

Lead Acetate: first artificial sweetener



Pompei fresco showing a banquet scene from the Casa dei Casti Amanti

Romans had few sweeteners besides honey, boiled grape juice in lead pots to Lead Acetate trihydrate produce a reduced sugar syrup called

crystals

defrutum, concentrated again into sapa. This syrup was used to sweeten wine & to sweeten & preserve fruit. Lead acetate or other lead compounds leaching into the syrup caused lead poisoning.



Artificial Sweeteners or Sugar Substitutes

Two types:

- 1) High intensity sweeteners saccharin, aspartame, acesulfame potassium, sucralose, stevia, etc.
- 2) Sugar alcohols sorbitol, mannitol, erythritol, xylitol

Chemical structure of sucrose and some high intensity sweeteners Sucrose (table sugar) Aspartame (NutraSweet, Equal) Saccharin (Sweet N' Low)

HO

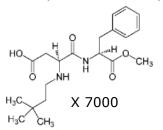
Saccharin (Sweet N' Low)

X 300

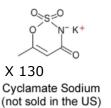
Sucralose (Splenda)

OH

Neotame (in Ice Breakers Mints)



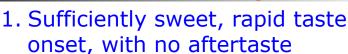
Acesulfame Potassium (Sunett, Sweet One)



X 30 N S O Na

Relative sweetness (X) compared to sucrose (1)

Requirements for commercially suitable sugar-substitute in foods and beverages



- 2. Non-toxic
- 3. Reasonable/competitive cost
- 4. Thermostable: resist cooking temperatures
- 5. Non or low caloric

How the Sugar Substitutes Stack Up

SACCHARIN (SWEET'N LOW, SUGAR TWIN)

Discovered 1879, first sold to the public in 1884, but became popular during sugar shortages in World War I.

How it's made Anthranilic acid, nitrous acid, sulfur dioxide and chlorine are combined with ammonia.

Flavor About 300 times sweeter than sugar. Its pronounced sweetness comes on immediately with a slight bitter or metallic aftertaste.

Cost 1.9 cents a packet.

ASPARTAME (EQUAL, NUTRASWEET)

Discovered 1965, first sold to the public in 1981.

How it's made The amino acids aspartic acid and phenylalanine are combined with methanol, an alcohol.

Flavor 200 times sweeter than sugar. It has a very forward, sweet taste with a sharp, clean finish.

Cost 3.3 cents a packet.

 $\begin{tabular}{ll} \textbf{SUCRALOSE (SPLENDA)} \\ The best-selling tabletop sweetener in the United States. Popular with bakers and food manufacturers. \\ \end{tabular}$

Discovered 1976, first sold to the public in 1998.

How it's made Sugar is chemically altered by the addition of chlorine.

Flavor 600 times sweeter than sugar. It lacks the sour bite or bitterness in some others. Still tastes like an artificial sweetener, but with a barely noticeable aftertaste.

Cost 4 cents a packet.

STEVIA (TRUVIA, PUREVIA, SWEETLEAF)

Extracted from plant leaves, a highly purified form was approved recently as safe for use in food.

Discovered Centuries ago, first sold for general use in 1971 in Japan and last year in the United States.

How it's made Sweetening agents called glycosides are removed from the leaves of the stevia plant.

Flavor 300 times sweeter than sugar. Its flavor is slow to start and can have a pronounced aftertaste that some describe as licorice or menthol. New versions have tamed that somewhat.

Cost 9.9 cents a packet.



Saccharin





- Benzoic sulfimide, a coal tar derivative, 300-400 x sweeter than sucrose, sweet taste detectable at 1: 100,000 dilution, stable at physiological pH & temperature, does not accumulate in body, excreted unchanged, no known metabolite.
- History: 1879 synthesized accidentally by American chemist, Constantin Fahlberg, at Johns Hopkins University 1880-1900 manufactured only in Germany, rigidly controlled by 6 firm cartel, Dye Trust



Saccharin: history

- 1901 John Queeny, purchasing agent for a pharmaceutical house, saw commercial use for saccharin as synthetic sweetener in USA, filed papers of incorporation for **Monsanto** Chemical Works. Arranged with Sandoz, Switzerland, to get a proficient chemist. Dye Trust tried to drive out competition by price cutting, almost succeeded.
- 1906 US Pure Food and Drug Act passed. Saccharin-containing foods challenged under this law as "adulterated" but President Theodore Roosevelt supported its use



Saccharin: testimonial

1911 Queeny founder of Monsanto was having difficulty acquiring data on safety of saccharin

"I always completely disagreed about saccharin, both as to the label and as to its being deleterious....I have used it myself for many years as a substitute for sugar in tea and coffee without feeling the slightest bad effects. I am continuing to use it now. Faithfully yours, T. Roosevelt"



Saccharin

Labeling history

- 1911 US government states that foods containing saccharin were adulterated
- 1912 US government decision that saccharin is not harmful
- 1973 FDA requires warning potential carcinogen
- 2001 FDA declares saccharin safe for consumption
- 2010 EPA states that saccharin is no longer considered a potential hazard to human health.

