Helping Your Clients Make Sense of Low- and No-Calorie Sweeteners

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Sponsored by the American Beverage Association
With You Today

Moderator:
Hope E. Wershow, MMSc, RD, CDE, BC-ADM
- President of the American Association of Diabetes Educators
- Owner, Hope Wershow Associates, LLC

Speaker:
Serna Magnuson, PhD
- Atkins Fellow
- BMagnuson Consulting

Speaker:
James D. Hill, PhD
- Anschutz Professor and Director of the Anschutz Health and Wellness Center, University of Colorado
Agenda

- Introduction of Speakers
- History, Safety and Regulation
- Weight Control and Low- and No-calorie sweeteners
- Questions/Discussion
- CE Credit Information
Learning Objectives

1. Understand the safety and regulation of low- and no-calorie sweeteners, as well as their long history of use.

2. Understand the science that supports the use of low- and no-calorie sweeteners in diabetes prevention and treatment.

3. Be able to provide science-based information to answer patients' questions about the efficacy and safety of using low- and no-calorie sweeteners for diabetes management.
Disclosures

- Hope Warshaw – Consultant to Calorie Control Council, McNeil Nutritionals, LLC (manufacturers of Splenda® Sweetener Products), Weber Shandwick
- Berna Magnuson – No disclosures
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SETTING THE RECORD STRAIGHT:
SAFETY AND REGULATION OF LOW-AND NO-CALORIE SWEETENERS

Berna Magnuson, PhD, ATS Fellow
BMagnuson Consulting
## Regulatory Categories of No- and Low-calorie Sweeteners

<table>
<thead>
<tr>
<th>Food additive</th>
<th>Generally Recognize as Safe</th>
<th>Dietary Supplm</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Safety data assessed by FDA before approval</td>
<td>• Safety data assessed by expert panel</td>
<td>• Not approved for use in foods and beverages</td>
</tr>
<tr>
<td>• FDA responsible for safety</td>
<td>• Manufacturer responsible for safety</td>
<td>• Manufacturer responsible for safety</td>
</tr>
</tbody>
</table>

http://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm397716.htm
<table>
<thead>
<tr>
<th>Sweetener</th>
<th>Regulatory status</th>
<th>Sweetness to sugar</th>
<th>Other names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acesulfame-K</td>
<td>Food additive</td>
<td>200X</td>
<td>Sunett, Sweet One, NutraSweet, Equal</td>
</tr>
<tr>
<td>Aspartame</td>
<td>Food additive</td>
<td>200X</td>
<td></td>
</tr>
<tr>
<td>Luo Han Fruit</td>
<td>Generally Recognized as Safe</td>
<td>300X</td>
<td>Monk fruit, Nectresse</td>
</tr>
<tr>
<td>Saccharin</td>
<td>FDA-approved interim regulation</td>
<td>300X</td>
<td>Sweet and Low, Sugar Twin</td>
</tr>
<tr>
<td>Steviol glycosides</td>
<td>Generally Recognized as Safe</td>
<td>30 – 300X</td>
<td>Truvia, PureVia, and others</td>
</tr>
</tbody>
</table>
Safety = absence of risk

Risk = Hazard (Potential to cause harm) \times Exposure

Risk is the combination of hazard or potential to cause harm and exposure.
Hazard evaluation of sweeteners

- What is the composition of the sweetener?
- What happens to the compound when we consume it?
- Many safety studies in animals
- And in humans!
Hazard evaluation of sweeteners

Required for approval:
- Short- and long-term toxicity studies
- Must test in at least 2 animal species, usually more
- Carcinogenicity
- Genetic toxicity
- Reproductive toxicity
  - before and during pregnancy
- Teratogenicity – effect on development
- Also human clinical studies
ADI = amount "that can be ingested daily over a lifetime without appreciable health risk"

- Based on highest level shown to have no observed effect in long-term animal studies.
- Apply 100 fold "safety factor"

No observed effect level/100 = ADI in mg/kg body weight/day

- ADI applies to entire population, children, pregnant women, and adults.
- Adjust amount according to body weight.
Safe for pregnant women? Children?
Answer = Yes, for approved sweeteners!
This question MUST be answered in safety testing before sweetener is approved for use in foods and beverages!
What is Aspartame?

FDA ADI: 0-50 mg/kg/day
For 150 lb person ~ 97 packets of sweetener/day

Structure: 2 amino acids & methyl group
• Aspartic acid (aspartate)
• Phenylalanine
These are commonly found in foods!

http://www.caloriecontrol.org/sweeteners-and-life/sugar-substitutes/aspartame
Aspartame digestion

Aspartame does not enter blood or body as a whole. Just like foods and proteins, aspartame is completely digested in intestine by digestion enzymes. Components of digestion same as from other foods.

