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Aspartame in the Diet: A Contribution to the Debate on Safety and Health Impact

Authors:

1. Milena Biernikiewicz, student
   Faculty of Medicine, Wroclaw Medical University Wybrzeże Ludwika Pasteura 1, 50-367 Wroclaw, Poland
   milenabiernikiewicz@gmail.com, https://orcid.org/0009-0006-7288-6965
2. Julia Biernikiewicz, student
   Faculty of Medicine, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
   biernikiewiczjulia@gmail.com, https://orcid.org/0009-0004-1192-9365
3. Anna Wilewska, student
   Faculty of Medicine, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
   wilewskaanna2000@gmail.com, https://orcid.org/0009-0001-5136-4598
4. Bartosz Pomirski, student
   Faculty of Medicine, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
   bartosz.pomirski@gmail.com, https://orcid.org/0009-0004-4868-0073

5. Agata Pomirska, student
   Faculty of Medicine, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
   pomirska.agata@gmail.com, https://orcid.org/0009-0009-5367-7123
6. Konstanty Alabrudziński, student
   School of Medicine Collegium Medicum University of Warmia and Mazury in Olsztyn, Oczapowskiego 2, 10-719 Olsztyn, Poland
   konstanty.alabrudzinski@gmail.com, https://orcid.org/0009-0008-4729-0937
7. Agnieszka Borowiec, MD
   The Regional Specialist Hospital in Biala Podlaska Terebelska 57-65 21-500 Biala Podlaska, Poland
   borowiec.agn@gmail.com, https://orcid.org/0000-0002-1428-170X
8. Kinga Borowiec, student
   Faculty of Medicine, Medical University of Warsaw Żwirki i Wigury 61, 02-091 Warsaw, Poland
   kingaborowiec07@gmail.com, https://orcid.org/0009-0000-5546-9787
9. Paulina Kwaśniewska, student
   Faculty of Medicine, Medical University of Warsaw Żwirki i Wigury 61, 02-091 Warsaw, Poland
   paulinakwasniewska12@gmail.com, https://orcid.org/0009-0009-4677-3387
10. Artur Hovsepyan, student
    Faculty of Medicine, Pomeranian Medical University of Szczecin Rybacka 1, 70-204 Szczecin
    arturik10011@gmail.com, https://orcid.org/0009-0003-0930-5839

Abstract

Introduction

Global sugar consumption remains at alarmingly high levels, far exceeding World Health Organization recommendations. This raises the question of whether sweeteners, as low-sugar substitutes, can become a key solution to help people switch to healthier alternatives. WHO guidelines suggest limiting free sugars to less than 10% of daily energy intake, with further

benefits for reducing it to below 5%. Such changes can improve overall health and reduce the risk of obesity, diabetes, cardiovascular diseases, and cancer. Among many sugar substitutes, aspartame is one of the most widely used synthetic sweeteners.

Purpose

The purpose of this article is to review the health effects of aspartame, focusing on its safety, cancer risk, impact on metabolism, obesity, diabetes, and other long-term effects. This paper aims to present scientific evidence on aspartame's safety, including studies supporting its use and those raising concerns. It also discusses potential risks, especially for individuals with phenylketonuria, and provides expert recommendations for its consumption.

Conclusion

Aspartame, a widely used sugar substitute, has caused controversy due to concerns about its long-term health effects, such as potential cancer and neurodegenerative risks. However, most health organizations consider aspartame safe when consumed in moderation. Despite some studies linking it to health issues, there is insufficient evidence to confirm these risks in humans. People with phenylketonuria should avoid aspartame, but for most, it is safe within recommended daily intake limits.

Materials and methods: Our review is based on an analysis of material collected in 'Pubmed', 'Google Scholar' and other scientific articles using the keywords: aspartame, aspartame safety, aspartame controversy.

Keywords: aspartame, aspartame safety, aspartame controversy

Introduction

Aspartame is a synthetic sweetener that has been widely used in the food and pharmaceutical industries. It is often used in carbonated beverages, powdered drinks and various food products. It was discovered by James M. Schlatter in 1965 [1], and its popularity has grown since 1981, when it was first approved by the US Food and Drug Administration (FDA) as a safe ingredient for use in food.

Due to its extremely high sweetness, which exceeds that of sucrose by 200 to 300 times, aspartame has become a popular choice in the food industry. It is characterized by a clean taste, similar to that of sugar, without unwanted metallic or bitter notes. In addition, aspartame is significantly cheaper than sugar, making it an attractive option for food manufacturers [2].

