



# 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

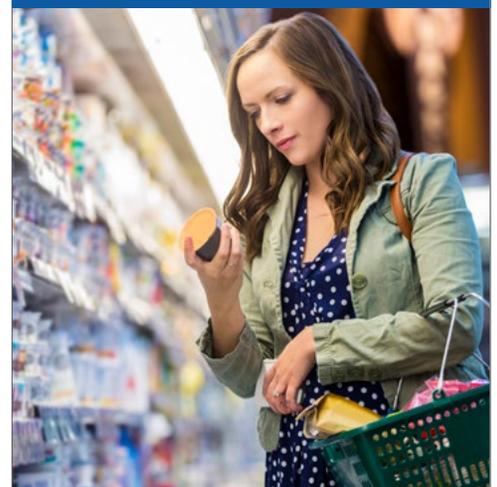
beverage manufacturers as an ingredient in beverages (such as diet sodas, light or low-sugar juices and flavored waters), canned fruits, condiments, dairy products (such as ice cream, flavored milk and yogurt) and other foods (such as baked goods, cereals, chocolate and other confections) and syrups. 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 In The Raw®, SLENDA® 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).<sup>1</sup> 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.<sup>1,2</sup>

## 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.<sup>3</sup> 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.<sup>4,5,6</sup> 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.<sup>9</sup> 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.<sup>10</sup> 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.

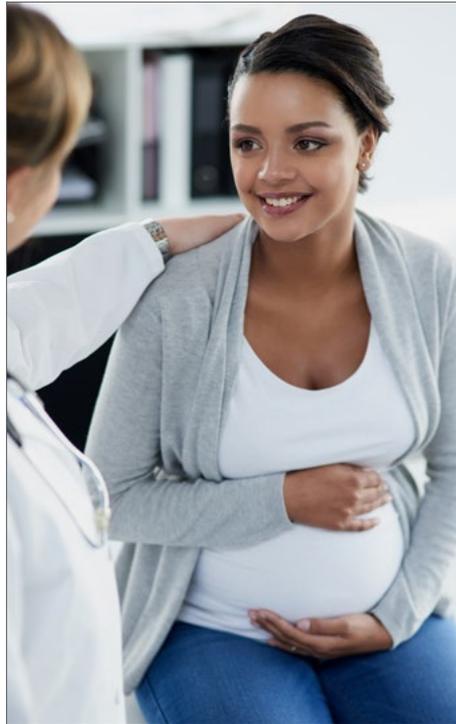
of Health, Labour and Welfare; Food Standards Australia New Zealand; and Health Canada. Based on the conclusions of these global authorities, stevia sweeteners are currently permitted for use in more than 60 countries. For more on the FDA GRAS process, see the **“What is GRAS?”** sidebar on page 2.

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.<sup>8,70</sup> 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.<sup>8</sup> 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.<sup>11</sup> 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.<sup>5</sup> 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,<sup>12</sup> current intake of low-calorie sweeteners is considered to be well within acceptable levels.<sup>8</sup> 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.<sup>13</sup> 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.<sup>14</sup> One of the notable exceptions 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.<sup>15</sup> 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.<sup>16</sup> 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.<sup>17,18</sup> 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.<sup>19–23</sup> 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.<sup>24–26</sup>

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.”<sup>27</sup> 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](#).<sup>28,29</sup>

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,<sup>30,31</sup> 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,<sup>32</sup> 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 it 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.<sup>33</sup>

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.<sup>34</sup> 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.<sup>35</sup> 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.<sup>36</sup> 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.<sup>37-39</sup>

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.<sup>40,41</sup> 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.<sup>42</sup> 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.<sup>43</sup>

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.<sup>44-47</sup> 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.<sup>39</sup>

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.<sup>37-39, 48-51</sup> 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.<sup>52</sup> 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.<sup>53</sup>

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.<sup>35</sup> As stated by Mela, et al.,<sup>47</sup> some study designs allow for the analysis of outcomes between caloric and non-caloric alternatives,<sup>38,51</sup> while others do not.<sup>35</sup>

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.<sup>51</sup> 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.<sup>54</sup>

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



## STEVIA SWEETENERS AT A GLANCE

**SCIENTIFIC NAME:** *Stevia rebaudiana* Bertoni

**BRAND NAME:** Truvia®, Pure Via®, Stevia In The Raw®, SLENDA® Naturals Stevia Sweetener, SweetLeaf®, Enliten®

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

healthfully, exercising regularly, getting enough sleep, and maintaining social support networks are all important factors in achieving weight loss and weight-maintenance goals.

