

Aspartame

A GUIDE FOR CONSUMERS,
POLICYMAKERS AND THE MEDIA



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The Association of Food, Beverage
and Consumer Products Companies

The **Grocery Manufacturers Association (GMA)** represents the world's leading food, beverage and consumer products companies. The association promotes sound public policy, champions initiatives that increase productivity and growth and helps to protect the safety and security of the food supply through scientific excellence. The GMA Board of Directors is comprised of chief executive officers from the Association's member companies. The \$2.1 trillion food, beverage and consumer packaged goods industry employs 14 million workers, and contributes over \$1 trillion in added value to the nation's economy. For more information, visit the GMA web site at www.gmaonline.org.

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TABLE OF CONTENTS

Foreword	1
Executive Summary	3
Introduction	5
Basic Facts About Aspartame	5
<i>What is Aspartame?</i>	5
<i>Regulatory Status</i>	5
<i>Consumption Levels</i>	6
<i>Uses in Foods and Beverages</i>	6
<i>Aspartame in the Body</i>	6
Diet and Health Benefits	6
<i>Dental Health</i>	6
<i>Weight Management</i>	7
Safety Evaluation	7
<i>Phenylketonuria</i>	8
<i>Cancer</i>	8
<i>Nervous System and Behavior</i>	8
<i>Headaches</i>	8
<i>Allergies</i>	9
<i>Diabetes</i>	9
Summary	10
References / Bibliography	11

FOREWORD

This paper addressing aspartame, a non-nutritive sweetener, is one in a series published by the Grocery Manufacturers Association (GMA) to evaluate and explore the science behind some of the most talked-about food-related issues of importance to consumers and policymakers.

The Grocery Manufacturers Association represents the world's leading food, beverage and consumer products companies. The Association promotes sound public policy, champions initiatives that increase productivity and growth, and helps to protect the safety and security of the food supply through scientific excellence. One of the Association's goals is to ensure that the laws and regulations governing food marketing and production are feasible, practical and based on sound information.

Each of our science policy articles includes a review of key scientific peer-reviewed published articles, regulatory considerations, food, beverage, and non-food consumer product applications, and market insights. The Association's goal in publishing these white papers is to provide current, scientifically accurate resources to journalists, health professionals, policy makers, interested consumers, and other stakeholders.

For more information, visit the Grocery Manufacturers Association web site at www.gmaonline.org/science/index.cfm. ■

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EXECUTIVE SUMMARY

Non-nutritive sweeteners, including aspartame, are used in a variety of food and beverage products. Today, aspartame is approved for use in more than 100 countries, including the United States, Canada, countries in the European Union, Japan, Australia and New Zealand. ^(1,2)

The aspartame database now contains more than 500 studies. It has been extensively studied in animals and humans since its discovery more than four decades ago. Few ingredients have been subject to the extent of research that has been conducted on aspartame. In addition to hundreds of individual studies on animals and humans, extensive literature reviews have been conducted to summarize the existing research. During more than three decades, research has shown aspartame to be safe. Despite certain pseudoscientific claims on the Internet, well-designed peer-reviewed research overwhelmingly shows that aspartame does not cause cancer, abnormal neural function, seizures, memory loss, headaches, diminished learning abilities or allergic reactions. (*Peer review is a process of subjecting research to scrutiny by experts and helps prevent the injection of unsubstantiated claims, conflict of interest and personal views in scientific literature.*)

It is the position of the American Dietetic Association that consumers can safely enjoy a range of nutritive and non-nutritive sweeteners when consumed in a diet that is guided by current federal nutrition recommendations, such as the *Dietary Guidelines for Americans* and the *Dietary References Intakes*, as well as individual health goals. ⁽³⁾ Beyond a well established safety track record, peer-reviewed studies have shown aspartame effective in helping people lose weight and reduce calorie intake. ⁽⁴⁾

This review summarizes scientific research, regulatory history, consumption and uses in foods and beverages, with attention to refuting misinformation commonly disseminated by a small but vocal group of anti-aspartame activists. Consumers deserve balanced, scientific information about non-nutritive sweeteners, including aspartame. The extensive peer-reviewed research over time, as well as regulatory agency and expert committee reviews, speaks to aspartame's safety as a non-nutritive sweetener. ■

INTRODUCTION

Aspartame was discovered in 1965 and after extensive pre-market safety and toxicology testing was approved by the U.S. Food and Drug Administration (FDA) in 1981. More than 30 years have passed since initial pre-market research began on aspartame, and since then the research database has grown to over 500 related studies.

Aspartame is a sweetening ingredient in approximately 6,000 food and beverage products worldwide. On average, aspartame consumption is only a fraction of the safe intake levels established by food safety authorities.