Aspartame (ll-aspartyl- ll-len-methyl-ester) consists of two natural amino acids: phenylalanine and aspartic acid, joined by methanol. After ingestion, aspartame is metabolized by intestinal enzymes (esterase and peptidase) to 3 amino acid isolates, phenylalanine (50%), aspartic acid (40%) and methanol (10%) . Phenylalanine is further converted in the liver to tyrosine, which in turn is converted to catecholamines such as dopamine, norepinephrine and epinephrine. Elevated plasma concentrations of phenylalanine and aspartic acid can affect brain neurochemistry, leading to increased transport of these amino acids into the brain.

As a large, neutral amino acid, phenylalanine competes with other amino acids for binding to neurotransmitter transport. Excess phenylalanine can lead to reduced levels of catecholamines, serotonin and dopamine. Aspartic acid is metabolized in the liver to lysine and methionine. At high concentrations, it can cross the blood-brain barrier and interact with NMDA receptors, leading to neurodegeneration.

Methanol metabolism varies among species. In primates, methanol is converted to formaldehyde and then to formic acid. Formic acid is then metabolized to carbon dioxide and water, and folic acid is also involved in this process. High concentrations of formic acid can lead to metabolic acidosis, so people with low levels of folic acid are at greater risk of its harmful effects [2].

Phenylalanine and aspartic acid occur naturally in many protein-rich foods, such as meat, dairy products and vegetables. Although methanol can be harmful in large quantities, the amount of methanol formed by the breakdown of aspartame is minimal-it is much less than the natural methanol content of fruits and vegetables [3].

Because aspartame is a source of phenylalanine, people with phenylketonuria should avoid excessive use of aspartame.

Aspartame and obesity and weight control

According to the World Health Organization (WHO), more than one billion adults worldwide are overweight, which is defined as a body mass index (BMI) of more than 25 kg/m². Of this group, at least 300 million people are considered obese, with a BMI of 30 kg/m² or more [4]. Overweight and obesity are associated with a number of serious conditions that have significant public health implications. These include hypertension, cardiovascular disease, diabetes, depression and increased risk of cancers such as breast, endometrial, colon and prostate cancer [5,6].

The replacement of sugar with sweeteners was intended to reduce total energy intake, which could ultimately lead to weight loss in the population. While these assumptions seem promising, so far there have been no conclusive results on this issue. Some studies suggest that swapping sugar-sweetened beverages for those with artificial sweeteners does not affect total energy intake, and may even lead to an increase [7,8]. Participants often compensate for the caloric deficit resulting from the use of artificial sweeteners by increasing their energy intake later. Moreover, there is evidence to suggest that both sugar-sweetened beverages and those with artificial sweeteners may intensify subjective feelings of hunger, leading to greater caloric intake and potential weight gain. These issues require further research [9,10]. Assessing the effect of artificial sweeteners on the increase in obesity is complicated. For some people, consumption of diet products becomes an excuse for excessive caloric intake from other sources. As a result, it is difficult to determine conclusively whether obesity is directly related to the consumption of products containing artificial sweeteners, such as aspartame, or whether it is due to an overall excess of calories in the diet [11].

Aspartame and diabetes

Studies on aspartame have shown that this low-calorie sweetener has no significant effect on blood glucose and insulin levels, making it safe for people with diabetes. It is even recommended as a sugar substitute due to its low caloric value.

In a study of 62 patients with insulin-dependent and insulin-independent diabetes mellitus, there were no significant differences in fasting glucose levels, postprandial glucose levels or glycated hemoglobin (HbA1c) levels between the group consuming aspartame and the placebo group. These results indicate that aspartame has no adverse effect on glycemic control in people with diabetes, making it a safe sugar substitute for this group of patients [12].

Aspartame safety

Aspartame has been the subject of much controversy over the potential side effects of its use. Among the concerns are headaches, feelings of fatigue, hearing impairment, allergies, skin problems and also anxiety, depression and insomnia. In addition, there are doubts about its effect on increased cancer risk [13,14]. As a result, the topic of aspartame remains the subject of intense debate among scientists, doctors and consumers.

Potential carcinogenic properties

Aspartame has attracted controversy because of its potential health risks, including concerns about its carcinogenic effects. These concerns are particularly related to the metabolism of aspartame in the body, which leads to the formation of formaldehyde, a substance considered a potential carcinogen.

The acceptable daily intake (ADI) of formaldehyde according to the World Health Organization (WHO) is 0.2 mg per kilogram of body weight [15]. In turn, the International Agency for Research on Cancer (IARC) classifies aspartame as a substance for which there is limited evidence of carcinogenicity in humans (Group 2B [16]) . IARC documents indicate a dose of 40 mg per kilogram of body weight as theoretically safe [17].