## 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.<sup>55</sup> 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.<sup>34,48</sup> 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,<sup>26,43</sup> and some randomized trials have demonstrated the opposite effect—including a decrease in hunger<sup>52</sup> and reduced dessert intake among those who drank low-calorie-sweetened beverages compared with those who drank water.<sup>55</sup> Others have shown no effect of stevia sweeteners on satiety,<sup>57,58</sup> as well as a reduction in overall daily calorie intake compared with a full-sugar control,<sup>57</sup> 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.<sup>59</sup> 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.<sup>60</sup>

## 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,<sup>61</sup> as observed in a 2003 *in vitro* study.<sup>62</sup>



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.<sup>11,63-66</sup>

Currently, no standards exist to define a healthy human microbiome.<sup>67</sup> 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.<sup>68</sup> 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.<sup>68</sup> 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.<sup>26</sup>

## 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.

## REFERENCES

1. [Magnuson BA](#), Carakostas MC, Moore NH, Poulos SP, Renwick AG. Biological fate of low-calorie sweeteners. *Nutr Rev*. 2016 Nov;74(11):670-689.
2. [Roberts A](#), Renwick AG. Comparative toxicokinetics and metabolism of rebaudioside A, stevioside, and steviol in rats. *Food Chem Toxicol*. 2008 Jul;46 Suppl 7:S31-9.
3. [U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition](#). Import Alert 45-06 [Internet]. Silver Spring, MD: U.S. Food and Drug Administration; 2019 August 16 [cited 2020 November 20].
4. [Joint FAO/WHO Expert Committee on Food Additives](#). Evaluation of certain food additives and contaminants: Sixty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives. Geneva, Switzerland. 2009.
5. [EFSA ANS Panel](#) (EFSA Panel on Food Additives and Nutrient Sources). Scientific Opinion on safety of steviol glycosides for the proposed uses as a food additive. *EFSA Journal*. 2010 Apr;8(4):1537.
6. [EFSA Panel on Food Additives and Flavourings](#) (FAF), Younes M, Aquilina G, Engel KH, Fowler P, Frutos Fernandez MJ, Fürst P, Gürtler R, Gundert-Remy U, Husøy T, Manco M, Mennes W, Moldeus P, Passamonti S, Shah R, Waalkens-Berendsen I, Wölfle D, Wright M, Degen G, Giarola A, Rincon AM, Castle L. Safety of a proposed amendment of the specifications for steviol glycosides (E 960) as a food additive: to expand the list of steviol glycosides to all those identified in the leaves of *Stevia Rebaudiana Bertoni*. *EFSA J*. 2020 Apr 29;18(4):e06106.
7. [Renwick AG](#). The use of a sweetener substitution method to predict dietary exposures for the intense sweetener rebaudioside A. *Food Chem Toxicol*. 2008 Jul;46 Suppl 7:S61-9.
8. [Martyn D](#), Darch M, Roberts A, Lee HY, Yaqiong Tian T, Kaburagi N, Belmar P. Low-/No-Calorie Sweeteners: A Review of Global Intakes. *Nutrients*. 2018 Mar 15;10(3):357.
