

1. **What have studies shown about a possible association between specific artificial sweeteners and cancer?**

**Saccharin**

Studies in laboratory rats during the early 1970s linked saccharin with the development of bladder cancer. For this reason, Congress mandated that further studies of saccharin be performed and required that all food containing saccharin bear the following warning label: "*Use of this product may be hazardous to your health. This product contains saccharin, which has been determined to cause cancer in laboratory animals.*" Subsequent studies in rats showed an increased incidence of urinary bladder cancer at high doses of saccharin consumption, especially in male rats. However, mechanistic studies (studies that examine how a substance works in the body) have shown that these results apply only to rats. Human epidemiology studies (studies of patterns, causes, and control of diseases in groups of people) have shown no consistent evidence that saccharin is associated with bladder cancer incidence.

Because the bladder tumors seen in rats are due to a mechanism not relevant to humans, and because there is no clear evidence that saccharin causes cancer in humans, saccharin was delisted in 2000 from the U.S. National Toxicology Program's *Report on Carcinogens*, where it had been listed since 1981 as a substance reasonably anticipated to be a human carcinogen (a substance known to cause cancer). More information about the delisting of saccharin is available at <http://ntp.niehs.nih.gov/ntp/roc/eleventh/append/appb.pdf> on the Internet. The delisting led to legislation, which was signed into law on December 21, 2000, repealing the warning label requirement for products containing saccharin.

**Aspartame**

Aspartame, distributed under several trade names (e.g., Nutrasweet® and Equal®), was approved in 1981 by the FDA after numerous tests showed that it did not cause cancer or other adverse effects in laboratory animals. Questions regarding the safety of aspartame were renewed by a 1996 report suggesting that an increase in the number of people with brain tumors between 1975 and 1992 might be associated with the introduction and use of this sweetener in the United States. However, an analysis of then-current NCI statistics showed that the overall incidence of brain and central nervous system cancers began to rise in 1973, 8 years prior to the approval of aspartame, and continued to rise until 1985. Moreover, increases in overall brain cancer incidence occurred primarily in people age 70 and older, a group that was not exposed to the highest doses of aspartame since its introduction. These data do not establish a clear link between the consumption of aspartame and the development of brain tumors.

Recently, a laboratory experiment found more lymphomas and leukemias in rats fed very high doses of aspartame (equivalent to drinking 8 to 2,083 cans of diet soda daily) (1). However, there were some inconsistencies in the findings. For example, the cancers found in the treated rats were not specific to aspartame, and the number of cancer cases did not rise with increasing amounts of aspartame as would be expected. Subsequently, the NCI examined human data from the NIH-AARP Diet and Health Study of over half a million retirees. Increasing consumption of aspartame-containing beverages was not associated with the development of lymphoma, leukemia, or brain cancer (2). More information about aspartame can be found in the *FDA Statement on Aspartame*, which is available at <http://www.cfsan.fda.gov/~lrd/tpaspart.html> on the Internet.

**Acesulfame potassium, Sucralose, and Neotame**

In addition to saccharin and aspartame, there are three other artificial sweeteners currently permitted for use in food in the United States. Acesulfame potassium (also known as ACK, Sweet One®, and Sunett®) was approved by the FDA in 1988 for use in specific food and beverage categories, and was later approved as a general purpose sweetener (except in meat and poultry) in 2002. Sucralose (also known as Splenda®) was approved by the FDA as a tabletop sweetener in 1998, followed by approval as a general purpose sweetener in 1999. Neotame, which is similar to aspartame, was approved by the FDA as a general purpose sweetener (except in meat and poultry) in 2002. Before approving these sweeteners, the FDA reviewed more than 100 safety

studies that were conducted on each sweetener, including studies to assess cancer risk. The results of these studies showed no evidence that these sweeteners cause cancer or pose any other threat to human health.

### **Cyclamate**

Because the findings in rats suggested that cyclamate might increase the risk of bladder cancer in humans, the FDA banned the use of cyclamate in 1969. Upon the reexamination of cyclamate carcinogenicity and the evaluation of additional data, scientists concluded that cyclamate was not a carcinogen or a co-carcinogen (a substance that enhances the effect of a cancer-causing substance). A food additive petition is currently filed with FDA for the reapproval of cyclamate. The FDA's concerns about cyclamate are not cancer related.

