The Safety of Artificial Sweeteners

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Introduction

There are four non-nutritive, artificial sweeteners or alternative sweeteners commonly used in the United States and Canada - acesulfame (*Sunette*), aspartame (*Equal, NutraSweet*), saccharin (*Sweet 'N Low*), and sucralose (*Splenda*).1,2 These agents are used by millions of people each day. However, these sweeteners have received negative publicity over the years. They have been blamed for many ailments including cancer, brain tumors, brain damage, seizures, chronic fatigue syndrome, lupus, multiple sclerosis, and many others.3,4 However, a review of the literature does not support causality between these artificial sweeteners and serious adverse effects [Evidence level B; lower quality RCT, clinical cohort studies, historical control studies, epidemiologic studies].

Saccharin

Saccharin has been available for over 100 years. It is 300 times sweeter than sugar.2,4 Saccharin was used extensively during both World Wars, since sugar was scarce. However, in the 1970's, the Food and Drug Administration began to review this substance previously considered "generally recognized as safe" or GRAS.4,5 Studies performed in the early 1970's on rats fed large amounts of saccharin raised concerns about bladder cancer. Later, it was thought that bladder cancer was due to impurities in the product rather than the saccharin itself. But, in 1977, a Canadian study showed that it was the saccharin that was responsible for bladder cancer. The FDA proposed withdrawing saccharin from the market, but was met with public resistance. Proponents of saccharin pointed out that the dose of saccharin used in the study that found a link between saccharin and bladder cancer was much higher than the expected daily intake by humans. As an intermediate step, Congress proposed a two-year moratorium on any ban of the sweetener. This act also required the labeling (which has since been removed), "Use of this product may be hazardous to your health." This act has been repeatedly renewed and saccharin has remained on the market.4,5

The National Cancer Institute has stated that "epidemiologic studies do not provide clear evidence" to an association with cancer in humans. In addition, the National Toxicology Program removed saccharin from its list of "anticipated carcinogens" in 2000 because "extensive review determined that the rodent cancer data are not sufficient to meet the current criteria..."5,6 Finally, many authoritative organizations including the American Diabetes Association, American Dietetic Association, American Cancer Society, and American Medical Association support the safety of saccharin.1,4,6

Aspartame

Aspartame has been available in the United States and Canada since 1981.7,8 It is 180 to 200 times sweeter than sugar.4,9 It is available as a tabletop sweetener and is also included in many products including beverages, chewing gum, desserts, and cereals. It is made by chemically reacting the amino acids phenylalanine and aspartic acid. The Food Directorate of Health Canada has established an acceptable daily intake of 40

mg/kg of body weight per day and the FDA has set an acceptable daily intake of 50 mg/kg of body weight per day.5,8 In order to assess common intake levels, 5,200 Canadian households were monitored for their aspartame intake and the actual consumption was found to be significantly lower than the acceptable daily intake.8

There are allegations that aspartame leads to cancer, brain tumors, seizures, multiple sclerosis, hair loss, dementia, behavioral disturbances in children, and allergic reactions. None of these allegations has ever been proven in clinical trials.2,4,7-10 In addition, some claim that since aspartame is metabolized to methanol, it is toxic. However, small amounts of methanol are part of the normal diet. In fact, many fruits and vegetables are metabolized to small amounts of methanol. The amounts produced from aspartame and fruits and vegetables are too small to cause any harm. Methanol does not accumulate in the body but rather is serially metabolized to formaldehyde, to formic acid, and finally to water and carbon dioxide.8

One disadvantage of aspartame is that it can degrade when heated. When aspartame is exposed to heat in a liquid, it breaks down to diketopiperazine. However, animal toxicity studies show that even if 100% of the aspartame contained in a beverage was broken down, the amount of diketopiperazine would still be well below the FDA acceptable daily intake amount.5

In conclusion, aspartame has been thoroughly tested and studied by both the FDA and Health Canada and found to be safe.4,8,9

However there is one specific population in whom aspartame should be avoided; people with the condition phenylketonuria or PKU, a disorder of amino acid metabolism. Accumulation of phenylalanine can lead to neurological, behavioral and dermatologic problems in this population. Since aspartame contains phenylalanine, patients with PKU should not use it.2-4

Acesulfame Potassium

Acesulfame potassium was approved in 1988.2,4 It is 200 times sweeter than sugar.4,9 While initially it was used as a tabletop sweetener, it is now found in many products such as beverages, candy, and baked goods. It is often combined with other sweeteners such as aspartame. Benefits include a long shelf life and the ability to use it in cooked or baked foods.2,4

As with the other artificial sweeteners, rumors about the link between acesulfame potassium and cancer continue to surface.11 Acesulfame potassium has been extensively studied and was found to be safe.1,4 The acceptable daily intake is 15 mg/kg of body weight per day. However, since it is so much sweeter than sugar, only minimal amounts are needed to sweeten foods and it is estimated that daily intake is only about 20% of the acceptable amount.5

Sucralose

Sucralose is 600 times sweeter than sugar.4,9 It was approved for use in 1998 in the U.S. and 1992 in Canada.2,4 It is used as a tabletop sweetener as well as in desserts and beverages. It is available in a granular form and can be used in cooking and baking. It is made from sugar, by replacing three hydroxyl groups with chlorine atoms. Less than

25% of the dose is absorbed and the small amount that is absorbed is excreted unchanged in the urine.2,4

Rumors on the internet highlight the fact that sucralose is made by substituting chlorine atoms on the sugar molecule making it a chlorocarbon similar to the pesticide DDT. The websites claim that chlorocarbons have long been famous for causing autoimmune diseases and organ, genetic, and reproductive damage.12 However, this oversimplification is flawed. Chlorine is naturally found in many foods, beverages, and drinking water. By adding chlorine atoms to sugar, it becomes inert and is not metabolized by the body. The chlorine in sucralose also makes it heat-stable so that it can be used in cooking and baking.13

Prior to approval in the U.S., it was evaluated in more than 110 studies and found to be safe in animals and humans. It did not cause cancer, reproductive abnormalities, or neurologic changes.4,5 While sucralose alone does not cause dental caries, the bulking agents that it is often mixed in may have cariogenic potential.2

Cyclamates

There are three chemical forms of cyclamate: cyclamic acid, calcium cyclamate, and sodium cyclamate. In 1969, on the basis of studies in which laboratory rodents developed cancer after being fed a 10:1 mixture of cyclamate: saccharin, the FDA banned cyclamates as a sweetener or for use in foods. Since 1970, cyclamates have been available in Canada only as a table-top sweetener. Health Canada requires a package statement that the sweetener be used only on the advice of a physician. In Canada, cyclamate is available under the brand name of *Sugar Twin*.14

Thaumatin

Thaumatin is another non-nutritive sweetener that is a plant protein derived from *Thaumatococcus daniellii.* It is not available in the U.S. but is available in Canada for use only in chewing gum, breath fresheners, and salt substitutes.14

Conclusion

In moderation, saccharine, aspartame, acesulfame potassium, and sucralose appear to be safe. The FDA and Health Canada have set acceptable daily intakes, and studies show that normal diets contain amounts of these sweeteners well below these intake values. While patients may experience idiosyncratic adverse effects such as headaches and insomnia, there does not appear to be a link between artificial sweeteners and serious adverse effects.

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