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Artificial Sweeteners and Their Health Implications: A Review

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Abstract

Artificial sweeteners are widely used in the food industry as substitutes for sugar, offering sweetness without the caloric content. Artificial sweeteners have become ubiquitous in the modern food and beverage industry as low-calorie alternatives to sugar. This paper provides a comprehensive overview of artificial sweeteners, encompassing their types, development history, taste profiles, and applications in various products. Additionally, it explores the scientific evidence surrounding the potential health implications associated with the consumption of artificial sweeteners. The document delves into the diverse classes of artificial sweeteners, including aspartame, sucralose, saccharin, acesulfame potassium, and stevia glycosides, examining their chemical structures and sweetness intensity. The taste perception of these sweeteners is discussed, elucidating the mechanisms through which they interact with taste receptors on the human tongue. Moreover, the paper critically analyzes the controversial aspects of artificial sweetener consumption, addressing debates on their safety and potential links to adverse health effects. Studies on the impact of artificial sweeteners on metabolism, gut microbiota, and long-term health outcomes are reviewed to provide a balanced perspective on the current state of scientific knowledge. In addition to scientific considerations, the document explores the regulatory landscape governing the use of artificial sweeteners in various regions. A comparative analysis of regulatory frameworks sheds light on the differing approaches taken by authorities to ensure the safety and labeling of artificial sweeteners. This paper consolidates existing knowledge on artificial sweeteners, offering insights into their development, taste characteristics, and potential health implications. The synthesis of scientific evidence and regulatory perspectives aims to inform consumers, health professionals, and policymakers about the complex landscape of artificial sweeteners in the contemporary food industry. Future directions for research and potential advancements in the field are also discussed, emphasizing the need for ongoing investigation to enhance our understanding of these widely used sugar substitutes.

Keywords: Artificial sweetener, health implications.

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Introduction

Artificial sweeteners are compounds that provide a taste sensation hundreds or even thousands of times sweeter than sugar without contributing any significant calories to the diet[1-4]. They are commonly known as artificial sweeteners, non-nutritive sweeteners, or synthetic sugar substitutes. These sweeteners are typically either chemically synthesized or derived from naturally occurring substances such as herbs or sugar [5-12]. By using artificial sweeteners, only small amounts are needed to achieve the desired level of sweetness, making them a popular choice for people looking to reduce their sugar intake or manage their calorie consumption [13-19]. Due to their intense sweetness compared to table sugar, artificial sweeteners require much smaller quantities to achieve the same level of sweetness. This characteristic is particularly advantageous considering that excessive consumption of table sugar is associated with various health risks, including diabetes, hypertension, and heart disorders. In response to these concerns, researchers have directed their efforts towards the production of artificial sweeteners and the isolation of naturally occurring compounds with sweetening properties. By promoting the use of artificial sweeteners and exploring natural alternatives, the aim is to mitigate the prevalence of disorders linked to the overconsumption of sugar in the diet (FDA2008). Artificial sweeteners may not fully satisfy hunger signals like sugar does, potentially leading to increased cravings or overeating.

These sweeteners provide the sweetness of sugar without adding calories and typically have a minimal impact on blood sugar levels [19]. The effect food has on post-meal blood sugar levels, called the "glycemic response," has made dietary sweeteners a sought-after alternative to sucrose for both consumers and food producers. Recently, there has been increased attention on these products due to their effects on glucose regulation.

Unlike sucrose, most sweeteners have varying concentrations that result in changing aftertastes, ranging from pleasant sweetness to unpleasant bitterness or metallic flavors [6]. Additionally, these sweeteners have been associated with several significant side effects, including mental illnesses, bladder cancer, heart failure, brain tumors, and psychological issues [15]. Some of the most commonly used non-caloric sweeteners belong to a group that includes substances like saccharin, cyclamate, aspartame, neotame, sucralose, and acesulfame potassium (acesulfame K). These sweeteners are significantly sweeter than sucrose, ranging from 30 to 13,000 times more potent, owing to their artificial composition. Known as low-calorie sweeteners, intense sweeteners, or non-nutritive sweeteners (NNS), they offer strong sweetness with negligible or zero calories per gram. These artificial sweeteners find applications in various products such as mouthwashes, nutritional supplements, and beverages calories per gram [15].