Analyses indicate that the consumption of one liter of diet soda can lead to the conversion of about 100-200 mg of aspartame into 10-20 mg of formaldehyde. This amount, depending on one's perspective, may raise concerns or be considered acceptable. Consequently, the topic of aspartame's safety and metabolism remains the subject of much research and discussion in the scientific community.

An article by Philip J. Landrig and Kurt Straif, published in April 2021, discusses important findings regarding aspartame and its potential carcinogenic effects. The researchers highlight that aspartame, a commonly used artificial sweetener, is associated with an increased risk of malignant tumors in rodents, especially after prenatal exposure. This suggests that aspartame's carcinogenic risk may affect offspring at lower doses than those affecting adult rodents. The study confirmed that 92.3% of cancers diagnosed in rodents exposed to aspartame were indeed malignant, which contrasts with earlier critics who questioned the original diagnoses, pointing to possible confounding factors such as Mycoplasma infections. The authors underscore the public health significance of these findings, calling on national and international health agencies to re-evaluate their assessments of aspartame, particularly in the context of prenatal and early postnatal exposures [18].

The following study that takes a closer look at the safety of aspartame consumption was published in the journal PLOS Medicine under the title “Artificial sweeteners and cancer risk: results from the NutriNet-Santé population-based cohort study” provides new information on the link between artificial sweetener consumption and cancer risk. The results suggest that higher intake of these substances may be associated with an increased risk of various types of cancer, especially in women. The study's authors emphasize that these observations should be interpreted with caution, as there is a need for further research to confirm these findings and clarify the mechanisms by which artificial sweeteners may affect cancer risk [19].

Despite numerous studies, there is still a lack of solid scientific evidence supporting aspartame's harm to humans. An article published in Nature on July 14, 2023 reports that the World Health Organization (WHO) has classified aspartame as “possibly carcinogenic.” This means that while the available evidence is insufficient, there are some signals that may suggest a potential risk. So far, human studies have not shown convincing evidence to support the claim that aspartame is carcinogenic [20].

Prenatal exposure to low-calorie sweeteners, including aspartame

Several animal studies have shown that prenatal exposure to low-calorie sweeteners, including aspartame, can affect infant health outcomes. They point to a risk of premature birth, increased infant weight, offspring preference for sweet foods, and to elevated fasting blood glucose levels and reduced insulin sensitivity in later life. Consequently, it is recommended that pregnant and lactating women avoid aspartame [21-23].

Potential epileptic effects

Aspartame has been accused of increasing the risk of epileptic seizures, prompting researchers to conduct an experiment on eighteen epilepsy sufferers who regularly consumed the sweetener. The study involved 16 adults and two children, who were given meals containing high doses of aspartame (50 mg/kg, higher than the recommended dose) and meals without aspartame as a control group (placebo).

The results showed that aspartame had no effect on the frequency of epileptic seizures. The number of seizures did not differ significantly between the aspartame and placebo groups, suggesting that there is no direct relationship between aspartame consumption and epileptic seizures [24].

Potential allergy and skin problems

A clinical trial published in 1993 examined hypersensitivity reactions to aspartame in patients with a history of urticaria and angioedema. Twenty-one participants were recruited over four years and given different doses of aspartame (50, 300, 600 mg) and placebo in a double-blind study.

The results showed that the number of allergic reactions was similar in both groups, suggesting no significant statistical differences ($p = 1.00$). In addition, the incidence of other adverse reactions was also comparable ($p \geq 0.29$). The study's conclusions indicate that aspartame and its metabolites do not cause urticarial reactions or angioedema more often than placebo in hypersensitive subjects [25].

A double-blind, randomized trial conducted in the United Kingdom compared a group of people reporting hypersensitivity to aspartame with a non-hypersensitive group. Participants were given snack bars containing 100 mg of aspartame or not, with at least a seven-day interval between each administration. The results showed no significant differences in responses between the sensitive and non-sensitive groups, suggesting that there are no adverse effects associated with acute aspartame consumption [26].

Some studies suggest that aspartame ingestion can lead to the onset of skin problems-systemic contact dermatitis (SCD). There is a possibility that aspartame can induce this condition, manifested by inflammation of the skin, which may be related to the accumulation of formaldehyde, which is a metabolite of aspartame. However, to induce formaldehyde accumulation, aspartame consumption would have to be at very high levels. Such side effects have been observed in both adults and children. For example, in an 11-year-old patient who struggled with general dermatitis and eyelid inflammation, discontinuation of an aspartame-containing product resulted in improvement of symptoms. Similarly, a 60-year-old patient with six months of eyelid inflammation also experienced complete resolution of symptoms within a week after discontinuing an aspartame-based sweetener [27,28].

