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Stevia, Nature's Zero-Calorie Sustainable Sweetener

A New Player in the Fight Against Obesity

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Stevia is a plant native to South America that has been used as a sweetener for hundreds of years. Today, zero-calorie stevia, as high-purity stevia leaf extract, is being used globally to reduce energy and added sugar content in foods and beverages. This article introduces stevia, explaining its sustainable production, metabolism in the body, safety assessment, and use in foods and drinks to assist with energy reduction. The article also summarizes current thinking of the evidence for the role of nonnutritive sweeteners in energy reduction. Overall, stevia shows promise as a new tool to help achieve weight management goals. Nutr Today. 2015;50(3):129–134

WHERE DOES STEVIA COME FROM?

Stevia is a naturally sourced, zero-calorie sweetener that has been used as a natural sugar substitute and flavoring ingredient for hundreds of years. The stevia plant is native to South America and was first consumed there over 200 years ago when the indigenous people used leaves of the plant to sweeten beverages or chewed them for their sweet taste. The plant leaves, often called "sweet herb," were dried and used to sweeten teas and medicines or simply chewed as a sweet treat.

The stevia plant was first scientifically recorded in 1899 as *Eupatorium rebaudianum* by Moises Santiago de Bertoni, in Paraguay. In 1905, it was later defined as *Stevia rebaudiana*, a member of the sunflower (Asteraceae) family.

Stevia, as a plant extract, was first commercially adopted as a sweetener by Japan in the 1970s, where it is still a popular ingredient today. Stevia is cultivated mostly in Paraguay, Kenya, China, and the United States and within many other parts of the world, including Vietnam, Brazil, India, Argentina, and Colombia.

Stevia Definitions

Stevia is the generic term used to refer to different forms of the sweetener, including the whole plant Stevia (*S rebaudiana* Bertoni) and the leaves where the sweet compounds are found. Stevia extract is a generic name for a preparation made by steeping the leaves of the Stevia plant to extract the sweet compounds from the leaf material.

On the other hand, high-purity stevia leaf extract contains 95% or greater steviol glycosides. Only high-purity stevia extracts meeting this specification are approved by major regulatory agencies, including the Joint Food and Agriculture Organization/World Health Organization (WHO) Expert Committee on Food Additives and Codex Alimentarius (Codex) for use in foods and beverages.

The term "stevia" as used in this article refers to high-purity stevia leaf extract.

Stevia is a sweetener and a natural origin plant extract that has been consumed for over 200 years. However, high-purity stevia leaf extract is now on the market today.

STEVIA'S SWEETNESS

The sweet-tasting components of stevia are called steviol glycosides, which are naturally present in the stevia leaf. There are 11 major steviol glycosides (Figure 1), of which rebaudioside A and stevioside are the most abundant. Figure 2 shows the basic chemical structure of all steviol glycosides. Purified stevia leaf extracts can contain one

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Steviol glycosides	Sweetening power relative to sucrose
Stevioside	150–300
Rebaudioside A	200-400
Rebaudioside B	300-350
Rebaudioside C	50-120
Rebaudioside D	200–300
Rebaudioside E	250–300
Rebaudioside F	Not available
Rubusoside	110
Steviolmonoside	Not available
Steviolbioside	100-125
Dulcoside A	50–120

FIGURE 1. The 11 major steviol glycosides in the stevia plant.

steviol glycoside or several different glycosides, which can be up to 250 to 300 times sweeter than sucrose.[1]

STEVIA PRODUCTION

Figure 3 illustrates the process used to extract steviol glycosides from the stevia leaf and shows how they are filtered and purified.[2]

The process of purifying stevia into high-purity stevia leaf extract is similar to how other plant-based ingredients, such as cane sugar or natural vanilla extract, are made through a series of steps beginning with the harvested, raw plant material through to the end product. The process begins by drying the leaves and then steeping them in hot water. Next, the liquid extract is filtered and purified with water or in some cases in combination with food-grade alcohol. If food-grade alcohol is used, it is later removed and no significant amount of alcohol remains in the end product. Other processes may be used in some cases. Further technical details are available in the cited article by Prakash et al.[3]

The purified steviol glycosides are the same molecules as originally found in the leaf. High-purity stevia leaf extracts (>95% steviol glycosides) are required to meet US and European regulatory approvals and safety standards for foods and beverage use.

