COMPLIMENTARY WEBINAR

Stevia: The Science Behind the Sweet

PRESENTED BY

Keith Ayoob,
EdD, RDN, FAND

EARN
1 CEU
FREE

November 8, 2023
2-3pm ET

INTERNATIONAL STEVIA COUNCIL

Diane Welland #24016 is approved by the CDR to offer 1.0 CPEU for this webinar.

Accreditation Statement

Stevia: The Science Behind the Sweet awards 1.0 CPEU in accordance with the Commission on Dietetic Registration's CPEU Prior Approval Program.

Disclosures

Keith Ayoob, EdD, RDN, FAND, faculty for this event, has the following relevant financial relationship(s) to disclose: he is a scientific advisory board member for the McCormick Science Institute and a consultant for Calorie Control Council, The Glutamate Association, and Potatoes USA. He has received honoraria from the International Stevia Council, and he is a former consultant to the National Cattleman's Beef Association and Bayer Crop Science.

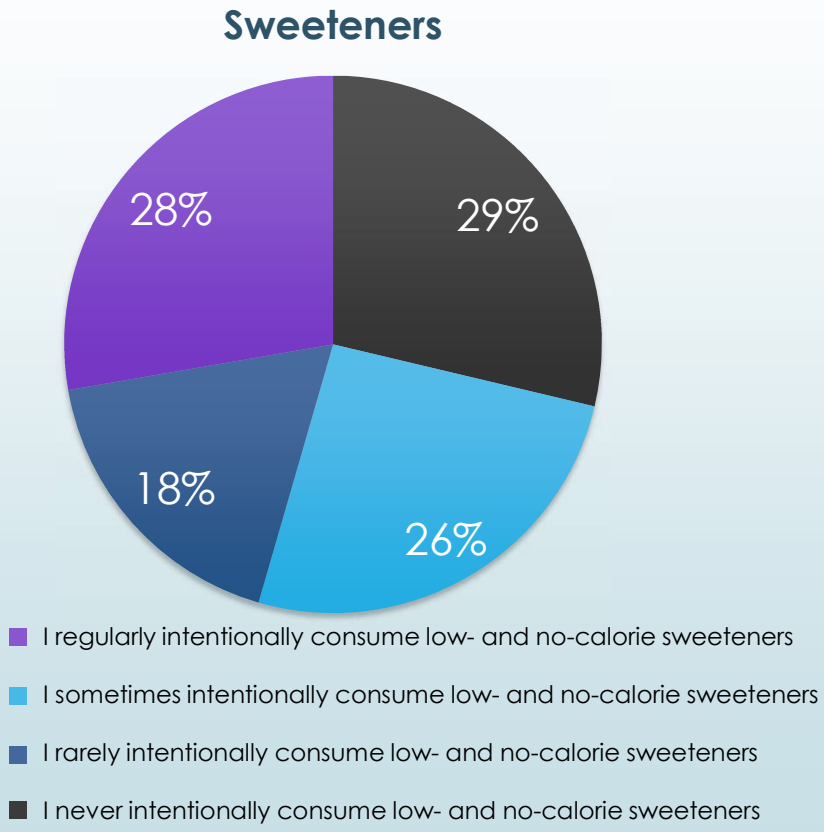
Learning Objectives

1. Interpret the key motivators propelling heightened interest in sugar reduction.
2. Understand the foundations of stevia sweeteners from their origins to their evolution as a leading solution to reduce sugar consumption.
3. Educate clients on the extensive regulatory reviews and scientific studies affirming stevia's health and safety credentials.
4. Detail the positive health implications associated with stevia and highlight innovative ways to help clients' meet their sugar-reduction goals.

THE STATE OF SWEET

How Do ***Consumers*** View Sweeteners?