Regulatory authorities in more than 100 countries have approved aspartame for human consumption, and all major food safety authorities and expert committees have concluded aspartame is safe, including the Joint Expert Committee on Food Additives of the Food and Agricultural Organization/World Health Organization, Scientific Committee on Food of the European Commission, Health Canada, United Kingdom's Food Standards Agency, French Food Safety Agency and Food Standards Australia New Zealand.⁽⁵⁾ In fact, the FDA has affirmed the safety of aspartame 26 times over a period of 23 years.

Note about terminology: Non-nutritive sweeteners are also known as sugar substitutes, and the following adjectives are also used: low-calorie, non-caloric, artificial, alternative and high-intensity. In this paper, we use the term non-nutritive sweetener.

BASIC FACTS ABOUT ASPARTAME

What is Aspartame?

Aspartame is a non-nutritive sweetener used in a wide variety of foods and beverages, including low-calorie beverages, calorie-reduced foods and table-top sweeteners. Aspartame consists of two amino acids — phenylalanine and aspartic acid — linked to a methyl ester.⁽²⁾ Amino acids, including the two in aspartame, occur naturally in foods and in the human body, as building blocks of protein. Methanol, which can be derived from the methyl ester, also occurs naturally in many foods, such as fruits and fruit juices.

Aspartame was discovered accidentally by a scientist at G.D. Searle research laboratories who was working to develop a small protein molecule. An intermediate substance (later known as aspartame) spilled onto his hands, and he noticed an intense sweet taste when he later licked his fingers. In 1970, researchers proposed its use as an artificial sweetener.⁽²⁾

A white powder with no odor, aspartame is extremely sweet to humans — 160 to 220 times sweeter than table sugar.⁽³⁾ Because aspartame is so sweet, very little is needed to sweeten a food or beverage.

Regulatory Status

Aspartame is one of five non-nutritive sweeteners (others include acesulfame-potassium (or acesulfame-K), neotame, saccharin, and sucralose) that have been approved by the FDA.^(6, 26) After extensive safety tests, the FDA approved aspartame in 1981 for use as a sweetener in chewing gum and in dry form, for example, in cereals, pudding mixes and tabletop sweeteners). In 1983, the FDA expanded approval of aspartame uses to include beverages. In 1996, aspartame was approved by the FDA as a “general purpose” sweetener for all foods and beverages.⁽⁶⁾

During the review of sweeteners as potential food additives, the FDA considers the following:⁽³⁾

- How is it made?
- What are the properties of the sweetener in foods and beverages?
- How much of the sweetener will be consumed and will certain groups be particularly susceptible?
- Is the sweetener safe and does it cause adverse effects to the individual or offspring, including cancer or chronic toxicity?

Routine toxicology testing is used for approval of sweeteners and other food additives. Such testing establishes a safety limit for food additives that is expressed as the Acceptable Daily Intake (ADI): the estimated amount per body weight that a person can safely consume on an average day every day over a lifetime without risk. The ADI is set conservatively, typically 100 times below the maximum level at which no observed effects occur in animals.⁽²⁷⁾

The FDA established an ADI of 50 mg/kg body weight for aspartame. That level translates into a 165 pound (75 kg) person (average adult male) consuming about 21 12-ounce cans of aspartame-sweetened soft drinks daily over a lifetime.⁽⁷⁾ In Europe and Canada, the ADI for aspartame is set slightly lower, at 40 mg/kg of body weight per day.

Today, aspartame is approved for use in more than 100 countries, including the United States, Canada, countries in the European Union, Japan, Australia and New Zealand.^(1, 2) Aspartame has been extensively studied in animals and humans for more than two decades. In fact, the FDA has affirmed the safety of aspartame 26 times over a period of 23 years.

Consumption Levels

For each of the five approved sweeteners, including aspartame, estimated intakes are well below the ADI.⁽³⁾ Even among people who consume aspartame at the top 10 percent of population consumption (among the total U.S. population), their intake is below 3 mg/kg body weight per person per day, or only 6 percent of the FDA's ADI.⁽⁵⁾ Specific to diet beverage consumers, a study of approximately 285,000 men and 189,000 women conducted by the National Institutes of Health (NIH) showed average aspartame consumption to be about 7 percent of the ADI.⁽⁸⁾ Estimated intakes of non-nutritive sweeteners in children are well below the ADI, with aspartame intake averaging 10.4 percent of the ADI.⁽³⁾

Uses in Foods and Beverages

Aspartame is used as an ingredient in approximately 6,000 food and beverage products. In the United States, the largest use of aspartame is in low-calorie beverages.⁽²⁾ Aspartame also is used as an ingredient in breath mints, cereals, chewing gum, flavored water products, frozen ice cream novelties, fruit spreads, sugar-free gelatin, hard and soft candies, ice cream toppings, sugar-free ice creams, iced teas, jams and jellies, juice blends and juice drinks, nutritional bars, sugar-free puddings, table-top sweeteners and yogurts.⁽⁹⁾ In fact, aspartame may be found in virtually any product labeled “sugar-free” or “reduced sugar” and in many “low calorie,” “reduced calorie” or “calorie free” foods.