European Food Safety Authority Review of Aspartame, Dec 2013
## There are many dietary sources of aspartame digestion products

<table>
<thead>
<tr>
<th>Food</th>
<th>Phenylalanine (mg)</th>
<th>Aspartic acid (mg)</th>
<th>Methanol (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartame-sweetened</td>
<td>90</td>
<td>72</td>
<td>18</td>
</tr>
<tr>
<td>Soft drink (340 ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-fat milk (340 ml)</td>
<td>606</td>
<td>953</td>
<td>-</td>
</tr>
<tr>
<td>Tomato Juice (340 ml)</td>
<td>58</td>
<td>346</td>
<td>107</td>
</tr>
<tr>
<td>Orange juice</td>
<td>24</td>
<td>180</td>
<td>23</td>
</tr>
</tbody>
</table>
Saccharin

- Currently - limited use in North America
- Most (95%) rapidly absorbed in the small intestine;
- Absorbed saccharin is rapidly excreted in urine.
- Small amount (5%) to colon and excreted in feces.
- April 2014: Health Canada reviews safety and extends allowed uses.
- ADI: 0-5 mg/kg/day
- For 150 lb person ~ 8.6 packets of sweetener/day

**Steviol glycosides**

- Purified from the leaves of a South America shrub.
- Are many different forms.
- All have common steviol backbone, different number and position of attachments of glucose.
- Rebaudioside A (Reb A) - sweetest, most abundant steviol glycoside

\[ \text{ADI} = 0 - 4 \text{ mg steviol equivalents/kg body weight/day} \]

Applies only to extracts purified to contain \( \geq 95\% \) steviol glycosides.

- Need to convert from steviol equivalents to glycosides
- i.e. ADI for Reb A = 0 - 12 mg rebaudioside A/kg/day
- 150 lb person = 30 packets of tabletop sweetener/day

Steviol glycosides

Steviol glycosides are not absorbed.

Glucose units removed by bacteria in large intestine.

Steviol absorbed in large intestine, modified by liver, and excreted.

http://globalsteviainstitute.com/health-professionals/nutrition-health
Sucralose

- Structure similar to sugar, but 600X sweetening potency.
- Only a small amount of sucralose is absorbed and excreted in urine.
- Most (85%) of ingested sucralose is not absorbed into the body; is eliminated in the feces unchanged.
- **Gut microflora unable to hydrolyse sucralose**
- ADI: 0-15 mg/kg/day
- For 150 lb person ~ 68.2 packets of sweetener/day

Risk is the combination of hazard or potential to cause harm and exposure.
Intense sweetness = low levels of use

Sweetness intensity of non-caloric sweetener

\[ \text{Intense sweetness} = \frac{\text{200-600}}{\text{Sugar}} \]
<table>
<thead>
<tr>
<th>Sweetener</th>
<th>Sweetness Intensity *</th>
<th>Amount to replace 25 g of sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartame</td>
<td>~ 200 x</td>
<td>125 mg</td>
</tr>
<tr>
<td>Saccharin</td>
<td>~ 300 x</td>
<td>80 mg</td>
</tr>
<tr>
<td>Sucralose</td>
<td>~ 600 x</td>
<td>40 mg</td>
</tr>
</tbody>
</table>
To determine exposure

Using food intake surveys, calculate consumption of foods that will contain sweetener:
- Average and high users
- Different ages and sex
- Special populations, such as diabetics, children

**Intakes must be lower than ADI for all users, including highest consumers.**

Example: Aspartame intakes remain well below ADI in recent review by EFSA.

How much do we eat? Estimated Daily Intake (EDI)

- **Aspartame**: EDI = 6% of ADI at the 90th percentile in general adult population;
- **Saccharin**: EDI = 12% of ADI;
- **Sucralose**: EDI = 32% of ADI for adults and children over age two.

International Food Information Council (IFIC) Foundation

http://www.foodinguider.org/Content/5438/Final%20Revised%20CPE%20Module_6-1-12.pdf
But – what about all the studies reporting adverse effects?

- How can we know what to believe?
- How can we explain the different opinions?
- Must look carefully at study, not just abstract or press release!
“Artificial sweeteners induce glucose intolerance by altering the gut microbiota”

- Compounds tested in mouse study:
  aspartame, saccharin, sucralose.
- All remaining experiments with saccharin and extrapolated results to all “artificial sweeteners”.
- Conclude “non-caloric sweeteners directly contribute to glucose intolerance, metabolic disease and obesity”.

