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## IUNS 21<sup>st</sup> ICN International Congress of Nutrition

### "From Sciences to Nutrition Security"





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## 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



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## **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





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## **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 reducedcalorie-reduced-sugar foods with sweeteners/stevia



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# **WHO: Global obesity**

Male

#### Female



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World Health Organization



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

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### IDF projection: Global diabetes will worsen 2015: 415 million $\rightarrow \rightarrow \rightarrow 2040$ : 641 million

Estimated number of people with diabetes worldwide and per region in 2015 and 2040 (20-79 years)





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### **Obesity: Gateway to Complications**





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### **WHY STEVIA?**





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### Worldwide Call for Healthy Lifestyles, Reductions in Calorie & Sugar Consumption

Dietary guidance by global & national health organizations

#### for ALL AGE GROUPS:

- $\downarrow$  Foods & beverages high in total/added sugars
- $\downarrow$  Added sugar to <10% of total calories, aim for <5% (WHO, 2015)







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## Evidence-based systematic reviews & meta-analyses



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### 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



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## 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

#### EFSA Journal 2010;8(4):1537.



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## **STEVIA & CV RISK FACTORS**



- Various pharm doses
- Stevioside showed:
  - Small reduction in FBG (p<0.00001)</li>
  - Small reduction in blood pressure (p=0.03)
- No dose-response relationship

Onakpoya & Heneghan: Eur J Prev Card 2015; 22(12) 1575–1587.





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## **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



**Fig. 2.** Mean ± standard error of the mean fasting glucose concentrations (mg/dL) at baseline (average of values at weeks -2 and 0) and 4, 8, 12, and 16 weeks of treatment for subjects receiving rebaudioside A (n = 60) or placebo (n = 62). Error bars are shown above the data points for rebaudioside A and below the data points for placebo.

Maki KC, et al., Food Chem Toxicol 2008;46 Suppl 7:S47-53.



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



#### • Animal studies:

- $\downarrow$  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

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



- Seems to have "targetspecific" 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

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# STEVIA: REAL LIFE





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### Expert Consensus Statement on Low/No-calorie Sweeteners



International Sweeteners Association

- Help reduce energy intake when they replace highcalorie 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

Gibson et al, *Nutrition Bulletin* 2014; 39:386-389



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### Stevia: Hunger, Satiety & Food Intake

#### Preload (tea, crackers, sweet cream cheese) 20 min before test meals:

- 290 kcal stevia/aspartame
- 493 kcal sucrose

SMOKE FREE EVENT

- <u>202 kcal sucrose removed</u> **Results**:
- No differences in hunger or satiety across groups
- Low-cal SS did not compensate at subsequent meals & ate less overall

Anton SD, et al., Appetite, 2010; 55:37-43



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### 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: <u>NO</u>
  <u>compensation</u> at subsequent meals, & ate less overall



Anton SD, et al., *Appetite*, 2010; 55:37-43



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

- 8 thru 13 year-olds
  PREFERRED steviasweetened choc milk
- Parental acceptance of the label:
  - Label-conscious parents
    PREFERRED stevia
  - "Traditional" parents preferred the sugar-sweetened



Li et al. *J Food Sci*. 2015; 80(5): S1083-1092

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### 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

Miller PE et al., Am J Clin Nutr, 2014; 100(3):765-77.



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### 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/m<sup>2</sup>; 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

Miller PE et al., Am J Clin Nutr, 2014; 100(3):765-77.