Saccharin & cancer

May, 2000 National Institute for Environmental Health Sciences (NIEHS) removed saccharin as a potential cancer-causing agent because tests that showed it caused tumors in rats did not apply to humans. It had been delisted as a carcinogen since 1981.

Studies now indicate that rat bladder tumors arise from mechanisms that are not relevant to the human situation.

information about delisting of saccharin is available at

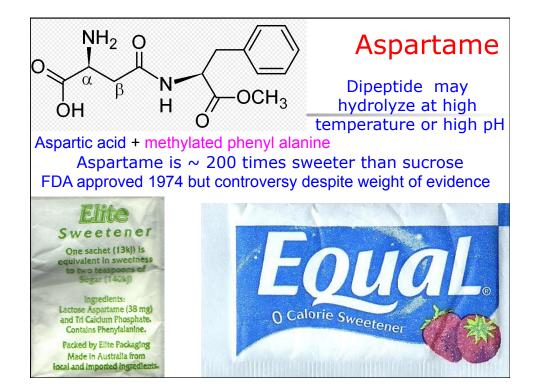
http://ntp.niehs.nih.gov/ntp/roc/eleventh/
append/appb.pdf



Artificial sweeteners induce glucose intolerance by altering the gut microbiota MOUSE BLOOD-GLUCOSE LEVELS 250 (mg dl 1) Fed glucose in water 150 Fed glucose in water 150 Minutes after ingestion

Mice consuming of commonly used Non-caloric Artificial Sweeteners (NAS) formulations developed glucose intolerance through induction of compositional and functional alterations to the intestinal microbiota.

Suez et al. Nature Sept 2014



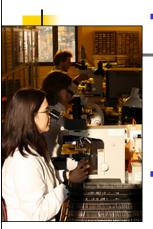
Aspartame: carcinogen?



Dr. Morando Soffritti, a cancer researcher in Bologna, Italy, who led tests of aspartame on 1,900 rats, calls it a possible carcinogen.

- results of his team's 7 year study on aspartame found
 that the sweetener was associated with unusually high rates of lymphomas, leukemias and other cancers in rats that had been given doses of it starting at what would be equivalent to four to five 20-ounce bottles of diet soda a day for a 150-pound person.
- The study was conducted at the European Ramazzini Foundation of Oncology and Environmental Sciences, a nonprofit organization

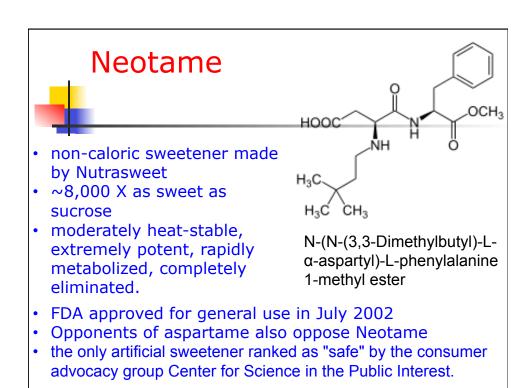
Aspartame: carcinogen?



- In US, the FDA says it has also taken note of the study. "We don't see any concerns at this stage," said George H. Pauli, associate director for science policy at Office of Food Additive Safety, F.D.A. . "We've gone through a humongous amount of data on aspartame over the years."
- Putting restrictions on aspartame would come at a significant cost. Food companies and consumers around the world bought about \$570 million worth of it last year. New regulatory action on aspartame would also jeopardize the billions of dollars worth of products sold with it.



Claims that aspartame causes: migraines, panic attacks, seizures, skin problems, weight gain, intestinal disorders, lupus, fibromyalgia, multiple sclerosis, blindness and death have not been substantiated but they persist.



