

here's no mistaking it: Americans love to eat. Enjoying good food with good company is one of life's great pleasures. And yet, frequent overindulgences can have a detrimental impact on conditions like obesity and type 2 diabetes, which take a substantial toll on individuals, communities and our healthcare system. Replacing foods and beverages high in calories and added sugars with ones that are lower in sugar is one option to help reduce intake of excess calories. In turn, this may help reduce the risk of obesity and related chronic diseases. One group of low-calorie sweeteners, purified extracts from the stevia leaf (referred to in this fact sheet as "stevia sweeteners"), are used in foods and beverages as a way to lower intake of added sugars while still providing satisfaction from enjoying something sweet. This fact sheet will examine many topics of interest around stevia sweeteners and health so that you can make informed decisions about their place in your diet.

WHAT ARE STEVIA SWEETENERS?

Stevia sweeteners are derived from the leaves of the Stevia rebaudiana (Bertoni) plant, an herbal shrub native to South America. The stevia plant has been used for food and medicinal purposes for hundreds of years, and its leaves and crude extracts have been sold as dietary supplements. Purified extracts of the sweet substances found in the stevia leaf, called steviol glycosides, are considered to be generally recognized as safe (GRAS) by the U.S. Food and Drug Administration (FDA). However, whole stevia leaves and crude leaf extracts are not permitted to be sold as sweeteners in the U.S. because there is not enough toxicological information on these products, according to the FDA.

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) (Magnuson 2016). Some steviol glycosides are also made through processes called bioconversion and fermentation, which allow sweeter and less bitter stevia rebaudiosides, such as reb M, to be produced on a larger scale.

BY THE INTERNATIONAL FOOD INFORMATION COUNCIL FOUNDATION



Purified steviol glycosides are not absorbed in the upper gastrointestinal tract and therefore do not contribute to any calories to our diet. 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 (Magnuson 2016, Roberts 2008).

Stevia sweeteners are 200-350 times sweeter than sugar and contribute sweetness to foods and beverages without adding calories. Stevia sweeteners are found in 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. Stevia sweeteners are used in beverages and foods like soft drinks, juices, dairy products, canned fruits, syrups and condiments. Because they are stable at high temperatures, stevia sweeteners can be used in baked goods. However, a food containing stevia sweeteners may be slightly different in appearance, texture and taste than the same food made with sugar, as sugar contributes to the structure and texture of foods.

Like all no- and low-calorie sweeteners, only very small amounts of stevia sweeteners are needed to achieve the sweetness of sugar. To make measuring and pouring easier, they are typically blended with common, approved food ingredients. This is why a packet of stevia sweeteners seems equal in quantity to a packet of table sugar, for example.

ARE STEVIA SWEETENERS SAFE TO CONSUME?

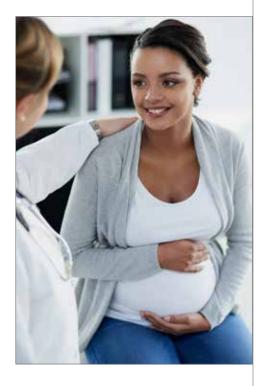
YES. High-purity steviol glycosides received no objection from the FDA for generally recognized as safe (GRAS) status from the <u>FDA</u> in 2008, a category which requires expert consensus that

a food ingredient is safe for its intended use. However, whole stevia leaf and crude stevia extracts do not have FDA approval for use in foods or drinks. Leading global health authorities such as the European Food Safety Authority (EFSA), Joint FAO/WHO Expert Committee on Food Additives (JECFA), the Japan Ministry of Health and Welfare, Food Standards Australia New Zealand and Health Canada have also found purified stevia sweeteners to be safe.

Because all steviol glycosides are metabolized to one common end product, steviol, the JECFA established an acceptable daily intake (ADI) for stevia sweeteners of 4 milligrams of steviol equivalents per kilogram of body weight (mg/kg) per day. This is equivalent to 12 mg/kg reb A per day and 10 mg/kg stevioside per day. The ADI represents an amount 100 times less than the quantity of stevia sweeteners found to be safe in research studies. While information on dietary exposure to stevia sweeteners is limited in the United States, estimates of daily intake are below the ADI (Renwick 2008). 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 (Martyn 2018).

