Health and Wellness of Stevia as a Sweetener

Keith T. Ayoob, EdD, RDN, FADN
Associate Professor Emeritus,
Albert Einstein College of Medicine, New York
October 17, 2017
Conflict of Interest Disclosure

Consultant with the Calorie Control Council
Advisory Board, Global Stevia Institute (GSI)
GSI is supported by PureCircle Ltd,
a global leader in purified stevia leaf extract production
Session objectives

• Explore the extent of the global health epidemics of obesity and type 2 diabetes.
• Discuss specifics of global health recommendations to reduce intake of added sugars and the role played by zero-calorie sweeteners in achieving these recommendations.
• Explore the unique role plant-based stevia may have in helping diabetics manage blood glucose levels.
• Learn and apply information related to the benefits of natural-origin stevia and the opportunities and challenges in developing reduced-calorie-reduced-sugar foods with sweeteners/stevia.
WHO: Global obesity

Male

Female

Prevalence of obesity*, ages 18+, 2014 (age standardized estimate)

Male

Female

Note: For mapping purposes, the map shows identical values for Sudan and South Sudan. These values concern the former Sudan as it existed prior to July 2011.

* Body Mass Index ≥30 kg/m²

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
IDF projection: Global diabetes will worsen

2015: 415 million → → → 2040: 641 million

Estimated number of people with diabetes worldwide and per region in 2015 and 2040 (20-79 years)
Obesity: Gateway to Complications

- Obesity
  - Type 2 Diabetes
    - Hypertension
    - Retinopathy
    - CV Risk
    - Met Syndrome
WHY STEVIA?
Worldwide Call for Healthy Lifestyles, Reductions in Calorie & Sugar Consumption

Dietary guidance by global & national health organizations for ALL AGE GROUPS:

- ↓ Foods & beverages high in total/added sugars
- ↓ Added sugar to <10% of total calories, aim for <5% (WHO, 2015)
Evidence-based systematic reviews & meta-analyses
CONCLUSIONS OF EFSA REVIEW: STEVIOL GLYCOSIDES

• IN-VITRO STUDIES:
  – Stimulate insulin secretion from islet cells
  – Up-regulate key genes controlling insulin secretion,
  – Positively impact insulin signaling & release

• ANIMAL STUDIES:
  – Improved insulin sensitivity & plasma glucose levels in normal, type-2 diabetic or obese rats
  – ↓blood glucose levels, possibly by enhancing insulin secretion and regulating gluconeogenesis.

EFSA Journal 2010;8(4):1537
CONCLUSIONS OF EFSA REVIEW ON STEVIOL GLYCOSIDES

HUMAN STUDIES:

• In normal & type 2 diabetics, up to 1000 mg steviol glycoside preparation:
  – Most studies showed no negative effect on glucose homeostasis, acknowledged some studies showed reduced post-prandial glucose in diabetics
  – No effect on blood pressure in normal or type-2 diabetics
  – Doses were larger than would be consumed in foods & beverages

STEVIA & CV RISK FACTORS

- *Meta-analysis* of 9 human RCT studies
- Various pharm doses
- Stevioside showed:
  - Small reduction in FBG (p<0.00001)
  - Small reduction in blood pressure (p=0.03)
- No dose-response relationship

Stevia: Suitable for Diabetics

- 16-week study,
- 122 diabetic adults
- 1000mg Reb A stevia/day (4 x 250 mg)

Results:
- Carb/GL: no effect
- HbA1C: no effect
- FBG, serum insulin: no effect
- Well tolerated – even at pharmacologic dose

2013 REVIEW: POTENTIAL ROLE FOR STEVIA IN INSULIN RESISTANCE AND DIABETES

• **Animal studies:**
  - ↓ lipid peroxidation when pre-fed with stevia
  - Stevioside & steviol ↑ insulin secretion
  - suggests slower/reduced progression of diabetic co-morbid complications

• **Human studies:**
  - ↓ postprandial glucose levels when fed meals supplemented with stevioside, vs both sucrose and aspartame.

