lower caloric intake. Several nonnutritive sweeteners have been accepted by the US Food and Drug Administration as safe and have shown good safety over time. However, data are scarce on long-term benefits for weight management in children and adolescents or on the consequences of long-term consumption. Continued research is needed.”

http://pediatrics.aappublications.org/content/135/3/575.full.pdf


About NNS: “Use of nonnutritive sweeteners (NNSs) has the potential to reduce overall calorie and carbohydrate intake if substituted for caloric (sugar) sweeteners 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.”

http://care.diabetesjournals.org/content/36/11/3821.full.pdf


About NNS: “There is no proof that these sweeteners, at the levels consumed in human diets, cause cancer. Aspartame, saccharin, and sucralose are a few of the non-nutritive sweeteners approved for use by the FDA. Current evidence does not show a link between these compounds and increased cancer risk…”


Summary: The value of reducing sugar-sweetened beverages (SSBs) to reduce weight is discussed briefly. Data from two RCTs demonstrating greater weight loss with the replacement of low calorie sweetened beverages for SSBs are detailed. These RCTs, by Tate et al. (2012) and Peters et al. (2014) are cited. (See summaries under Weight Management section.)

http://www.eatrightpro.org/~/media/eatrightpro%20files/practice/position%20and%20practice%20papers/position%20papers/weightmanagementashx


About NNS: “Additional improvements in nutrient density of sweet-tasting products could be obtained if nonnutritive sweeteners are used as a tool to replace added sugars and help...
META-ANALYSES, SYSTEMATIC AND LITERATURE REVIEWS


**Summary:** Sucralose has been extensively studied and evaluated by researchers and regulatory agencies around the world. This publication offers an in-depth review of the broad array of studies conducted over the forty year history including the effects of sucralose on growth, development, reproduction, neurotoxicity, immunotoxicity, carcinogenicity and overall health status, including human studies on the effects of sucralose in people with diabetes. The review of more recent studies focused on carcinogenic potential and the effect of sucralose on the gut microbiota and potential impact on glycemic control. The review concludes sucralose is safe for its intended use as a NNS. Due to the extensive length of this review a “pocket guide” summary was created and is available here: http://www.splendaprofessional.com/sites/splenda_hcp/files/Magnuson_Pocket_Guide_2017.pdf


**Summary:** This systematic review covers a large and lengthy body of evidence including numerous types of animal human studies using varied designs. Studies were conducted with various NNS including several currently available or approved by the U.S. FDA. Conclusions are consistent with other systematic reviews of NNS that demonstrate decreased energy intake and body weight with consumption of NNS used in place of added sugars. http://www.nature.com/ijo/journal/vaop/ncurrent/full/jio2015177a.html


**Summary:** This systematic review culled studies from six different literature databases to identify prospective cohort studies (PCS) and randomized controlled trials (RCTs) in children and adults with four month or longer duration. Six PCS and 4 RCTs were included. Results showed that replacing Sugar Sweetened Beverages with a variety of low-calorie beverage alternatives demonstrate a favorable effect on long term body weight. http://www.andjrn.org/article/S2212-2672(15)00112-4/fulltext


**Summary:** This paper, which analyzed research about how human NNS consumption may change the appetite for and intake of sweet tasting products, draws three main conclusions: 1) no consistent relationship exists to demonstrate a heightened appetite for sweet foods, 2) some research shows use of NNS is associated with consumption of less sweets, 3) intervention studies in children and adults show use of NNS can reduce intake of caloric sweeteners and support weight loss efforts. http://link.springer.com/article/10.1007%2Fs13679-014-0133-8#/page-1


**Summary:** This meta-analysis analyzed results from randomized control trials (RCTs) and prospective cohort studies on NNS and body weight, fat mass, BMI, and waist circumference. It showed that in RCTS NNS reduced body weight compared to placebo and modestly, but “significantly” reduced BMI, fat mass, and waist circumference. This meta-analysis was accompanied by the editorial referenced below by Hill.
http://ajcn.nutrition.org/content/early/2014/06/18/ajcn.113.082826.full.pdf+html

https://academic.oup.com/ajcn/article/100/3/739/4576421

SAFETY AND CARCINOGENICITY


**Summary:** This comprehensive review covers commonly used NNS, including aspartame, saccharin, stevia leaf extract (steviol glycoside) and sucralose. It details the biological fate of these NNS, including their absorption, distribution, metabolism, and excretion pathways. The review also compares the chemical differences between these NNS and notes their global regulatory status. This article helps healthcare providers’ and their clients’ overcome potential concerns and hesitancy about using NNS to prevent and/or manage chronic health conditions.
https://academic.oup.com/nutritionreviews/article/74/11/670/2281652


