"Sucralose" is a one-hour of self-study continuing professional education (CPE) Level-1 module for Registered Dietitian Nutritionists (RDNs) and Dietetic Technicians, Registered (DTRs).

Level I: Assumes that the participant has little or no prior knowledge of the area(s) covered.

The focus of this CPE activity is to increase the core knowledge of the user.

Suggested Learning Need Codes:

- 2030: Food additives
- 2080: Food toxicology
- 4080: Food labeling
- 5370: Weight management

Suggested Performance Indicators

8.1.2 Applies knowledge of food and nutrition as well as the biological, physical and social sciences in practice.

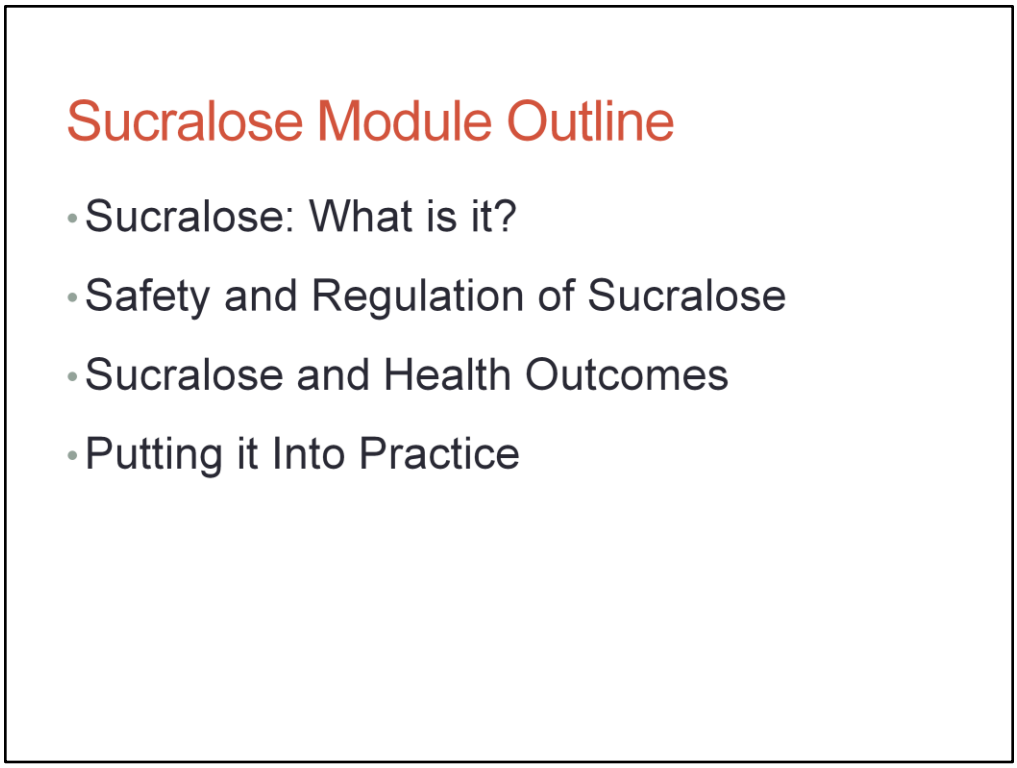
8.3.6 Keeps abreast of current nutrition and dietetics knowledge and trends.

Learning Objectives:

1. List the characteristics of sucralose that relate to its use as a sweetener and its safety as a food additive.
2. Discuss the FDA approval process for sucralose as a food additive
3. Explain safe levels of consumption of foods and beverages sweetened with sucralose within the context of the Acceptable Daily Intake (ADI) level for sucralose.
4. Advise patients and the public on the appropriate use of sucralose based on age, life stage, and health status of the individual.
5. Advise patients and the public on the appropriate use of sucralose in packaged food and beverages and in cooking.

Upon completion of this module, dietetic professionals will be able to:

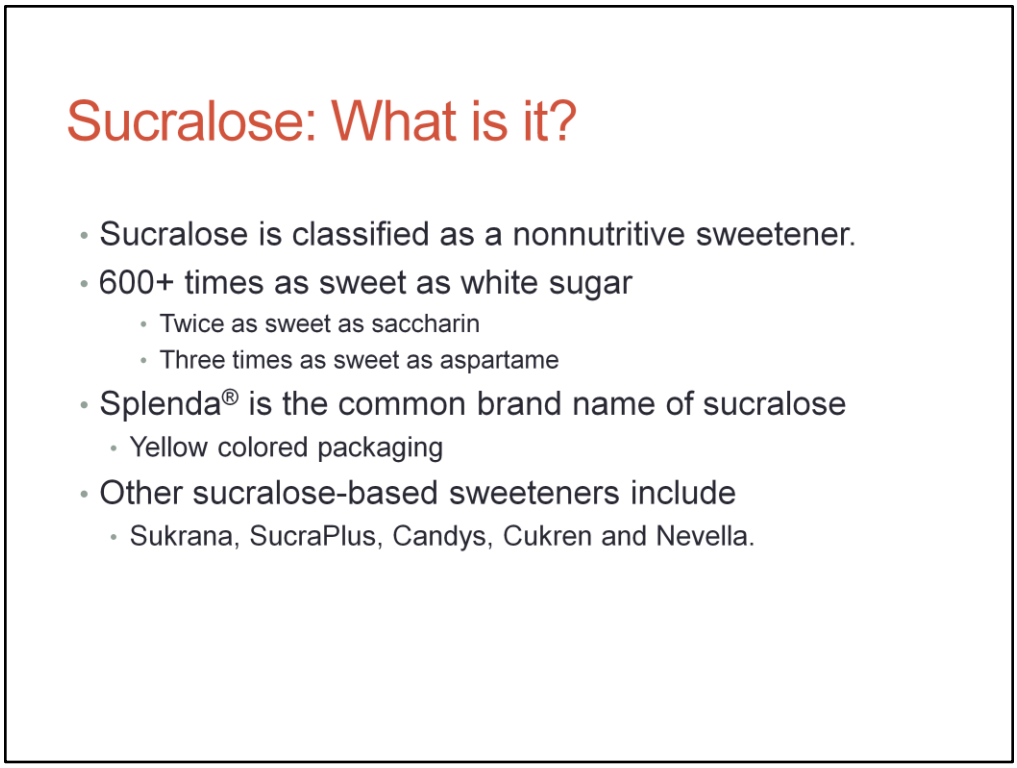
1. List the characteristics of sucralose that relate to its use as a sweetener and its safety as a food additive.
2. Discuss the FDA approval process for sucralose as a food additive
3. Explain safe levels of consumption of foods and beverages sweetened with sucralose within the context of the Acceptable Daily Intake (ADI) level for sucralose.
4. Advise patients and the public on the appropriate use of sucralose based on age, life stage, and health status of the individual.
5. Advise patients and the public on the appropriate use of sucralose in packaged food and beverages and in cooking.



Sucralose Module Outline

- Sucralose: What is it?
- Safety and FDA Regulation of Sucralose
- Sucralose and Health Outcomes
- Putting it Into Practice

SUCRALOSE: WHAT IS IT?