## **2. Where can people find additional information about artificial sweeteners?**

For more information about artificial sweeteners, contact the FDA at:

Address: 5600 Fishers Lane  
Rockville, MD 20857

Telephone: 1-888-INFO-FDA (1-888-463-6332)

Internet Web site: <http://www.fda.gov/>

### **Selected References**

1. Soffritti M, Belpoggi F, Esposti DD, et al. First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats. *Environmental Health Perspectives* 2006; 114(3):379-385.
2. Lim U, Subar AF, Mouw T, et al. Consumption of aspartame-containing beverages and incidence of hematopoietic and brain malignancies. *Cancer Epidemiology Biomarkers Prevention* 2006; 15.

## **Aspartame - Other Sweeteners**

Many people want to know what other artificial sweeteners they can safely use instead of aspartame. My first recommendation is NOT to use any chemical sweeteners at all, but merely use natural sugars or learn to adjust to the natural sweetness of raw foods themselves.

I have provided a list of alternative artificial sweeteners available on the market today, even though I am not recommending their use over natural sweeteners. I do recommend them above aspartame, nonetheless, as their side effects are less harmful to human health.

The best thing to do is avoid all artificial and chemical sweetener substitutes. They have NO food value, trick the body into thinking it is eating something sweet, and they have by-products of harmful toxic side effects. And remember that aspartame was discovered as an ulcer drug, not a sweetener. Every diet drink you used to drink was a dose of medication .

#### **Aspartame Information:**

- [Aspartame Side Effects](#)
- [Aspartame Case Histories](#)
- [Artificial Sweeteners](#)
- [Phenylalanine](#)
- [Phenylketonuria](#)

#### **Aspartame Detoxification:**

- [How to Detox](#)
- [Read about SweetPoison](#)
- [Contact Janet Hull](#)

## **Information on Aspartame and Other Chemical Sweeteners:**

## Acesulfame K

Acesulfame Potassium (K) was approved for use by the FDA as a safe artificial sweetener in July, 1988. It is a derivative of acetoacetic acid. Unfortunately, several potential problems associated with the use of acesulfame have been raised. They are based largely on animal studies since testing on humans remains limited. The findings showed the following:

Acesulfame K stimulates insulin secretion in a dose dependent fashion thereby possibly aggravating reactive hypoglycemia ("low blood sugar attacks").

Acesulfame K apparently produced lung tumors, breast tumors, rare types of tumors of other organs (such as the thymus gland), several forms of leukemia and chronic respiratory disease in several rodent studies, even when less than maximum doses were given. According to the Center for Science in the Public Interest, it was petitioned on August 29, 1988 for a stay of approval by the FDA because of "significant doubt" about its safety.

Dr. H.J. Roberts, Aspartame (NutraSweet) Is It Safe?, Charles Press, page 283/84.

## Aspartame (commonly misspelled as aspartame)

Aspartame, a dipeptide of aspartic acid and a methyl ester of phenylalanine, is approved for use in pharmaceutical products and is being used increasingly in chewable tablet and sugar-free formulations. Labels for both prescription and nonprescription products must include the phenylalanine content. The major consideration in the use of aspartame in children is in patients with autosomal recessive phenylketonuria. Although heterozygotes do not appear to have clinically significant increases in phenylalanine after ingestion of even large amounts (equivalent to 24 12-oz cans of diet beverages), homozygotes with strict dietary restrictions should avoid aspartame. Children without dietary restrictions could safely ingest 10 mg/kg/d. [37-40]. Dietary consumption of aspartame is typically less than 5 mg/kg/d[41]; young children, however, could ingest considerably more. For example, a 2-year-old child weighing 12 kg consumes 17 mg/kg from drinking one 12-oz can of diet soda and one serving of a sweetened product (eg, cereal, pudding, gelatin, or frozen dessert).

Headache is the most common adverse side effect attributed to aspartame but is seldom confirmed by single-dose double-blind challenge. Up to 11% of patients with chronic migraine headaches reported headaches triggered by aspartame; however, a double-blind challenge with three doses of 10 mg/kg given every 2 hours triggered no more headaches than did placebos in patients with vascular headaches believed to be exacerbated by aspartame. A small, double-blind 4-week trial showed an increase in frequency of headaches after ingestion of 1200 mg/d, indicating that a longer challenge period may be necessary.

In anecdotal reports, aspartame has been linked to various neuropsychiatric disorders, including panic attacks, mood changes, visual hallucinations, manic episodes, and isolated dizziness. A small, double-blind crossover study of patients with major depression revealed a higher incidence of reactions in these patients compared with nondepressed volunteers after administration of 30 mg/kg for 7 days; symptoms included headache, nervousness, dizziness, memory impairment, nausea, temper outbursts, and depression. None of these conditions has been rigorously proven to be caused by aspartame, but carefully conducted double-blind challenges may be indicated in patients with histories that suggest aspartame as a cause. Patients with underlying mitral valve prolapse or affective disorders may be at increased risk for neuropsychiatric effects; several studies have shown that individuals without psychiatric or seizure disorders do not demonstrate these effects.