Low-calories sweetener

Artificial sweeteners like Aspartame, Acesulfane-K, Neotame, Saccharin, Sucralose, Cyclamate, and Altima have been deemed safe for human consumption and are known for their taste-enhancing properties. These sweeteners do not provide energy to the body as they are non-nutritive. A summary of data regarding high-intensity sweete Artificial sweeteners like Aspartame, Acesulfane-K, Neotame, Saccharin, Sucralose, Cyclamate, and Altima have been deemed safe for human consumption and are known for their taste-enhancing properties. These sweeteners do not provide energy to the body as they are non-nutritive. A summary of data regarding high-intensity sweeteners is presented in **Table 1**.

Table 1 List of High-intensity sweeteners.

Low-Calorie Sweetener	Brand Name	Sweetness as compared with sugar	Acute	Acceptable Daily Intake*
Aspartame	Equal®, NutraSweet®, Sugar Twin®	200 times sweeter than sugar	Headache, Dizziness, Dry face, Nausea, Vomiting	75**
Acesulfame-K	Sunett®, Sweet One®	200 times sweeter than sugar	Headache	23
Saccharin	Sweets' Low®, Sweet Twin®, Necta Sweet®	200-700 times sweeter than sugar	Diarrhea, Vomiting	45
Sucralose	Splenda®	600 times sweeter than sugar	Diarrhea	23
Neotame	Newtame®	7,000-13,000 times sweeter than sugar	Hepatotoxic at high doses, Headache	23
Advantame	No brand names	20,000 times sweeter than sugar	-	4,920

**(maximum number of tabletop sweetener packets per day)*

Saccharin

Saccharin, the first and oldest artificial sweetener, has been utilized for over a century to enhance the flavor of food and beverages without adding extra calories. It has been approved for use by the FDA in over 100 countries [7].

At Johns Hopkins University, researchers Fahlberg and Remsen discovered saccharin in 1879. Saccharin experienced significant commercial success during periods of sugar shortages, including World Wars I and II. [1].

In 1997, the FDA proposed a ban on saccharin due to concerns about bladder cancer in animals exposed to large amounts of the sweetener. Foods containing saccharin were required to carry a label warning consumers of potential health risks and the association with cancer in experimental animals. Labels included statements such as "Use of this product may be hazardous to your health." However, in 2000, the National Toxicology Program concluded that mechanistic studies, which examine how substances function in the body, indicated that the findings were limited to rats. Therefore, saccharin should no longer be classified as a potential carcinogen. Human epidemiological studies have not consistently found a link between saccharin consumption and the incidence of bladder cancer [18].

Neatome

Aspartame derivatives represent the latest generation of artificial sweeteners, receiving FDA approval in 2002. With no calories, they are 30–60 times sweeter than aspartame itself and 6000–10,000 times sweeter than sucrose.

Following the commercial success of aspartame, there were calls for the development of a new sweetener with additional properties such as improved heat stability, fewer limitations, and enhanced sweetness potency, allowing for reduced usage and cost. In response, researchers synthesized thousands of compounds based on aspartame's structure. Among these, neotame emerged with the desired characteristics and was approved by the FDA in 2002 for general use. Neotame is a dipeptide derivative of phenylalanine and aspartic acid, with a molecular composition similar to aspartame. Due to its strong heat resistance, it is utilized as a sweetener in various culinary products, including soft drinks, jellies, processed fruits, syrups, chewing gum, and gelatins. Studies suggest that over 90% of neotame is eliminated from the body through fecal matter [8].

Acesulfame-K

This high-intensity, non-nutritive, white crystalline sweetener can be utilized for various purposes and has been deemed non-carcinogenic [4].

Chemists Karl Claus and Jensen discovered acesulfame-K in 1967 while researching oxathiazinone dioxides, stumbling upon its sweet flavor by accident among several different compounds. In 1988, acesulfame-K gained approval in the US for various purposes, including use as a tabletop sweetener. It received FDA approval for use in beverages in 1998, notably to mitigate the bitter aftertaste associated with aspartame.

The FDA continues to endorse the use of acesulfame-K in low-calorie and diabetic foods. Notably, acesulfame-K is not stored or metabolized by the body; it is rapidly absorbed and excreted unchanged in urine. Its stability at high temperatures makes it suitable for use in baked goods, and it is employed in over 4,000 products across more than 90 countries. Additionally, acesulfame-K contains the mineral potassium, which is naturally present in the human body (Wikipedia).

Aspartame

Aspartame is a widely used low-calorie sweetener found in beverages and various low-calorie or reduced-calorie foods. It is commonly used as a tabletop sweetener and is also added to dry mixes, gums, and breakfast cereals. While aspartame itself is low in calories, it breaks down in the body to provide roughly 4 calories of energy per gram.

