An Introduction to Low-and No-Calorie Sweetener Uses in Foods and Beverages in the United States

Corey Scott, PhD
Principal Scientist, Cargill, Inc
corey_scott@cargill.com
## Disclosures

<table>
<thead>
<tr>
<th><strong>AFFILIATION/FINANCIAL INTERESTS</strong> (prior 12 months)</th>
<th><strong>ENTITIES</strong></th>
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<tbody>
<tr>
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<td>Owner</td>
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<td>Speakers Bureau</td>
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<tr>
<td>Stock Shareholder</td>
<td>Cargill, Inc; General Mills</td>
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<tr>
<td>Employee</td>
<td>Cargill, Inc</td>
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<tr>
<td>Other</td>
<td>Paid employee of Cargill, manufacturer and marketer of LNCS</td>
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TODAY’S FOCUS

Introduction of LNCS as a Means to Reduce Added Sugars

Uses of LNCS in Foods and Beverages and Challenges

General Toxicological, Safety and Efficacy

Clinical study outcomes supporting benefits of using Stevia for weight management| FNCE © 2023
Why Add Sugars to Foods and Beverages?

- Besides bringing sweetness, sugars also have important **nutritive, sensorial, physical and organoleptic properties**.
  - Sweet taste
  - Texture
  - Water binding
  - Preservation

- Sugar reductions/sugar intake is a health focus.

- Sugars can be reduced/replaced, but today there is not one single ingredient that can replace all the functions of sugars in food.
IFIC 2023 Health and Safety Survey on Added Sugars

Source: IFIC 2023
Global Added Sugar Intake Recommendations

• Risk of tooth decay, overweight, obesity (WHO, US DGA, EFSA)
• 2009-AHA- less than 150 and 100 calories for men and women
• 2018-WHO- Less that 10% total energy strong recommendation
  - less than 5% as a conditional recommendation
• 2020-2025- USDGA-Reduce to 10% total energy
  • Added sugars are used in for many reasons
• 2023 EFSA TUL on Added/Free Sugars “As low as possible”
• FDA has issued added sugar labeling
• Sugar taxes and warning labels exists in some regions
LNCS—Sugar Substitutes that Provide Sweetness with No Calories

- Sucralose
- Aspartame
- Cyclamate (not in US)
- Acesulfame-K
- Saccharin
- Steviol glycosides
- Advantame
- Neotame
- Neohesperidine DC
- Thaumatin
- Monk-fruit

Diverse molecules
- Sweetening potency
- Chemical structure
- Stability
- Artificial
- Plant based
- Protein
- Excreted
- Absorbed
- Act on different receptors

Make up 95%+ of the global sweetener market
LNCS Are Highly Scrutinized

America's Most Popular Artificial Sweetener Damages Our DNA, Scientists Say
BY PANDORA DREMAN ON 6/23 AT 1:00 PM EDT
A Sugar Replacement May Be Linked to Heart Attacks and Strokes. Don't Throw Out Your Stash Yet

The Link Between Highly Processed Foods and Brain Health

New Warning About Zero-Calorie Sugar Substitute: What Experts Are Saying About Erythritol

How fake sugars sneak into foods and disrupt metabolic health

New Evidence That Ultra-Processed Foods May Increase Cancer Risk

Commonly used sweetener found linked to anxious behaviour in mice

Artificial sweetener erythritol linked to heart attack and stroke: Study
LNCS Uses in the Food Industry

Media
“Forget tobacco, sugar is our new addiction problem.”

Health Professionals
“You AND your children are overweight. Cut your sugar intake.”