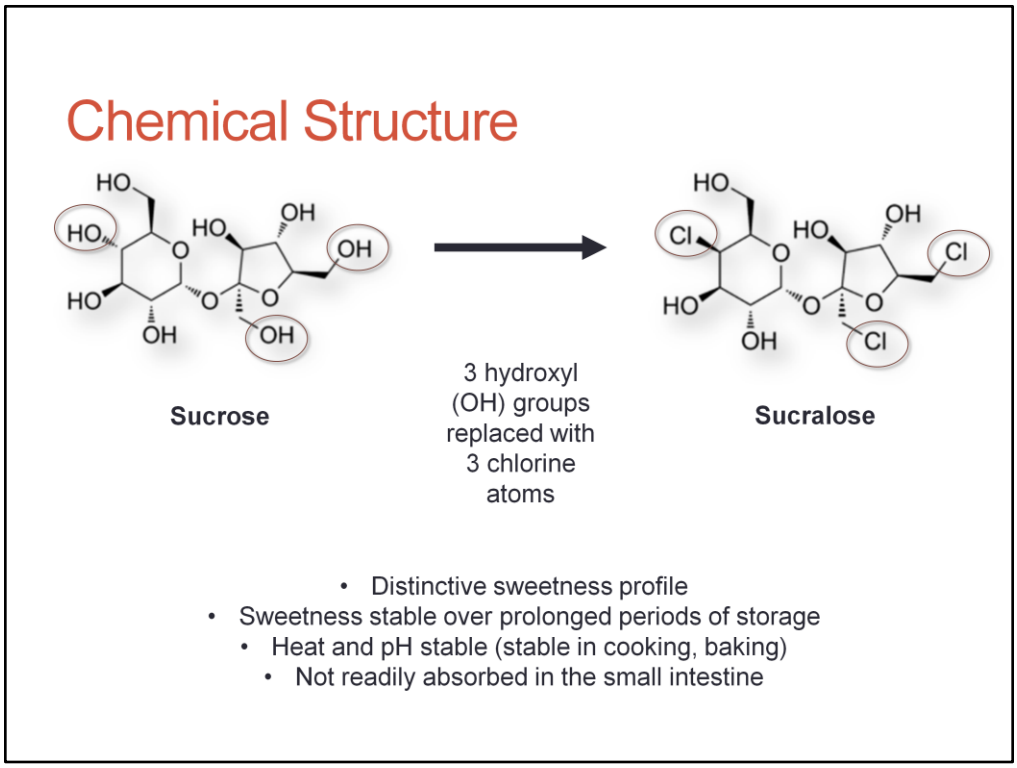


Sucralose is classified as a nonnutritive sweetener. (Fitch and Keim 2012) Though not the sweetest of all nonnutritive sweeteners, it is 600-1000 times as sweet as table sugar and 2-3 times as sweet as saccharin and aspartame, respectively. (NCBI 2015) Its most common commercial name is Splenda®. Sweetener packets containing sucralose are yellow for easier identification and differentiation from other commercial sweeteners. Other sucralose-based sweeteners include: Sukrana, SucraPlus, Candys, Cukren, and Nevella.

Sucralose in Food and Beverages

- Sucralose can be found in:
  - Diet drinks
  - Low carbohydrate meal replacements
  - Reduced carbohydrate foods
  - Pre-prepared dairy foods
  - Condiments
  - Candy and gums

Products sweetened with sucralose have been found to retain their sweetness throughout extended periods of storage and therefore help extend the shelf-life of foods in which it is used. (CCC Sucralose 2015) Products that contain sucralose include carbonated and other sweet drinks, reduced-carbohydrate meal replacements and foods, dairy foods, condiments, candy, and chewing gum.



Sucralose is produced from the disaccharide sucrose and chloride. The three hydroxyl groups (OH) on sucrose are replaced with three chlorine atoms.

The unique chemical structure of sucralose results in a product that has a distinctive and stable sweetness profile. It is heat- and pH-stable over a broad range of conditions. As a result, sucralose can be used in baking. As for calories, it is not readily absorbed in the small intestine, and passes intact into feces. Therefore, sucralose imparts negligible calories to the diet. (TOXNET 2012; Grotz AND Munro 2009)

The chlorine that is used to make sucralose is a familiar chemical element. Chlorine is a natural component of foods, including: salt (sodium chloride), lettuce, tomatoes, mushrooms, and peanut butter. It is part of more complex molecules naturally found in foods such as peas and potatoes. In addition, chlorine is added to most public drinking water supplies as an antimicrobial agent. (Briggs and Wahlqvist 1998)

Sucralose: Absorption and Metabolism

- Metabolism is well understood
- Approximately 85% of ingested sucralose is not absorbed
- About 15% of ingested sucralose is passively absorbed
- Absorbed sucralose is not recognized as a carbohydrate and provides no energy to the body
- Sucralose does not accumulate in body compartments
- Most sucralose is eliminated, unchanged in feces

Metabolism of sucralose is well understood. (Rodero et al 2009) Approximately 85% of consumed sucralose is not absorbed in the small intestine. As a result of its low absorption rate, sucralose provides no energy to the body. Excretion of unabsorbed sucralose is primarily through feces. About 15% of ingested sucralose is passively absorbed due to its small size and solubility in water. It is distributed to essentially all tissues, but does not accumulate. Rather, it is excreted through urine. (Grotz and Munro 2009)

Sucralose: Metabolism

- Consumption, even at very high levels, has virtually no impact on blood constituents, such as:
  - Amino acids
  - Methanol
  - Glucose
- Research shows that sucralose has no negative gastrointestinal effects:
  - No gas or bloating
  - No osmotic effect (diarrhea)

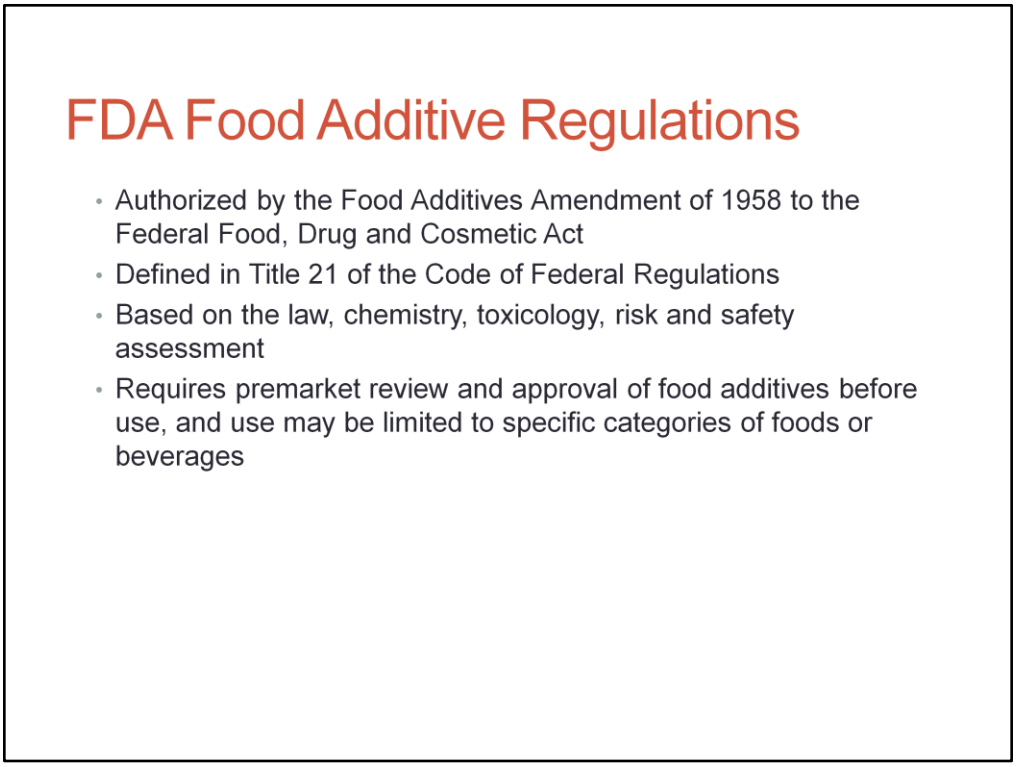
Sucralose consumption, even at very high levels, has virtually no impact on blood amino acids, methanol levels, or blood glucose. (Rodero et al 2009) Unabsorbed or undigested food components that move into the large intestine undergo gut bacteria fermentation. Common side effects of these processes can include gas and bloating, and depending on the substance, diarrhea. However, sucralose does not produce these undesirable gastrointestinal effects, suggesting it is not fermented by gut bacteria. (Grotz and Munro 2009)

SAFETY & REGULATION OF SUCRALOSE

FDA Safety Standards

A reasonable certainty of no harm under the intended conditions of use.

It is noteworthy that the FDA requires that all foods and beverages meet the same standard of safety, specifically described as "..the reasonable certainty of no harm under the intended conditions of use…" New food ingredients are presumed to be unsafe until they are proven safe on the basis of scientific data. The burden of proof lies with the company that petitions the FDA for approval of an ingredient for use in the food supply.