Suez et al., Nature, 2014
Questions to consider

- How can aspartame affect gut microbiota when does not enter colon?
- How can sucralose affect gut microbiota when not metabolised by microflora?
- What doses were used? Dose response?
- Any effect on other dietary factors that affect gut microbiota or glycemic response?
11 weeks exposure via drinking water, followed by antibiotic treatment.

- Doses based on water consumption reported:
  - Saccharin = 3656 mg/kg/d as compared to ADI = 0-5 mg/kg/d
  - Aspartame = 1600 mg/kg/d as compared to ADI = 0-50 mg/kg/d
  - Sucrose = 2000 mg/kg/d as compared to ADI = 0-15 mg/kg/d

Combine 3 treatment groups (n=60) to compare to 3 control groups.

Not valid in conflict with controlled clinical studies in humans.

Required for approval which demonstrated no effect on glycemic indices with chronic use.

Suez et al., Nature, 2013
Liquid & food intake shown only for 4 of 20 mice/group and 72 hr of 11 weeks.

Huge differences in water/sugar liquid intake.
Over 50% reduction in mouse chow in some groups.

Dramatic impact on other nutrients, fiber and other fermentable components that affect microbiome. Not considered in paper.
Final Comments

- The safety of use of low calorie sweeteners has been extensively evaluated worldwide.
- But health effect of low-calorie sweeteners continues to be subject of many studies.
- Study design, interpretation of results and consideration of all factors are critical for assessment of validity of conclusions.
- Regulatory agencies worldwide continue to review and confirm safety of use.
For more information

Food and Drug Administration websites:
- http://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm397716.htm
- http://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm397725.htm#SummaryTable
- http://www.fda.gov/aboutfda/transparency/basics/ucm214864.htm

Calorie Control Council:
http://www.caloriecontrol.org/

European Food Safety Authority:
http://www.efsa.europa.eu/

Health Canada
LOW- AND NO-CALORIE SWEETENERS IN WEIGHT MANAGEMENT:

WHAT DOES THE EVIDENCE SHOW?

James O. Hill, PhD
Anschutz Professor, Executive Director
Anschutz Health and Wellness Center
University of Colorado
All FDA-approved low calorie sweeteners meet the same standards of safety and are safe for consumption, including pregnant women and children.

All FDA-approved sweeteners are safe.

http://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm397725.htm
Epidemiologic studies are confusing

- Some studies show association of low- and no-calorie sweeteners (LCS) with:
  - Increased body weight\(^1\,\(^2\)
  - Decreased body weight\(^3\) or
  - Both increased/decreased body weight\(^4\)

Health Authorities Recommend LCS as Way to Cut Calories, Lose Weight

“There are some data to suggest that NNS may be used in a structured diet to replace sources of added sugars and that this substitution may result in modest energy intake reductions and weight loss.”
- American Heart Association American Diabetes Association 2012 Position Statement

“NNS, when substituted for nutritive sweeteners, may help consumers limit carbohydrate and energy intake as a strategy to manage blood glucose or weight.”
- Academy of Nutrition and Dietetics 2012 Position Statement

American Heart Association American Diabetes Association

An analysis of dietary patterns by Piernas, et al. showed that both study groups reduced total energy, carbohydrates, total sugar, added sugar and other calorie containing nutrients, however, the diet beverage group had a greater reduction of desserts compared to the water drinkers at 6 months.

Take-Home Messages

• The diet beverage group showed a greater likelihood of achieving a 5% weight loss compared with control
  • OR: 2.29; 95% CI: 1.05, 5.01; P=0.04

• The water group did not significantly differ from control in odds of achieving 5% weight loss

The Effects of Water and Non-Nutritive Sweetened Beverages on Weight Loss During a 12-week Weight Loss Treatment Program

Jane E. Finn, JoAnn A. Reif, Lambdin Penrod, Mary E. Waterlow, and James F. Reif

Objective: To examine the efficacy of non-nutritive sweetened beverages (NNS) in water for weight loss during a 12-week behavioral weight loss treatment program.

Methods: The participants were assigned to two groups in a prospective, randomized, controlled trial: those drinking 32 oz of water and those consuming an equal volume of water plus NNS (2 oz). The results of the weight loss (7 weeks) and maintenance (5 weeks) phases were analyzed to determine the effectiveness of the NNS as a weight loss aid.

Results: The NNS group experienced significantly greater weight loss than the water group during the weight loss phase. The maintenance phase revealed no significant differences between the two groups.