SUSTAINABILITY

Stevia requires lower inputs of land, water, and energy to produce the same amount of sweetness found in other natural sweeteners. A carbon and water footprint assessment from one of the largest stevia producers, using sweetness equivalence for comparison, found an 82% reduction in carbon footprint for stevia compared with beet sugar and a 64% reduction compared with cane sugar. The water footprint for stevia was 92% lower than beet sugar and 95% lower than cane sugar (www.purecircle.com). The carbon footprint was calculated following Publically Available Standard 2050 (PAS 2050)—the foremost methodology for product lifecycle analysis of carbon emissions that contribute to greenhouse gases. This method incorporated embedded carbon in the agricultural inputs and ingredients used in the processes as well as all direct emissions from operations and transportation of goods, emissions from purchased electricity, and emissions from sources not owned or controlled by company, but only directly related to the supply chain. Water footprint calculation followed the Water Footprint Assessment Methodology as set out by the Water Footprint Network and incorporated green (rain) and blue (irrigation or process) water that went into stevia production.

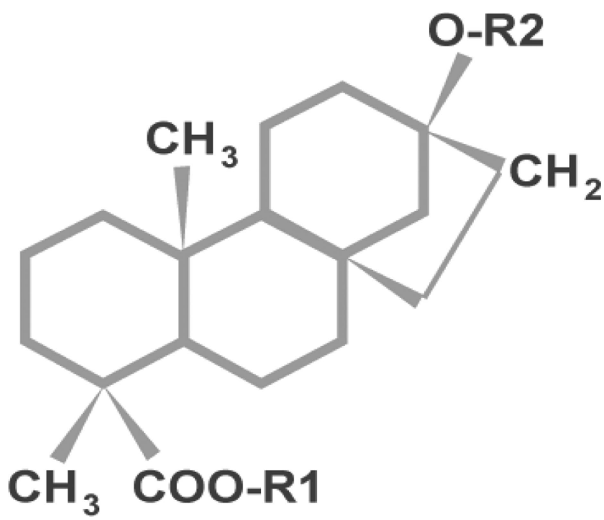

FIGURE 2. The chemical structure of the steviol backbone for steviol glycosides found in the stevia plant. The "R" structures indicate placement of the various glycoside molecules, which results in the variety of steviol glycosides present in the leaf.

