

Safety and Benefits of Alternative Sweeteners

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On behalf of
Calorie Control Council



The Calorie Control Council

Alternative Sweeteners Available for Use

Intense sweeteners

- **Advantame**
- **Acesulfame K**
- **Aspartame**
- **Cyclamate**
- **Monk Fruit Extract**
- **Neotame**
- **Saccharin**
- **Stevia**
- **Sucralose**

Polyols

- **Erythritol**
- **Isomalt**
- **Lactitol**
- **Maltitol**
- **Mannitol**
- **Polyglycitol**
- **Sorbitol**
- **Xylitol**

Approved around the world



- **All sweeteners approved for use by JECFA have been thoroughly tested and ADIs established.**
- **Maximum use levels in foods and beverages ensure no consumer exceeds ADI for each sweetener.**
- **Use of new sweeteners & mixtures lowers risk of exceeding ADI.**

So if these sweeteners are safe, why is there controversy?



In most cases, controversy based on

- **Adverse effects seen in high dose animal experiments**
 - But are not relevant at ADI levels;
- **Experimental protocol not physiologically relevant;**
- **Associations in observational studies reported as causation.**

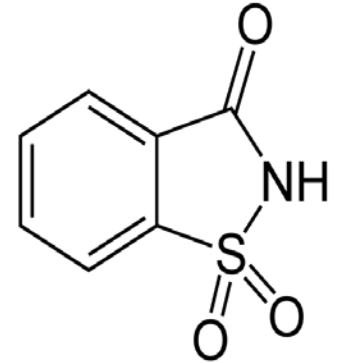
Good news (no effects) does not make interesting story so not told.

Adverse effects in high dose animal experiments not relevant at ADI levels

Examples:

- cyclamate and saccharin;
- early studies reported evidence of bladder cancer at high doses;
- extensive mechanism studies show does not occur at lower amounts and mechanism not relevant to humans because of difference in metabolism and excretion;
- included 24 yr study in monkeys showing no evidence of increased cancer.

Saccharin



- **Most (95%) absorbed in the small intestine;**
- **Absorbed saccharin is rapidly excreted in urine.**
- **Small amount (5%) to colon and excreted in feces.**
- **Clear evidence that not a carcinogen in humans**
- **April 2014 : Health Canada reviews safety and extends allowed uses**

- **ADI: 0-5 mg/kg/day**

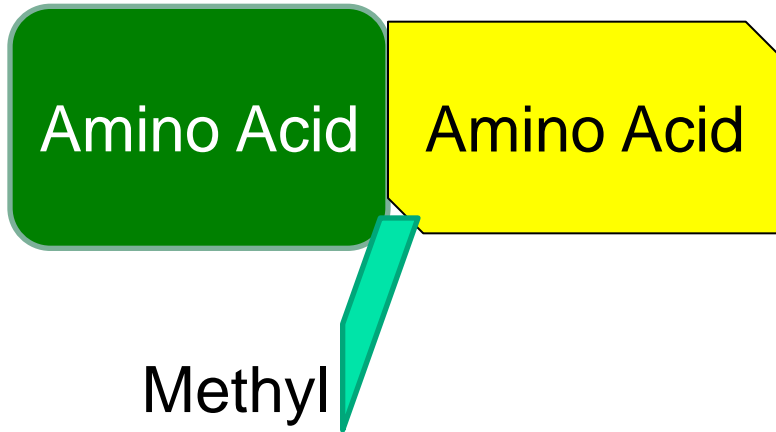
Majority of epidemiological studies find no association between low-calorie sweeteners & cancer

Author	Type of study (N)	Consumption	Conclusions
Olney (1996)	# brain tumors cases in US	Not measured	Increased after approval
Gurney (1997)	56 brain tumor cases 94 controls	Dietary recall - Personal interview	No association
Hardell (2001)	30 brain tumor cases 45 controls	Recall of low-calorie soft drinks.	No association
Bunin (2005)	315 child brain tumor cases, 315 controls	Food frequency by mothers	No association
Lim (2006)	Prospective 473,984 subjects, 5 yr. Hematopoietic and brain cancers	Food frequency questionnaires	No associations
Gallus (2007)	Case control; various cancers (8976 cases, 7028 controls)	Food frequency questionnaires	No association
Bosetti (2009)	Case control; various cancers (1010 cases, 2107 controls)	Food frequency questionnaires	No association
Schernhammer (2012)	Prospective: 22 yr. Nurses' Health (77,218 F); Health Professionals (47,810 M). Hematopoietic cancers	Food frequency questionnaires every 4 years	No association when combined cohorts. Weak positive with separate
McCullough (2014)	Prospective: 10 yr. Cancer Prevention cohort; (100,442 M&F) Non-Hodgkin lymphoma	Food frequency questionnaires every 2 years	No association with aspartame or diet beverage consumption