Advatame



- HO TO THE PERSON OF THE PERSON
- non-caloric high intensity sweetener developed by Japan's Ajinomoto Co.
- N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-α-L-aspartyl]-L-phenylalanine 1-methyl ester

 20,000 X as sweet as sucrose

- FDA approved for general use in foods and beverages except meat and poultry as a food additive May 2014
- Animal studies have found no evidence for carcinogenicity or developmental toxicity



Splenda:Sucralose

Twice shelf life of Aspartame Heat stable

FDA approve 1998

Can't Get Enough

Splenda's popularity, particularly among food manufacturers eager to cater to calorie-counting consumers, has led to a surge in the number of new products using the artificial sweetener.

900

NEW PRODUCTS USING SPLENDA INTRODUCED EACH YEAR

300

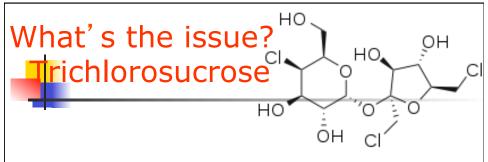
Through Dec. 13
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Manufacturer can not keep up with demand, rationing supplies

New products using Splenda soared from 573 in 2003 to 1,330 in 2004

Include not just sodas gums, also breakfast cereals, orange juice, salad dressings, bread Feb 2005 reported as accounting for 51% market share artificial sweeteners.





- Advertising claims by Splenda "Made from sugar, so it tastes like sugar" dispute hinges on the role of language in creating and defining the product.
- Merisant argues that advertising implying that Splenda is natural and is sugar without calories, is untrue it is an artificial sweetener made in the laboratory.



What's at stake?

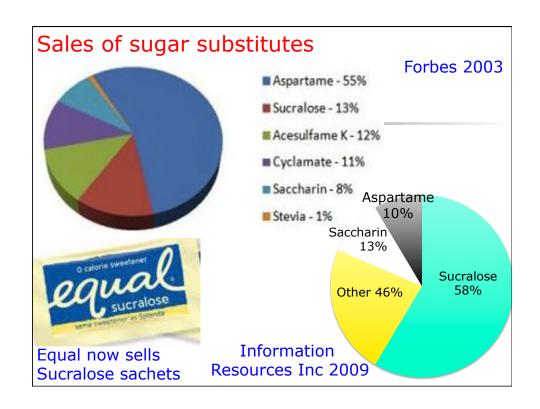
Leadership of the fiercely competitive \$1.5 billion artificial sweetener market of more than 6,000 consumer products like Diet Coke, Diet Pepsi and many more, not just in packets and bulk

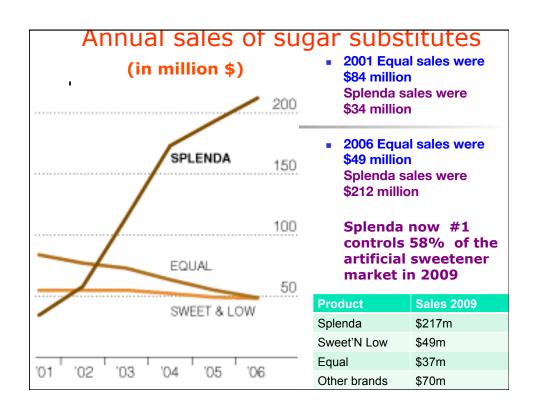
Annual sales of sugar substitutes



- 2001 Equal sales were\$84 millionSplenda sales were\$34 million
- 2006 Equal sales were \$49 millionSplenda sales were \$212 million

Splenda now #1 controls 62% of the artificial sweetener market





Over-the-counter sugar substitutes

Tabletop sweeteners / Sachets

us market share in 2010

Sweet' n Low 11% Equal 6.5%

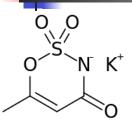
Splenda 45.5% Truvia/Stevia 13.8%



- Sweet'n Low (Cumberland Packing Co.) contains saccharin as the sweetening agent
- Equal (Merisant Worlwide) contains aspartame as the sweetening agent
- Splenda (McNeil Nutritionals) & Nevella (Heartland Sweeteners LLC) contains sucralose as the sweetening agent
- Truvia(Cargil) contains rebaudioside A

Acesulfame potassium

Brand: Sunett and Sweet One, Hoechst Celanese



Calorie-free sugar substitute, 200 times sweeter than sucrose, sweetness quickly perceptible, stable under heat and moderately acidic and basic conditions, can be used in baking or products that require long shelf life.

Approved by FDA 1988 for use in dry food products, beverages, protein shakes and pharmaceutical products. In 2003 general purpose approval.

In carbonated drinks it is almost always used in conjunction with another sweetener, such as aspartame or sucralose.

