

Objectives

- Identify the Non-Nutritive Sweeteners (NNS) approved by the FDA as food additives and as Generally Recognized as Safe (GRAS)
- Review the public and professional concerns surrounding NNS and the origin of these considerations in the literature
- Compare research results to consensus by health agencies
- Apply the evidence base to practice for patients with diabetes and obesity to improve outcomes
- Navigate the conflicting messages surrounding NNS use to better educate patients and the public

NNS: Background

- NNS are several hundred to several thousand times sweeter than sucrose
- NNS are different from sugar alcohols, like sorbitol and xylitol, which are considered nutritive at 2 kcal/gram
- Foods labeled as "sugar free" may contain NNS, sugar alcohols, or both
- Most NNS are regulated in the U.S. by the FDA as food additives
- Other types of sweeteners are granted GRAS status
- NNSs are ubiquitous in the U.S. population's diet

(Shwide-Slavin, Swift, & Ross, 2012) (CFR - Code of Federal Regulations Title 21)

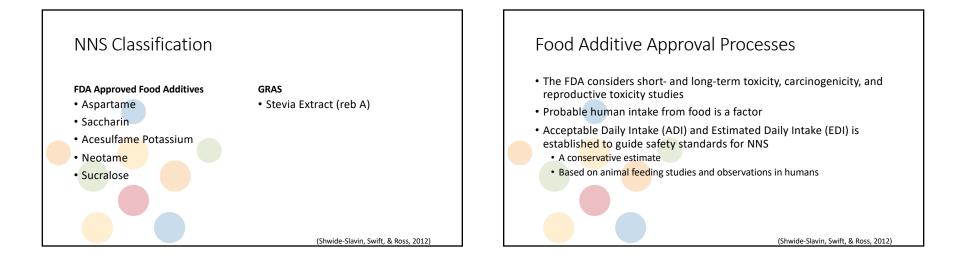
Definitions

- Food Additives are "any substance the intended use of which results ... in its becoming a component of ... or affecting the characteristics of any food."
- GRAS is "any substance that is intentionally added to food ... and generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use

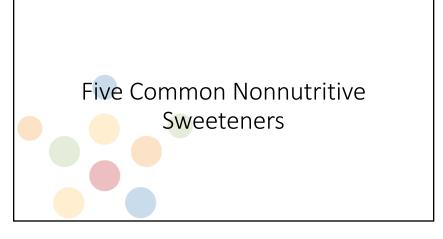
(Shwide-Slavin, Swift, & Ross, 2012) (CFR - Code of Federal Regulations Title 21) From Food Safety Magazine, published by the FDA "For a substance to be GRAS, the scientific data and information about the use of a substance must be widely known and there must be a consensus among qualified experts that those data and information establish that the substance is safe under the conditions of its intended use. GRAS determinations made in this manner are said to be made through scientific procedures.

For a **food additive**, privately held data and information about the use of a substance are sent by the sponsor to FDA, which evaluates those data and information to determine whether they establish that the substance is safe under the conditions of its intended use (21 CFR 171.1). Thus, for a food additive, FDA determines the safety of the ingredient; whereas a determination that an ingredient is GRAS can be made by qualified experts outside of government."

(Food Safety Magazine, 2006)



	Acceptable	Daily Intakes a	nd Expected Daily I	ntakes for Nonnutritive Sw	eeteners
NNS	Sweetening power compared to sucrose	ADI (mg/kg body weight/day)	EDI as a percentage of ADI in adults (%)	ADI equivalents in 12 oz can of zero-calorie diet soda each day over a lifetime (based on 150 lb body weight)	ADI equivalents in packets of tabletop sweetener each day over a lifetime (based on 150 lb body weight)
Ace-K	200 x	15	20%	25	20
Aspartame	200 x	50	6%	17	97
Saccharin	300 x	5	12%	2	9
Sucralose	600 x	5	32% (includes children > 2 years of age)	5	68
Stevia (expressed as steviol)	200-300 x	0-4	20-30%	N/A (sodas containing stevia are not widely available)	30