The FDA regulation of food additives is authorized by the Food Additives Amendment of 1958 to the Federal Food, Drug and Cosmetic Act (FFD&C Act) and defined in Title 21 of the Code of Federal Regulations. (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=170). The regulations are based on careful consideration of the law, as well as chemistry data, toxicology data, and risk and safety assessments (Rulis and Levitt 2009). Premarket review and approval by FDA is required before a food additive may be used in foods or beverages, and the approval specifies the particular uses that are allowed. http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm253328.htm.

FDA Safety Evaluation: Intake Levels

- EDI: Estimated Daily Intake
  - Conservative estimation of probable consumer exposure to the additive
- HNEL: Highest No Effect Level
  - Animal studies data
  - The highest level that can be consumed without negative consequences
- ADI: Acceptable Daily Intake
  - HNEL x 1/100 = ADI

https://www.flickr.com/photos/safari_vacation/5929769873

FDA evaluation of safety includes examination of the chemical identidy, purity, and technical specifications of the ingredient, the estimated daily intake (EDI), highest no-effect level (HNEL), and acceptable daily intake (ADI) (http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm253328.htm#answer).

- The EDI is the conservative estimation of probable consumer exposure to the food additive based on projected lifetime average exposure, assuming large serving sizes, high frequency of eating, and high concentration of the additive in foods. Estimates of intake can be challenging due to the use of a variety of sweeteners in foods and beverages, as well as limited information regarding the quantity of sweeteners used in some products. The EDI is expressed in mg per kg body weight per day (mg/kg/d) in humans.
- The HNEL is determined based on animals studies and represents the highest level of intake that can be consumed without negative consequences. A considerable amount of research is considered, including studies assessing toxicity (genetic, reproductive, chronic), carcinogenicity, pharmacokinetic properties, environmental information, and any other information available.
- The ADI is an adjusted HNEL. The ADI is adjusted in two ways. First, an additional 10 fold “safety” or “uncertainty” factor is added to account for any potential underestimation of risk to humans due to extrapolation from animal studies. A second adjustment factor of 10 is applied to account for individual variation among humans. Therefore, the ADI value

represents the HNEL x 1/100.

FDA Safety Evaluation and Regulatory Decision

- FDA compares the EDI and ADI.
  - If EDI > ADI, FDA will NOT allow safety conclusions
  - If EDI < ADI, FDA *may* issue a safety decision consistent with "reasonable certainty of no harm"
- Additional research may be required
- Other risk assessment techniques may be applied
- An advisory committee may be consulted
- Published in Federal Register with adequate and reasonable time for public's right to review and respond

The FDA uses a comparison of the EDI and ADI to make a safety decision. (Rulis et al 2009) If the EDI is greater than the ADI, the FDA will NOT allow safety conclusions to be made. If the EDI is lower than the ADI, then the FDA *may* issue a safety decision consistent with the standard that there is a "reasonable certainty of no harm under the intended conditions of use." Still, additional research, such as clinical trials, such as to assess blood glucose homeostasis, drug interactions, or potential allergenicity, may be required by the FDA. And additional risk assessment techniques may be utilized. When a decision is made, it is published in the Federal Register, allowing adequate and reasonable time for the public's right to review and respond to the regulatory decision.

Sucralose Discovery and Approval History

- 1976: Discovered, and patented
- 1987: Original FDA petition filed
- 1991: Approved for use in Canada
- 1998: Approved for use in United States
- 2000: Approved for use in European Union (EU)

- Sucralose is permitted for use in more than 100 countries

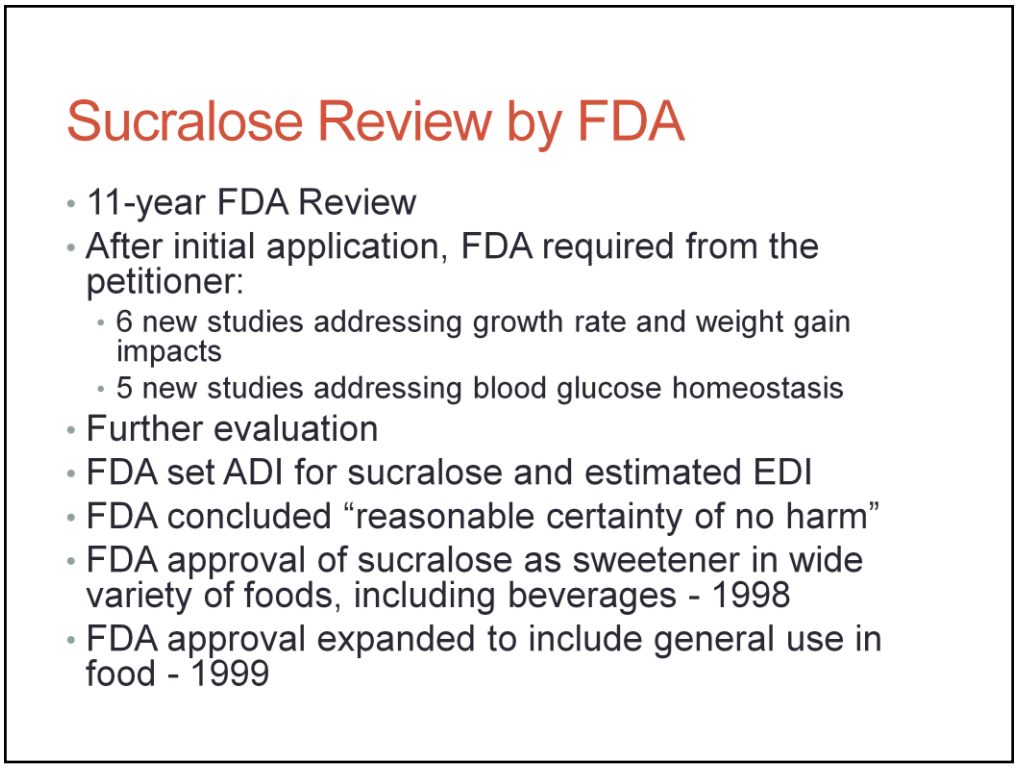
Sucralose was discovered in 1976 by scientists working for Tate & Lyle and patented in the same year. Though the original petition was filed with the FDA in 1987, Canada was first to approve sucralose for use in foods in 1991, (Health Canada 2013) followed by the U.S. in 1998 (FDA 1998), and the European Union in 2000. (Mortensen 2006) According to the International Sweeteners Association, sucralose is permitted for use in more than 100 countries. (ISA 2012)

Chronology of FDA Food Additive Approval or GRAS Affirmation of Nonnutritive Sweeteners

Sweetener	Approved
Saccharin	1977 (GRAS) 2000 (all warnings repealed) (general use)
Aspartame	1981 (specific foods) 1983 (soft drinks) 1996 (general use)
Acesulfame potassium (Ace-K)	1988 (dry foods) 1998 (nonalcoholic beverages) 2003 (general purpose)
Sucralose	1998 (general use)
Neotame	2002 (general use)
Stevia	2008 (GRAS)
Luo han guo (monk fruit)	2010 (GRAS)
Advantame	2014 (general use)

This table chronicles FDA regulatory decisions regarding nonnutritive sweeteners approved through the food additive petition process (FDA December 2014) and comments regarding those evaluated through the GRAS process. (FDA 2015) These include saccharin, aspartame, acesulfame potassium, sucralose, neotame, stevia, luo han guo (monk fruit), and advantame. Those sweeteners with multiple years listed reflect that the FDA evaluation process for ingredient use in foods is sometimes conducted over several years for different categories of foods.

(For additional information on other NNS, refer to the FDA web page on "High-Intensity Sweeteners" at http://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm397716.htm.)



The approval process for sucralose illustrates the thorough approach used by FDA in reviewing food additive petitions. Sucralose was under review at the FDA for 11 years. (Rulis et al 2009) During the course of the FDA's safety evaluation process, its scientists identified two central questions that needed to be resolved. As a result, the petitioner was required to conduct an additional six new studies to address an issue concerning the growth rate and body weight gain of the test animals. An additional five new studies were required to resolve concerns about blood glucose homeostasis. In the end, FDA scientists reviewed eleven additional studies that were not part of the original petition.