Mohd-Radzman et al. *Evid Based Comp Alt Med.* 2013; Article ID: 718049
2013 REVIEW:

POTENTIAL ROLE FOR STEVIA IN INSULIN RESISTANCE AND DIABETES

- Seems to have “target-specific” effect:
  - Reduces hyperglycemia in human subjects (1 gm dose)
  - No effect in normo-glycemic conditions
  - Suggests no danger of hypoglycemia

Mohd-Radzman et al. Evid Based Comp Alt Med. 2013; Article ID: 718049
STEVIA: REAL LIFE
Expert Consensus Statement on Low/No-calorie Sweeteners

- Help reduce energy intake when they replace high-calorie ingredients.
- Can enhance wt loss in free-living conditions when used as part of a behavioral weight loss program.
- May benefit post-prandial glucose & insulin in both healthy people & those with diabetes.
- Won’t increase appetite, no discernable effect on satiety.
- Have dental benefits when used in food & beverages

Stevia: Hunger, Satiety & Food Intake

Preload (tea, crackers, sweet cream cheese) 20 min before test meals:
- 290 kcal stevia/aspartame
- 493 kcal sucrose
- **202 kcal sucrose removed**

Results:
- No differences in hunger or satiety across groups
- Low-cal SS did not compensate at subsequent meals & ate less overall

Stevia Leaf Extract Helps Blunt Blood Glucose Level in a Reduced-Calorie Meal

Results:
• No differences in hunger or satiety across groups
• Low-cal SS: NO compensation at subsequent meals, & ate less overall

Kids, Sugar, & Chocolate Milk: Sucrose vs. Stevia & Monk Fruit

- 8 thru 13 year-olds PREFERRED stevia-sweetened choc milk

- Parental acceptance of the label:
  - Label-conscious parents PREFERRED stevia
  - “Traditional” parents preferred the sugar-sweetened

Recent Meta-analysis on Low-Calorie Sweeteners (LCS) & Body Weight and Composition

- Data from 15 RCTs and 9 prospective cohort studies
- Among the excluded factors:
  - Reviews & commentaries w/ no new studies
  - Duplicates or non-randomized
  - ≤2 weeks duration
  - LCS not reported/identified
  - Not prospective
- Result of meta-analysis of prospective studies:
  - No association between LCS and BMI or fat mass

Recent Meta-analysis on Low-Calorie Sweeteners (LCS) & Body Weight and Composition

- **RCT studies**: Substituting LCS options for their *regular-calorie* versions: showed that it modestly but significantly reduced all outcomes
  - Modest weight loss, -0.80 kg
  - BMI: -0.24 kg/m²; Fat mass: -1.10 kg; WC: -0.83 cm
  - Significance consistent among age & gender groups

- **CONCLUSION**:
  - LCS were a useful tool for compliance with weight loss & weight maintenance plans

# Meta-analysis: Significant Body Weight Reduction, Low-energy sweeteners vs. SSB & Water

## Adults

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Follow-up (months)</th>
<th>Sample size</th>
<th>Weight (%)</th>
<th>WMD [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kendall et al, 1968 (M+F)</td>
<td>3</td>
<td>59</td>
<td>7.4</td>
<td>-0.40 [-2.75, 1.95]</td>
</tr>
<tr>
<td>Blackburn et al, 1997 (F)</td>
<td>40</td>
<td>163</td>
<td>11.5</td>
<td>-5.10 [-6.29, -3.91]</td>
</tr>
<tr>
<td>Raben et al, 2002 (M+F)</td>
<td>2.5</td>
<td>41</td>
<td>11.8</td>
<td>-2.60 [-3.71, -1.49]</td>
</tr>
<tr>
<td>Reid et al, 2007 (F)</td>
<td>1.25</td>
<td>66</td>
<td>12.4</td>
<td>-0.45 [-1.39, 0.49]</td>
</tr>
<tr>
<td>Nijke et al, 2009 (M+F)</td>
<td>6</td>
<td>77</td>
<td>13.9</td>
<td>-0.09 [-0.49, 0.31]</td>
</tr>
<tr>
<td>Reid et al, 2010 (M+F)</td>
<td>1.25</td>
<td>53</td>
<td>11.9</td>
<td>-0.49 [-1.58, 0.60]</td>
</tr>
<tr>
<td>Tate et al, 2012a (M+F)</td>
<td>6</td>
<td>210</td>
<td>11.8</td>
<td>-0.80 [-1.90, 0.30]</td>
</tr>
<tr>
<td>Maersk et al, 2012a (M+F)</td>
<td>6</td>
<td>22</td>
<td>5.6</td>
<td>-1.20 [-4.25, 1.85]</td>
</tr>
</tbody>
</table>