Acesulfame-Potassium

- Branded as Sunett, Sweet & Safe, and Sweet One
- Tests done on rats in 1970s had poor design and were inconclusive of carcinogenity
- Approved in 1988 for use in food products and as a tabletop
- sweetener
- Expanded for use in beverages in 1998
- Approved as a general sweetener in 2003
- Often blended with other sweeteners which may or may not be
 nutritive



(Shwide-Slavin, Swift, & Ross, 2012) (Center for Food Safety and Applied Nutrition, FDA) (Schaefer, 2017) (Karstadt 2006)

Aspartame

- Branded as NutraSweet and Equal
- Controversial among consumers due to associations with cancer, seizures, hyperactivity, multiple sclerosis, and other ailments
- Broken down into two amino acids, aspartic acid and phenylalanine, and methanol
 - Methanol is converted to formaldehyde by the liver
- There is more methanol from commonly consumed "natural" foods than from aspartame sweetened beverages
- Foods with aspartame must carry the phenylketonuria (PKU) warning

(Shwide-Slavin, Swift, & Ross, 2012) (USDA National Nutrient Database for Standard Reference, Release 26) (About Aspartame. n.d.)

Saccharin

- Branded as Sweet'N Low, Necta Sweet, Sweet Twin, and Sugar Twin
- The only NNS in the U.S. from 1970-1981
- Controversial because it was removed from the GRAS list in 1972 due to association with bladder cancer in rats
 - Resulted in a warning label requirement on foods containing saccharin
- Further research determined the animal study findings were not relevant to humans and used human epidemiological findings to change its safety status
- In 2000, warning label requirements were repealed

(Shwide-Slavin, Swift, & Ross, 2012)

Sucralose

- Branded as Splenda and Nevella
- Made from a sucrose molecule with three chlorine atoms replacing 3 of the hydrogen oxygen groups
- Approved by the FDA in 1998 for use in 15 food and beverage categories
 - The broadest initial approval of any food additive
- Limited research showing negative outcomes with sucralose use

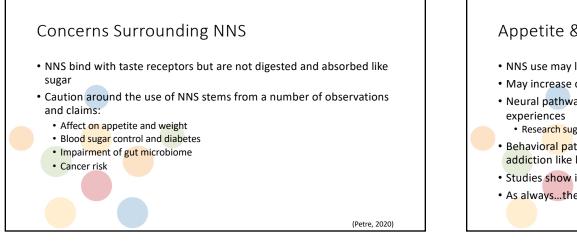
(Shwide-Slavin, Swift, & Ross, 2012) (Pepino, 2013)

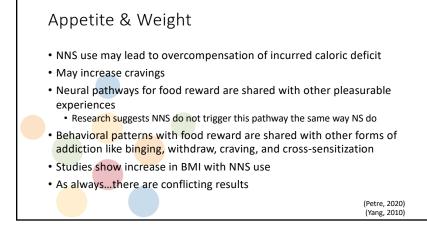
Stevia

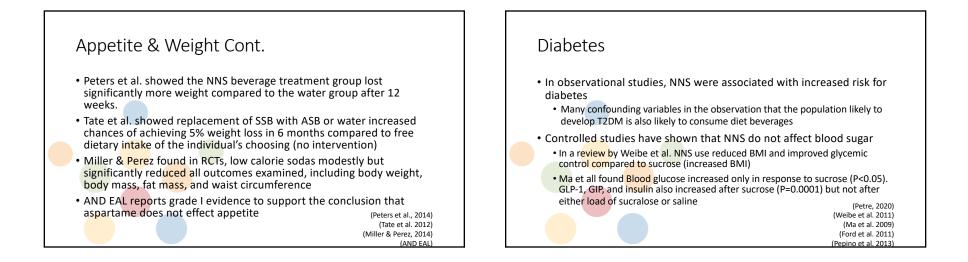
- Branded products contain stevia combined with a bulking agent to improve taste
 - SweetLeaf inulin
 - PureVia dextrose and cellulose
 - SunCrystals cane sugar
 - Truvia erythritol
- Reb A added to GRAS list in 2008
- Stevia is generally trusted by consumers because of its natural source
- Whole stevia leaves and crude leaf extracts are not permitted to be sold as sweeteners in the U.S.