The results of the original studies submitted to FDA and the additional studies requested by FDA, in addition to other reviewed materials, allowed the FDA to set the ADI for sucralose and conclude a "reasonable certainty of no harm under the intended conditions of use" (recall that this is the FDA's standard of safety). (FDA 1998) The FDA decision, published in the *Federal Register* in 1998, (FDA) was for approval of sucralose as a sweetener for use in a wide variety of foods, including beverages. Subsequently, the allowed use of sucralose was expanded to include general use in food. (FDA 1999) (Recall that food additive approval specifies how the ingredient may be used, including what foods it can be used in. Therefore, food additives may be approved for use in specific foods and/or beverages, and may later be approved for general use in any food or beverage.)

Sucralose and the Estimated Daily Intake (EDI) for Adults

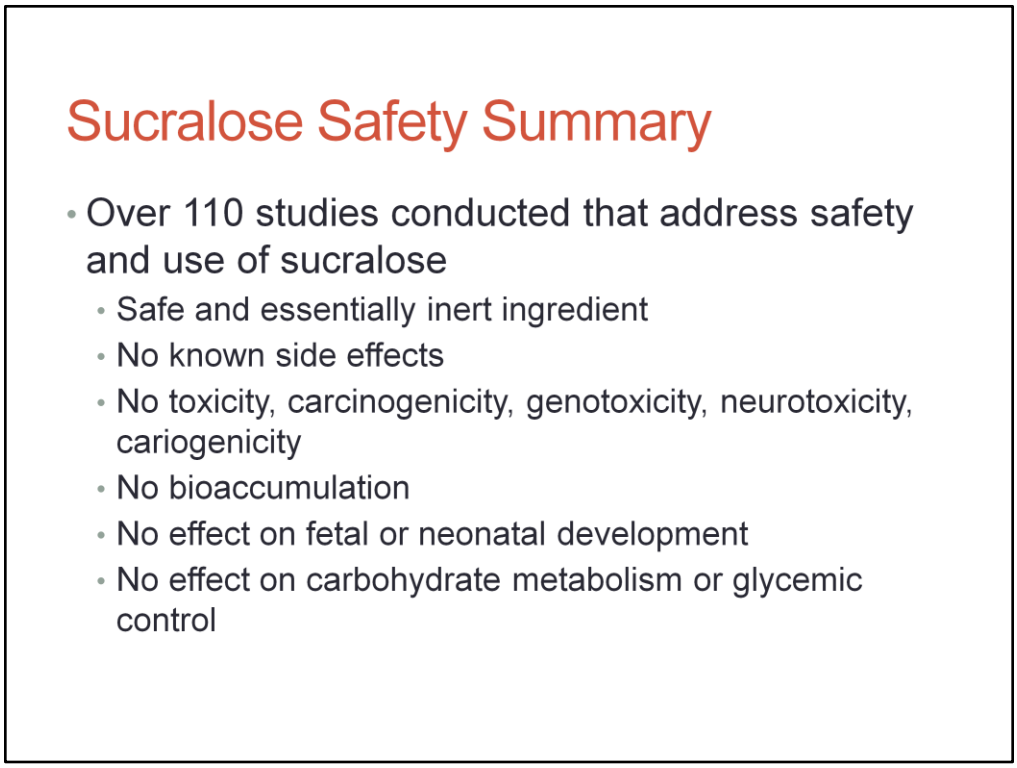
- Sucralose Estimated Daily Intake (EDI)
  - 1.6 mg/kg bw/day
- Sucralose Acceptable Daily Intake (ADI)
  - 5 mg/kg bw/day
- EDI < ADI → contributed to FDA safety conclusion

Recall that the EDI for adults is based on conservative assumptions including an assumed aggressive replacement of sugar with sucralose. (Rulis 2009) The EDI (Estimated Daily Intake) for sucralose is 1.6 mg/kg/d (based on the 90th percentile EDI). (FDA 1998) The FDA conclusion regarding the safety of sucralose is based partly on the fact that the EDI is lower than the ADI of 5 mg/kg/d. (FDA 1998 and 1999)

How Much Sucralose Can an Individual Safely Consume?

Sweetener	ADI (mg/kg/d)	132 lb. (60 kg) person	
		mg/d	packets/d
Acesulfame K	15	900	23
Aspartame	50	3,000	75
Saccharin	15	900	45
Sucralose	**5**	**300**	**23**
Advantame	32.8	1,968	4,920

The chart above shows the amounts of various tabletop sweetener packets a 132-lb (60-kg) individual would have to consume to reach the ADI for those sweeteners. (FDA May 2014) Note that although the ADI for sucralose is lower than some of the other sweeteners, smaller amounts are used in foods.



Over 110 studies have been conducted that address safety and the use of sucralose. (Grotz and Munro 2009) Conclusions from these studies can be summarized as follows:

- It is a safe and essentially inert ingredient.
- There are no known side effects.
- It is not toxic, carcinogenic, genotoxic, neurotoxic, or cariogenic.
- It does not bioaccumulate.
- There is no effect on fetal or neonatal development.
- There is no effect on carbohydrate metabolism or glycemic control.

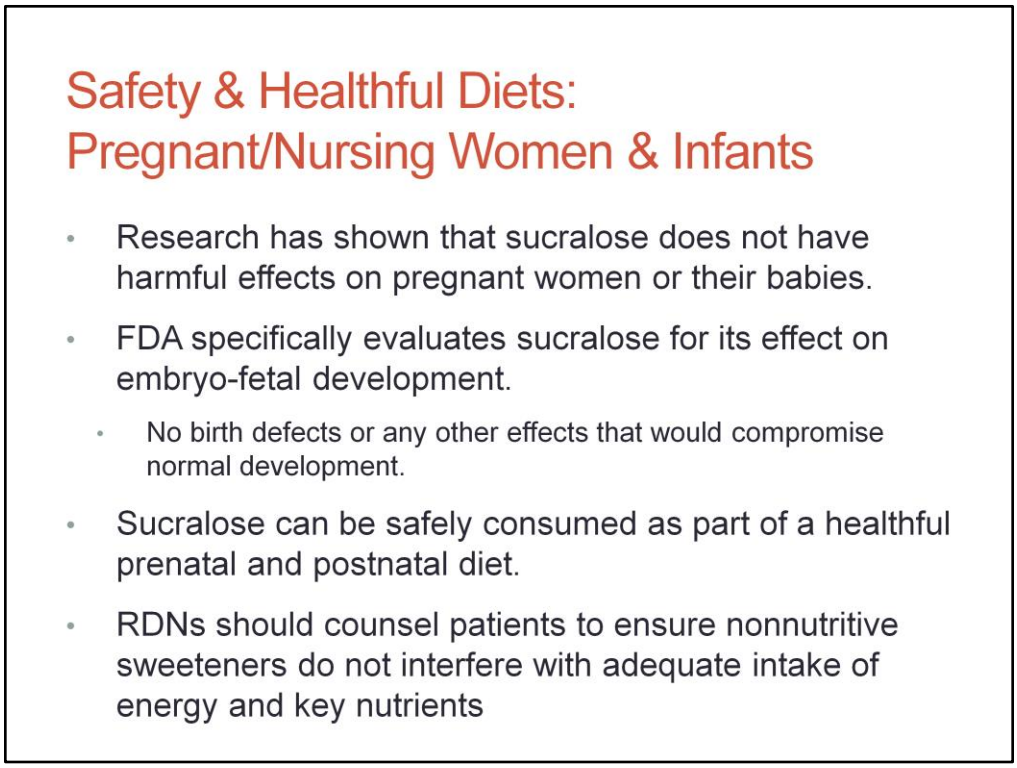
Safety & Healthful Diets: Children

- Unique considerations with children:
  - Smaller body size
  - Periodic tendency to eat a limited number of foods
- Risk reduced by
  - Food producers use of sweetener blends versus only one type
  - Parents continued promotion of variety and decreasing proportion of sweet-tasting foods in children's diets
- Used in nutrient-dense foods, nonnutritive sweeteners can encourage key nutrient intakes without extra kcal

Smaller body size for people of any age is relevant to sweetener safety, as the ADI is based on body weight. Children also may periodically eat a limited number of foods due to evolving preferences, therefore could more easily consume the ADI for a particular sweetener. It is important to encourage parents to promote and practice moderation and variety in a child's food choices and overall diet in order to reduce the risk of excessive consumption of any food or food constituent, including both nutritive and nonnutritive sweeteners and sweet tasting foods in general.