Aspartame is slightly soluble in water and alcohol but not in fats and oils. In dry form, aspartame is very stable, but it degrades in liquids and at high temperatures over time.

During the first years after approval, aspartame was sold exclusively by the patent holder under the brand name NutraSweet. Since the expiration of the patent in 1992, aspartame has been sold by several suppliers under different brand names.⁽¹⁰⁾

Aspartame in the Body

In the digestive system, aspartame breaks down into its three components — the two amino acids, aspartic acid and phenylalanine, and methanol — which are then absorbed into the body. Naturally occurring in other foods, these components are used in normal body functions.

Importantly, the milligram amounts of aspartic acid, phenylalanine and methanol that come from consuming aspartame are very small compared to what's ingested from other foods and beverages. The mean daily intake

from all foods and supplements is 6.5 grams for aspartic acid and 3.4 grams for phenylalanine.⁽¹¹⁾ Further, a serving of non-fat milk provides about six times more phenylalanine and 13 times more aspartic acid as compared to an equivalent amount of diet beverage sweetened only with aspartame.⁽³⁾ Likewise, a serving of tomato juice provides about six times more methanol compared to an equivalent amount of diet beverage with aspartame.⁽³⁾ Humans also produce methanol — approximately one gram daily from fruits and vegetables. In contrast, methanol generated from aspartame is about 0.033 grams/daily.⁽²⁾ Methanol metabolizes to formaldehyde, which is rapidly further metabolized. The body produces formaldehyde naturally and, in fact, humans produce and metabolize more than 50 grams of formaldehyde daily.⁽²⁾

DIET AND HEALTH BENEFITS

Sweeteners, whether caloric or non-caloric, add enjoyment to eating. Non-nutritive sweeteners, including aspartame, add sweetness with reduced energy to foods/beverages. By increasing palatability of nutrient-dense foods/beverages, sweeteners can promote diet healthfulness. And some studies have shown that individuals who use foods with non-nutritive sweeteners, as compared to those who do not, have significantly higher intakes of vitamins and minerals.⁽¹²⁾

It is the position of the American Dietetic Association that consumers can safely enjoy a range of nutritive and non-nutritive sweeteners when consumed in a diet that is guided by current federal nutrition recommendations, such as the *Dietary Guidelines for Americans* and the *Dietary Reference Intakes*, as well as individual health goals.⁽³⁾

Dental Health

Risk of dental caries is dependent on a number of factors, including frequency of meals, snacks and tooth-brushing, and consumption of fluoridated water. Carbohydrate-containing foods, including sugars, provide a substrate for the acid-producing bacteria that promote dental decay. However, non-nutritive sweeteners, including aspartame, do not promote dental caries.^(3, 28)

Weight Management

Concerning weight management, aspartame does not increase hunger or caloric intake in those who use it.^(2, 13) In fact, the use of non-nutritive sweeteners as a substitute for sucrose offers one way of helping people to reduce the energy density of their diet without adversely affecting taste acceptability. Researchers reviewed 15 studies to consider aspartame's impact on weight loss, weight maintenance and energy intakes in adults.⁽⁴⁾ The studies that examined the effect of substituting sugar with either aspartame alone or aspartame in combination with other non-nutritive sweeteners on energy intake or bodyweight were included in the review. The studies which used soft drinks as the vehicle for aspartame used about two to six cans or bottles of soft drinks every day. When comparing aspartame to sucrose, average calorie reduction was 10 percent. A significant reduction of about 3 percent was seen in bodyweight. Given that the weighted average study length was 12 weeks, the estimated rate of weight loss was around 0.2 kg/week for a 75-kg adult (about 0.5 pounds per week). Nevertheless, these compensation values are derived from short-term studies. More data are needed over the longer term to determine whether a tolerance to the effects is acquired. The meta-analyses of human studies demonstrate that using foods and drinks sweetened with aspartame instead of sucrose can result in a significant reduction in both energy intakes and bodyweight.