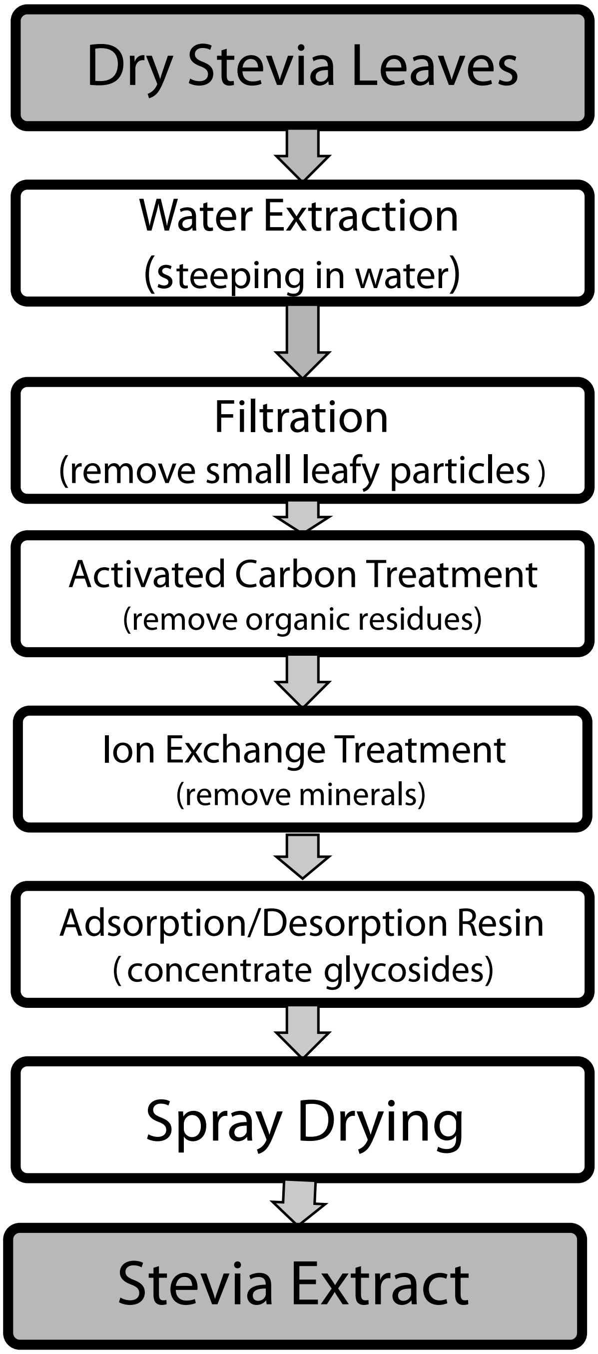

FIGURE 3. The processing steps used to obtain high-purity stevia leaf extract from the stevia plant.

In addition, stevia is creating opportunities for farmers in countries such as Kenya, Paraguay, and Brazil to grow profitable crops that support public health goals.

PURIFIED STEVIA LEAF EXTRACT

High-purity stevia extract contains 95% or greater steviol glycoside content and is often referred to as stevia, steviol glycosides, stevia extracts, purified stevia leaf extract, high-purity stevia, or rebiana. Only high-purity stevia extracts meeting this specification are approved by major regulatory agencies, including the Joint Food and Agriculture Organization/WHO Expert Committee on Food Additives[4] and Codex, for use in foods and beverages. For simplicity, the term "stevia" as used in this article refers to purified steviol glycosides.

Stevia in Your Foods and Drinks

Food scientists continue to explore ways to use stevia-based sweeteners. Proposed uses for high-purity stevia leaf extracts include soft drinks, canned fruit and jams, ice cream and other dairy products, cakes and desserts, and alcoholic beverages.

Stevia Metabolism

The backbone of all steviol glycosides is steviol, to which various glycoside (glucose) groups attach to form the variety of sweet compounds in stevia (Figure 2). Steviol glycosides pass through the upper gastrointestinal tract fully intact. Gut bacteria in the colon hydrolyze steviol glycosides into steviol by snipping off their glucose units. Steviol is then absorbed via the portal vein and primarily metabolized by the liver, forming steviol glucuronide, which is primarily excreted in the urine. Research shows that there is no accumulation of stevia (or any component or by-product of stevia) in the body and that it passes through the body during metabolism. Energy from fermentation of glucose units (usually assessed as 2 kcal/g) is so low that it is minimal, and so, effectively, stevia can be said to provide zero calories.[5,6]

High-purify stevia leaf extract is not metabolized, so it provides zero calories.