Experimental protocol not physiologically relevant

- **Example:**
- **Studies where sweetener added directly to cells or injected into animals.**
 - Bypass effect of digestion and absorption (or lack of absorption).
 - Very important for aspartame, steviol glycosides and sucralose.

What is Aspartame?



About 200 X sweetening potency as sugar.

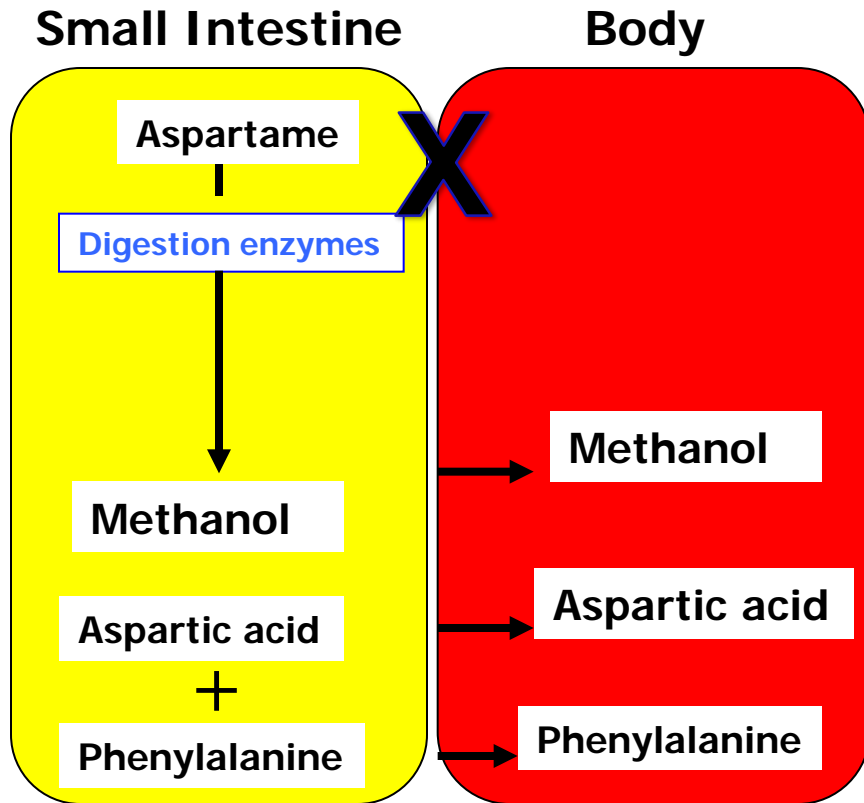
**JECFA ADI:
0-40 mg/kg/day**

Structure: 2 amino acids & methyl group

- Aspartic acid (aspartate)
- Phenylalanine

These are commonly found in foods!

Aspartame digestion







Aspartame does not enter the body as a whole.

Just like foods and proteins, aspartame is completely digested in intestine by digestion enzymes.

Components of digestion of aspartame are same as from other foods.

Other dietary sources of aspartame digestion products

Food	Phenylalanine (mg)	Aspartic acid (mg)	Methanol (mg)
Aspartame-sweetened Soft drink (340 ml) 	90	72	18
Non-fat milk (340 ml) 	606	953	-
Tomato Juice (340 ml) 	58	346	107
Orange juice (340 ml) 	24	180	23

How many servings to reach the safe level established by JECFA?