WHO / Dietary Guidelines
Added sugars should not exceed 10% of total daily intake

Brand Mgr
I need to reduce sugar in my product, but it won’t sell unless it TASTES good

Nutrition Facts
FDA changes to Nutrition Facts Panel to include “Added Sugars”

Sugar taxes

Industry Responsibility
Pressure on the food industry to “fix the obesity epidemic” by reducing calories

Consumer FEAR:
• I’m afraid I am / my child is obese or could get diabetes
• I’m afraid of artificial sweeteners, but what exactly does ‘natural’ mean?”
LNCS Have a Very Wide Use in Foods and Beverages

As a Food/Beverage Ingredient

Diet Soda
Light Yogurt
Medicines
Energy Drinks
Oral Care Products

Pure Compound, mg
Mixed compound, g

“Tabletop”
- Stevia
- Sucralose
- Aspartame/Ace K
- Monk Fruit
Use of LNCS to Improve Sweetness Profile

Blending of LNCS provides Sweetness improvements
LNCS Work on Sweet Taste Receptors on Tongue

Figure provided by Loic Briand
Biological Fate on LNCS Is Diverse

Acesulfame Potassium & Saccharin

- Ingestion
- Absorption
- Systemic circulation
- Kidneys
- Urinary excretion
- Fecal excretion

Aspartame

- Ingestion
- Absorption
- Liver metabolism of methanol
- Utilized for protein synthesis and metabolism

Steviol Glycoside

- Ingestion
- Absorption of steviol
- Liver metabolism to glucuronide
- Colonic microflora cleave glycoside linkage (no glucose absorption)
- Kidneys
- Urinary excretion

Sucralose

- Ingestion
- Little absorption
- Fecal excretion


SOT FDA Colloquia on Emerging Toxicological Science Challenges in Food and Ingredient Safety
Production of Artificial LNCS–Sucralose

Sucrose → Sucralose

1) CPh₂Cl (XS) β-picoline cat. DMAP
2) Ac₂O

Sucrose → 2 → 3

HCl(g)
toluene

1-butylamine
EtOAc/hexane
55 °C

Sucralose

1) SOCl₂, Ph₃PO
2) cat. NaOMe MeOH
Production of Artificial LNCS–Aspartame

\[
\text{L-Phenylalanine} \xrightarrow{\text{MeOH/HSO}_4} \text{L-Phenylalanine methyl ester} + \text{L-Aspartic acid}
\]

\[
\text{Aspartame}
\]
Stevia Leaf Composition
- Stevioside 2.5%
- Reb A 7.75%
- Reb B 0.01%
- Reb C 1.04%
- Reb D 0.21%
- Reb M 0.10%
- Reb F 0.14%
- Dulcoside A 0.05%
- Steviolbioside 0.05%
- Rubusoside 0.01%
- Other Leaf material 88%

Steviol Glycosides Composition
- Stevioside
- Reb A
- Reb B
- Reb C
- Reb D
- Reb M
- Reb F
- Dulcoside A
- Steviolbioside
- Rubusoside

88% leaf material not used/sweet
 Reb M & Reb D <1% of the leaf

Example of LNCS Production–Stevia from Leaf
Stevia Production via Fermentation
Other Novel Plant Based Sweeteners

- Brazzein
- Monatin
- Neoculin
- Miraculin
- Glycyrrhizin
- Monellin

Challenges:
- Only sweet under acidic conditions, long lasting sweetness, not heat stable, low sweetness, not pH stable, low solubility, licorice aftertaste
- Supply chain, costs and regulations

Optimal Sweetener Selection for Foods and Beverages Is Critical

**Type of sweeteners**
- Sucralose
- Aspartame
- Acesulfame-K
- Saccharin
- Steviol glycosides
- Advantame
- Neotame
- Neohesperidine DC
- Aspartame-acesulfame salt
- Thaumatin
- Monk-fruit
Example of LNCS Selection for Beverages

1. Taste Profile
2. Processing
3. Shelf-life

Sweetener Blends:
- Sucrose Control (SEV 8)
- Stevia Reb A/Thaumatin
- Stevia Reb M
- Mogroside V/Stevia Reb M
- Sucralose/Ace K
- Neotame