(Shwide-Slavin, Swift, & Ross, 2012) (Food Insight, 2019)









Diabetes Cont.

- Conversely, one small study showed that ingesting sucralose before a glucose tolerance test increased in peak plasma glucose concentrations compared to ingesting water before the test among obese participants who do not regularly consume NNS
- Compared with the control condition, sucralose ingestion caused:
 - a greater incremental increase in peak plasma glucose concentrations,
 greater incremental increase in insulin,
 - greater peak insulin secretion,
 - decrease in insulin clearance, and
 - decrease in insulin sensitivity.

(Petre, 2020) (Weibe et al. 2011) (Ma et al. 2009) (Ford et al. 2011) (Pepino et al. 2013)

Gut Microbiome

- Gut health plays a major role in human health including weight status, blood sugar control, metabolic syndrome, and immunity
- One study on 7 human subjects found that saccharin disrupted the gut microbiome and resulted in poor blood sugar control among 4 of the participants
 - With fecal transplant to mice from these 4 subjects, the mice also developed poor blood sugar control
 - Mice transplanted from the non-responder subjects did not develop the poor blood sugar control
- More research is needed

(Petre, 2020) (Suez et al. 2014)

Professional Consensus Cancer · Controversy emerged in 1970 with a study on mice that found The Dietary Guidelines for Americans has updated its recommendation on artificial sweeteners increased risk of bladder cancer after being fed extremely high doses • The Committee recommends these food ingredients [LCS] be considered as of saccharin and cyclamate an option for managing body weight... the evidence base used to draw these Mice metabolize saccharin differently than humans conclusions was limited, but viewed as sufficient to acknowledge such beverages [LCSBs] may be a useful aid in weight management in adults. Since this time, dozens of human studies have found no association • ADA statement acknowledges artificial sweeteners can reduce calorie with increased risk of cancer with NNS and carbohydrate consumption when dietary overcompensations are • U.S. and European authorities agree that when consumed within the avoided ADI, there is no increased cancer risk • 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 (Petre, 2020) (DGA 2015-2020) (Gallus et al. 2007) (ADA, 2020)



Teaching Points	Related Information for Clients	
Compare the nutrition facts label of regular products and artificially sweetened products including calorie and fat content in addition to carbohydrate content	Regular fruit-flavored yogurt (6 oz): • 1500 calories* • 2 g total fat* • 26 g total carbohydrate* Regular soda (12 oz): • 145 calories • 0 g total fat • 40 g total carbohydrate	Light/fat-free fruit-flavored yogurt (6 oz): • 90 calories* • 0 g total fat* • 17 g total carbohydrate* Diet soda (12 oz): • 1 calorie • 0 g total fat • 0 g total carbohydrate
* Nutrition data updated compared to the	e original graphic which contained errors	
		(Shwide-Slavin, Swift, & Ross, 2012)

Application in Practice – Teaching Tips About Nonnutritive Sweeteners

	Related Information for Clients
Help reduce confusion about abel claims like "sugar-free" or 'no sugar added" which can be misleading	 "Sugar-free" or "no sugar added" on a food label does not mean the food is carbohydrate or calorie free. These products may have as many carbohydrates and calories as the regularly sweetened product, if not more. Products may be labeled as either "low calorie" or "reduced calorie" if they in fact are lower in calories than the original product. "Reduced" or "less" sugar indicated a sugar reduction of 25% compared to the original product. If a food is not lower in calories, the label must state that it is "not a low-calorie food," "not a reduced-calorie food," or "not for weight control."