### RE estimate for adult subgroup

- Sig. test of ES = 0. Z = -2.280, p = 0.023
- Het.: p < 0.001, I² = 90.5% 

## Children

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Follow-up (months)</th>
<th>Sample size</th>
<th>Weight (%)</th>
<th>WMD [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Ruyter et al, 2012 (M+F)</td>
<td>18</td>
<td>641</td>
<td>13.7</td>
<td>-1.02 [-1.52, -0.52]</td>
</tr>
</tbody>
</table>

### Overall RE estimate for LES vs sugar-sweetened beverages

- Sig. test of ES = 0. Z = -2.544, p = 0.004
- Het.: p < 0.001, I² = 69.2% 

## Overall RE estimate for LES vs sugar-sweetened beverages

<table>
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<tr>
<th>Author, year</th>
<th>Follow-up (months)</th>
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<th>Weight (%)</th>
<th>WMD [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tate et al, 2012b (M+F)</td>
<td>6</td>
<td>213</td>
<td>38.7</td>
<td>-0.60 [-1.77, 0.57]</td>
</tr>
<tr>
<td>Maersk et al, 2012b (M+F)</td>
<td>6</td>
<td>25</td>
<td>10.0</td>
<td>-0.50 [-3.42, 2.42]</td>
</tr>
<tr>
<td>Peters et al, 2014 (M+F)</td>
<td>3</td>
<td>303</td>
<td>51.4</td>
<td>-1.86 [-2.72, -1.00]</td>
</tr>
</tbody>
</table>

### Overall RE estimate for LES vs water

- Sig. test of ES = 0. Z = -2.479, p = 0.013
- Het.: p = 0.197, I² = 36.4% 

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2015 Meta-analysis:
LCS, body weight, & energy intake

Conclusion of human studies:

“The preponderance of evidence from all human randomized controlled trials indicates that LES do not increase EI or BW, whether compared with caloric or non-caloric (for example, water) control conditions.”

“Overall, the balance of evidence indicates that use of LES in place of sugar, in children and adults, leads to reduced EI and BW, and possibly also when compared with water.”

Summary of Stevia’s Benefits for a Healthy Lifestyle, Overweight/Obesity & Diabetes

• Weight Management
  – Foods with stevia may help with a long-term modest effect on body weight, BMI, & waist circumference

• Appetite
  – Foods with stevia help lower total calorie intake, WITHOUT over-consumption later in the day.

Summary of Stevia’s Benefits for a Healthy Lifestyle, Overweight/Obesity & Diabetes

• Diabetes

  – Safe and appropriate for diabetics.
  – As a sugar replacer, may benefit blood glucose & insulin levels
  – Safety confirmed, no negative effect on glucose homeostasis

• Blood Pressure

  – Long-term use stevioside may have a small blood pressure lowering effect, but most studies used levels higher than the ADI.

Stevia & Sustainability

• For the same sweetness as sugar cane, stevia:
  – Uses 1/5th of the land
  – Uses only a fraction of the water

• Has few predators
  – less need for pesticides/herbicides

• Is a hardy crop
  – good for smaller plots of land,
  – ideal for small & large farms
  – Spares rainforest land

• Produces several crops per year in some parts of the world
Stevia: The body of evidence

- Stevia is a sustainable, plant-based natural-origin zero-calorie sweetener
- Substituting stevia for energy/sugar helps lower blood glucose and can help weight management by reducing sugar & energy intake
- Stevia can be useful by anyone wanting to reduce overall sugar intake & improve dietary quality
- Approved by all major regulatory bodies as safe & suitable for whole family