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

riation, year	(months)	size				We	ight (%)	WMD [95% CI]
Adults						2.		
Kanders et al, 1988 (M+F)	3	59	_		•	_	7.4	-0.40 [ -2.75 , 1.95 ]
Blackburn et al, 1997 (F)	40	163 -	-	_			11.5	-5.10[-6.29,-3.91]
Raben et al, 2002 (M+F)	2.5	41	-		_ :		11.8	-2.60[-3.71,-1.49]
Reid et al, 2007 (F)	1.25	66		-	-		12.4	-0.45[-1.39, 0.49]
Njike et al, 2009 (M+F)	6	11			-		13.9	-0.09[-0.49, 0.31]
Reid et al, 2010 (M+F)	1.25	53		-			11.9	-0.49[-1.58, 0.60]
Tate et al, 2012a (M+F)	6	210		-	-		11.8	-0.80[-1.90, 0.30]
Maersk et al, 2012a (M+F)	6	22				-	5.6	-1.20[-4.25, 1.85]
RE estimate for adult subg	roup				-			-1.41[-2.62,-0.20]
Sig. test of ES = 0: Z = -2.280 , p	= 0.023							
Het.: p < 0.001 , I^2 = 90.5 %					1			
Children	0.021							
de Ruyter et al, 2012 (M+F)	18	641		H			13.7	-1.02 [ -1.52 , -0.52 ]
Sig. test of ES = 0: Z = -2.854 , p = Het.: p < 0.001 , I^2 = 89.2 %	= 0.004	-6.00	I -4.00 Mean	I -2.00 difference	0.00 e (kg)	2.00		
Author, year	Follow-up (months)	Sample size				We	ight (%)	WMD [95% CI]
Author, year	Follow-up (months)	Sample size				We	ight (%)	WMD [95% CI]
Author, year Tate et al, 2012b (M+F) Maarsk et al. 2012b (M+F)	Follow-up (months)	Sample size			•	We	ight (%) 38.7	WMD [95% CI]
Author, year Tate et al, 2012b (M+F) Maersk et al, 2012b (M+F)	Follow-up (months)	Sample size			•	We	<b>ight (%)</b> 38.7 10.0	WMD [95% CI] -0.60 [-1.77, 0.57] -0.50 [-3.42, 2.42]
Author, year Tate et al, 2012b (M+F) Maersk et al, 2012b (M+F) Peters et al, 2014 (M+F)	Follow-up (months) 6 6 3	Sample size 213 25 303		-	•	We	<b>ight (%)</b> 38.7 10.0 51.4	WMD [95% CI] -0.60 [ -1.77 , 0.57 ] -0.50 [ -3.42 , 2.42 ] -1.86 [ -2.72 , -1.00 ]
Author, year Tate et al, 2012b (M+F) Maersk et al, 2012b (M+F) Peters et al, 2014 (M+F) Overall RE estimate for LE Sig. test of ES = 0: Z = -2.479, p = Het : p = 0.197   /2 = 38.4 %	Follow-up (months) 6 6 6 3 3 S vs water = 0.013	Sample size 213 25 303				We	<b>ight (%)</b> 38.7 10.0 51.4	WMD [95% CI] -0.60 [ -1.77 , 0.57 ] -0.50 [ -3.42 , 2.42 ] -1.86 [ -2.72 , -1.00 ] -1.24 [ -2.22 , -0.26 ]
Author, year        Tate et al, 2012b (M+F)        Maersk et al, 2012b (M+F)        Peters et al, 2014 (M+F)        Overall RE estimate for LE        Sig. test of ES = 0: Z = -2.479, p        Het: p = 0.197, IP2 = 38.4 %	Follow-up (months) 6 6 6 3 3 S vs water = 0.013	Sample size 213 25 303	-			We	<b>ight (%)</b> 38.7 10.0 51.4	WMD [95% CI] -0.60 [ -1.77 , 0.57 ] -0.50 [ -3.42 , 2.42 ] -1.86 [ -2.72 , -1.00 ] -1.24 [ -2.22 , -0.26 ]
Author, year        Tate et al, 2012b (M+F)        Maersk et al, 2012b (M+F)        Peters et al, 2014 (M+F)        Overall RE estimate for LE        Sig. test of ES = 0: Z = -2.479, p        Het: p = 0.197, l*2 = 38.4 %	Follow-up (months) 6 6 3 3 S vs water = 0.013	Sample size 213 25 303	-4.00		0.00	We	<b>ight (%)</b> 38.7 10.0 51.4	WMD [95% CI] -0.60 [ -1.77 , 0.57 ] -0.50 [ -3.42 , 2.42 ] -1.86 [ -2.72 , -1.00 ] -1.24 [ -2.22 , -0.26 ]

Rogers PJ et al, 2015. International J of Obesity, 10 Nov 2015; doi:10.1038/ijo.2015.177

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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."

Rogers PJ et al, 2015. International J of Obesity, 10 Nov 2015; doi:10.1038/ijo.2015.177





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### 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.

Onakpoya & Heneghan: *Eur J Prev Card* 2015; 22(12) 1575–1587.





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# 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.

Onakpoya & Heneghan: *Eur J Prev Card* 2015; 22(12) 1575–1587.



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## **Stevia & Sustainability**

- For the same sweetness as sugar cane, stevia:
  - Uses 1/5<sup>th</sup> 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







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## **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