9. [World Health Organization, Food and Agriculture Organization of the United Nations](#). Principles and Methods for the Risk Assessment of Chemicals in Food. Chapter 5. 2009.
10. [Renwick AG](#). Safety factors and establishment of acceptable daily intakes. *Food Addit Contam*. 1991 Mar-Apr;8(2):135-49.
11. [Purkayastha S](#), Kwok D. Metabolic fate in adult and pediatric population of steviol glycosides produced from stevia leaf extract by different production technologies. *Regul Toxicol Pharmacol*. 2020 Oct;116:104727.
12. [Sylvetsky AC](#), Jin Y, Clark EJ, Welsh JA, Rother KI, Tategawkar SA. Consumption of Low-Calorie Sweeteners among Children and Adults in the United States. *J Acad Nutr Diet*. 2017 Mar;17(3):441-448.e2.
13. [Dewinter L](#), Casteels K, Corthouts K, Van de Kerckhove K, Van der Vaerent K, Vanmeerbeeck K, Matthys C. Dietary intake of non-nutritive sweeteners in type 1 diabetes mellitus children. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*. 2016;33(1):19-26.
14. [Johnson RK](#), Lichtenstein AH, Anderson CAM, Carson JA, Després JP, Hu FB, Kris-Etherton PM, Otten JJ, Towfighi A, Wylie-Rosett J; American Heart Association Nutrition Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Quality of Care and Outcomes Research; and Stroke Council. Low-Calorie Sweetened Beverages and Cardiometabolic Health: A Science Advisory From the American Heart Association. *Circulation*. 2018 Aug 28;138(9):e126-e140.
15. [Baker-Smith CM](#), de Ferranti SD, Cochran WJ; COMMITTEE ON NUTRITION, SECTION ON GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION. The Use of Nonnutritive Sweeteners in Children. *Pediatrics*. 2019 Nov;144(5):e20192765.
16. [U.S. Department of Agriculture and U.S. Department of Health and Human Services](#). *Dietary Guidelines for Americans, 2020-2025*. 9th Edition. December 2020. Available at DietaryGuidelines.gov.
17. [Usami M](#), Sakemi K, Kawashima K, Tsuda M, Ohno Y. [Teratogenicity study of stevioside in rats]. *Eisei Shikenjo Hokoku*. 1995;(113):31-5. Japanese.
18. [Curry LL](#), Roberts A, Brown N. Rebaudioside A: two-generation reproductive toxicity study in rats. *Food Chem Toxicol*. 2008 Jul;46 Suppl 7:S21-30.
19. [Maki KC](#), Curry LL, Reeves MS, Toth PD, McKenney JM, Farmer MV, Schwartz SL, Lubin BC, Boileau AC, Dicklin MR, Carakostas MC, Tarka SM. Chronic consumption of rebaudioside A, a steviol glycoside, in men and women with type 2 diabetes mellitus. *Food Chem Toxicol*. 2008 Jul;46 Suppl 7:S47-53.
20. [Ajami M](#), Seyfi M, Abdollah Pouri Hosseini F, Naseri P, Velayati A, Mahmoudnia F, Zahedirad M, Hajifaraji M. Effects of stevia on glycemic and lipid profile of type 2 diabetic patients: A randomized controlled trial. *Avicenna J Phytomed*. 2020 Mar-Apr;10(2):118-127.
21. [Onakpoya LJ](#), Heneghan CJ. Effect of the natural sweetener, steviol glycoside, on cardiovascular risk factors: a systematic review and meta-analysis of randomised clinical trials. *Eur J Prev Cardiol*. 2015 Dec;22(12):1575-87.