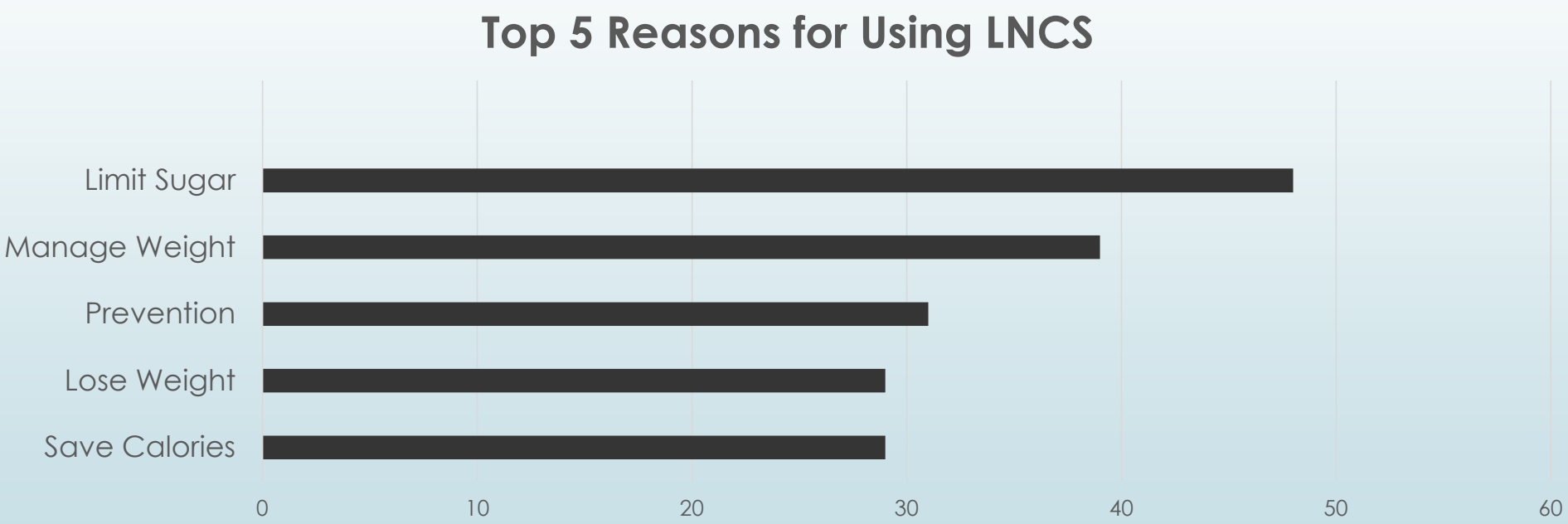
Consumer Consumption of LNCS



- 3 in 10 intentionally use LNCS
  - Of these, 1 in 3 do so ≥1x/day
- 1 in 4 use LNCS "sometimes"
- Slightly <half say they rarely or never do

Chart does not add up to 100% due to rounding.
Public perceptions of dietary sweeteners. (2023). Foodinsight.org. https://foodinsight.org/wp-content/uploads/2023/05/IFIC-Sweeteners-Survey-May-2023.pdf

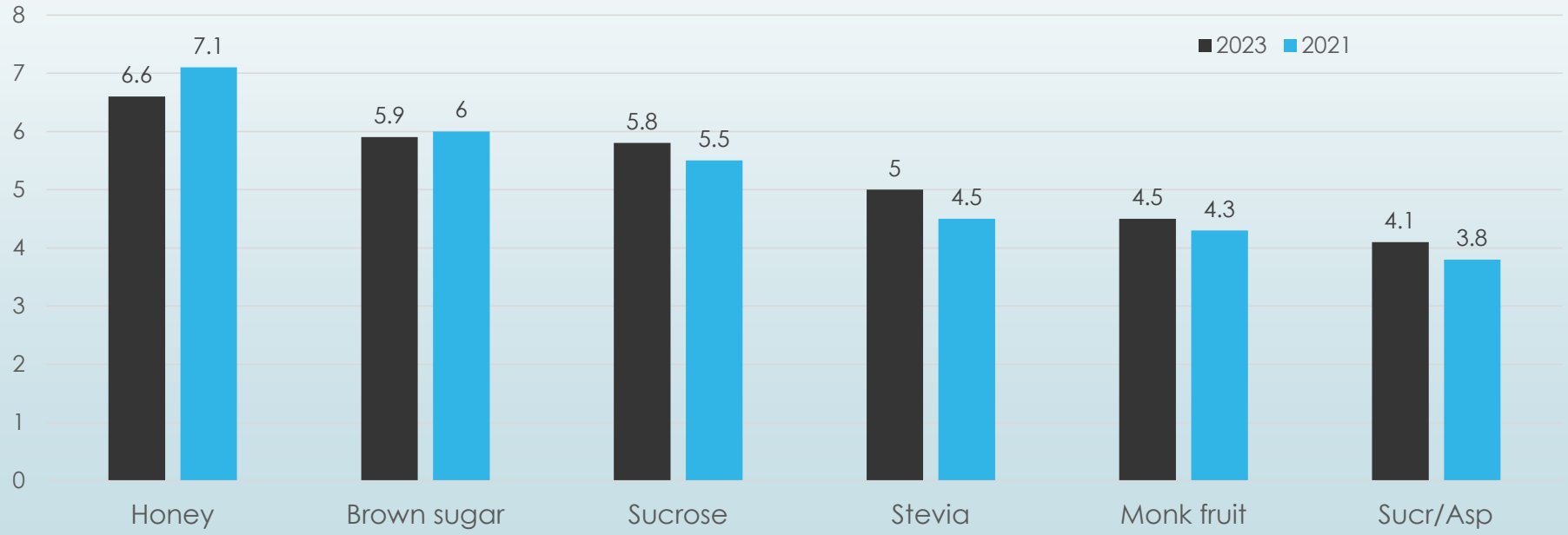
Among Those Who Use LNCS



Public perceptions of dietary sweeteners. (2023). Foodinsight.org. https://foodinsight.org/wp-content/uploads/2023/05/IFIC-Sweeteners-Survey-May-2023.pdf