The Claim: Artificial Sweeteners Cause Migraines



Artificial sweeteners have been linked in **anecdotal reports** to a variety of health problems for more than 30 years. But one of the more mysterious reported side effects is also among the most commonly mentioned, headaches.

Despite widespread anecdotal reports, most studies have not found an association between artificial sweeteners and headaches.

Alitame

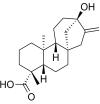


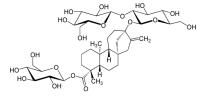
- Dipeptide: L-aspartic acid, D-alinine and a novel amine, Aclame[™], discovered by Pfizer Inc. Now owned by Cultor
- Relative sweetness: x 2,000 sucrose, clean sweet taste
- Metabolism: Aspartate metabolized normally, alanine amide excreted with minimal metabolic change
- Applications: can be used in beverages, baked goods, milk products, chewing gum, candies, pharmaceuticals & toileteries
- Status: Petition filed in USA 1986, now in abeyance, approved in Australia, New Zealand, Mexico, China





Stevioside





4 major steviol glycosides found in the stevia plant leaves are:

5-10% stevioside (250-300X of sugar)

2–4% rebaudioside A — most sweet (350–450X of sugar)

1-2% rebaudioside C

½-1% dulcoside A

The major compounds stevioside and rebaudioside, primarily responsible for the sweet taste of stevia leaves, were first isolated by French chemists, Bridel and Lavielle (1931)



Stevia Plant

Source of Truvia



Stevioside/Stevia

Marketed as Truvia (Cargill/Coca-Cola), PureVia (Pepsi), SweetLeaf

- Intensely sweet, naturally occurring compound found in leaves of small shrub, Stevia rebaudiana, also called yerba dulce, grows wild in Paraguay.
- Sweetness 300X that of sucrose
- Steroid glycoside, some antiandrogenic activity of its derivatives, steviol & dihydroisosteviol
- WHO in 2006 concluded stevioside and rebaudioside A are not genotoxic
- FDA 2008 approved them as GRAS, calling it "generally recognized as safe."



Truvia

Nature's Calorie-Free Sweetener

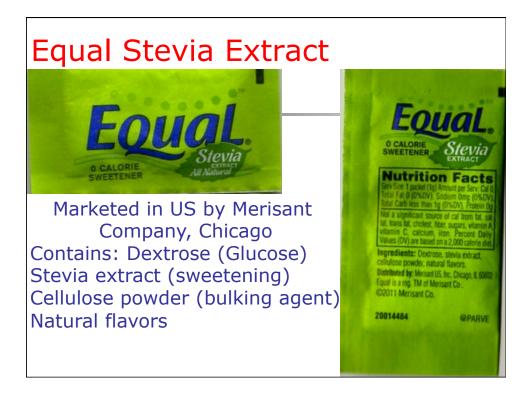
Marketed in USA since 2008 by Cargil Inc as powder or in packages as non-caloric sweetener. Ingredients: Erythritol, rebiana, natural flavors Rebiana is the trade name for high-purity rebaudioside A. Cargill has filed patents which give it exclusive rights to sell Rebiana in beverages.

In 2007 Coca-Cola Co. teamed up with Cargill Inc., an agribusiness and commodity trading group, to market a new calorie-free natural sweetener aimed at health-conscious consumers.

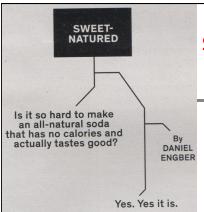


Supplement Facts:
Serving size:
1 packet (1g)
Amount per serving:
Calories 0,
Total Carb. 1g
(<1%DV*
Stevia Extract
(Stevia rebaudiana)
(leaf) 85mg
*Percent Daily Values
(DV) are based on
2000 calorie diet









"Natural" Sweetener for use in diet sodas

N.Y. Times Magazine 1-5-14



Real money profit is in diet drinks not sachets, consumers are not content to switch to "artificial" sweeteners. **Problem** Stevia, although sweet, has a bitter aftertaste that lingers. Unobtrusive in small doses (amount sprinkled in your coffee), it is ruinous in quantities used in diet soda.



Quest for "Super Stevia" without bitter aftertaste
Rebaudioside A is active ingredient

Rebaudioside-D PepsiCo Rebaudioside-X Coca-Cola Selected sweeter glycosides with less bitterness & aftertaste.

Next generation of "natural" sweeteners may come from come from yeast fermentation using G.M.O., cells with specific genes stuffed in their nuclei to make desired Rebaudioside.