Seizures have been reported via passive surveillance data collected by the FDA and in a few case reports. A recent analysis of FDA reports showed 41 cases of rechallenge with a temporal relationship to aspartame consumption. Most seizures occurred in patients who had an acceptable dietary intake, except for a 16-year-old who ingested up to 57 mg/kg of aspartame. Aspartame is generally considered safe for children with epilepsy. One study found increased spike-wave discharges in children with untreated absence seizures after a high dose of aspartame and suggested that children with poorly controlled absence seizures avoid aspartame.

## Saccharin

Foods containing saccharin no longer carry a label stating that the "use of this product may be hazardous to your health ...contains saccharin which has been determined to cause cancer in laboratory animals." This warning was lifted in 2001 by the American FDA as saccharin no longer has been connected to cancer in human beings.

Saccharin may be present in drugs in substantial amounts. Ingestion of the recommended daily dosage of chewable aspirin or acetaminophen tablets in a school-age child would provide approximately the same amount of saccharin contained in one can of a diet soft drink. This amount, relative to the body weight of a child younger than 9 or 10 years, ingested for prolonged periods would be considered as "heavy use," as defined in a major large-scale FDA/National Cancer Institute epidemiologic study. In this study, heavy use of artificial sweeteners was associated with a significantly increased risk for the development of bladder cancer. An independent review of this study concluded that there was no association. An investigation of saccharin performed by the American Medical Association in 1985 concluded that bladder changes were species-specific, were confined to the second generation of male rats, and occurred in association with large doses (equivalent to several hundred cans of diet soft drink per day). The no-effect level was equivalent to 500 mg/kg/d.[68,69] Saccharin is not genotoxic; the presumed mechanism of toxicity is the binding of saccharin to urinary proteins (not normally found in humans), creating a nidus for the formation of silicate crystals, which are cytotoxic to bladder epithelium.

Saccharin is an O-toluene sulfonamide derivative and causes similar dermatologic reactions. Cross-sensitivity with sulfonamides has been demonstrated; therefore, children with "sulfa" allergy should also avoid saccharin. Hypersensitivity can usually be confirmed by a radioallergosorbent test for saccharin. In a series of 42 patients with adverse effects resulting from consumption of saccharin in pharmaceutical agents, pruritus and urticaria were the most common reactions, followed by eczema, photosensitivity,

and prurigo. Other reactions include wheezing, nausea, diarrhea, tongue blisters, tachycardia, fixed eruptions, headache, diuresis, and sensory neuropathy.

Ingestion of saccharin-adulterated milk formula by infants was associated with irritability, hypertonia, insomnia, opisthotonos, and strabismus, which resolved within 36 hours after ingestion. Two anecdotal reports of an accidental overdose in an adult and a child discussed reactions of generalized edema, oliguria, and persistent albuminuria. Because of the paucity of data on the toxicity of saccharin in children, the American Medical

Association has recommended limiting the intake of saccharin in young children and pregnant women.

## Sucralose

Splenda, also known as sucralose, is an artificial sweetener, which is a chlorinated sucrose derivative. Facts about this artificial chemical are as follows:

### Pre-Approval Research

Pre-approval research showed that sucralose caused shrunken thymus glands (up to 40% shrinkage) and enlarged liver and kidneys.

### Recent Research

A possible problem with caecal enlargement and renal mineralization has been seen in post approval animal research.

### Sucralose Breaks Down

Despite the manufacturer's mis-statements, sucralose does break down into small amounts of 1,6-dichlorofructose, a chemical which has not been adequately tested in humans. More importantly, sucralose

must break down in the digestive system. If it didn't break down and react at all (as the manufacturer claims), it would not chemically-react on the tongue to provide a sweet taste. The truth is that sucralose does break down to some extent in the digestive system.

Independent, Long-Term Human Research

None. Manufacturer's "100's of studies" (some of which show hazards) were clearly inadequate and do not demonstrate safety in long-term use.

Chlorinated Pesticides

The manufacturer claims that the chlorine added to sucralose is similar to the chlorine atom in the salt (NaCl) molecule. That is not the case. Sucralose may be more like ingesting tiny amounts of chlorinated pesticides, but we will never know without long-term, independent human research.