The sugar substitute industry had its beginnings unexpectedly in 1879 when two scientists from Johns Hopkins University stumbled upon saccharin, a non-nutritive coal-tar byproduct that is 300 times sweeter than sugar. This discovery occurred by accident, as they were actually searching for a wonder medication.

Sucralose

Sucralose possesses a pleasant sweet taste, being approximately 450–650 times sweeter than sucrose, and closely resembles sucrose in quality and time intensity profile [2]. Additionally, it interacts moderately positively with other nutritive and non-nutritive sweeteners [3].

In 1976, sucralose was discovered. This non-nutritive sweetener is created by replacing three of the hydroxyl groups in the sucrose molecule with three chloride atoms (FDA, 2006).

Furthermore, sucralose does not degrade or de-chlorinate. To assess its safety, the FDA reviewed data from over 110 human and animal studies. Numerous studies were conducted to investigate potential harmful effects, such as neurological and reproductive cancers; however, none of these effects were found. Based on research indicating that sucralose is safe for human consumption, the Food and Drug Administration (FDA) approved its use. The FDA authorized sucralose for use as a general-purpose sweetener. The US has established an acceptable daily intake (ADI) of 5 mg/kg body weight per day for sucralose. According to USFDA calculations, the estimated daily consumption for percentile consumers is 1.6 mg/kg body weight/day (FDA, 1999).

Advantame

The FDA recently approved Advantame as a flavor enhancer and general-purpose sweetener, making it the most recent synthetic artificial sweetener to be approved. Advantame is created by combining aspartame and vanillin, resulting in an N-substituted derivative of aspartame. Unlike aspartame, Advantame can be consumed by individuals with phenylketonuria. Additionally, Advantame is stable in heat [5].

G. D. Searle made the discovery of aspartame in 1965 while researching novel remedies for stomach ulcers. During the evaluation of potential anti-ulcer medications, a biologist utilized tetrapeptide, a compound typically found in the stomach. As part of the synthesis process for tetrapeptide, the creation of an intermediate, aspartyl-phenylalanine methyl ester, was crucial. By chance, a small amount of this compound came into contact with the chemist's fingers. Unaware of its presence, the chemist licked their finger and tasted something pleasant. After determining the compound's low toxicity, further research ensued.

Aspartame received FDA approval in 1981 for use as a tabletop sweetener and again in 1996 for use as a general-purpose sweetener in various foods and beverages.

Uses of Artificial Sweetener

Due to aggressive marketing campaigns by manufacturers, people have been using non-nutritive sweeteners (NNS) excessively and sometimes even abusing them. Both lean and obese individuals consume these sweeteners because they are believed to reduce hunger and appetite, potentially leading to positive effects on body weight and the cardio-metabolic profile. Additionally, many diabetic patients opt to replace sugar in their diets with these "sugar-free" sweeteners [17].

Food and beverage drinks

The primary applications of artificial sweeteners are in the food and beverage industry, where the main goal is to reduce caloric content. These sweeteners are used either alone or in combination with other sugary ingredients. Depending on the type of product, artificial sweeteners can be used alone or with bulk sugar alternatives suitable for diabetic consumption in diabetic foods and beverages. Beverages account for over 50% of the sugar consumed by humans, making them an easy target for substituting artificial sweeteners, as sugar serves no significant functional purpose in beverages. Additionally, desserts and dairy products with fruit flavors are significant additional applications for artificial sweeteners.

Sweeteners for tables

Artificial sweeteners are manufactured in various forms for tabletop use at home, including powders, pills, spoon-by-spoon packets, and liquid formulations**.**

Medicines

When formulating medications for diabetics, artificial sweeteners are often incorporated to mask the unpleasant flavors and tastes of active ingredients, particularly bitterness. Syrups, soluble pills, and powders are common forms of medication that contain artificial sweeteners to improve palatability.

Makeup & cosmetics

Many cosmetics, especially those designed for oral hygiene, are sweetened to enhance customer satisfaction. Products such as mouthwash and toothpaste must be free of cariogenic (tooth decay-causing) components. Therefore, an extra amount of artificial sweetener is often added to achieve the desired level of sweetness without contributing to tooth decay.

Conclusion

Almost everyone enjoys indulging in sugary snacks, but frequent consumption of foods and beverages with high levels of added sugar can lead to the accumulation of empty calories. This can contribute to weight gain and increase the risk of serious health issues such as diabetes and heart disease. To mitigate these risks, it's important to consider substituting sugar with alternatives such as stevia, xylitol, aspartame, and others. These sugar substitutes can provide sweetness without the negative health impacts associated with added sugar consumption.

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