Advantage: lower cost

unbeholden to rain and sun and weeds, nor to the natural limits of plant biology. Ability to make specific glycoside.





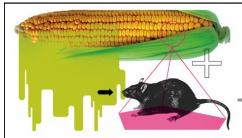
Nectresse (McNeil Nutritionals) contains
Ingredients: erythritol, sugar, monk fruit
extract, molasses, (<5cals/sachet)
Obtained from Chinese mountain-orchard melon
known as luo han guo or monkfruit.
Sold in tangerine colored packets as natural
product, sweetness 150-250X sucrose
GRAS 2009, FDA approval
Cost 7.5-15 cents/sachet
Discontinued

22

The Claim: Artificial Sweeteners Cause Migraines



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- Despite widespread anecdotal reports, most studies have not found an association between artificial sweeteners and headaches.



Worries about sweeteners (high fructose corn syrup)?

~55% Americans consider it a food safety issue Corn Refiners Association consider name change to corn sugar

For nutritional scientist all sugars, including those from sugar cane and beets, as well as HFCS are cause for concern due to obesity Calories from sugars now account for 16 percent total calories, a 50 percent increase from the 1970s

Sugar alcohols

Polyol Relative sweetness

sorbitol 0.5 mannitol 0.7 Xylitol 1.0

Can be metabolized, hence caloric sweeteners, but are not completely absorbed. Excess intake can cause diarrhea, intake should be limited. Used as sweetener in mouthwashes, toothpaste, chewing gum, but not major food additives. Cost of xylitol limits its use.



Erythritol

butane-1,2,3,4-tetraol

A sugar alcohol approved for use in USA and throughout much of the world. 60–70% as sweet as table sugar yet it is almost non-caloric, does not affect blood sugar, does not cause tooth decay, and is absorbed by the body, therefore unlikely to cause gastric side effects.

EMERALD FOREST SUGAR, INC.



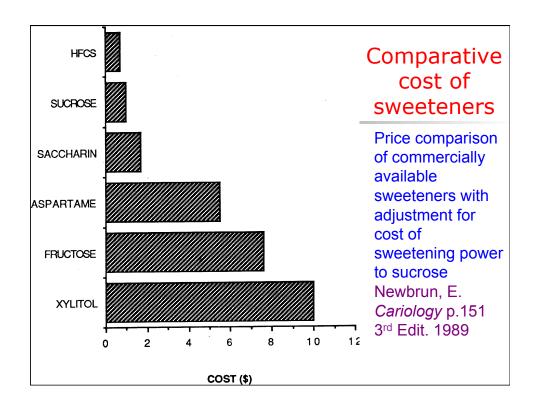
Company based in Broomfield, CO founded in 2003 to introduce consumers to xylitol. offers more than 25 products, including bulk xylitol and erythritol, and a variety of mints, fruit sours, gums and coffee shots containing xylitol, natural flavors and natural colors.

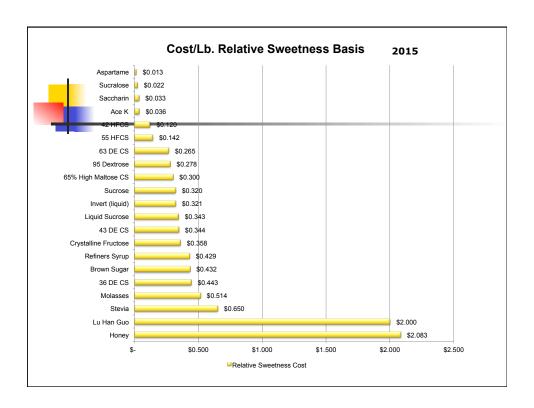
Diabetics and health conscious shoppers choose xylitol and erythritol because they taste great, help stabilize blood sugar levels and are guilt free. Safeway, Inc. is carrying Emerald Forest's all natural sweetener, Xylitol, in some stores.