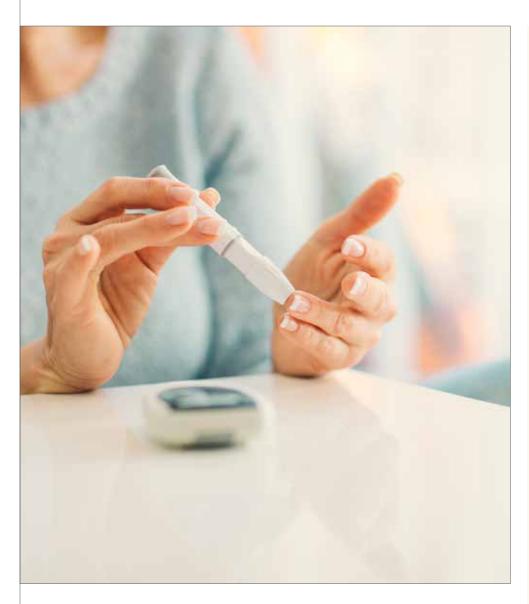
ARE STEVIA SWEETENERS SAFE FOR CHILDREN?

YES. Foods that include stevia sweeteners can add sweetness to a child's diet without contributing to increased calorie intake, sugar intake or risk of cavities. As with adults, current intake of low-calorie sweeteners in children is considered to be well within acceptable levels. Due to limited studies in children, however, the American Academy of Pediatrics does not have official recommendations on low-calorie sweetener intake.



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 (Curry 2008, Usami 1995). After reviewing the safety evidence, regulatory agencies like the JECFA, EFSA and FDA have all 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 should try to consume the necessary nutrients and calories for their baby's growth during pregnancy and breastfeeding, while taking care not to exceed their needs. This may include being mindful of all sources of sweeteners, whether they be from sugar or low-calorie sweeteners.



CAN PEOPLE WITH DIABETES CONSUME STEVIA SWEETENERS?

YES. Products containing stevia sweeteners provide a sweet taste and are often low or lower in carbohydrates, which is important for people who must monitor their carbohydrate intake. Stevia sweeteners do not raise blood sugar levels. The 2018 American Diabetes Association Standards of Medical Care in Diabetes state that, "The use of nonnutritive sweeteners may have the potential to reduce overall calorie and carbohydrate intake if substituted for caloric (sugar) sweeteners and without compensation by intake of additional calories from other food sources. Nonnutritive sweeteners are generally safe to use within the defined acceptable daily intake levels." One modeling study (Dewinter 2016) 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 manage a diet lower in carbohydrates and sugars. The researchers concluded that there is little chance for children with type 1 diabetes to exceed the ADI for stevia sweeteners. Nonetheless, people with diabetes should talk with a registered dietitian, healthcare professional or a certified diabetes educator for advice on healthy eating to improve blood sugar control.

WHAT IS AN ADI?

The acceptable daily intake, or ADI, is the average daily intake over a lifetime that is expected to be safe based on significant research (WHO 2009). It is usually derived by determining the highest intake level found to have no adverse effects in lifetime studies in animal models. These studies are required by FDA and other regulatory agencies around the world before permitting any new food ingredient. That amount is then divided by a safety factor (usually 100) to determine the ADI (Renwick 1991). The ADI is a conservative number that the vast majority of people will not reach.

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: 1) 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 2) 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.

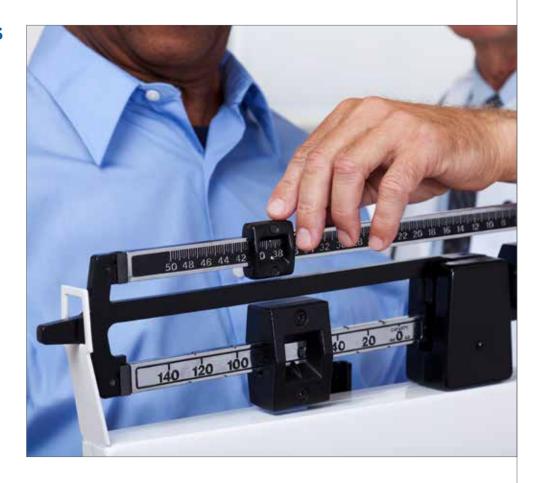
STEVIA SWEETENERS

WILL STEVIA SWEETENERS HELP ME LOSE OR MAINTAIN MY WEIGHT?