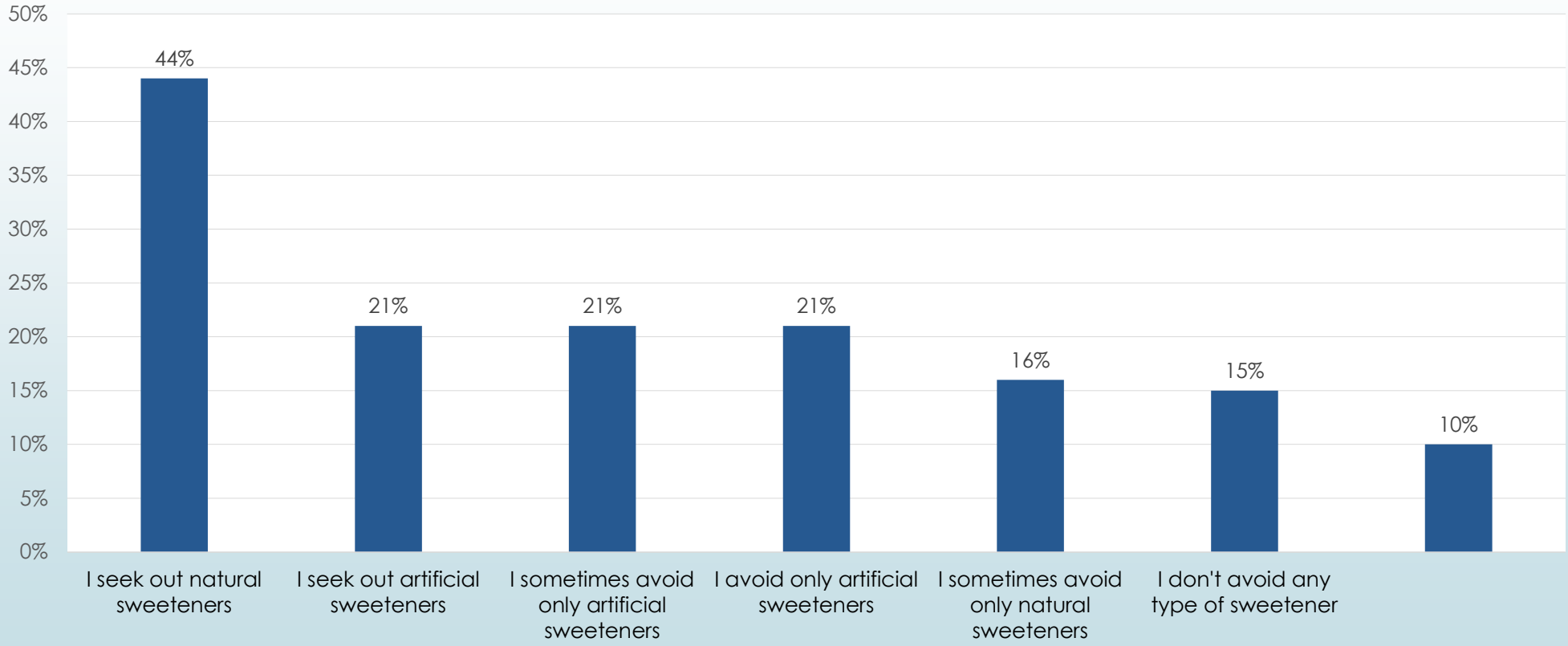
Consumers Still Prefer Caloric Sweeteners…
…but Not by Much

"On a scale of 1 to 10, with 1 = not at all likely and 10 = extremely likely, please indicate how likely you are to consume foods and beverages that include the following ingredient…"



Public perceptions of dietary sweeteners. (2023). Foodinsight.org. https://foodinsight.org/wp-content/uploads/2023/05/IFIC-Sweeteners-Survey-May-2023.pdf

Among Those Who Typically Consume LNCS



Public perceptions of dietary sweeteners. (2023). Foodinsight.org. https://foodinsight.org/wp-content/uploads/2023/05/IFIC-Sweeteners-Survey-May-2023.pdf

THE STEVIA STORY

Nature's *First* Zero-Calorie Sweetener

Stevia: A Plant-Based Sweetener

- Native to South America
- Used by indigenous Paraguayans for 600+ years
- 1901: "Discovered" by Moises Bertoni
- 1931: Steviol glycosides in the leaf are identified
- 1970s: Japan begins using stevia commercially

Ashwell M (2015) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4890837/

Steviol Glycosides

- = The sweet compounds in the stevia leaf
- Rebaudiana A, D, M, etc.: various steviol glycosides in the leaf
- Usually abbreviated as “Reb A,” “Reb D,” etc.
- Over 60 steviol glycosides now identified in the leaf

Samuel P et al. (2018) https://pubmed.ncbi.nlm.nih.gov/29982648/

How Sweet is Stevia? It Depends….