Conclusion

While it is unlikely that sucralose is as toxic as the poisoning people are experiencing from Monsanto's aspartame, it is clear from the hazards seen in pre-approval research and from its chemical structure that years or decades of use may contribute to serious chronic immunological or neurological disorders.

It is very important that people who have any interest in their health

stay aware from the highly toxic sweetener aspartame and other questionable sweeteners such as sucralose (Splenda), and acesulfame-k (Sunette, Sweet & Safe, Sweet One). Please see the extensive resources for sweeteners on the Healthier Sweetener Resource List. <http://www.holisticmed.com/sweet/>

<http://www.holisticmed.com/splenda/>

Mark D. Gold [mgold@holisticmed.com](mailto:mgold@holisticmed.com)

Aspartame Toxicity Information Center

35 Inman St., Cambridge, MA 02139 617-497-7843

<http://www.HolisticMed.com/aspartame/>

## Stevia

Another sweetener, stevioside, is championed by natural-foods advocates in the United States and is used in several countries, most notably Japan. Stevioside comes from the leaves of the stevia plant (*Stevia rebaudiana* Bertoni), a perennial shrub of the Asteraceae (Compositae) family native to Brazil and Paraguay. Stevia contains sweet-tasting glycosides, mainly stevioside; but also rebaudiosides A, B, C, D, and E; dulcoside A; and

steviolbioside. Stevioside has a slight bitter aftertaste and provides 250 to 300 times the sweetness of sugar. It is stable to 200°C (392°F), but it is not fermentable and does not act in browning reactions.

In the 1970s, the Japanese government approved the plant for use in food. Japanese food processors use stevioside in a wide range of foods: pickled vegetables, dried seafood, soy sauce and miso, beverages, candy, gums, baked goods and cereals, yogurt, ice cream, and as a tabletop sweetener. In salty applications, stevioside modifies the harshness of sodium chloride. Combining it with other natural and synthetic sweeteners improves taste and functionality.

FDA considers stevia leaves and stevioside as unapproved, non-GRAS food additives. In 1992, the American Herbal Products Association (AHPA) petitioned the FDA to declare stevia as GRAS, citing historical usage and referring to numerous toxicology studies conducted in Japan and other countries. The FDA rejected AHPA's petition, contending inadequate evidence to approve the product. The agency does allow the herb to be used in dietary supplements as covered by DSHEA (Dietary Supplement Health and Education Act).

## Tagatose

From the manufacturer's web page.

It looks like sugar, tastes like sugar, cooks like sugar... well technically, it is sugar. But it's sugar with almost no calories. It's 100-percent natural - not synthesized, unlike other "sweeteners" that are chemically synthesized or derived from sugar, Tagatose is a naturally occurring sugar. And SPHERIX has discovered and patented a way to make it available for use as a food additive as well as for a variety of other uses.

It's Tagatose, the only sweetener that tastes, looks, feels, and performs like table sugar. Tagatose can supply a major need for baked goods, ice cream, chocolates, chewing gum, and other food products that can't be met by low bulk of high-intensity sweeteners. And it's safe, with over ten years of safety research and numerous consultancies and world-renowned scientists reviewing the product. Scientifically known as D-tagatose, Tagatose occurs naturally in some dairy products and other foods. Our patented production process starts from whey, a dairy by-product. Tagatose has been determined to be a Generally Recognized As Safe (GRAS) substance in the U.S., with the FDA affirming the green light for the product with its "no objection" opinion, permitting its use in foods and beverages. Tagatose has also been determined GRAS for use in cosmetics and toothpastes, as well as in drugs.

About Tagatose: IS IT SAFE OR NOT?

BIOSPHERICS HAS HIGH HOPES FOR SWEETENER

April 16, 2001

Washington Post

Page E01

Jerry Knight

<http://www.washingtonpost.com/wp-dyn/articles/A21621-2001Apr15.html>

Last week was, according to this story, a long time coming for Gilbert Levin, the 76-year-old chairman of Biospherics Inc. After almost a decade of study, a panel of medical experts declared that an obscure low-calorie form of sugar that Levin has latched onto is safe to use in food.

The story says that Biospherics has collected \$2.5 million by licensing rights to make the sugar to a Scandinavian dairy cooperative, but the food safety panel's decision has the potential to open the spigot on what could become a gushing stream of royalty revenue on every pound of the product that goes into any food.