Food/Beverage	Adult 70 kg	Child 23 kg
Carbonated soft drink (12 oz.)	16	5
Powdered drink (8 oz.)	26	9
Gelatin dessert (4 oz.)	34	11
Tabletop sweetener (packet)	80	26

Aspartame Review by Food Safety Experts of new studies

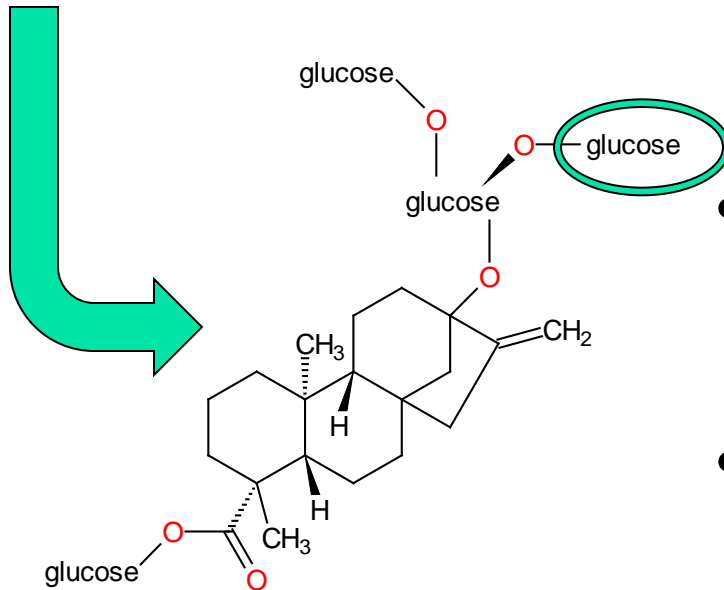
- Aspartame has been officially extensively reviewed **6 times** since first approved!
- Most recent – 2013
- Each time concluded:
 - Use of aspartame is safe
 - Including for pregnant women
 - No need to conduct further studies.

Reviewed by EU SCF and EFSA 1997, 2002, 2006, 2009, 2011, 2013; Magnuson and coauthors, 2007.

Stevia extracts

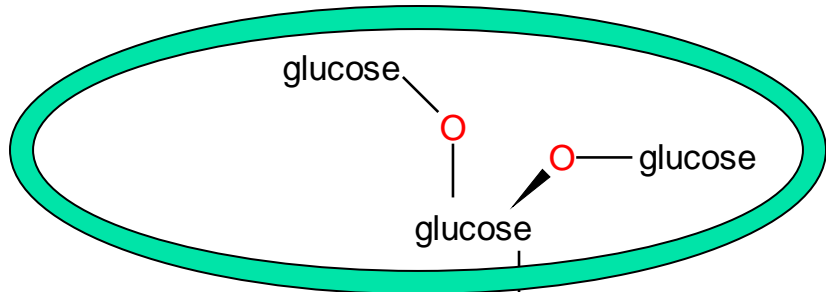


Extraction
and
purification

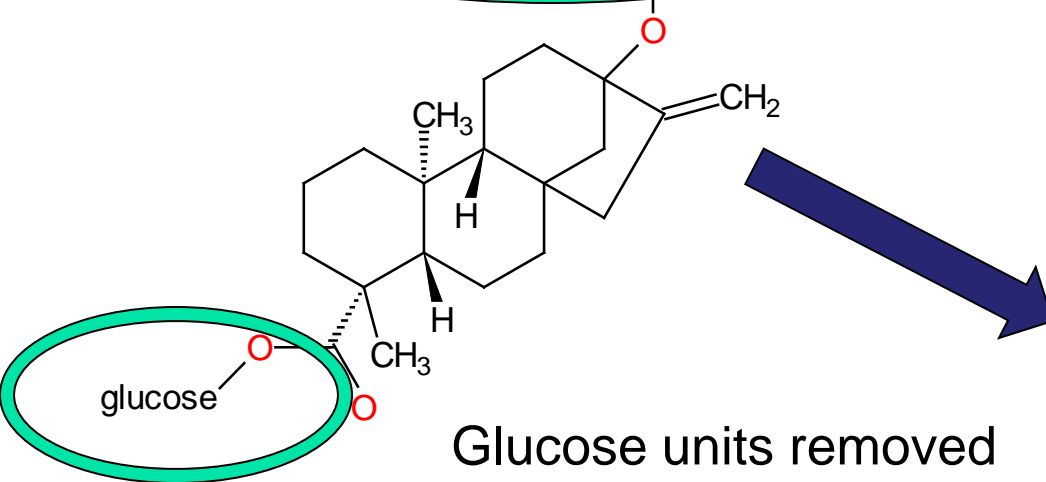


- Purified extracts from the leaves of the South America shrub - *Stevia rebaudiana*;
- Sweetness comes from steviol glycosides, such as rebaudioside A;
- Purified glycosides are 30-300x sweet as sugar;
- Glycosides contain glucose molecules.