Steviol Glycosides	Sweetening Potency Relative to Sucrose*
Rebaudioside A (Rebiana)	200 - 350
Rebaudioside B	150
Rebaudioside C	30
Rebaudioside D	221
Rebaudioside E	174
Rebaudioside F	200
Rebaudioside M	250
Rubusoside	114
Stevioside	111 - 210
Steviolbioside	90
Dulcoside A	30

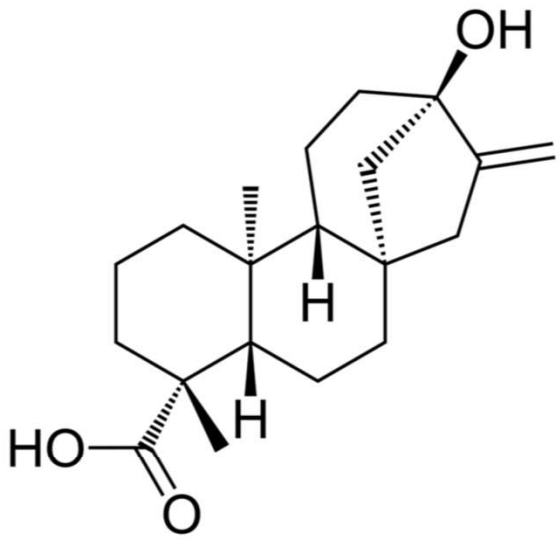
- 60+ steviol glycosides have now been isolated
  - Many are present in minute quantities
  - Some have additional flavor notes
- Ingredient aim: just the sweet

Samuel, P. et. al. (2018). Stevia leaf to Stevia sweetener: Exploring its science, benefits, and future potential. The Journal of Nutrition, 148(7), 1186S-1205S.

Steviol Glycosides: Complexity

- Over 60 sweet compounds found in the leaf
- Intensity varies: 50-350x the sweetness of sugar
- Each steviol glycoside has its own taste and sweetness intensity
- Steviol glycosides can vary in their best uses
  - Some are best in beverages but not in foods
  - Some work better than others in frozen foods
  - Some impart flavor notes that have specific applications
- The purest sweet taste? Reb M & Reb D
  - <1% of the steviol glycosides in the leaf

Samuel P et al. (2018) https://pubmed.ncbi.nlm.nih.gov/29982648/



Steviol

$C_{20}H_{30}O_3$

Commercial Production: Four Methods to Get the Sweet

- **Extraction**: crushed leaves and hot water; filter; purify with food-grade alcohol (later removed)
- **Bioconversion**: uses enzymes to convert extracted glycosides to desired ones (usually Reb D and Reb M)
- **Glucosylation**: steviol glycosides from leaf; glucose molecules are added via enzymes to produce 1 or more desired glycosides
- **Fermentation**: cultivated organisms convert sugars into steviol glycosides; fermentation is similar to the process in the leaf itself

https://internationalsteviacouncil.org/about-stevia/how-stevia-is-made/

Stevia Naturalness: Regardless of Production Method

- **NATURE-IDENTICAL**
- **Same structure** as steviol glycosides in the leaf
- **Same taste, purity, and uses** as if the steviol glycoside had been taken directly from the leaf
- Example:
  - Vitamin C/ascorbic acid: same structure whether obtained from foods or supplements

Overview of the safety and benefits of modern Stevia-based sweeteners effective, nature-based sugar management. International Stevia Council. https://internationalsteviacouncil.org/wp-content/uploads/2023/05/ISC-White-Paper_2023.pdf

Safety & Regulatory Approvals

Review of Safety Studies

- GRAS status since 2008
- Safety:
  - Studies since the 1980s have consistently demonstrated safety
- Safety confirmed by global scientific and regulatory authorities: FDA, EFSA, JECFA, Health Canada, Food Standards Aus/NZ, Japan Ministry of Health, others
- Based on high-purity (>95%) steviol glycosides

Samuel, P. et. al. (2018). Stevia leaf to Stevia sweetener: Exploring its science, benefits, and future potential. The Journal of Nutrition, 148(7), 1186S-1205S.

ADI and NOAEL

- ***Acceptable daily intake (ADI)***: Average daily intake over a lifetime that is expected to be safe for human consumption based on significant research. Derived from:
- ***No Observed Adverse Effect Level (NOAEL)***: Highest intake level found to have no adverse effects in lifetime studies in animal models, **divided by 100**.
  - ADI = 100 times lower than the max level found to have no adverse effects in toxicology studies
  - Adds a margin of safety that helps ensure that human intakes will be safe.

Food additives. (n.d.). Who.int. Retrieved September 20, 2023, from https://www.who.int/news-room/fact-sheets/detail/food-additives
Renwick, A. G. (1991). Safety factors and establishment of acceptable daily intakes. Food Additives and Contaminants, 8(2), 135–149. https://doi.org/10.1080/02652039109373964

Dietary Exposure Assessments

- Samuel et al concluded: "…based on estimated dietary exposure assessments from different countries and regions of the world, at typical patterns of consumption of foods and beverages containing steviol glycosides, it is unlikely that either adults or children, including diabetic adults and children, will exceed the ADI for steviol glycosides."
- Robust database of in vivo and in vitro studies: no evidence of genotoxicity

Samuel, P. et. al. (2018). Stevia leaf to Stevia sweetener: Exploring its science, benefits, and future potential. The Journal of Nutrition, 148(7), 1186S-1205S.

Dietary Exposure Assessments: Reproductive/Developmental Toxicity

Pertains to:

- Pregnant and lactating women
- Children over 2 years of age

→ No adverse effects, even after exposures to high doses of high-purity steviol glycoside before and during critical periods of fertility and pregnancy, during lactation, and *throughout growth and development* of the offspring to adulthood for 2 generations[1]

Urban et al (2008): "*Mutation and genotoxicity data…overwhelmingly affirm the genetic safety of stevia extracts*."[2]

1. Samuel, P. et. al. (2018). Stevia leaf to Stevia sweetener: Exploring its science, benefits, and future potential. The Journal of Nutrition, 148(7), 1186S-1205S.
2. Urban, J. D., et. al. (2013). Steviol glycoside safety: Is the genotoxicity database sufficient? Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association, 51, 386–390.