It'll be at least two years before consumers can eat anything sweetened with the stuff, but investors didn't wait to buy Biospherics stock. The story also notes there is no way of predicting whether food manufacturers will be as excited as Levin is about the sweetener called tagatose. It's a natural product, a chemical cousin of familiar sugars such as sucrose, fructose, dextrose and lactose. Tagatose, like table sugar, is a white crystal; it is 90 percent as sweet as ordinary sugar, but has one-third the calories.

Tagatose could be the product that converts Biospherics into what most people have always thought it was: a biotech company.

The story goes on to say that tagatose is most closely related to fructose, the sugar that's in honey, fruits and corn, Levin explained in an interview Friday. The chemical formulas for fructose and tagatose are identical. The two molecules look the same, but in tagatose, one atom of carbon juts off to the left of the main structure instead of off to right as it does in fructose.

Left-leaning sugars have fascinated Levin for more than 20 years. He first got interested in one that is a mirror image of table sugar. Think of the sugar molecule as a coil that curls around to the right. A backward sugar molecule that turns to the left was Levin's first interest. Levo-sugar it's called, for left-handed.

Levo-sugar is a confusing chemical to the human body. To the tongue, it tastes just like regular sugar. But the body has never swallowed left-handed sugar and can't digest it.

Levin spent the better part of the 1980s tinkering with left-handed sugar, attracting a lot of attention to Biospherics stock, but ultimately leaving a bad taste in the mouths of investors. The problem was that the company was never able to find a way to make left-handed sugar at a low enough price to give the company a high stock price. Every once in a while, Biospherics would announce some development in sweetener research, the stock would jump, and then it would drift back down.

The pattern continued in the 1990s after Levin shelved levo-sugar and shifted his team of researchers to tagatose.

The result has been an erratic stock with poor long-term performance. A \$100 investment in Biospherics on Dec. 31, 1995, had grown in value to \$151 at the end of 1998, but by the end of last year was back to \$111. As a benchmark, a \$100 investment in a Standard & Poor's 500-stock index mutual fund was worth \$232 at the end of last year.

The story also goes on to say that unlike drugs, foods don't have to be tested on humans, Levin explained. But Biospherics obtained a Maryland Industrial Partnership grant to finance human studies at the University of Maryland Medical School, which produced promising results for potential use by diabetics.

Diabetics can eat foods sweetened with tagatose without getting the unhealthful changes in their blood glucose levels that are caused by eating sugar.

The studies did, however, find that patients who consumed large amounts of tagatose experienced gastrointestinal distress, including diarrhea, nausea and flatulence. The intestinal problems apparently result because most tagatose passes through the digestive tract without being absorbed -- a key reason why it's lower in calories.

Those lower-bowel symptoms weren't a problem for most people who ate small amounts of the sweetener and Levin said he does not expect the reaction to be a problem for the uses Arla has in mind for tagatose.

<http://www.emedicine.com/MED/topic1653.htm>

Also, preliminary reports exist of the potential utility of agents that impede dietary carbohydrate absorption. Tagatose is one of the agents in this class undergoing trials.

The newest artificial sweetener on the block is sucralose (SPLENDA). It is not affected by heat and retains its sweetness in hot beverages, baked goods, and processed foods. This has some advantages, Roxland says. "Nutrasweet can't be stored for long periods and you can't cook with it, but Splenda is heat stable so you can use it in cooking."

There are others in the pike including alitame (brand name Aclame™), which is 2,000 times sweeter than sucrose. A petition for its use in a broad range of foods and beverages has been filed in the U.S.

Another sweetener is Cyclamate, which is a 30 times sweeter than sucrose but as such it has the least "sweetening power" of the commercially acceptable intense sweeteners. It was banned in the U.S. in 1970, but currently there is a petition at the FDA for reapproval.

Dihydrochalcones (DHCs) are noncaloric sweeteners derived from bioflavonoids of citrus fruits that are approximately 300 to 2,000 times sweeter than sucrose.

Glycyrrhizin, a noncaloric extract of licorice root, is 50-100 times sweeter than sucrose. It is approved for use in the U.S. as a flavor and flavor enhancer.

Stevioside comes from leaves of a South American plant and is 300 times sweeter than sucrose. It is currently approved for use in 10 countries, including Japan, Paraguay, and Brazil. It can be sold in the U.S. as a dietary supplement only.

Another potential sweetener is Thaumatin (Talin™), a mixture of proteins from a West African fruit that's approximately 2,000-3,000 times sweeter than sucrose. In the U.S., it's approved as a flavor enhancer for beverages, jams and jellies, condiments, milk products, yogurt, cheese, instant coffee and tea, and chewing gum.

Originally published March 25, 2005.

Medically updated on Nov. 1, 2006.