Steviol glycosides: metabolism

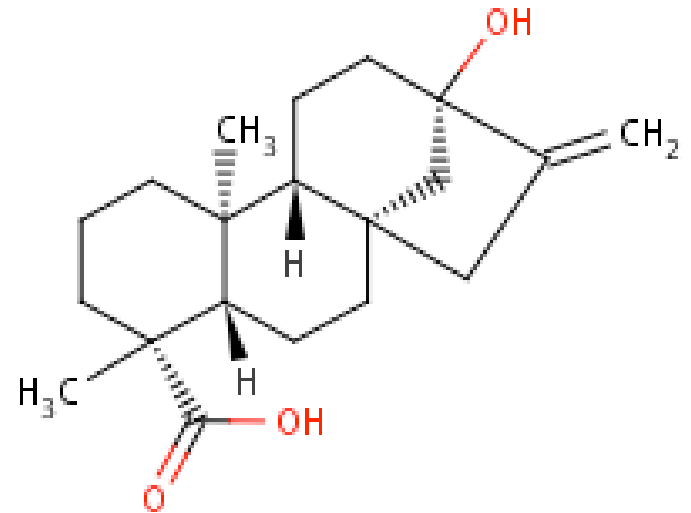


Steviol glycosides are not absorbed.



Glucose units removed by bacteria in large intestine. Time varies for different glycosides. All metabolized to steviol backbone.

Steviol



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

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

- **Reb A is 200-300 sweeter than sugar**

ADI = 0 - 4 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

Sucralose

- **Structure similar to sugar, but 600X sweeter.**
- **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**

JECFA assessment of sucralose

<http://apps.who.int/food-additives-contaminants-jecfa-database/PrintPreview.aspx?chemID=2340>

Experimental protocol not physiologically relevant

- **Example:**
- **Recent study on effect of artificial sweeteners on gut microbiota**
 - Protocol resulted in significant changes in total diet intake in mice; not considered.
 - Extensive well-controlled human clinical studies showing sweeteners do not effect blood glucose response.



Do low-calorie sweeteners increase appetite? body weight?

Answer – No!



- Hypothesis based on observational studies showing positive correlations between low-calorie sweeteners and body weight.
- Cause or result?
- **Association does not establish CAUSE!**

Studies conclude low-calorie sweeteners do not cause weight gain

- Meta-analysis: 16 studies assessing effect of aspartame on weight loss, found using foods and drinks sweetened with aspartame instead of sucrose results in a significant reduction in both energy intakes and body weight (de la Hunty *et al.*, 2006).
- No evidence that low-calorie sweeteners are cause of higher body weights in adults (Anderson *et al.*, 2012).
- Short-term randomized controlled trials find low-calorie sweetener use is BMI neutral or weight-reducing in overweight/obese adolescents. Long-term data are lacking (Foreyt *et al.*, 2012).

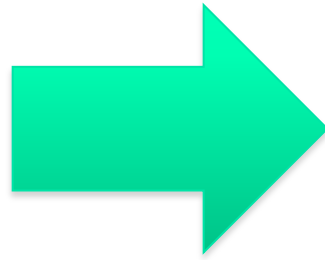
Meta-Analysis of Randomized Controlled Trials and Prospective Cohort Studies on LCS and Body Weight

15 randomized controlled trials (RCTs) and 9 prospective trials analyzed

- **RCTs:** LCS were significantly **associated with reduced** body weight, BMI, fat mass and waist circumference
- **Prospective trials:** modest **positive association** between consumption of LSC and changes in BMI with no significant associations for weight gain or fat mass

Conclusion: RCT demonstrate that substituting LCS for sugar modestly reduces body weight, BMI, fat mass, and waist circumference.

Conclusions on Benefits



Well-conducted clinical studies have shown that weight loss and weight maintenance is more successful with use of low-calorie sweeteners.

Conclusions on Safety

A large body of evidence is required to support safety, and is critically reviewed by health authorities.

All approved sweeteners are safe.

No evidence of adverse effects of non-nutritive sweeteners at levels of human consumption, by even highest users.

Thank you!

For More Information

- CalorieControl.org
- Acesulfamek.org
- Aspartame.org
- Cyclamate.org
- Fructose.org
- Polyol.org
- Saccharin.org
- Steviabenefits.org
- Sucralose.org



The Calorie Control Council