However, the ADI is set at a level to be safe for all consumers, including children and infants, as part of a healthy diet. (FDA 1998 and 1999) Furthermore, since most foods use a combination of sweeteners, it is not likely that the ADI for any one sweetener would be reached.

Sweetness may be useful in promoting the consumption of nutrient dense foods of importance to the growing child's diet, such as low-fat flavored milk, yogurts, and certain juices. Therefore, sucralose and other nonnutritive sweeteners can serve this purpose without increasing the caloric content of the diet.



Research has shown that sucralose does not have harmful effects on pregnant women or their babies. (Pope et al 2014) The FDA has specifically evaluated sucralose for its effect on embryo-fetal development and found no indications that birth defects or any other effects that would compromise normal development are connected to sucralose intake. (FDA 1998) Therefore the safety statement by the FDA reflects that sucralose can be safely consumed as part of a healthful prenatal and postnatal diet.

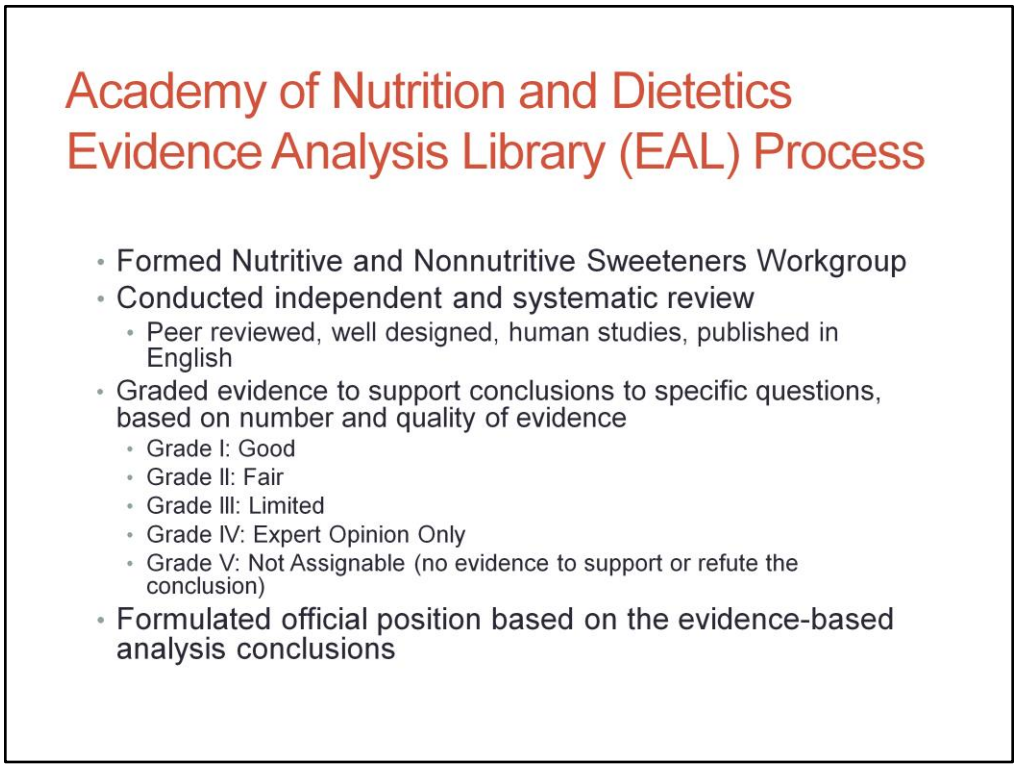
However, the RDN should counsel expectant mothers to ensure that use of nonnutritive sweeteners does not interfere with consumption of adequate kcal and key nutrients needed for the health of both mother and baby during pregnancy and lactation.

Reviewed by Other Regulatory and Scientific Agencies

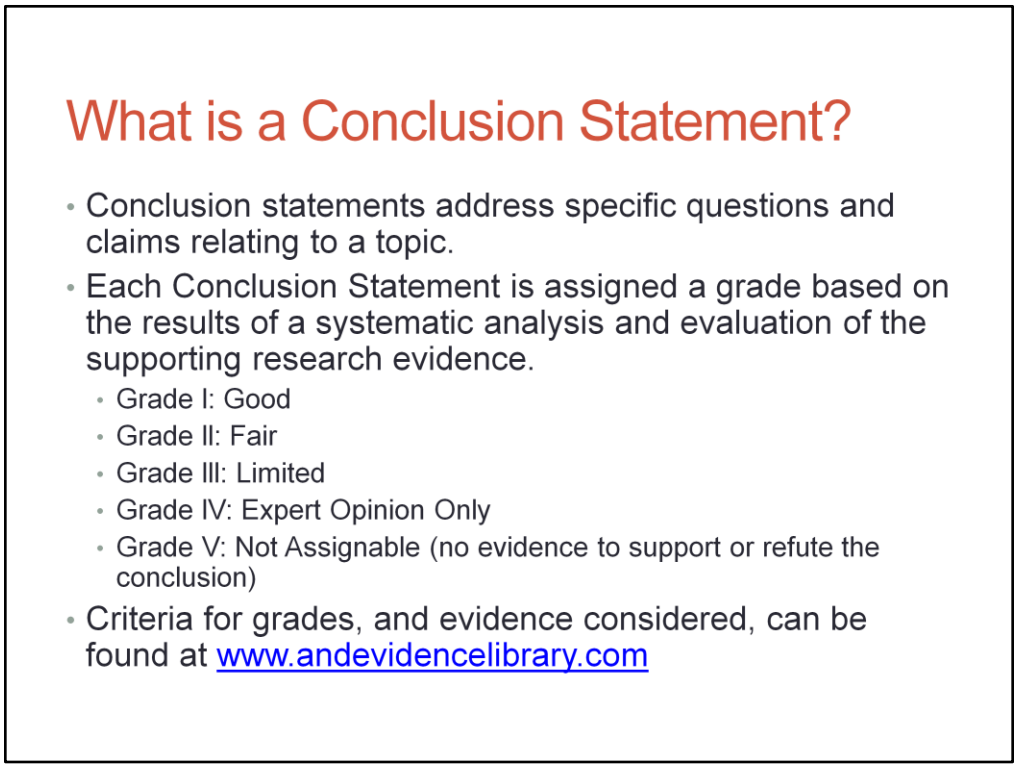
- The following third party and regulatory agencies have conducted independent evaluations for use of sweeteners, and uphold their appropriate and reasonable use.
  - U.S. Food and Drug Administration
  - U.S. National Institutes of Health, National Cancer Institute
  - Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives
  - European Union's Scientific Committee on Food
  - Health Protection Branch of Health and Welfare Canada
  - Food Standards Australia and New Zealand

In addition to the FDA, regulatory and scientific bodies around the world, including those listed here, acknowledge that the reasonable use, within the ADI, of nonnutritive sweeteners, including sucralose, is safe. (IFIC Foundation 2010)

Several health professional and health science organizations have reviewed nonnutritive sweetener research, focusing on application for health benefit (e.g., replacing added sugars for health benefits, effects on glycemic control in those with diabetes, etc). The American Diabetes Association (Gardner et al 2012; Evert et al 2013), Academy of Nutrition and Dietetics (Fitch et al 2012), American Heart Association (Gardner et al 2012) and Canadian Diabetes Association (Dworatzek et al 2011) have upheld the conclusions of FDA and others that the appropriate and reasonable use of nonnutritive sweeteners can be a part of an overall healthful eating plan.



The conclusions put forth in the Academy of Nutrition and Dietetics Position Paper on "Use of Nutritive and Nonnutritive Sweeteners" (Fitch et al 2012) were based on the Academy's Evidence Analysis Library (EAL) process. First, a Nutritive and Nonnutritive Sweeteners Workgroup was formed. The Workgroup conducted an independent and systematic review of the peer-reviewed, English-language literature, limited to well-designed human studies that addressed specific questions. They graded each paper for quality, and graded the overall evidence based on number and quality of studies. Finally, a separate committee formulated the official Academy position based on the EAL conclusions. The evidence relating to sucralose intake and health is documented in both the EAL (www.andeal.org) and the position paper. (Fitch and Keim 2012)



Conclusion statements address specific questions and claims relating to a topic. Each Conclusion Statement is assigned a grade based on the results of a systematic analysis and evaluation of the supporting research evidence.