22. [Romo-Romo A](#), Aguilar-Salinas CA, Brito-Cordova GX, Gomez Diaz RA, Vilchis Valentin D, Almeda-Valdes P. Effects of non-nutritive sweeteners on glucose metabolism and appetite regulating hormones: systematic review of observational prospective studies and clinical trials. *PLoS One*. 2016 Aug 18;11(8):e0161264.
23. [Nichol AD](#), Holle MJ, An R. Glycemic impact of non-nutritive sweeteners: a systematic review and meta-analysis of randomized controlled trials. *Eur J Clin Nutr*. 2018 Jun;72(6):796-804.
24. [Serra-Majem L](#), et al. IberoAmerican Consensus on Low- and No-Calorie Sweeteners: Safety, Nutritional Aspects and Benefits in Food and Beverages. *Nutrients*. 2018 Jun 25;10(7):818.
25. [Evert AB](#), Dennison M, Gardner CD, Garvey WT, Lau KHK, MacLeod J, Mitri J, Pereira RF, Rawlings K, Robinson S, Saslow L, Uelman S, Urbanski PB, Yancy WS Jr. Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report. *Diabetes Care*. 2019 May;42(5):731-754.
26. [Ashwell M](#), Gibson S, Bellisle F, Buttriss J, Drewnowski A, Fantino M, Gallagher AM, de Graaf K, Goscinny S, Hardman CA, Laviada-Molina H, López-García R, Magnuson B, Mellor D, Rogers PJ, Rowland I, Russell W, Sievenpiper JL, la Vecchia C. Expert consensus on low-calorie sweeteners: facts, research gaps and suggested actions. *Nutr Res Rev*. 2020 Jun;33(1):145-154.
27. [American Diabetes Association](#). 5. Facilitating Behavior Change and Well-being to Improve Health Outcomes: *Standards of Medical Care in Diabetes-2021*. Diabetes Care. 2021 Jan;44(Suppl 1):S53-S72.
28. [Diabetes Canada Clinical Practice Guidelines Expert Committee](#). Sievenpiper JL, Chan CB, Dworatzek PD, Freeze C, Williams SL. Nutrition Therapy. *Can J Diabetes*. 2018 Apr;42 Suppl 1:S64-S79.
29. [Dyson PA](#), Twenefour D, Breen C, Duncan A, Elvin E, Goff L, Hill A, Kalsi P, Marsland N, McArdle P, Mellor D, Oliver L, Watson K. Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes. *Diabet Med*. 2018 May;35(5):541-547.
30. [Sakurai M](#), Nakamura K, Miura K, Takamura T, Yoshita K, Nagasawa SY, Morikawa Y, Ishizaki M, Kido T, Naruse Y, Suwazono Y, Sasaki S, Nakagawa H. Sugar-sweetened beverage and diet soda consumption and the 7-year risk for type 2 diabetes mellitus in middle-aged Japanese men. *Eur J Nutr*. 2014 Feb;53(1):251-8.
31. [Imamura F](#), O'Connor L, Ye Z, Mursu J, Hayashino Y, Bhupathiraju SN, Forouhi NG. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. *BMJ*. 2015 Jul 21;351:h3576.
32. [Bleich SN](#), Wolfson JA, Vine S, Wang YC. Diet-beverage consumption and caloric intake among US adults, overall and by body weight. *Am J Public Health*. 2014 Mar;104(3):e72-8.
33. [Catenacci VA](#), Pan Z, Thomas JG, Ogden LG, Roberts SA, Wyatt HR, Wing RR, Hill JO. Low/no calorie sweetened beverage consumption in the National Weight Control Registry. *Obesity* (Silver Spring). 2014 Oct;22(10):2244-51.
34. [Fowler SPG](#). Low-calorie sweetener use and energy balance: Results from experimental studies in animals, and large-scale prospective studies in humans. *Physiol Behav*. 2016 Oct 1;164(Pt B):517-523.