Dietary Exposure Assessment

- All steviol glycosides (SGs) → metabolized to steviol
- ADI: 4 mg/kg/day of "steviol equivalents" (SE)
  - Example: 4 mg/kg/d of SE = 12 mg/kg/d of Reb A
- Global intakes[1]:
  - General population, adults and children: 0.4-0.7 mg/kg/d of SE
  - High intakes (>90%, includes diabetics): 1.1-1.7 mg/kg/d of SE
- EFSA 2014 reassessment of MAX intakes (>95%):
  - All intake levels remained <ADI
  - Only exception: Netherlands toddlers (4.3 mg/kg/d), considered by EFSA as dietetically insignificant[2]

Renwick AG. The use of a sweetener substitution method to predict dietary exposures for the intense sweetener rebaudioside A. Food Chem Toxicol 2008;46(Suppl 7):S61–9.
European Food Safety Authority. Scientific opinion on the revised exposure assessment of steviol glycosides (E960) for the proposed uses as a food additive. EFSA J 2014;1295:3639. https://www.efsa.europa.eu/en/efsajournal/pub/3639

Global Approval by Health and Safety Authorities

- Approved for use in >150 countries, by all categories of the population, ***including children and pregnant women***
- Global approval: all major regulatory authorities:
  - FDA
  - Joint Expert Committee on Food Additives (JECFA)
  - European Food Safety Authority (EFSA)
  - Health Canada
  - Food Standards Australia and New Zealand (FSANZ)

https://internationalsteviacouncil.org/resource-center/links/

Stevia Safety Established

- Stevia, authorized at the international level, has gone through safety assessments and received positive safety opinions from food safety authorities at the regional, national, and international levels
- Safe for human consumption by all categories of the population, ***including children and pregnant women***

Samuel P et al. (2018) https://pubmed.ncbi.nlm.nih.gov/29982648/
Stevia: A Great Ally to Control Calorie Intake. (2021, July 19). The Authoritative Voice for the Stevia Industry. https://internationalsteviacouncil.org/lifestyle-and-diet/stevia-a-great-ally-to-control-calorie-intake/

Transparent Labeling: Many Ways to Say "Stevia" on Labels

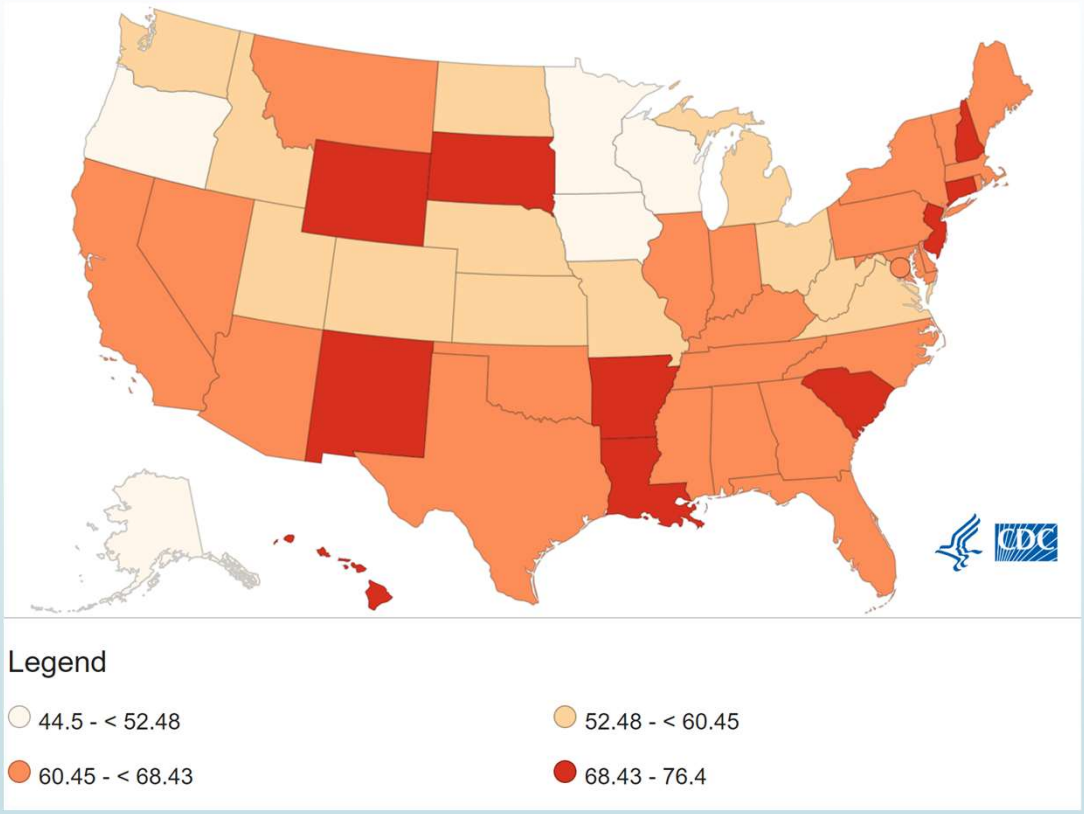
- Stevia leaf extract
- Stevia sweetener
- Stevia-based sweetener
- Stevia extract
- Steviol glycosides E960 (European labels)
- Reb A (Rebaudioside A)
- Reb M
- Stevioside
- Rebiana
- High-purity stevia