Grade I: Good
Grade II: Fair
Grade III: Limited
Grade IV: Expert Opinion Only
Grade V: Not Assignable (no evidence to support or refute the conclusion)

Criteria for grades, and evidence considered, can be found at www.andevidencelibrary.com.

It is noteworthy that the majority of evidenced reviewed by the FDA in its food additive regulatory decisions are animal studies, examining questions of toxicology that are not conducted in humans for ethical reasons. The Academy EAL, on the other hand, does not evaluate safety, but does evaluate human research documenting adverse effects. All conclusion statements included in the Academy position paper were grade III (meaning that there is limited available evidence to consider). (Fitch and Keim 2012)

EAL Conclusion on Adverse Events Related to Sucralose in Humans

"Limited research in humans, from peer-reviewed journals, did not find an association between adverse effects and the intake of sucralose in the general population. No data from longitudinal cohort studies were available for review."

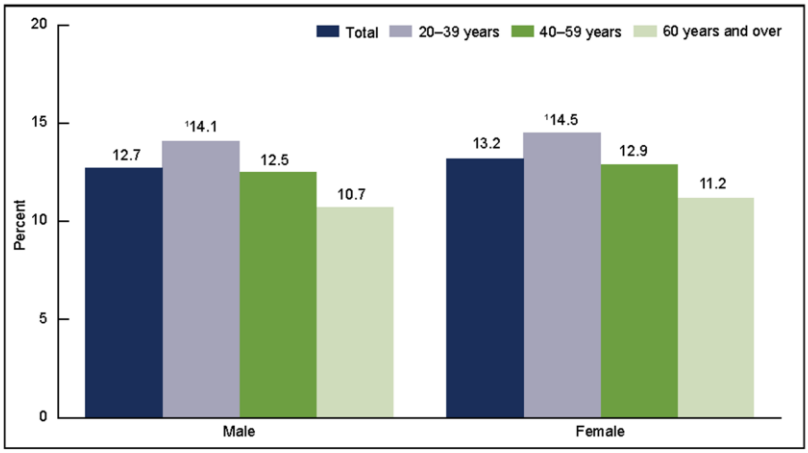
The EAL did not find an association between adverse events and the intake of sucralose in the general population in human, peer-reviewed research. (Fitch and Keim 2012) The available evidence was noted to be limited, and no data from longitudinal cohort studies were available for review.

Because the EAL does not evaluate animal studies, information regarding the FDA additive approval process and approvals for various NNS, including sucralose, are provided on the EAL website (https://www.andeal.org/topic.cfm?menu=4100&pcat=4859&cat=3230).

SUCRALOSE AND HEALTH

Percentage of Kilocalories From Added Sugars

Figure 2. Mean percentage of kilocalories from added sugars among adults aged 20 and over, by age group and sex: United States, 2005–2010



1Significant linear trend by age, $p < 0.05$.
NOTE: Estimates that were not age-specific were age adjusted to the 2000 U.S. standard population using the three age groups shown.
SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 2005–2010.

The 2005-2010 NHANES data suggest that in adults aged 20 and older, the mean percentage of kcal from added sugars is approximately 13%. (Ervin and Ogden 2013) Among adolescents (not shown in slide), average intake of added sugars is 16% of total daily kcal.

Added Sugar Intakes & Recommendations

Added Sugars	Dietary Guidelines	American Heart Association	World Health Organization
	2015-2020	2009	2015
%kcal/d	< 10	N/A	≤ 10
g/d	< 50*	25-38	≤ 50*
tsp/d*	<12*	6-9	≤ 12*

*Calculated based on 2,000 kcal/d diet

U.S. intake of added sugars is higher than recommended by the 2015-2020 Dietary Guidelines for Americans (HHS and USDA 2010), the American Heart Association (Johnson et al 2009), and the World Health Organization (WHO 2015). The World Health Organization recommends no more than 10% kcal/d from added sugars, with a conditional recommendation to reduce intakes to less than 5% kcal/d (noting that the evidence to do so is weaker than the ≤10% kcal/d recommendation, but may prove to be beneficial over the lifespan). Replacing added sugars with nonnutritive sweeteners (rather than simply adding nonnutritive sweeteners) may help individuals to meet these recommendations.

Adults: Weight Management

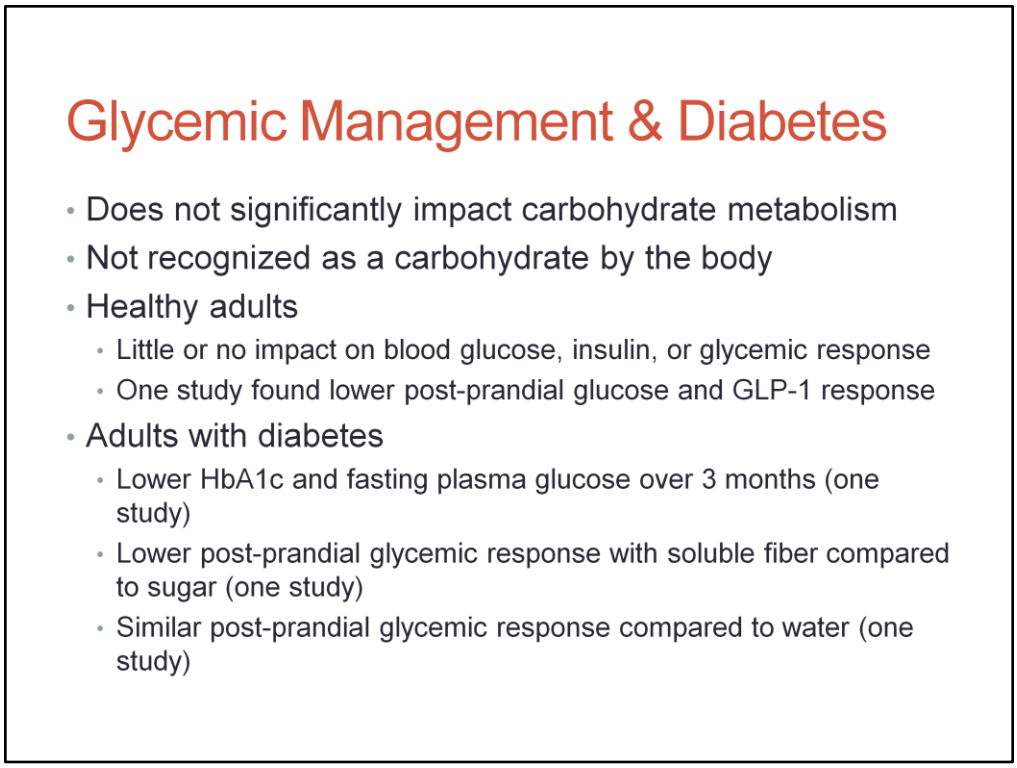
- Studies are limited
- Does not affect appetite or directly affect food intake in adults (two studies)
- Creates energy deficit only if sucralose displaces caloric sweeteners and not compensated with other caloric intake
  - + increased physical activity to improve weight loss efforts
  - In place of added sugars to meet Dietary Guidelines for Americans

While there are several weight management studies utilizing different types of sweeteners, there are few well-designed human studies specifically on sucralose and weight management. As noted in the AND position statement, (Fitch and Keim 2012), the EAL cites one study that found no increase in appetite attributable to sucralose. (Frank et al 2008) Another small study suggested sucralose does not increase food intake in adults, but could contribute to a negative energy balance when substituted for energy normally consumed from other sources. (Rodearmel et al 2007) The result of this type of substitution or displacement, in conjunction with increased physical activity, could positively impact weight loss efforts. The 2015-2020 Dietary Guidelines for Americans policy document notes, "…replacing added sugars with high-intensity sweeteners may reduce calorie intake in the short-term, yet questions remain about their effectiveness as a long-term weight management strategy." Further research is needed to understand how sucralose use may help individuals to meet weight management goals.