**Summary:** This article provides an in-depth review of the regulatory processes for NNS including the food additive approval process and the Generally Recognized as Safe (GRAS) used by the U.S. FDA. The same level of scientific evidence is required to support safety and ensure a reasonable certainty of no harm in both review processes. This review covers potential safety concerns, including carcinogenicity, effects on body weight gain, glycemic control and effects on the gut microbiome.


**Summary:** This comprehensive safety review of sucralose includes independently conducted and industry-funded research on sucralose chemistry, pharmacokinetics, metabolism, toxicity, genotoxicity, and long-term safety - including carcinogenicity. It concludes that sucralose is non-carcinogenic and safe for all consumers to use and supports four key points: 1) There is no evidence of chemical concerns or toxicity; 2) No metabolites in sucralose were found to be carcinogenic; 3) No changes to genes were observed to
GUT HEALTH, GLYCEMIC CONTROL, HUNGER AND APPETITE

A 12-week Randomized Clinical Trial Investigating the Potential for Sucralose to Affect Glucose Homeostasis. Grotz Vl, et al. Regulatory Toxicology and Pharmacology. 2017;88:22-33. **Summary:** This 12-week RCT on the impact of sucralose on glucose control and other metabolic parameters was a double-blind, parallel design with 47 normoglycemic male volunteers. Study subjects consumed “333.3 mg encapsulated sucralose or placebo three times a day at mealtimes, the equivalent to ~200 g of added sugars per meal. A1c, fasting glucose, insulin, and C-peptide levels were measured weekly. Adherence was carefully measured. Results showed glucose, insulin, C-peptide and A1c levels were within normal ranges throughout the study. The findings support that sucralose has no effect on glycemic control. The discussion offers a valuable review of recent research on NNS, glucose control and the impact of gastrointestinal sweet taste receptors.


Impact of Diet Composition on Blood Glucose Regulation. Russell WR, et al. Critical Reviews in Food Science and Nutrition, 2016;56(4):541-590. **Summary:** This review explores human studies on a range of dietary components and their impact on blood glucose levels in prevention and management of type 2 diabetes. The review includes the impact of the major macronutrients, micronutrients, nonnutrient phytochemicals, and low calorie sweeteners (NNS). It includes the range of research on various NNS related to glucose regulation including impact on gut hormones and glucose, C-peptide and insulin levels. The article concludes the use of NNS in subjects with or without diabetes does not affect glucose levels and are tools that may help people reduce or control calorie consumption.

http://dx.doi.org/10.1080/10408398.2013.792772

Low Calorie Sweeteners: Evidence Remains Lacking For Effects On Human Gut Function. Bryant C, McLaughlin J. Physiology & Behavior, 2016;164, Part B, 482-485. **Summary:** This review covers cellular, animal and clinical studies and puts results into context with the gut-brain axis and its regulation of food intake. Authors conclude human studies do not support a clinically meaningful effect of ingested NNS on hormones involved in gut signaling. Sucralose, aspartame and ace-K had no greater effect than water on secretion of GLP-1, insulin, PYY, or ghrelin, nor any impact on appetite. In summarizing the literature in humans, the authors state studies have consistently not shown that activation of sweet taste receptors by NNS placed in the human gut replicate any of the effects on gastric motility, gut hormones or appetite responses evoked by calorie-containing sugars.


Nonnutritive Sweeteners Are Not Supernormal Stimuli. Antenucci RG, et al. Int J Obes. 2015;39(2):254-9. **Summary:** Study participants were exposed to a series of taste tests with various caloric and nonnutritive sweeteners. Participants rated perceived sweetness. Results showed participants perceived the sweetness of NNS at lower concentrations than the caloric sweeteners and indicated caloric sweeteners all had higher sweetness ratings than NNS. Researchers concluded that results don’t support the claim that NNS produce a negative effect by over-stimulating peoples’ sweet taste receptors to produce supernormal stimuli.

http://www.nature.com/ijo/journal/v39/n2/full/ijo2014109a.html (abstract)