NOTE: Labeling requirements vary by country

(Framework for) Steviol Glycosides. (n.d.). Fao.org. Retrieved September 20, 2023, from https://www.fao.org/3/cb8031en/cb8031en.pdf

Effects and Health *Benefits*

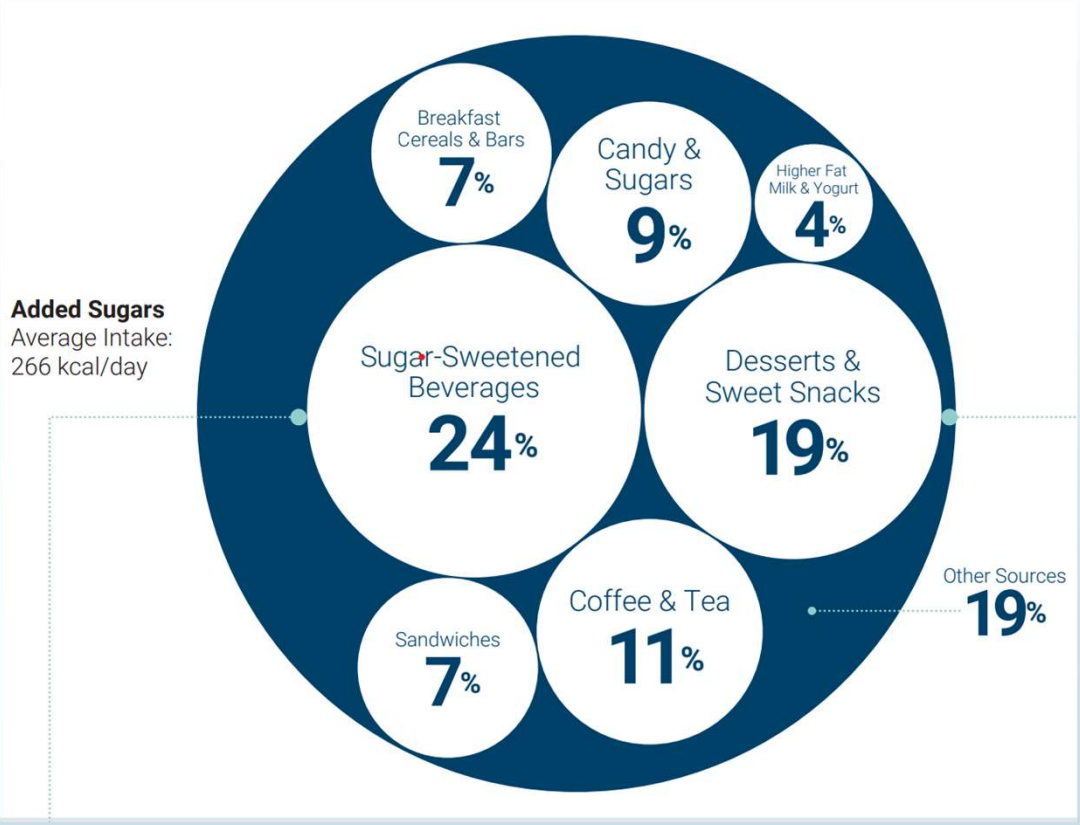
Reducing Intake of Added Sugars



- 63% of adults drink an SSB at least once daily
- Obesity 2000-2020
  - 2000: 31%
  - 2020: 41%

CDC. (2022, April 11). Get the facts: Sugar-sweetened beverages and consumption. Centers for Disease Control and Prevention. https://www.cdc.gov/nutrition/data-statistics/sugar-sweetened-beverages-intake.html