Stevia Safety

The Acceptable Daily Intake (ADI) is the amount of a substance that people can consume in food or beverages on a daily basis during their whole life without any appreciable risk to health. Several regulatory authorities have rigorously evaluated more than 200 peer-reviewed studies on animals and humans examining the safety of high-purity steviol glycosides. Based on this evidence, JECFA has established an ADI that applies to adults and children. The ADI is expressed as steviol equivalents of 4 mg/kg of body weight per day.[7] This equates to approximately 12 mg of high-purity stevia extracts/kg of body weight per day, using a conversion factor of 0.33. This ADI was established using a safety factor of 100, which includes a 10-times factor to account for potential differences between humans and animal species used in toxicological testing and a 10-times factor to account for potential differences within the human population, such as between children and adults. Thus, any potential increased susceptibility of children compared with adults to steviol glycosides has been addressed in the establishment of the ADI. For example, to put the ADI for high purity steviol glycosides into perspective, a 150-lb (70-kg) person would need to consume approximately 40 packets of a table top stevia sweetener that contain 21 mg steviol glycosides per packet daily for a lifetime to maximize the current ADI. Here is the calculation: A 70-kg person consuming the ADI (12 mg/kg per day) would consume 70 × 12 = 840 mg steviol glycosides per day. If a tabletop packet contained about 21 mg steviol glycosides, this person would need to consume 840 / 21 = 40 small tabletop packets per day to maximize the current ADI.

In the United States, high-purity stevia leaf extracts are considered GRAS (generally recognized as safe) by the US Food and Drug Administration. For more information about the Food and Drug Administration GRAS process, see http://www.ncbi.nlm.nih.gov/pubmed/18983884. There are many ways of producing purified steviol glycosides, and there are many GRAS notices.

Stevia has been shown to be safe in more than 200 studies, and JECFA has established an ADI of 4 mg/kg body weight per day, expressed as steviol equivalents, to guarantee this safety to consumers.

Role of Stevia in Energy Reduction and Weight Management

To fully discuss this issue, there are 4 distinct questions that need to be answered:

1. Does sugar contribute to greater energy intake and overweight and obesity?
2. Do sugar-sweetened beverages (SSBs) contribute to greater energy intake and overweight and obesity?
3. Does replacement of caloric sweeteners with nonnutritive sweeteners (NNS) facilitate weight loss or weight maintenance by helping reduce energy intake?
4. Does replacement of caloric sweeteners with stevia facilitate weight loss or weight maintenance by helping reduce energy intake?

Does Sugar Contribute to Greater Energy Intake and Overweight and Obesity?

The fact that "epidemiological studies do not show a positive association between total sugar intake and obesity" was one of the reasons why a positive European Food Safety Authority opinion was not given in 2011 for NNS reducing obesity.[8] Since that time, an important systematic review and meta-analysis,[9] commissioned by WHO, concluded that "Altering intakes of sugars, or SSB, is associated with changes in body weight (more consistently in adults than in children), which seem to be mediated via changes in energy intake because isoenergetic exchange of sugars with other carbohydrates is not associated with weight change." Thus sugar does seem to contribute to greater energy intake, but it cannot be said categorically to cause obesity.

Do SSBs Contribute to Greater Energy Intake and Overweight and Obesity?

This question has been hotly debated over recent years, and interesting viewpoints have been expressed on all sides (see Kaiser et al[10] and Hu[11]). The debate centers around which evidence should be considered (randomized controlled trials [RCTs] and cohort studies or just RCTs?) and how the evidence should be interpreted for policy purposes.

The most recent systematic review to address question 2 included 15 prospective studies and 5 RCTs in children and 7 cohort studies and 5 trials in adults. It concluded that SSB consumption promotes weight gain in children and adults.[12] The 15 RCTs in children showed reductions in body mass index gain when NNS were used to replace SSBs, and these benefits were more pronounced in overweight children compared with normal-weight children. The effects were even greater than those achieved with school-based education programs. The greatest effects were seen in the two most recent trials where great care had been taken to conceal the identity of the NNS sweetened drinks.[13,14] In one trial,[13] sugar was replaced with sucralose and acesulfame potassium and in the other SSBs was replaced with "diet drinks" with the sweetener not stated.[14] However, it should be noted that the latter trial found an effect after 1 year, but not 2 years, which was the primary outcome identified. In fact, a previous study by these authors found an effect only in the most overweight boys.[15]

Does Replacement of Caloric Sweeteners With NNS Facilitate Weight Loss or Weight Maintenance by Helping Reduce Energy Intake?