Application in Practice – Teaching Tips About Nonnutritive Sweeteners

Teaching Points

Explain that all calories count and that weight loss requires eating fewer calories than are expended

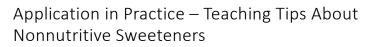
Related Information for Clients

 Total calorie intake should be the focus for weight management. This includes calories from fat and protein.

(Shwide-Slavin, Swift, & Ross, 2012)

Teaching Points	Related Information for Clients	
Teach nutrition label reading and note that carbohydrate content is the same between all forms of cows milk (skim, 2 %, whole etc.) it is naturally occurring sugar from lactose. Whole milk has more calories because of the fat.	 Whole milk (8 oz): 150 calories 70 calories from fat 8 g total fat* 35 mg cholesterol 120 mg sodium 12 g total carbohydrate 0 g dietary fiber 11 g sugar 8 g protein 	Skim milk (8 oz): • 90 calories • 0 calories from fat • 0 g total fat* • 35 mg cholesterol • 120 mg sodium • 12 g total carbohydrate • 0 g dietary fiber • 11 g sugar • 8 g protein

(Shwide-Slavin, Swift, & Ross, 2012)



Teach clients the names of NN	 Look for NNS in the ingredients list on packaged foods: Aspartame Sucralose Acesulfame-Potassium (Ace-K) Saccharin Reb A (stevia)

Application in Practice – Teaching Tips About Nonnutritive Sweeteners

Teaching Points

Help dispel myths about

nonnutritive sweeteners.

nonnutritive sweeteners and

learn more about the safety of

Related Information for Clients

Resources to learn about the safety of nonnutritive sweeteners: International Food Information Council: http://www.ific.org provide resources for clients to Academy of Nutrition and Dietetics: http://www.eatright.org "The Truth About Artificial Sweeteners or Sugar Substitutes" PDF download from www.andeal.org*

Application in Practice – Teaching Tips About Nonnutritive Sweeteners

Teaching Points Related Information for Clients Teach patients the sweetness intensity of nonnutritive sweeteners compared to sugar

Ace-K 200 X sweeter than sugar Aspartame 200 X sweeter than sugar Saccharin 300 X sweeter than sugar Sucralose 600 X sweeter than sugar Stevia 200-300 X sweeter than sugar

* Information updated from the original graphic

* Web address updated from the original graphic

(Shwide-Slavin, Swift, & Ross, 2012)

(Shwide-Slavin, Swift, & Ross, 2012)

Teaching Points	Related Information for Clients
Explain that patients can modify recipes by using nonnutritive sweeteners to reduce calories and sugar but that, in some cases, nonnutritive sweeteners can affect flavor, texture, browning, or cooking time.	 Cooking tips for nonnutritive sweeteners: Using nonnutritive sweeteners in place of 1 cup of sugar in a recipe saves 774 calories and 200 g carbohydrate. Nonnutritive sweeteners can completely replace sugar in recipes for sweet sauces, fruit pie fillings, cheesecakes, glazes, and beverages. Some recipes work better if you only partially replace sugar with nonnutritive sweeteners. Recipes that call for baking or browning require some sugar.
	(Shwide-Slavin, Swift, & Ross, 2012)

Application in Practice – Teaching Tips About Nonnutritive Sweeteners

Teaching Points	Related Information for Clients
	 Aspartame should be added to recipes after heating the ingredients to avoid a bitter taste. Although it is not harmful, aspartame is not recommended for use in baking because it is not heat stable and loses sweetness when heated. Saccharin and sucralose are heat stable and work well in baked products. But the lack of sugar may affect the structure, texture, and volume of the cooked item. You can replace sugar with an equal amount of sucralose, but the baking time will be quicker with the sucralose Adding ½ tsp. baking soda to a recipe helps the product rise in a short baking time
	(Shwide-Slavin, Swift, & Ross, 2012)