35. [Azad MB](#), Abou-Setta AM, Chauhan BF, Rabbani R, Lys J, Copstein L, Mann A, Jeyaraman MM, Reid AE, Fiander M, MacKay DS, McGavock J, Wicklow B, Zarychanski R. Nonnutritive sweeteners and cardiometabolic health: a systematic review and meta-analysis of randomized controlled trials and prospective cohort studies. *CMAJ*. 2017 Jul 17;189(28):E929-E939.
36. [Young J](#), Conway EM, Rother KI, Sylvestry AC. Low-calorie sweetener use, weight, and metabolic health among children: A mini-review. *Pediatr Obes*. 2019 Aug;14(8):e12521.
37. [Miller PE](#), Perez V. Low-calorie sweeteners and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohort studies. *Am J Clin Nutr*. 2014 Sep;100(3):765-77.
38. [Rogers PJ](#), Hogenkamp PS, de Graaf C, Higgs S, Lluch A, Ness AR, Penfold C, Perry R, Putz P, Yeomans MR, Mela DJ. Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *Int J Obes (Lond)*. 2016 Mar;40(3):381-94.
39. [Toews I](#), Lohner S, Küllenberg de Gaudry D, Sommer H, Meerpohl JJ. Association between intake of non-sugar sweeteners and health outcomes: systematic review and meta-analyses of randomised and non-randomised controlled trials and observational studies. *BMJ*. 2019 Jan 2;364:k4718.
40. [Mattes RD](#), Popkin BM. Nonnutritive sweetener consumption in humans: effects on appetite and food intake and their putative mechanisms. *Am J Clin Nutr*. 2009 Jan;89(1):1-14.
41. [Peters JC](#), Beck J. Low Calorie Sweetener (LCS) use and energy balance. *Physiol Behav*. 2016 Oct 1;164(Pt B):524-528.
42. [De Witt Huberts JC](#), Evers C, De Ridder DT. "Because I am worth it": a theoretical framework and empirical review of a justification-based account of self-regulation failure. *Pers Soc Psychol Rev*. 2014 May;18(2):119-38.
43. [Rogers PJ](#). The role of low-calorie sweeteners in the prevention and management of overweight and obesity: evidence v. conjecture. *Proc Nutr Soc*. 2018 Aug;77(3):230-238.
44. [Drewnowski A](#), Rehm CD. The use of low-calorie sweeteners is associated with self-reported prior intent to lose weight in a representative sample of US adults. *Nutr Diabetes*. 2016 Mar 7;6:e202.
45. [Sievenpiper JL](#), Khan TA, Ha V, Viguiouk E, Auyeung R. The importance of study design in the assessment of nonnutritive sweeteners and cardiometabolic health. *CMAJ*. 2017 Nov 20;189(46):E1424-E1425.
46. [Malik VS](#). Non-sugar sweeteners and health. *BMJ*. 2019 Jan 3;364:k5005.
47. [Mela DJ](#), McLaughlin J, Rogers PJ. Perspective: Standards for Research and Reporting on Low-Energy ("Artificial") Sweeteners. *Adv Nutr*. 2020 May 1;11(3):484-491.
48. [Sylvestry AC](#), Rother KI. Nonnutritive sweeteners in weight management and chronic disease: a review. *Obesity (Silver Spring)*. 2018 Apr;26(4):635-640.
49. [Laviada-Molina H](#), Molina-Segui F, Pérez-Gaxiola G, Cuello-García C, Arjona-Villicaña R, Espinosa-Marrón A, Martínez-Portilla RJ. Effects of nonnutritive sweeteners on body weight and BMI in diverse clinical contexts: Systematic review and meta-analysis. *Obes Rev*. 2020 Jul;21(7):e13020.
50. [Ebbeling CB](#), Feldman HA, Steltz SK, Quinn NL, Robinson LM, Ludwig DS. Effects of Sugar-Sweetened, Artificially Sweetened, and Unsweetened Beverages on Cardiometabolic Risk Factors, Body Composition, and Sweet Taste Preference: A Randomized Controlled Trial. *J Am Heart Assoc*. 2020 Aug 4;9(15):e015668.
51. [Rogers PJ](#), Appleton KM. The effects of low-calorie sweeteners on energy intake and body weight: a systematic review and meta-analyses of sustained intervention studies. *Int J Obes (Lond)*. 2021 Mar;45(3):464-478.
52. [Stamataki NS](#), Crooks B, Ahmed A, McLaughlin JT. Effects of the Daily Consumption of Stevia on Glucose Homeostasis, Body Weight, and Energy Intake: A Randomised Open-Label 12-Week Trial in Healthy Adults. *Nutrients*. 2020 Oct 6;12(10):3049.