Substituting foods and beverages sweetened with stevia sweeteners for their full-sugar counterparts can play a role in weight loss or weight management. In a survey of members of the National Weight Control Registry, the largest study of successful weight-loss maintainers, over 50 percent of all respondents stated that they regularly consume low-calorie beverages, 78 percent of whom felt that doing so helped control their calorie intake (Catenacci 2014).

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 (Miller 2014, Rogers 2016). For example, in one study, over 300 participants were assigned to consume either water or low-calorie sweetened beverages for one year as part of a weight loss program. Those who were assigned to the low-calorie sweetener group lost 6.21 kg on average, compared to those in the water group, who lost 2.45 kg (Peters 2016). However, clinical trials on the effect of stevia sweeteners on body weight have not yet been published.

Some observational studies have demonstrated an association between low-calorie sweeteners and increased weight and waist circumference (Fowler 2016). Observational studies, which examine the relationship between an exposure (such as intake of stevia sweeteners) and an outcome (such as body weight or a health condition), are not able to establish cause and effect. This is because they are not randomized. so they cannot control for all of the other exposures or factors that may be causing or influencing the 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 (Mattes 2009). 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 be greater than the calories saved by ordering the diet beverage. These additional calories may contribute to weight gain or prevent further weight loss. It has also been suggested that people who are already overweight or obese may begin to choose low-calorie sweetened foods and beverages as one method for losing weight (Drewnowski 2016). This makes it difficult to assume that the use of a low-calorie sweetener can be the cause of weight gain, but it may reflect how low-calories sweeteners are typically used in the diet. RCTs may therefore represent the efficacy of low-calorie sweeteners. while observational studies may be reflecting their real-world effectiveness.

Recent systematic reviews and metaanalyses (a scientific approach that combines findings from many studies into one powerful analysis) have concluded that, overall, findings from observational studies showed no association between low-calorie sweetener intake and body weight, and a small positive association with body mass index (BMI) (Miller 2014, Rogers 2016).

It is important to note that losing and maintaining one's weight often require multiple simultaneous approaches.

Making a single change, such as substituting foods and beverages made with low-calorie sweeteners for full-calorie, sugar-containing products, is just one approach. Lifestyle and behavior practices like reducing total calorie intake, eating a healthful diet, exercising regularly, getting enough sleep and maintaining social support networks are all important factors in achieving weightloss and weight-maintenance goals.

STEVIA SWEETENERS



EMERGING RESEARCH:

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 (Singh 2014). Substituting full-calorie and sugar-containing foods with their counterparts made with low-calorie sweeteners has exhibited a similar effect on reward pathways, but without contributing additional calories.

Some have expressed concern that activating reward pathways without delivering sugar to the body may have unintended consequences, and the role that low-calorie sweeteners play in appetite and food cravings is a developing area of research. As noted in recent reviews (Fowler 2016, Sylvetsky & Rother 2018), some research in animal models has demonstrated changes in food intake and appetite-related hormones after consuming low-calorie sweeteners. And yet, similar effects have not been seen in humans. To date there is no strong evidence that low-calorie sweeteners, including stevia sweeteners, enhance appetite or cravings in humans (Rogers 2017), and some randomized trials have demonstrated the opposite effect—including a decrease in hunger (Peters 2016) and reduced dessert intake compared to those who drank water (Piernas 2013). Others have shown no effect of stevia sweeteners on satiety (Anton 2010, Tey 2017) and a reduction in overall daily energy intake compared to a full-sugar control (Anton 2010), which is 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. Additionally, a recent study demonstrated a reduction in hunger after consuming cookies made with stevia sweeteners compared to control cookies (Ahmad 2018).