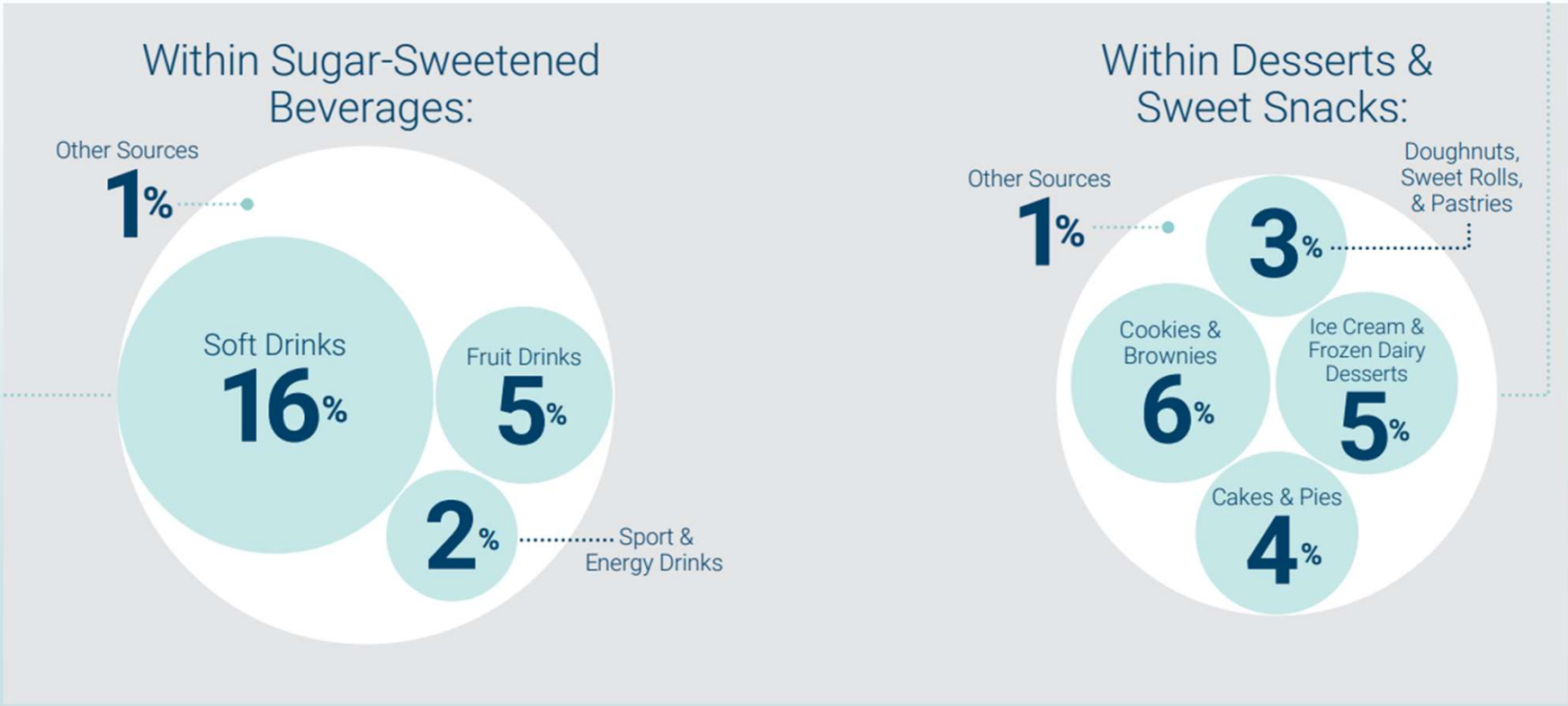
Added Sugars: Sources and Average Intakes U.S. Population Ages 1 and Older



- 52% of added sugars are from "empty-calorie" foods
  - Sugar-sweetened beverages
  - Desserts and sweet snacks
  - Candy and sugars
- Stevia: ideally suited to naturally replace many of these added sugars

U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at DietaryGuidelines.gov.

Sugar Intake from "Empty-Calorie" Foods



U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at DietaryGuidelines.gov.

RCTs: Stevia, Blood Glucose, and Insulin Levels

- Anton (2010): Human RCT, CO design
- Lean and obese adults, normal BG
- Steviol glycosides or aspartame (290 kcals) replaced sucrose (493 kcals) in pre-loads to test meals

Findings:

- "*Stevia preloads significantly reduced postprandial glucose levels compared to sucrose preloads (p<.01), and postprandial insulin levels compared to* ***both aspartame and sucrose preloads*** *(p<.05).*"
- Did NOT compensate by eating more at meals
- Similar satiety as when consuming sucrose pre-load

Anton SD, et. al. Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels. Appetite 2010;55:37–43.

RCTs: Stevia, Blood Glucose, and Insulin Levels: *Without* Dietary Manipulation?

- Gregerson, RCT, T2D adults:
  - 1,000 mg steviol glycosides OR 1,000 maize
  - All subjects stopped taking hypoglycemic meds prior to testing
  - Isocaloric test meal: no differences in calories, sugar, CHO
- Results:
  - Significant ↓ BG, trend towards ↑blood insulin (p=.08)
  - 40% ↑ in AUC insulin/AUC glucose ratio

Gregersen S, et. al. Antihyperglycemic effects of stevioside in type 2 diabetic subjects. Metabolism. 2004;53:73–6.

LNCS Review by Rogers, et al: Do LNCS Impact Sugar Intake?

- 56 studies, human and animal
- Duration: from 10 days to 1 year
- Subjects were normal weight, overweight, and obese
- 83% substituted LNCS for sugar

Rogers PJ et al (2016). https://pubmed.ncbi.nlm.nih.gov/26365102/

LNCS Review by Rogers, et al: Do LNCS Impact Sugar Intake?

Findings:

- Overall energy compensation: only 50%
- Adults: 43%
- Children: 70%
- *No differences when LNCS compared with water*

Could LNCS *INCREASE* Energy Intake?