SAFETY EVALUATION

Typically, pre-market ingredient safety studies are conducted on animals rather than risk humans to exposure. Such was the case with aspartame prior to its approval in 1981. Many additional studies have been conducted since then. Few ingredients have been subject to the extent of research that has been conducted on aspartame.

Thus, over three decades of studies exist from animal toxicity studies to human epidemiological, clinical and case studies, which attest to the safety of aspartame. These safety studies have occurred around the world and aspartame's safety has been affirmed by FDA and international regulatory and scientific bodies.

Several scientific literature reviews have been conducted, including a recent review of more than 500 studies that was published in the September 2007 issue of the peer-reviewed journal *Critical Reviews in Toxicology*.⁽²⁾ The review was conducted by an international panel from ten universities and medical schools and included leading experts in the areas of toxicology, epidemiology, metabolism, pathology and biostatistics. Examining extensive research about aspartame and cancer, neurological func-

tion, reproductive health and behavior, the group concluded that no credible evidence exists that aspartame causes or promotes cancer or, in general, that aspartame in the diet has any impact on the nervous system, learning or behavior. The international panel's conclusions:

- Aspartame's metabolism is well understood and is similar to that of other common foods and ingredients. Aspartame consumption, even at levels much higher than that expected under typical circumstances, has virtually no impact on levels of other blood constituents such as amino acids, methanol or glucose.
- Aspartame is a well-studied sweetener for which safety is clearly documented and well established through extensive laboratory testing, animal experiments, epidemiological studies, and human clinical trials.
- Controlled and thorough scientific studies confirm aspartame's safety and find no credible link between consumption of aspartame at levels found in the human diet and conditions related to the nervous system and behavior, nor any other symptom or illness.
- Aspartame is well documented not to be genotoxic (damages DNA), and there is no credible evidence that aspartame is carcinogenic.
- Aspartame does not increase hunger in those that use it; to the contrary, studies indicate it might be an effective tool as part of an overall weight management program.
- Aspartame is a well-characterized, thoroughly studied, non-nutritive sweetener that has a long history of safe use in the food supply and can help reduce the caloric content of a wide variety of foods.

Another multi-center aspartame safety review was conducted by 24 researchers and published in a 2002 supplement to *Regulatory Toxicology and Pharmacology*.⁽⁵⁾ The expert group concluded:

The testing of aspartame has been far beyond the standard safety testing required to evaluate the safety of a food additive. When all the research on aspartame, including evaluations in both the pre-marketing and post-marketing periods, is examined as a whole, it is clear that aspartame is safe, and there are no unresolved questions regarding its safety under conditions of intended use.

Phenylketonuria

The only known dietary consumption issue related to aspartame is for individuals with phenylketonuria (PKU). PKU is a rare, genetically inherited condition (inborn error of metabolism) in which a baby is born without the ability to metabolize the amino acid phenylalanine. People with PKU do not produce the enzyme phenylalanine hydroxylase, which is needed to break down an essential amino acid called phenylalanine. Without the enzyme, levels of phenylalanine and closely-related substances build up in the body, potentially causing brain damage and other harm to the central nervous system. Fortunately, PKU is easily diagnosed at birth (with virtually every state requiring PKU screening at birth) and is treatable. The regimen involves a diet that is extremely low in phenylalanine, particularly when a child is growing, and for pregnant and lactating women with PKU. Those who strictly follow the diet into adulthood have better physical and mental health. For those with PKU, any foods containing phenylalanine, including aspartame, should be avoided. The FDA requires that products containing aspartame have the following statement prominently displayed on labels: “PHENYLKETONURICS:

CONTAINS PHENYLALANINE.”⁽¹⁴⁾

Cancer

Long-term studies on aspartame and cancer now include seven chronic studies of at least two years in duration with mice and rats. Beyond animal studies, several epidemiological studies also show no association between cancer and aspartame consumption. A number of studies have been subject to extensive peer and regulatory review. In all cases, the authoritative agencies conclude that aspartame does not have carcinogenic or cancer-promoting activity.⁽²⁾

The U.S. National Toxicology Program studied aspartame in three transgenic or genetically manipulated mouse strains. Exposure to aspartame had no effect on the survival of any of the animal groups, nor was any tumor caused by aspartame. At aspartame levels equivalent to 7,500 mg/kg body weight (2,500 times the amount typically consumed), no evidence of cancer-causing or -promoting properties was seen.⁽¹⁵⁾

Subsequently, the Soffritti group studied lifetime aspartame consumption in rats, indicating a carcinogenic effect.^(16, 17) However, numerous expert reviews, including ones conducted by the FDA and the European Food Safety Authority, identified potential flaws in the research (such as lack of commonly-accepted experimental design) and concluded the studies do not provide evidence of carcinogenicity of aspartame.^(2, 18, 19)

Epidemiological studies, including several case-control

studies and one prospective study with nearly 474,000 people, have shown that aspartame does not promote cancer in either adults or children.^(8, 20-22) These studies are significant because they have included large study populations and studied real-life conditions regarding consumption of aspartame in foods and beverages. For adults and children, the studies demonstrate a lack of biologic or experimental evidence to support hypotheses that aspartame causes brain cancer, or cancers in other sites in the human body.