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<tr>
<th>Sweetener Blends</th>
<th>Liking</th>
<th>Sweet intensity</th>
<th>Bitterness intensity</th>
<th>JAR Sweet</th>
<th>JAR After taste</th>
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<tbody>
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<td>Sucrose</td>
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Project SWEET Consortium, SWEETPROJECT.EU
For Solid Foods, Bulking Agents Are Needed with LNCS

Bulking agents provide similar properties and (some) sweetness as sugar.
Examples-Chocolate, yogurts, cookies/cakes, breakfast cereals

Bulking agents include
  Polyols
  Inulin
  Maltodextrin
  Fiber
  Fats
  Proteins

Considerations to processing must be noted, i.e., pH, temperature, etc.
Regulations vary (i.e., in Europe: food category, caloric reduction and dose specific)
Standard of identity must also be preserved when adding NNS and bulking agents
Beverage vs. Food Ingredient Labels with LNCS

Sugar Sweetened Beverage (150 kcal)
- Carbonated water, Sucrose, Acid, Color, Flavor, Caffeine

Diet Beverage (0 kcal)
- Carbonated water, Acid, Color, Flavor, Sweetener, Caffeine

Dark Chocolate Bar (325 kcal)
- Sucrose, Cocoa Liquor, Cocoa Butter, Lecithin, Vanilla Flavor

Dark Chocolate Bar 30% Reduced Sugar (310 kcal)
- Sucrose, Maltitol, Cocoa Liquor, Cocoa Butter, Lecithin, Vanilla Flavor, Sweetener

No Added Sugar Dark Chocolate Bar (260 kcal)
- Polydextrose, Cocoa Liquor, Cocoa Butter, Lecithin, Vanilla Flavor, Sweetener

Low Calorie Confection Bar (245 kcal)
- Maltitol, Erythritol, Cocoa Liquor, Cocoa Butter, Calcium Carbonate, Lecithin, Vanilla Flavor, Sweetener

Project SWEET Consortium, SWEETPROJECT.EU
Regulatory Approval of LNCS–Steviol Glycosides

>95% Pure Steviol Glycosides FDA GRAS in 2008 •

Study Types to confirm Safety (FDA)
1. Genetic Toxicity Tests
2. Short Term Rodent
3. Sub Chronic Rodent
4. Sub Chronic Non-Rodent
5. One year non rodent
6. Two-year rodent chronic toxicity/carcinogenicity
7. Reproductive Study
8. Developmental study
9. Metabolism and pharmacokinetic
10. Human clinical studies

• Food and Chemical Toxicology– Volume 46 (2008)–Rebaudioside A: An Assessment of Safety

In vitro and in vivo metabolism:

Steviol formation

• Common metabolic pathway for all steviol glycosides – bridges to published safety data

Purkayashta et al., 2016. Regul Toxicol Pharmacol.
Safety of LNCS and Acceptable Daily Intake (ADI) Level

<table>
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<tr>
<th>Sweetener</th>
<th>ADI</th>
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<tr>
<td>Saccharin</td>
<td>5 mg/ kg of body weight</td>
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<tr>
<td>Cyclamate</td>
<td>7 mg/ kg of body weight</td>
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<tr>
<td>Aspartame</td>
<td>50 mg/ kg of body weight</td>
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<tr>
<td>Sucralose</td>
<td>15 mg/ kg of body weight</td>
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<tr>
<td>Acesulfame-K</td>
<td>15 mg/ kg of body weight</td>
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<tr>
<td>Stevia</td>
<td>4 mg/ kg of body weight</td>
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Source: FDA.  
ADI: acceptable daily intake; FDA: food and drug administration.

ADI is average daily consumption over a lifetime  
Based on No Observed Adverse Effects Level (NOAEL)  
NOAEL is divided by 100  
ADI is set by JECFA and based on rodent studies  
Studies show that at the highest intakes, NNS use to not go over the ADI
LNCS are diverse molecules and are useful tools in reducing added Sugars.

Selection of LNCS has challenges for Foods and Beverages Uses.

LNCS go through an approval process and Safety is well established.
Thank You!