Children: Weight Management

- Studies are limited
- Does not increase food intake in children
- Overweight children who increased walking by 2000 steps/day and eliminated 100 kcal/day by using sucralose prevented further weight gain
- Long-term studies needed to assess impact of sucralose use on achieving and maintaining healthy weight in children

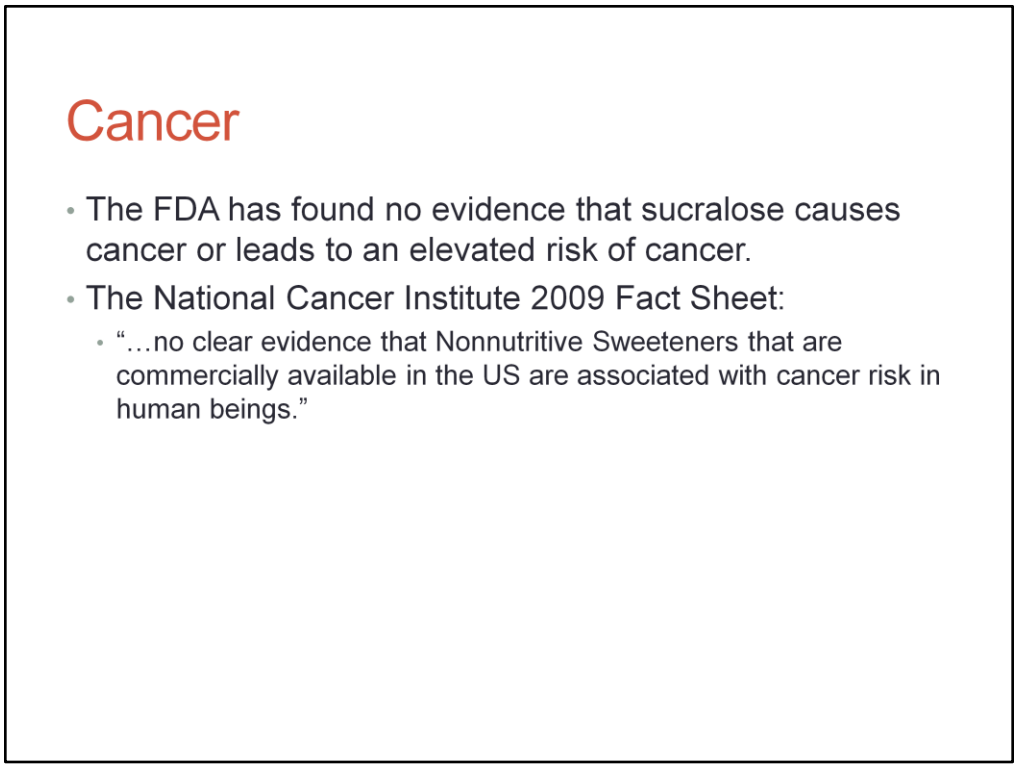
Sucralose has not been shown to cause increased food intake in children. (Rodearmel et al 2007) The researchers also documented that overweight children could prevent further weight gain by walking another 2,000 steps and eliminating 100 kcal each day using products sweetened with sucralose (Splenda®). This was one of the first times clinical evidence suggested that overweight children could effectively prevent excess weight gain by making small changes to their lifestyle. However, further research, including long term studies in child and adolescent populations, are needed to establish a correlation between sucralose intake and weight management in children.



As previously mentioned, sucralose does not appear to significantly impact carbohydrate metabolism because it is not recognized by the body as a carbohydrate. (Rodero et al 2009) This is consistent with studies reviewed by the Academy of Nutrition and Dietetics Evidenced Analysis Library (EAL), supporting its conclusion: "Limited evidence from three controlled trials (Mezitis et al, 1996; Reyna et al, 2003; Grotz et al, 2003) showed little or no effects of sucralose on metabolic effects, including blood glucose in adults; however, the trials were of small size and used varying doses of sucralose for different lengths of time."

Subsequent to the EAL review, a small study with healthy males demonstrated no differences in post-prandial glycemic response with consumption of sucralose alone, sucralose in combination with Ace-K, or water. (Wu et al 2013) In another small study, post-prandial glucose and GLP-1, but not insulin, was higher with sucralose compared to water. (Temizkan et al 2015)

In those with diabetes, as noted in the EAL conclusions, one study found a decrease in HbA1c and fasting plasma glucose levels over 3 months with sucralose versus placebo. (Grotz et al 2003) In a study conducted in Greece, replacing sugar with sucralose and soluble fiber in a dessert was shown to have beneficial postprandial glycemic effects in people with diabetes, although in this study it is impossible to distinguish whether there may be an effect of sucralose independent of or in synergy with soluble fiber. (Argyri et al 2013) In a small sample of adults with newly diagnosed type 2 diabetes, sucralose or water was consumed before an oral glucose tolerance test, and there were no differences in glucose, insulin, or GLP-1 response.



The FDA has found no evidence that sucralose causes cancer or leads to an elevated risk of cancer. (FDA 1998) As noted in the The National Cancer Institute Fact Sheet, "Artificial Sweeteners and Cancer," there is "…no clear evidence that nonnutritive sweeteners that are commercially available in the US are associated with cancer risk in human beings." (NCI 2009)

Potential Interaction with Gut Microbiome

- Gut microbiome linked to risk factors for chronic disease
  - Metabolic syndrome, obesity, diabetes, etc.
  - Proportion of bacterial species important
  - Metabolites of bacterial digestion of food components may be more important
  - Sucralose reaches colon (microbiome) intact
- However:
  - Early studies document sucralose excreted intact in feces
  - Limited human studies on sucralose and gut microflora
  - Gut microflora respond to many food components, foods, and dietary patterns

There is increasing interest in the impact of foods, food components, and dietary and other lifestyle patterns on the gut microbiome. While in the past research has focused on the effects of the diet on the gut locally (e.g., improving gut motility, reducing absorption of specific components from food, etc.), researchers have begun to detect connections between the balance of bacterial species in the gut and systemic health. Moreover, while detecting changes in the proportions of bacterial species is of interest, scientists have asked what, if any, effects these changes are having on health. The metabolites produced by the microbiome are increasingly understood to affect human health, and may be more informative than any documented changes in the gut microflora. Therefore, the fact that sucralose reaches the colon intact justifies research investigating potential interactions between the sucralose molecule and the gut microbiome. However, early studies documented the presence of sucralose, unchanged, in feces. (Roberts et al 2000, Sims et al 2000, John et al 2000) Very few studies have specifically studied the potential interactions of sucralose with the gut microbiome. As such studies are conducted, the potential confounding of results by other dietary factors must always be assessed.

Potential Interaction with Gut Microbiome

- One animal study documented microflora changes with sucralose
  - Both good and bad bacterial species increased
  - No observed health effects
  - Methodological flaws
- One animal study claimed: "artificial sweeteners induce glucose intolerance by altering gut microbiota"
  - Three different sweetener-fed groups were combined for statistical analysis, suggesting that all three sweeteners had similar effects
  - Gut microbiome in mice fed sucralose was unchanged
- Exploration of dietary impacts on the gut microbiome is ongoing.

One study has documented changes in the gut microflora with ingestion of sucralose in rats. (Abou-Donai et al 2008) However, both good and bad bacterial species were increased and there were no observed health effects related to the changes in the microbiome. There were flaws in the study design, as well, including use of an inappropriate control group diet and lack of adequate control or measure of food or energy intake. (CCC 2008)

The authors of a more recent paper concluded that "artificial sweeteners induce glucose intolerance by altering the gut microbiota." (Suez et al 2014) In the mouse study reported in this paper, while separate groups were fed different types of sweeteners (sucralose, saccharin, aspartame), all three groups were combined for statistical analysis. When examined separately, the sucralose group showed no significant differences from its control group. Also, liquid and food intake were reported for only 4 of 20 mice per group, and for only 3 days of the 11 weeks of study. Multiple dietary components and foods have been documented to affect the gut microbiome, therefore dietary intake data is important in such studies.

Certainly, this is an area of research that will continue to be explored.