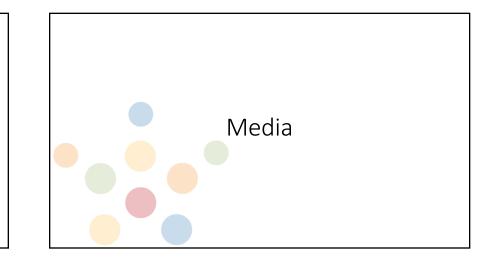
Application in Practice – Teaching Tips About Nonnutritive Sweeteners

Teaching Points	Related Information for Clients
(Continued from last slide)	 A blend of sugar and sucralose or stevia extract (for example, Truvia) is recommended for use in baking to maintain structure. This can reduce calories and carbohydrate from sugar by 50%. Using stevia will require a replacement of "filler" (for example, fiber fill) because its sweetness potency causes a loss of volume of the baked good. Flatten cookies with a fork before baking because cookies made with nonnutritive sweetners will not spread like the full-sugar versions.
	(Shwide-Slavin, Swift, & Ross, 2012)

Application in Practice – Teaching Tips About Nonnutritive Sweeteners

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Teaching Points	Related Information for Clients
(Continued from last slide)	 Activate yeast with 2 tsp. sugar before using nonnutritive sweeteners to replace sugar in bread products. To maintain browning on bread products, brush them with an egg wash (1 egg mixed with 1 Tbsp. water) before baking. Sprinkling cinnamon or nutmeg can help replace the color of normal browning in baked goods.
	(Shwide-Slavin, Swift, & Ross, 2012)

Teaching Points	Related Information for Clients
Provide Patients with sources for recipes incorporating nonnutritive sweeteners.	Recipes using nonnutritive sweeteners can be found: On the internet: American Diabetes Association: www.diabetes.org Diabetes Care and Education Practice Group of the Academy of Nutrition and Dietetics: www.dce.org The Food Network Website (search term "sugar substitute"): http/www.foodnetwork.com In magazines: Diabetes Forecast: www.forecast.diabetes.org Diabetes Self-Management: www.diabetesselfmanagement.com Diabetic Cooking: www.diabeticcooking.com



Media Messaging Patients are confronted with headlines that sensationalize the research results and provoke fear around NNS use Often, only a fragment of a study finding is included and authors apply this to support the overall effect of the article Anticipate questions that patients may bring as a result of this type of reporting



Source Evaluation

- Patient should be encouraged to evaluate sources of information with consistent criteria
 - Is this author credible?
 - Is it a personal opinion or a professional consensus?
 - Does this source feature testimonials as evidence to support the claims?
 - Is this source designed to sell a product with health promises?
 - Does the source include citations?

Patient Groups

- The following groups of patients are more likely to consume NNS
 - Diabetes
 - Bariatric Surgery
 - Medical Weight Loss
 - Athletes or anyone who uses sports supplements
- Translating the research findings in perspective of the amount and quality of evidence is critical to educating patients
 - Compare the NNS intake in a typical diet containing artificially sweetened supplements and food to the ADI
 - High variability among patients so must use an individualized approach

Key Takeaways

- The majority of the concern around NNS came from initial animal studies that have since been refuted
- Current research results are confusing due to the different methodologies and lack of standardization between comparators
- One of the most important factors when discussing NNS requires urging patients to NOT replace the calories saved by NNS with other sources of intake
- Replacing sugar sweetened beverages with water is ideal, however there is enough consensus for artificially sweetened beverages to have a place in an overall healthy diet pattern

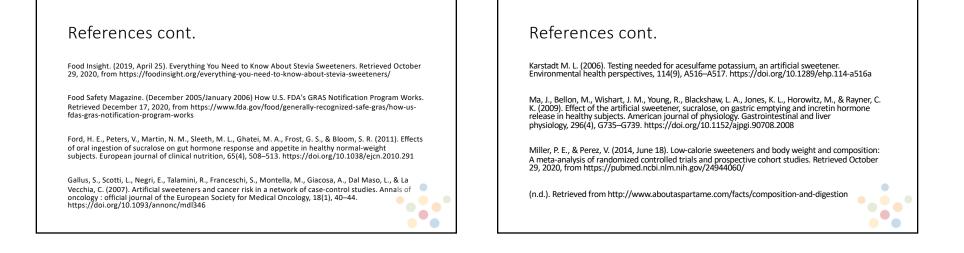
References

American Diabetes Association. (2020, January 01). Standards of Medical Care in Diabetes-2020. Retrieved from https://care.diabetesjournals.org/content/43/Supplement_1/S7