Non-Nutritive Sweeteners: No Class Effect on the Glycaemic or Appetite Responses to Ingested Glucose. Bryant CE, et al. Eur J Clin Nutr. 2014;68:629-631. **Summary:** This study examined the individual effect of acesulfame-K (AceK), aspartame and saccharin responses on glycemia and appetite in humans when consumed in combination with glucose in commonly used amounts. Results showed no additional effect of aspartame or saccharin on glucose response any time during the 60 minute post-ingestion period. No NNS individually had an effect on perceptions of hunger or fullness.

http://www.nature.com/ijo/journal/v68/n5/full/ijo201419a.html (abstract)

WEIGHT MANAGEMENT

The Role of Low-Calorie Sweeteners in the Prevention and Management of Overweight and Obesity: Evidence v. Conjecture. Rogers Pj. Proceedings of the Nutrition Society. 2017;23:1-9 (Published ahead of print online) **Summary:** This paper reviews evidence about the impact of LCS on energy intake and weight control, and further examines three claims regarding the effect of LCS on energy intake and preference for sweetness. The claims examined in this paper were 1) “sweet taste confusion” – energy disruption hypothesis, 2) the “sweet tooth” hypothesis and 3) the conscious overcompensation hypothesis; with the findings being that there is little or no evidence for their support. The author concludes that “intervention studies demonstrate that consumption of LCS in place of (some) sugar in the diet reduces energy intake and body weight.”


Low Calorie Sweetener (LCS) Use And Energy Balance. Peters, JC, Beck J. Physiology & Behavior, 2016;164, Part B, 524-528. **Summary:** This review details over thirty years of research and reviews on NNS, energy balance and weight management. The authors summarize the observational longitudinal cohort studies that early on suggested the promotion of weight gain and others, while more recent studies nearly uniformly show either weight loss or the prevention of weight gain. Two recent meta-analyses cited here are summarized (Miller, et al, Rogers, et al). The authors conclude: “RCTs are consistent in showing a benefit of LCS which suggest that simple behavioral engagement by individuals attempting to control their weight is a sufficiently strong signal to overcome any potential mechanism that might act to promote energy intake and weight gain.”

Sugar- and Artificially Sweetened Beverages and Intrahepatic Fat: A Randomized Controlled Trial.
Summary: Over a 12 week study period this RCT compared the impact of Artificially Sweetened Beverages (ASB) with Sugar-Sweetened Beverages (SSB) on intrahepatic fat among overweight adults who usually consumed two or more 22- fl. oz. of SSB daily. Results showed participants consuming ASB had significantly decreased total energy, carbohydrate, and sugar intake. Subjects continuing to consume SSB showed no differences in intake. Dietary changes in the ASB group were accompanied by a significant decrease in intrahepatic fat.

Low/No Calorie Sweetened Beverage Consumption in National Weight Control Registry (NWCR).
Summary: This study surveyed consumption of beverages with NNS in NWCR members with sustained weight loss for > 7 years. Results showed 53% regularly consumed NNS beverages, 10% regularly consumed sugar-sweetened beverages (SSB). 78% of NNS consumers reported they helped control caloric intake. Choice of beverage was “very important” for weight loss (42%) and weight maintenance (40%).

Replacing Caloric Beverages with Water or Diet Beverages for Weight Loss in Adults: Main Result of the Choose Healthy Options Consciously Everyday (CHOICE) Randomized Control Trial.
Summary: CHOICE was a 6-month RCT with 3 groups: 1) diet beverage, 2) water or 3) control. Eligible subjects had to consume > 280 kcal/day sweetened beverages and commit to making a dietary change. Diet beverage and water groups substituted > 2 servings/day of sweetened beverage with a diet beverage or water, respectively. Results: At 6 months diet beverage drinkers were more likely to achieve a 5% weight loss than water drinkers. A secondary analysis Piernas, et al. (http://ajcn.nutrition.org/content/97/3/604.full.pdf+html) showed both study groups reduced total energy, carbohydrate, and added sugars. Diet beverage group participants reduced dessert consumption more than water drinkers.
http://ajcn.nutrition.org/content/95/3/555.full.pdf+html

Summary:
The literature cited here is consistent with the extensive evidence base on NNS which concludes that NNS can be used safely and efficaciously as part of a healthy eating pattern. Summaries of other and older publications are available at http://www.splendaprofessional.com/studies-science. Using nonnutritive sweeteners, can assist people with managing their weight and/or various aspects of metabolic health by reducing calories, total carbohydrate and added sugars.

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