PUTTING IT INTO PRACTICE

Recommendations Regarding Intake of Nonnutritive Sweeteners

- Dietary Guidelines for Americans 2015-2020
  - Potential for "high-intensity sweeteners" to replace added sugars, reducing calories in short term
  - Recommendation for added sugars < 10% total kcal
  - Need more long-term research to evaluate effectiveness for weight management
- World Health Organization
  - No direct mention of nonnutritive sweeteners

Currently there are no intake recommendations for nonnutritive sweeteners by the Dietary Guidelines for Americans or the World Health Organization. (HHS and USDA 2015; WHO 2015) The 2015-2020 Dietary Guidelines for Americans does note the potential for "high-intensity sweeteners" to assist in reducing added sugars intakes in the short term, and that more long-term research is needed on effectiveness in weight management. (HHS and USDA 2015)

Terms used on Food Labels to Identify Sweeteners

Nonnutritive Sweeteners
Acesulfame Potassium/K
Aspartame
Neotame
Saccharin
Sucralose
Luo han guo (Monk Fruit) Extract
Stevia
Advantame

Nutritive Sweeteners
Fruit juice concentrates, Nectars
Date sugar, Honey
Syrups: Corn, High Fructose Corn, Sorghum, Maple, Malt
Molasses
Dextrose & Anhydrous Dextrose
Sugars: Brown, Confectioner's, Invert, Raw, White granulated
Lactose, Maltose, Sucrose, Fructose
Polyols (Sugar Alcohols): Sorbitol, Mannitol, Xylitol, Maltitol syrup, Lactitol, Erythritol, Isomalt, Hydrogenated Starch Hydrolysates

Consumers who read a food label list of ingredients will be faced with many terms that indicate the presence of nutritive or nonnutritive sweeteners. This table includes the nonnutritive and nutritive sweetener names as found on food labels and packaging.

Kilocalories Saved with Substitutions of Nonnutritive Sweeteners

Product	kcal	In Place of	kcal saved
Table top sweetener (one packet)	0	2 tsp. sugar	32
Fat-free, light yogurt (6 oz.)	80	Fat-free yogurt (6 oz.)	95
Sugar-free syrup (1/4 cup)	20	Regular Syrup (1/4 cup)	180
Sugar-free preserves (1 tbsp.)	10	Regular preserves (1 tbsp.)	40
Sugar-free pudding (1/2 cup)	60	Regular Pudding (1/2 cup)	70
Diet Soda (12 oz.)	0	Regular soda (12 oz.)	127

Small changes in caloric intake can lead to big impacts on energy intake over time. A habitual energy imbalance of about 50-100 kcal per day could produce either a gradual weight gain or weight loss. Therefore, one option may be to substitute a nonnutritive sweetener for sugar to help achieve a daily energy deficit. The table above shows the energy saved by such replacements in a variety of foods and beverages.

Working with Clients and Consumers

- Read, review, and discuss the literature.
- Translate research for clients and consumers.
- Remind clients that sucralose must displace intake of nutritive sweeteners in order to create an energy deficit.
- Provide practical tips for creating an energy deficit:
  - Replace nutritive with non-nutritive sweeteners in beverages and recipes, keeping serving sizes the same.
  - Reduce food intake throughout the day.
  - Help those with diabetes to account for carbohydrates versus sugar on labels.

http://jackkennard.com/?s=latte+art

For the best client care, dietetic professionals should regularly read and review the literature regarding sweeteners. Examine the data reported in studies and compare against study conclusions. Inconsistencies are a red flag that warrant discussion with colleagues and further reading to understand what, if any, implications the study may have. A thorough understanding of the body of evidence is necessary in order to translate evidence into actionable advice for the public.

Help patients and the broader public to understand:

- For sucralose or any nonnutritive sweetener to help consumers with weight management goals, total calories eaten and calories burned by physical activity must result in an energy deficit for weight loss, and energy balance for weight maintenance.
- No food ingredient should be consumed in excess.
- Overall eating habits and other lifestyle factors matter more than individual food ingredients.

Provide practical tips for helping patients to reduce calories, reduce added sugar intake, or for those with diabetes, control carbohydrate intake:

- Replace nutritive with noon-nutritive sweeteners in beverages and recipes, keeping serving sizes the same. Because there are a variety sucralose products available to consumers, check web sites for recipes developed with specific products to ensure best results.
- Reduce portion sizes throughout the day.
- Label-reading skills are critical for helping those with diabetes account for the

carbohydrate content of foods, even if they are “sugar-free.”

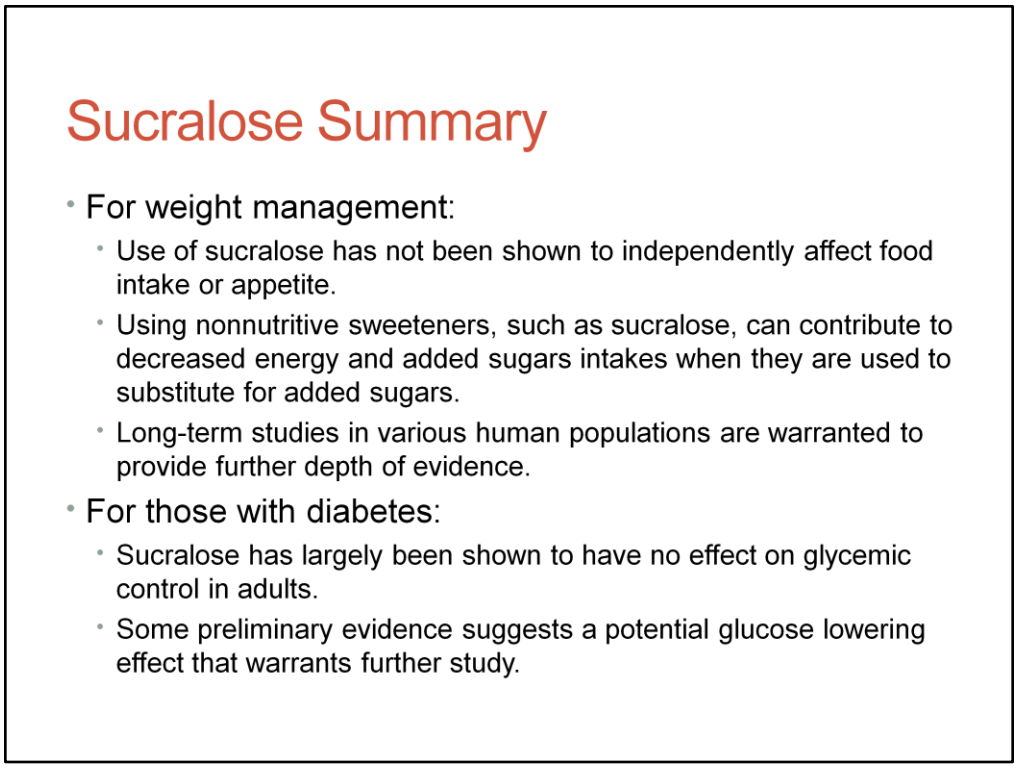
SUMMARY

Sucralose Summary

- The unique chemical structure of sucralose prevents its absorption, therefore it can be used to sweeten without imparting calories to foods.
- Sucralose was thoroughly reviewed by the FDA before approval as a safe food additive, and has also been deemed safe by several other regulatory and scientific organizations.

In summary:

- The unique chemical structure of sucralose prevents its absorption, therefore it can be used to sweeten without imparting calories to foods.
- Sucralose was thoroughly reviewed by the FDA before approval as a safe food additive, and has also been deemed safe by several other regulatory and scientific organizations.



- For weight management:
  - Use of sucralose has not been shown to independently affect food intake or appetite.
  - Using nonnutritive sweeteners, such as sucralose, can contribute to decreased energy and added sugars intakes when they are used to substitute for added sugars.
  - Long-term studies in various human populations are warranted to provide further depth of evidence.
- For those with diabetes:
  - Sucralose has largely been shown to have no effect on glycemic control in adults.
  - Some preliminary evidence suggests a potential glucose lowering effect that warrants further study.

Nonnutritive Sweeteners Summary

- Dietetics professionals can use this information, along with continued review of evolving science, to help clients and consumers make educated decisions about the use and value of sweeteners as a part of their daily diets.
  - For all nonnutritive sweeteners, learning to make substitutions is the key.

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