These discrepancies underscore an area in which animals and humans are inherently different as research subjects. In humans, the link between food and physiology, psychology and personal experiences is unmistakably complex, and the translation of animal research to this area of study should be viewed with caution.

DO STEVIA SWEETENERS AFFECT BLOOD SUGAR CONTROL?

Foods and beverages made with stevia sweeteners are frequently recommended to people with diabetes as an alternative to sugar-sweetened foods and beverages. Extensive research shows that stevia sweeteners do not raise blood sugar levels in humans (Nichol 2018, Romo-Romo 2017, Maki 2008), and a recent consensus statement by experts in nutrition, medicine, physical activity and public health concluded that the use of low-calorie sweeteners in diabetes management may contribute to better glycemic control (Serra-Majem 2018).

Many medical, nutrition and public health organizations around the world, backed by a large body of evidence, support the consumption of low-calorie sweeteners by people with diabetes. These individuals, or those who are at risk for developing diabetes, should be mindful of food and beverage intake from all sources, including those containing low-calorie sweeteners and sugars. It is important to discuss nutrition with a doctor or registered dietitian and to eat a healthful, balanced diet to keep blood sugar levels under control.

A few observational studies have demonstrated an association between low-calorie sweetener consumption and risk for type 2 diabetes (Sakurai 2014, Imamura 2015), but these studies are not able to directly link cause and effect and as with the studies on body weight and obesity, they are at risk of confounding. Given that overweight—and obese individuals tend to consume more low-calorie sweetened beverages as compared to lean individuals (Bleich 2014), this is a critical omission.

STEVIA SWEETENERS

EMERGING RESEARCH:

WHAT ABOUT THE MICROBIOME?

The microbes living in our intestinal tract have become recognized as potentially significant contributors to our health, though research on the gut microbiome is still in its infancy. Despite the gut microbiota being integral to the metabolism of steviol glycosides, to date there is no evidence that stevia sweeteners meaningfully impact the composition or function of the gut microbiome (Wang 2018, Li 2014, Kunová 2014, Denina 2014). However, randomized clinical trials have not vet been conducted in humans. There are significant differences between the microbiome profiles from one person to another, and research has shown that the gut microbiome changes in response to normal changes in the diet (David 2014). A great deal of research is still needed to identify a microbiome profile and degree of diversity considered to be "optimal" in populations and in individuals.





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®

COMMON NAMES SEEN ON FOOD LABELS: Reb A, rebiana, stevia leaf extract, stevia extract, steviol glycosides

DATE OF GRAS STATUS BY FDA: Generally Recognized as Safe status confirmed in 2008 for use in foods and beverages

NUMBER OF TIMES SWEETER THAN SUGAR: 200-350

SAFE FOR CHILDREN? Yes

SAFE FOR PREGNANT AND BREASTFEEDING WOMEN? Yes

WHAT IS THE BOTTOM LINE?

All types of foods and beverages can have a place in our diets, including those made with stevia sweeteners. Stevia sweeteners have been considered GRAS in the United States since 2008, and their safety has been acknowledged by many international health agencies.

Stevia sweeteners' impact on and association with chronic conditions like obesity and diabetes have been studied. Observational studies linking low-calorie sweeteners to weight gain inherently cannot demonstrate a causal relationship, while randomized clinical trials consistently support that low-calorie sweeteners like stevia sweeteners can be useful in nutritional strategies to assist with weight

loss and weight maintenance goals. Stevia sweeteners do not negatively impact blood sugar or insulin levels in randomized trials. Research continues on emerging issues like the effect of low-calorie sweeteners on 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-calorie sweeteners such as stevia may be one tool to help control sugar intake and keep calories in check, which are important components of maintaining a healthy body weight. and reducing risk for diet-related disease.

REFERENCES

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.

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;55:37-43.

<u>Bleich SN</u>, 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.

<u>Catenacci VA</u>, 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.