Conclusions: These findings suggest that consuming NNS in conjunction with a comprehensive behavioral weight loss program may aid in weight loss maintenance.

Key words: Weight loss, behavioral therapy, non-nutritive sweetener.
Note: This is the more conservative analysis because we are assuming that those who dropped from the study were not very successful with weight loss.
NNS~ 13 pounds
Water~ 9 pounds

Difference of ~ 4 pounds
Note: This analysis includes only those that completed the study. Those that dropped are not included. Dropout was similar in both groups.
NNS~ 14 lbs
Water~ 10 lbs
Diet Beverages Help People Lose Weight

Researchers showed that dieters who drank diet beverages as part of an overall weight loss program were able to lose weight over 12 weeks.

DIET BEVERAGE DRINKERS:
- Averaged 1.5 lbs weight loss
-Reported feeling significantly less hungry
- Were more likely to shed 5% of their body weight
- Lost a two-fold greater drop in total cholesterol levels
The RCT analysis demonstrated that NNS reduced body weight compared to placebo and modestly, but “significantly” reduced BMI, fat mass, and waist circumference. These results supports existing evidence that judicious substitution of NNS and foods sweetened with them does not cause weight gain and may actually help people manage their weight. No correlation was found between NNS consumption and body weight or fat mass in the nine observational cohort studies analyzed.
Low- and No-Calorie sweetened beverages help “successful losers”
Longer-Term Intervention Trial: 
Adding Low- and No-Calorie Sweeteners 
to a Multidisciplinary Program

- Randomized controlled trial
- N=163 obese women
- Subjects assigned to
  - Aspartame + multidisciplinary program
  - Multidisciplinary program alone (advised to abstain from using aspartame)
- Study duration: 1 year of treatment 
  + 2 year follow-up period

Aspartame Group Achieved Greatest Weight Loss

Beverage Consumption
Weight Loss Maintainers vs. Always-Normal Weight Subjects

Cross-sectional study
Subjects
172 long-term weight loss maintainers
BMI: 22 kg/m²
Maintained ≥10% weight loss for 11.5 years
131 always-normal weight individuals
BMI: 21.3 kg/m²
No history of overweight
24-hour dietary recalls
Recent enrollees of the NWCR (N=837) who had completed the 2005 version of the Block Food Frequency questionnaire.
Long-term Successful Weight Control
Predictors of one-year weight regain
final multivariate model

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<tr>
<th></th>
<th>B</th>
<th>Beta</th>
<th>T</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased restraint</td>
<td>-.1</td>
<td>.079</td>
<td>1.96</td>
<td>.05</td>
</tr>
<tr>
<td>Increased disinhibition</td>
<td>.5</td>
<td>.295</td>
<td>7.4</td>
<td>.0001</td>
</tr>
<tr>
<td>Decreased water</td>
<td>.0</td>
<td>.134</td>
<td>5.4</td>
<td>.0001</td>
</tr>
</tbody>
</table>

- Decreasing water intake only beverage related to higher risk of weight regain.
- Neither increases nor decreases in consumption of diet beverage or soft drink related to weight regain.
Appetite and Hunger

- Most studies and reviews conclude that non-nutritive sweeteners do not affect appetite or hunger or desire for sweetness in adults.1-4

- … also note that future research is needed.5,6

Pregnancy

- All FDA-approved low- and no-calorie sweeteners are approved for use by pregnant and lactating women.
- The position of the Academy of Nutrition and Dietetics is that their use is acceptable during pregnancy.
- One study from 2010 among 59,334 Danish women found an association between intakes of soft drinks with NNS and pre-term births.
  - Incidence of pre-term birth was low and finding has not been confirmed in other studies.

Conclusions

- **Strong support** for a modest positive effect on weight with low- and no-calorie sweeteners.

- Many research studies in humans with **consistent findings** from prospective studies and randomized controlled trials.

- **No current scientific reason to recommend against use** of low- and no-calorie sweeteners for those trying to lose weight.
Low- and no-calorie sweeteners are tools that:

- Improve glycemic, lipid, HTN control
- Support weight loss/control
- Help prevent and delay disease progression
Questions?
For more information

- American Beverage Association: www.letsclearitup.com
- Calorie Control Council www.caloriecontrol.org
- EFSA www.efsa.europa.eu/
- FDA on stevia: www.fda.gov/aboutfda/transparency/basics/cm214864.htm

- E-mail: b.magnuson@utoronto.ca
- E-mail: james.hill@ucdenver.edu