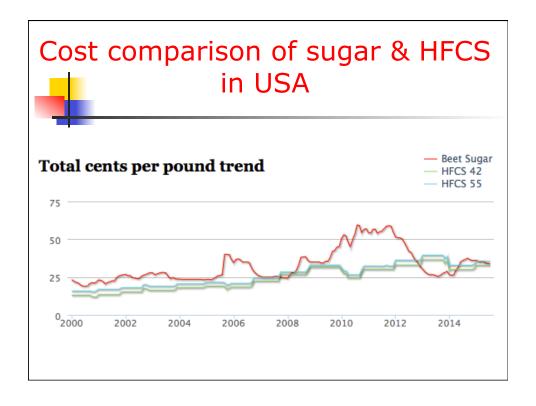
Requirements for sugar substitutes



- 1. Have sufficient sweetening power
- 2. Be nontoxic, non-carcinogenic
- 3. Be reasonably inexpensive
- 4. Be thermostable (i.e. resist cooking temperatures)





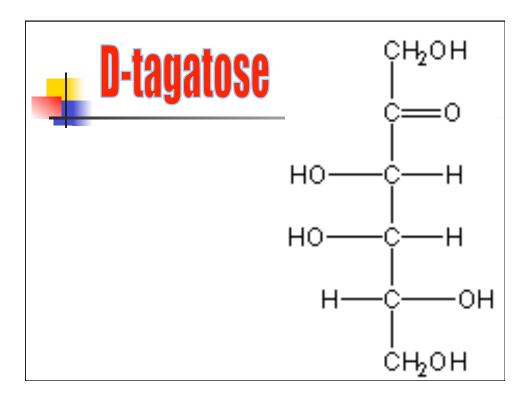




Tagatose



- Rare monosaccharide found in trace amounts in dairy foods (yogurt, cheese), can be derived from whey, a dairy byproduct
- Sweetness 92, same bulk and browning as sucrose
- Low caloric (1.1 to 1.4 kcal/g) because only ~ 20% is absorbed
- Safe for teeth, does not drop plaque pH below 5.7 in vivo tests
- GRAS claim (Arla Foods, Denmark) permitting use in foods and beverages, drugs and medications. FDA response pending



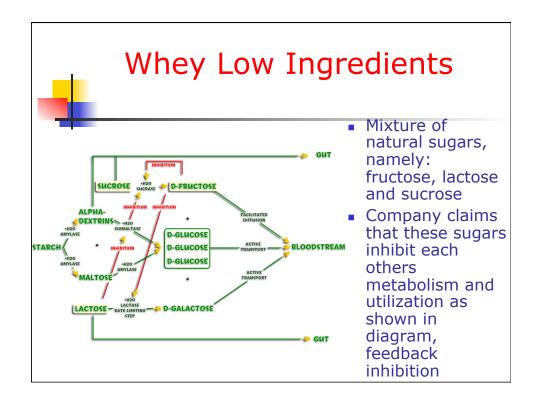


- Whey: a milk serum, separating as a watery liquid from curd after coagulation, as in making cheese
- Whey Low a commercial table top sweetener, cost ~ \$5/lb
- Sweetening ingredients: fructose, lactose, sucrose
- Claims; lower calories (1.9 cals/g), lower glycemic index, "great for diabetics," sweetness=sucrose



Here is why Whey Low is the Most Sensational Sugar Substitute Ever:

·100% Natural ·Tastes Exactly like sugar · 75% fewer Calories than sugar · 70-80% lower Glycemic Index than sugar · Only 1 Effective Carb per Serving · Easy to Use! Whey Low is a One-for-One substitute for sugar in ALL food applications. Whey Low is perfect for baking. Cakes and cookies cannot tell the difference, and neither will you. · So whether you are a Low-Calorie, Smart-Carb, or Low-Carb Dieter, a Type 1 or Type 2 Diabetic, or simply Health-Conscious, Whey Low is the choice for you.

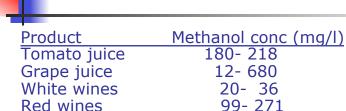


Whey Low health benefit claims



- By controlling your body weight, you reduce your risk for these overweight-related diseases
- Helps you control after-meal blood sugar excursions
- Helps you realize a healthier immune system
- May help you avoid or postpone osteoporosis





Soft drink (aspartame) 55

Brandv

Dietary sources are only partial contributors to totalbody pool of methanol. Protein methylation also results in formation of methanol as end product

181-2425

Whey Low^{MT} VivaLac Inc.

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Methanol content of juices & beverages

Product	<u>Methanol conc (mg/l)</u>
Tomato juice	180- 218
Grape juice	12- 680
White wines	20- 36
Red wines	99- 271
Brandy	181- 2425
Soft drink (asparta	ame) 55

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Saccharin & cancer

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Studies now indicate that rat bladder tumors arise from mechanisms that are not relevant to the human situation.





What are the facts?

Splenda contains sucralose, made by chlorinating sucrose (sugar) in the laboratory and adding bulking agents dextrose and maltodextrin.

Sucralose is 600 X as sweet as sucrose so much less is required.