- The concept: LNCS "uncouple" sweetness from energy content
- Fantino (2018) review: LNCS beverage intake with meals:
  - No increase in total energy intake
  - No increase in macronutrient intake
  - No increase in sweet foods selected
- Evidence runs ***CONTRARY*** to concerns that LNCS enhance calorie intake or preference for sweetness.

Fantino M, et. al. Beverages containing low energy sweeteners do no differ from water in their effects on appetite, energy intake and food choices in healthy, non-obese French adults. Appetite 2018;125:557–65.

Stevia and Blood Pressure

- 6 RCTs,
  - 8 clinical arms
  - Duration: 4 weeks – 2 years
  - Dose range: 750mg-1500 mg/day
- Healthy adults: ***No significant difference*** between stevia and placebo on BP
- T2D adults w/ HTN, on meds: no impact on BP
- T2D adults, mild HTN, not on meds: modest lowering effect

Chan P, et al. A double-blind placebo-controlled study of the effectiveness and tolerability of oral stevioside in human hypertension. Br J Clin Pharmacol 2000;50:215–20.
Hsieh MH, et al. Efficacy and tolerability of oral stevioside in patients with mild essential hypertension: a two-year, randomized, placebo-controlled study. Clin Ther 2003;25: 2797–808.

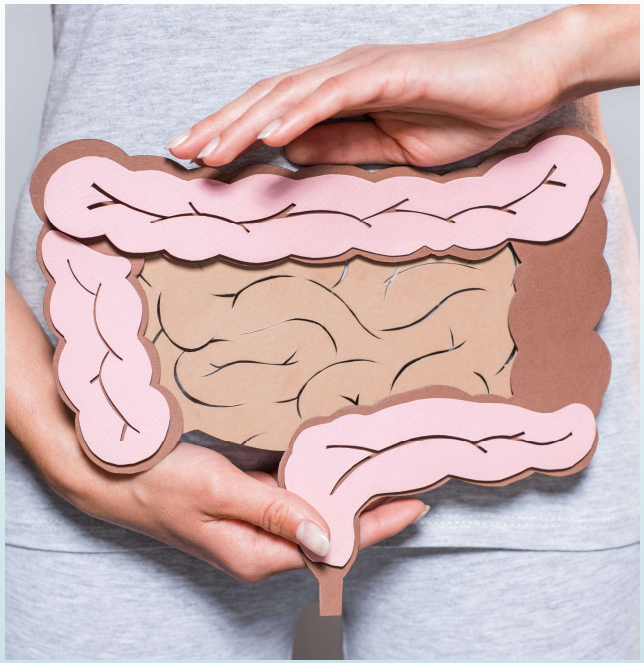
Stevia and Blood Pressure

- Meta-analysis of 7 RCTs of stevia's effect on BP vs. placebo
  - Included acute, single meal doses, and longer-term settings
  - NSD on systolic BP
  - Significant (p=.03) but small decrease in diastolic BP (MD: -2.98 mm Hg)
- Take-aways in stevia and BP:
  - Results had no or modest impact on BP
  - Studies used supplemental doses, 3-4x ADI, so not applicable to culinary use
  - Further reinforces safety of steviol glycosides

Onakpoya IJ, Heneghan CJ. Effect of the natural sweetener, steviol glycoside, on cardiovascular risk factors: a systematic review and meta-analysis of randomised clinical trials. Eur J Prev Cardiol 2015;22:1575–87.

Steviol Glycosides, Metabolism, and Gut Microbiome

- Most LNCS are NOT metabolized by gut bacteria
- Stevia IS metabolized in the gut
  - Steviol glycosides → undergoes "deglycosylation" → steviol backbone absorbed
  - Quickly modified in liver → excreted in urine as steviol glucuronide
- Bacteroides are responsible for the deglycosylation
- No significant impact on gut – bacteroides is already extremely abundant in gut



THE CHEW: Stevia's Role in Dental Health

- Gamboa and Chavez (2012) demonstrated:
  - Very mild oral anti-microbial properties of stevia vs. vancomycin and azithromycin
- Zanela (2002) compared a rinse of stevia and fluoride:
  - Had no advantages vs. rinse of chlorhexidine with fluoride
- Most evidence indicates stevia is non-cariogenic, but is a better option than sucrose, which is very cariogenic

Gamboa F, Chaves M. Antimicrobial potential of extracts from Stevia rebaudiana leaves against bacteria of importance in dental caries. Acta Odontol Latinoam 2012;25:171–5.
Zanela N, Bijella M, Rosa O. The influence of mouthrinses with antimicrobial solutions on the inhibition of dental plaque and on the levels of Mutans streptococci in children. Pesqui Odontológica Bras 2002;16:101–6.

STEVIA: Easy Growing

- Easy to grow on a large scale
- Grown throughout the world
- NOT a new food!
- Leaves have historically been eaten fresh, dried, and used for extracts for >400 years

Putting It Into Practice

Conclusions

- Stevia is a safe, low-calorie sweetener
- Using stevia to replace sugar is a tool for reducing intake of added sugars
- If added sugars are consumed to excess, replacing them with stevia can be a useful strategy for reducing excess calories and managing weight
- There's no evidence that LNCS or stevia-containing foods result in any increase in appetite for sugar or sweet products

Questions?

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