In 2006, we published a systematic review and meta-analysis to look at the evidence for the effect of NNS, mainly aspartame, on weight loss, weight maintenance, and energy intakes in adults. It addressed the question of how much energy is compensated for and whether the use of sweetened foods and drinks is an effective way to lose weight.[16] We demonstrated that using foods and drinks sweetened with NNS, instead of sucrose, results in a significant reduction in both energy intakes (about

10%) and body weight; the estimated rate of weight loss was about 0.2 kg/wk. Some compensation for the substituted energy does occur, but this is only about one-third of the energy replaced and is probably less when using soft drinks sweetened with NNS because of the smaller compensation usually found for liquids as opposed to foods. However, these results and the compensation values were derived from short-term studies, and more data were needed over the longer term to determine whether a tolerance to the effects of NNS is acquired.

Some progress was made when studies on overweight subjects were separated from those on normal-weight subjects.[17] In this case, the 6 pertinent studies taken altogether showed no overall benefit. However, when the 3 studies performed in overweight subjects were looked at separately, these authors reported a significant benefit on body mass index by replacing sugar with NNS.

However, we still urgently needed a systematic review and meta-analysis of good-quality longer-term recent studies to specifically address question 3: "Does replacement of caloric sweeteners with NNS facilitate weight loss or weight maintenance by helping reduce energy intake?" This was provided in mid-2014.[18] These authors concluded that data from 15 RCTs, which provide the highest quality of evidence for examining the potentially causal effects of NNS intake, indicated that substituting NNS options for their regular-calorie versions results in a modest weight loss and may be a useful dietary tool to improve compliance with weight loss or weight maintenance plans.

Does Replacement of Caloric Sweeteners With Stevia Facilitate Weight Loss or Weight Maintenance by Helping Reduce Energy Intake?

Although there have been many studies on stevia that have produced results confirming the safety of stevia, and there is evidence that stevia does not affect satiety,[19] no long-term trials have been reported that look at the effectiveness of stevia in weight control. However, as reported above, many studies and overviews have been published that report trials undertaken with other NNS, mainly aspartame. We have no reason to believe that the effectiveness of stevia replacing sugar in drinks and foods would lead to different conclusions. More research in humans will be important to clarify the role of stevia in long-term energy reduction.

We need studies to confirm the role of stevia in long-term weight reduction and maintenance.

CONCLUSION

Stevia is a natural-origin sweetener that is increasing the options for reduced sugar and reduced energy foods and beverages. Stevia shows promise as a tool to help lower energy intakes, which may lead to the reduction and prevention of obesity.

