not make up for the deficit by eating more calories later in the day.

A 2020 randomized controlled trial examined the influence of sweetness (with or without calories) on appetite and food intake. Researchers found that subjects who consumed water sweetened with stevia experienced reduced feelings of hunger before a meal when compared with those who consumed plain water.[59] They also found that consuming stevia-sweetened water reduced subsequent food intake compared with matching volumes of plain water, water containing maltodextrin or water sweetened with glucose or sucrose. Additionally, a 2018 randomized controlled trial demonstrated a reduction in hunger after consuming cookies made with stevia sweeteners compared with control cookies.[60]

WHAT ABOUT THE GUT MICROBIOME?

Although research on the gut microbiome is still in its infancy, the microbes living in our intestinal tract have become recognized as potentially significant contributors to our health. Gut microbiota are integral to the metabolism of steviol glycosides, a process that research has shown to have a limited effect on the composition of the human gut microbiome itself,[61] as observed in a 2003 *in vitro* study.[62] However, randomized clinical trials have not yet been conducted in humans, and to date there is no evidence that stevia sweeteners meaningfully impact the composition or function of the gut microbiome.[11,63–66]

Currently, no standards exist to define a healthy human microbiome.[67] There are significant differences among microbiome profiles of different people, and research has shown that the gut microbiome can quickly respond to normal changes in the diet.[68] International experts have noted that huge variabilities in microbiome profiles makes it difficult to distinguish normal variation from adverse effects.

A 2019 literature review found no conclusive evidence that low-calorie sweeteners negatively impact gut microbiota.[68] In 2020, a panel of experts on low-calorie sweeteners came to a similar conclusion that, at this time, data on the effects of low-calorie sweeteners on the human gut microbiota are limited and do not provide adequate evidence that they impact gut health at doses that are relevant to human consumption.[26]

WHAT'S THE BOTTOM LINE?

All types of foods and beverages, including those made with stevia sweeteners, can have a place in a variety of healthy eating patterns. Stevia sweeteners have been considered GRAS in the U.S. since 2008, and their safety has been acknowledged by many international health agencies. The impact of low-calorie sweeteners on, and association with, chronic conditions like obesity and type 2 diabetes have been studied. Observational studies linking low-calorie sweeteners to risk for type 2 diabetes and weight gain inherently cannot demonstrate a causal relationship and suffer from methodological issues like confounding and reverse causality. In contrast, randomized controlled trials consistently support that low-calorie sweeteners can be useful in nutritional strategies to assist with weight loss and/or weight-maintenance goals. Stevia sweeteners do not negatively impact blood glucose or insulin levels in randomized controlled trials. While the role of the gut microbiome in health is still being explored, the available research does not suggest that low- and no- calorie sweeteners such as stevia sweeteners adversely affect the gut microbiome.

Adopting a healthful, active lifestyle that is tailored to personal goals and priorities is vital to supporting one's well-being. Choosing foods and beverages sweetened with low- and no-calorie sweeteners such as stevia sweeteners is one way to reduce consumption of added sugars and keep calories in check—important components in maintaining health and reducing the risk for lifestyle-related diseases.

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