Nervous System and Behavior

Research examining aspartame and neurological function, behavior and biochemistry has been intensive. Studies that mimic human exposure do not show any evidence of neurological impact.⁽²⁾ For example, studies of rats and primates show aspartame has no impact on seizure susceptibility, even when administered prenatally.⁽²⁾

The majority of studies investigating aspartame and learning or memory have used multiple doses and multiple tests. These studies report that aspartame has no effect on learning or memory, even with aspartame doses as unrealistically high as 4 percent of the diet.⁽²⁾

Headaches

In general, headaches are extremely common. The World Health Organization estimates that in developed countries, tension-type headaches affect two-thirds of men and over 80 percent of women.⁽²³⁾ Particularly because headaches are so common, anecdotal reports cannot be used to determine with certainty whether aspartame is associated with headaches. Several studies have been conducted to determine if there is an association between aspartame and headaches. As a group, these studies have yielded conflicting results, with some reporting no effect and others suggesting that a small subset of the population may be susceptible to aspartame-related headaches. Some of the studies are very small and experienced high drop-out rates, making conclusions less strong.⁽²⁾ Further, when considering numerous human studies with aspartame, the results and observations show no association between aspartame and headaches. Thus, the weight of the scientific evidence indicates aspartame does not cause headaches.⁽⁵⁾

Allergies

Anecdotal reports of allergic reactions to aspartame prompted two double-blind, placebo-controlled food challenge studies (the gold standard of allergy research protocol) on hypersensitivity to aspartame in the early 1990s, both funded by the federal government. Neither study showed aspartame to cause allergic reactions.

In one study, NIH researchers recruited subjects through local newspapers and worked closely with the local community of allergists and dermatologists in an attempt to recruit subjects with reported hypersensitivity reactions to aspartame. A total of 61 self-referrals and physician referrals were screened, with 20 referrals evaluated in clinic. After this evaluation, 12 patients underwent single- and double-blind challenge with up to 2,000 mg of aspartame. None of the participants had a clearly reproducible adverse reaction to aspartame. The researchers thus concluded, "It is difficult to recruit study subjects with a history of hypersensitivity reactions to aspartame...subjects who believed themselves allergic to aspartame did not have reproducible reactions."⁽²⁴⁾

In the second study, researchers from multiple research and medical institutions evaluated individuals who had experienced hives and other skin reactions, allegedly associated with consumption of an aspartame-containing product. Despite extensive recruiting efforts over four years, only 21 subjects could be enrolled. The subjects were given a placebo and aspartame, increasing doses (50, 300, 600 mg) at 8:00 a.m., 10:00 a.m., and noon. Four reactions were observed: Two followed aspartame ingestion and two followed placebo ingestion. These results indicate that aspartame is no more likely than placebo to cause hives and other skin reactions in subjects with a history of reported hypersensitivity to aspartame.⁽²⁵⁾

Diabetes

Aspartame, like other non-nutritive sweeteners, may assist in control of blood glucose and weight management, both of which are important in diabetes control.⁽³⁾ The multi-center aspartame safety review published in a 2002 supplement to *Regulatory Toxicology and Pharmacology* addressed animal and human studies examining diabetes and aspartame, indicating no adverse effects occurred.⁽⁵⁾

SUMMARY

- 1.** Misinformation about aspartame and its safety abounds. Consumers need balanced, scientifically based information about aspartame.
- 2.** More than three decades of research and experience in the food supply have shown aspartame to be safe.
- 3.** Hundreds of individual studies, expert panel reports and regulatory authority reviews all conclude that aspartame is safe for use as a non-nutritive sweetener.
- 4.** Regulatory authorities and recognized research experts concur aspartame does not cause cancer, abnormal neural function, seizures, memory loss, headaches, diminished learning abilities or allergic reactions.
- 5.** For consumers interested in reducing sugar or caloric intake, non-nutritive sweeteners, including aspartame, provide flavorful options. In fact, short-term studies (duration of 12 weeks or less) indicate aspartame is effective in helping people lose weight and reduce calorie intake.

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The Association of Food, Beverage
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