 $2015-2020 \ Dietary \ Guidelines. \ (n.d.). \ Retrieved from \ https://health.gov/our-work/food-nutrition/2015-2020-dietary-guidelines$

Center for Food Safety and Applied Nutrition. (n.d.). Additional Information about High-Intensity Sweeteners. Retrieved October 29, 2020, from https://www.fda.gov/food/foodadditives-petitions/additional-information-about-high-intensity-sweeteners-permitted-usefood-united-states

CFR - Code of Federal Regulations Title 21. (n.d.). Retrieved from https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=170.3



References cont.

(n.d.). Retrieved from https://www.andeal.org/topic.cfm?cat=4612

Pepino, M. Y., Tiemann, C. D., Patterson, B. W., Wice, B. M., & Klein, S. (2013). Sucralose affects glycemic and hormonal responses to an oral glucose load. Diabetes care, 36(9), 2530–2535. https://doi.org/10.2337/dc12-2221

Peters, J., Wyatt, H., Foster, G., Pan, Z., Wojtanowski, A., Veur, S., . . . Hill, J. (2014, May 26). The effects of water and non-nutritive sweetened beverages on weight loss during a 12-week weight loss treatment program. Retrieved October 29, 2020, from https://onlinelibrary.wiley.com/doi/10.1002/oby.20737

Petre, A., MS, RD, (NL). (2020, August 19). Artificial Sweeteners: Good or Bad? Retrieved October 29, 2020, from https://www.healthline.com/nutrition/artificial-sweeteners-good-or-bad



References cont.

Schaefer, A. (2017, November 11). Acesulfame Potassium: Is It Safe? Retrieved October 29, 2020, from https://www.healthline.com/health/is-acesulfame-potassium-bad-for-me

Shwide-Slavin, C., Swift, C., & Ross, T. (2012, May 01). Nonnutritive Sweeteners: Where Are We Today? Retrieved from https://spectrum.diabetesjournals.org/content/25/2/104

Suez, J., Korem, T., Zeevi, D., Zilberman-Schapira, G., Thaiss, C. A., Maza, O., Israeli, D., Zmora, N., Gilad, S., Weinberger, A., Kuperman, Y., Harmelin, A., Kolodkin-Gal, I., Shapiro, H., Halpern, Z., Segal, E., & Elinav, E. (2014). Artificial sweeteners induce glucose intolerance by altering the gut microbiota. Nature, 514(7521), 181–186. https://doi.org/10.1038/nature13793

Tate DF;Turner-McGrievy G;Lyons E;Stevens J;Erickson K;Polzien K;Diamond M;Wang X;Popkin B;. (2012, February 1). Replacing caloric beverages with water or diet beverages for weight loss in adults: Main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. Retrieved October 29, 2020, from https://pubmed.ncbi.nlm.nih.gov/22301929/

References cont.

U.S. Department of Agriculture, Agricultural Research Service. 2013. USDA National Nutrient Database for Standard Reference, Release 26. Methods and Application of Food Composition Laboratory Home Page, http://www.ars.usda.gov/nea/bhnrc/mafcl

Wiebe N;Padwal R;Field C;Marks S;Jacobs R;Tonelli M;. (2011, November 17). A systematic review on the effect of sweeteners on glycemic response and clinically relevant outcomes. Retrieved October 30, 2020, from https://pubmed.ncbi.nlm.nih.gov/22093544/

Yang, Q. (2010). Gain weight by "going diet?" Artificial sweeteners and the neurobiology of sugar cravings. YALE JOURNAL OF BIOLOGY AND MEDICINE, 83, 101-108.