53. [Peters JC](#), Beck J, Cardel M, Wyatt HR, Foster GD, Pan Z, Wojtanowski AC, Vander Veur SS, Herring SJ, Brill C, Hill JO. The effects of water and non-nutritive sweetened beverages on weight loss and weight maintenance: A randomized clinical trial. *Obesity (Silver Spring)*. 2016 Feb;24(2):297-304.
54. [Dietary Guidelines Advisory Committee](#). *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC. 2020
55. [Singh M](#). Mood, food, and obesity. *Front Psychol*. 2014 Sep 15;9:25.
56. [Piernas C](#), Tate DF, Wang X, Popkin BM. Does diet-beverage intake affect dietary consumption patterns? Results from the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. *Am J Clin Nutr*. 2013 Mar;97(3):604-11.
57. [Anton SD](#), Martin CK, Han H, Coulon S, Cefalu WT, Geiselman P, Williamson DA. Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels. *Appetite*. 2010 Aug;55(1):37-43.
58. [Tev SL](#), Salleh NB, Henry J, Forde CG. Effects of aspartame-, monk fruit-, stevia- and sucrose-sweetened beverages on postprandial glucose, insulin and energy intake. *Int J Obes (Lond)*. 2017 Mar;41(3):450-457.
59. [Stamataki N](#), Scott C, Elliott R, McKie S, Bosscher D, McLaughlin J. Stevia Beverage Consumption prior to Lunch Reduces Appetite and Total Energy Intake without Affecting Glycemia or Attentional Bias to Food Cues: A Double-Blind Randomized Controlled Trial in Healthy Adults. *The Journal of Nutrition*, Volume 150, Issue 5, May 2020, Pages 1126-1134.
60. [Ahmad J](#), Khan I, Johnson SK, Alam I, Din ZU. Effect of Incorporating Stevia and Moringa in Cookies on Postprandial Glycemia, Appetite, Palatability, and Gastrointestinal Well-Being. *J Am Coll Nutr*. 2018 Feb;37(2):133-139.
61. [Ruiz-Ojeda FJ](#), Plaza-Diaz J, Sáez-Lara MJ, Gil A. Effects of Sweeteners on the Gut Microbiota: A Review of Experimental Studies and Clinical Trials. *Adv Nutr*. 2019 Jan 1;10(suppl\_1):S31-S48.
62. [Gardana C](#), Simonetti P, Canzi E, Zanchi R, Pietta P. Metabolism of stevioside and rebaudioside A from Stevia rebaudiana extracts by human microflora. *J Agric Food Chem*. 2003 Oct 22;51(22):6618-22.
63. [Kunová G](#), Rada V, Vidallac A, Lisova I. Utilisation of steviol glycosides from Stevia rebaudiana (Bertoni) by lactobacilli and bifidobacteria in in vitro conditions. *Folia Microbiol (Praha)*. 2014 May;59(3):251-5.
64. [Li S](#), Chen T, Dong S, Xiong Y, Wei H, Xu F. 2014. The effects of rebaudioside A on microbial diversity in mouse intestine. *Food Sci Technol Res*. 2014 May;20(2):459-467.
65. [DeniDa I](#), Semjonovs P, Fomina A, Treimane R, Linde R. The influence of stevia glycosides on the growth of Lactobacillus reuteri strains. *Lett Appl Microbiol*. 2014 Mar;58(3):278-84.
66. [Wang QP](#), Browman D, Herzog H, Neely GG. Non-nutritive sweeteners possess a bacteriostatic effect and alter gut microbiota in mice. *PLoS One*. 2018 Jul 5;13(7):e01990868.
67. [Merten C](#), Schoonjans R, Di Gioia D, Peláez C, Sanz Y, Maurici D, Robinson T. Editorial: Exploring the need to include microbiomes into EFSA's scientific assessments. *EFSA J*. 2020 Jun 29;18(6):e18061.
68. [David LA](#), Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, Ling AV, Devlin AS, Varma Y, Fischbach MA, Biddinger SB, Dutton RJ, Turnbaugh PJ. Diet rapidly and reproducibly alters the human gut microbiome. *Nature*. 2014 Jan 23;505(7484):559-69.
69. [Lobach AR](#), Roberts A, Rowland IR. Assessing the in vivo data on low/no-calorie sweeteners and the gut microbiota. *Food Chem Toxicol*. 2019 Feb;124:385-399.
70. [Tran NL](#), Barraij LM, Hearty AP, Jack MM. Tiered intake assessment for low- and no-calorie sweeteners in beverages. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*. 2021 Feb;38(2):208-222.