Potential increased risk of developing multiple sclerosis

Speculation about a link between aspartame and multiple sclerosis was based on the toxicity of formic acid, which is produced by the conversion of methanol during the breakdown of aspartame. The Multiple Sclerosis Society of Canada, in its Medical Update Memo statement, unequivocally rejected these allegations. The organization based its position on studies that prove that consuming large amounts of aspartame-containing foods and beverages causes only

minor changes in blood levels of methanol and formic acid, thus showing no link to the development of multiple sclerosis [29].

Autism

Autism is a neurodevelopmental disorder that manifests as difficulties in communication, social interaction and the presence of repetitive behaviors. Numerous studies suggest that genetic, environmental and immunological factors may play a role in the pathogenesis of autism.

The link between aspartame and Autism Spectrum Disorder (ASD) was noted in 1983, when an increase in ASD cases coincided with the growing consumption of diet drinks containing this popular sweetener [30]. There was speculation that aspartame's effect on ASD may have been related to the process of metabolizing methanol, which could lead to DNA and RNA deactivation. These changes have been observed in the brains of ASD sufferers [31]. Nevertheless, studies have shown that aspartame alone does not cause autism [32].

Methanol was previously present in other products such as canned vegetables and cigarette smoke, and this did not result in higher rates of ASD. Moreover, when Pepsi Cola removed aspartame from its beverages for a time, it did not reduce the rate of autism in the United States [33].

Dental benefits

The potential benefit of low/no calorie sweeteners (including aspartame) in tooth decay when consumed in place of sugars has been noted.

Dental caries is one of the most prevalent chronic diseases in the world, characterized by local destruction of hard dental tissues. It is a multifactorial disease that occurs in the presence of a

pathogenic biofilm and frequent exposure to sugars. Aspartame , as a non-nutritive sweetener, is gaining popularity in the context of oral health. In vitro studies have analyzed the effects of non-nutritive sweeteners (including aspartame) on the bacterial biofilm, particularly on Streptococcus mutans and Streptococcus sanguinis, which play a key role in caries processes. The results show that non-nutritive sweeteners significantly inhibit the growth and acid production of S. mutans, which translates into a reduction in the biofilm's cariogenic potential. In addition, a favorable change in the ratio of S. mutans to S. sanguinis was observed in biofilms with non-nutritive sweeteners, suggesting a better microbial balance. Increased pH values and decreased extracellular polysaccharide (EPS) production indicate a reduced risk of caries when using low-nutritive sweeteners instead of sucrose. In conclusion, non-nutritive sweeteners not only do not promote the development of caries, but may also promote oral health by stabilizing the microbiome [34].

DISCLOSURE

Author`s contribution:

Conceptualization: Milena Biernikiewicz, Anna Wilewska, Artur Hovsepyan , Konstanty Alabrudziński , Kinga Borowiec

Methodology: Milena Biernikiewicz, Agnieszka Borowiec, Artur Hovsepyan, Konstanty Alabrudziński

Software: Bartosz Pomirski, Agata Pomirska, Anna Wilewska, Paulina Kwaśniewska, Bartosz Pomirski

Check:Agata Pomirska, Julia Biernikiewicz, Anna Wilewska , Kinga Borowiec, Bartosz Pomirski

Fornal Analysis:Agata Pomirska, Julia Biernikiewicz, Agnieszka Borowiec, Paulina Kwaśniewska, Bartosz Pomirski

Resources: Julia Biernikiewicz, Milena Biernikiewicz, Agnieszka Borowiec, Artur Hovsepyan , Kinga Borowiec, Paulina Kwaśniewska

Data Curation: Agnieszka Borowiec, Kinga Borowiec, Julia Biernikiewicz, Anna Wilewska, Artur Hovsepyan, Agata Pomirska, Konstanty Alabrudziński, Milena Biernikiewicz

Writing-rough preparation:Paulina Kwaśniewska, Bartosz Pomirski, Agata Pomirska, Konstanty Alabrudziński, Julia Biernikiewicz, Agnieszka Borowiec

Writing-review and editing: Kinga Borowiec, Milena Biernikiewicz, Anna Wilewska, Konstanty Alabrudziński, Milena Biernikiewicz

Supervision: Anna Wilewska, Paulina Kwaśniewska, Bartosz Pomirski, Agata Pomirska, Paulina Kwaśniewska

Project Administration: Agnieszka Borowiec, Bartosz Pomirski, Konstanty Alabrudziński, , Kinga Borowiec, Artur Hovsepyan , Milena Biernikiewicz

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