<u>Curry LL</u>, Roberts A, Brown N. Rebaudioside A: two-generation reproductive toxicity study in rats. *Food Chem Toxicol*. 2008;46:S21-30.

<u>David LA</u>, Maurice CF, Carmody RN, Gootenburg 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):559-63.

<u>Denina I</u>, Semjonovs P, Fomina A, Treimane R, Linde R. The influence of stevia glycosides on the growth of Lactobacillus reuteri strains. *Lett Appl Microbiol*. 2014;58:278-84.

<u>Dewinter L</u>, 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.

<u>Drewnowski A</u>, 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.

<u>Fowler SPG</u>. 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.

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.

<u>Kunová G</u>, Rada V, Vidaillac A, Lisova I. Utilisation of steviol glycosides from Stevia rebaudiana (Bertoni) by lactobacilli and bifidobacteria in in vitro conditions. *Folia Microbiol (Praha)*. 2014:59:251-5

<u>Li S</u>, Chen T, Dong S, Xiong Y, Wei H XF. The effects of rebaudioside A on microbial diversity in mouse intestine. *Fd Sci Technol Res.* 2014;20:459-67.

Magnuson BA, Carakostas MC, Moore NH, Poulos SP, Renwick, AG. Biological fate of low-calorie sweeteners. *Nutr Rev.* 2016 Nov;74(11):670-689.

Maki KC, Curry LL, Reeves MC, Toth PD, McKenney JM, Farmer MV, Schwartz SL, Lubin BC, et al. 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.

Martyn D, Darch M, Roberts A, Lee HY, Yagiong Tian T, Kaburagi N, Belmar P. Low/No-Calorie Sweeteners: A Review of Global Intakes. *Nutrients*. 2018 Mar 15;10(3).

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.

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.

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 May 15.

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.

<u>Piernas C</u>, 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.

Renwick AG. Safety factors and establishment of acceptable daily intakes. *Food Addit Contam.* 1991 Mar-Apr;8(2):135-49.

Renwick AG. The use of a sweetener substitution method to predict dietary exposures for the intense sweetener rebaudioside A. Food Chem Toxicol. 2008;46(Suppl 7):561-9.

<u>Roberts A</u>, Renwick AG. Comparative toxicokinetics and metabolism of rebaudioside A, stevioside, and steviol in rats. *Food Chem Toxicol*. 2008 Jul;46 Suppl 7:S31-9.

Rogers PJ. Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including metaanalyses, of the evidence from human and animal studies. *Int J Obes.* 2016 Mar 40(3):381-94.

Rogers PJ. The role of low-calorie sweeteners in the prevention and management of overweight and obesity: evidence v. conjecture. *Proc Nutr Soc.* 2017 Nov 23:1-9.

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.

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. doi: 10.1007/s00394-013-0523-9.

<u>Serra-Majem L</u>, et al. Ibero-American consensus on low- and no-calorie sweeteners: safety, nutritional aspects and benefits in food and beverages. *Nutrients*. 10:818.

<u>Singh M.</u> Mood, food, and obesity. *Front Psychol.* 2014;5:925. <u>Sylvetsky AC</u>, Rother KI. Nonnutritive sweeteners in weight management and chronic disease: a review. *Obesity* (Silver Spring). 2018 Apr;26(4):635-640.

<u>Tey SL</u>, Salleh NB, Henry J, Forde CG. Effecs of aspartame-, monk fruit-, stevia- and sucrose-sweetened beverages on postprandial glucose, insulin and energy intake. *Int J Obes (Lond)*. 2017;41:450-7.

<u>US Food and Drug Administration</u>. GRAS notice 619. Purified steviol glycosides. US Gras Notice Inventory. 2016.

<u>Usami M</u>, Sakemi K, Kawashima K, Tsuda M, Ohno Y. Teratogenicity study of stevioside in rats. Eisei Shikenjo Hokoku. 1995;(113):31-5.

Wang QP, Browman D, Herzog H, Neely CG. Non-nutritive sweeteners possess a bacteriostatic effect and alter gut microbiota in mice. PLoS One. 2018 Jul 5;13(7):e0199080.

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.