REFERENCES

1. Prakash I, Markosyan A, Bunders C. Development of next generation stevia sweetener: rebaudioside M. *Foods*. 2014; 3(2):162–175.
2. Food and Drug Administration, Center for Food Safety and Applied Nutrition (CFSAN)/Office of Food Additive Safety, December 17, 2008. Agency Response Letter GRAS Notice No. GRN 000252.
3. Prakash I, Dubois GE, Clos JF, Wilkens KL, Fosdick LE. Development of rebiana, a natural, non-caloric sweetener. *Food Chem Toxicol*. 2008;46(suppl 7):S75–S82.
4. JECFA (Joint FAO/WHO Expert Committee on Food Additives). Compendium of Food Additive Specifications. Monograph 5. Steviol glycosides. 2008. http://www.fao.org/ag/agn/jecfa-additives/details.html?id=898.
5. 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;51(22): 6618–6622.
6. EFSA Panel on Food Additives and Nutrient Sources (ANS). Scientific Opinion on the safety of steviol glycosides for the proposed uses as a food additive. *EFSA J*. 2010;8(4):1537.
7. JECFA (Joint FAO/WHO Expert Committee on Food Additives). Safety evaluation of certain food additives. Presented at the 69th meeting of the Joint FAO/WHO Expert Committee on Food Additives; 2008; Rome.
8. EFSA Panel on Dietetic Products Nutrition and Allergies (NDA). Scientific Opinion on the substantiation of health claims related to intense sweeteners and contribution to the maintenance or achievement of a normal body weight (ID 1136, 1444, 4299), reduction of post-prandial glycaemic responses (ID 4298), maintenance of normal blood glucose concentrations (ID 1221, 4298), and maintenance of tooth mineralisation by decreasing tooth demineralisation (ID 1134, 1167, 1283) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA J*. 2011;9(6):2229.
9. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. *BMJ*. 2013;346:e7492.
10. Kaiser KA, Shikany JM, Keating KD, Allison DB. Will reducing sugar-sweetened beverage consumption reduce obesity? Evidence supporting conjecture is strong, but evidence when testing effect is weak. *Obes Rev*. 2013;14(8):620–633.
11. Hu FB. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obes Rev*. 2013; 14(8):606–619.
12. Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *Am J Clin Nutr*. 2013;98(4):1084–1102.
13. de Ruyter JC, Olthof MR, Kuijper LD, Katan MB. Effect of sugar-sweetened beverages on body weight in children: design and baseline characteristics of the Double-blind, Randomized INtervention study in Kids. *Contemp Clin Trials*. 2012;33(1): 247–257.
14. Ebbeling CB, Feldman HA, Chomitz VR, et al. A randomized trial of sugar-sweetened beverages and adolescent body weight. *N Engl J Med*. 2012;367(15):1407–1416.

15. Ebbeling CB, Feldman HA, Osganian SK, Chomitz VR, Ellenbogen SJ, Ludwig DS. Effects of decreasing sugar-sweetened beverage consumption on body weight in adolescents: a randomized, controlled pilot study. *Pediatrics*. 2006;117(3):673–680.
16. de la Hunty A, Gibson S, Ashwell M. A review of the effectiveness of aspartame in helping with weight control. *BNF Nutr Bull*. 2006; 31:115–128.
17. Mattes RD, Shikany JM, Kaiser KA, Allison DB. Nutritively sweetened beverage consumption and body weight: a systematic review and meta-analysis of randomized experiments. *Obes Rev*. 2011;12(5):346–365.
18. 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;100(3): 765–777.
19. Anton SD, Martin CK, Han H, et al. Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels. *Appetite*. 2010;55(1):37–43.

CALENDAR

International Society of Behavioral Nutrition and Physical Activity
June 3–6, 2015; Edinburgh, Scotland
http://www.isbnpa2015.org/

International Conference on Weight Loss and Fitness
July 13–15, 2015; Philadelphia, Pennsylvania
http://weightloss-fitnessconference.conferenceseries.net/

Society for Nutrition Education and Behavior Annual Meeting
July 25–28, 2015; Pittsburgh, Pennsylvania
http://www.sneb.org/

Healthy Aging Summit
July 27–28, 2015; Washington, DC
http://www.2015HealthyAgingSummit.org

Academy of Nutrition and Dietetics Food & Nutrition Conference & Expo
October 2–6, 2015; Nashville, Tennessee
http://www.eatright.org/fnce/sessionproposals/

15th International Nutrition & Diagnostics Conference
October 5–8, 2015; Prague, Czech Republic
http://www.indc.cz/en/registration/abstracts/abstractregistration-form/

Omics International: 4th International Conference and Exhibition on Nutrition
October 26–28, 2015; Chicago, Illinois
http://www.nutritionalconference.com/

American Public Health Association (APHA) Annual Meeting
October 31 to November 4, 2015; Chicago, Illinois
https://www.apha.org/events-and-meetings/annual

11th International Food Data Conference "Food Composition Data and Public Health Nutrition"
November 3–5, 2015; Hyperbad, India
Contact Longvah T (tlongvah@gmail.com) for more information

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