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Are Artificial Sweeteners a Healthier Alternative to Sugar? - Systematic Review

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ABSTRACT

Introduction: Sweeteners are a popular alternative to sugar, especially in the context of the fight against obesity and diabetes. Thanks to their low calorie content, they are gaining supporters among health-conscious people. The food industry uses both natural sweeteners, such as stevia or erythritol, and synthetic sweeteners, such as aspartame or saccharin. Despite their recognition as safe in recommended doses, there is ongoing debate about their long-term health effects. This controversy highlights the need for further research into their effects on the human body. This paper analyses the properties, benefits and risks of different types of sweeteners. Particular attention is given to their role in the diet of people with diabetes and their effects on the gut microbiome.

Aim of the Study: The aim of this study is to investigate the effects of sweeteners on human health and to assess their suitability as sugar substitutes in the diet of the modern consumer. The study also attempts to identify the benefits and potential risks of their use.

Materials and Methods: An analysis of papers available in PubMed was performed. The following keywords were used: sweeteners, artificial sweeteners, erythritol, acesulfame potassium, sucralose, aspartame, alternative to sugar.

Basic results: Sweeteners, both natural (e.g. stevia, erythritol) and synthetic (e.g. aspartame, sucralose), are being used as alternatives to sugar due to concerns about the health risks associated with excessive consumption of white sugar. Research indicates that sweeteners can help reduce calorie intake and control blood sugar levels, although their long-term health effects remain uncertain. Some studies raise concerns about potential metabolic or gut microbiota changes, but conclusive evidence is lacking. Regulatory bodies such as the FDA consider approved sweeteners to be safe within established daily limits. Despite their benefits, further research is needed to fully understand the long-term health effects of sweeteners.

Conclusion: Sweeteners are an alternative to sugar that is growing in popularity, particularly in the context of combating obesity and diabetes. Their variety, from natural to synthetic, allows for a wide range of dietary applications. Although they are considered safe in certain doses, they still raise questions about their long-term health effects. They can support weight control and glucose levels, but are not a one-size-fits-all solution. A moderation approach and further research to better understand their effects is key.

Keywords: sweeteners, artificial sweeteners, erythritol, acesulfame potassium, sucralose, aspartame, alternative to sugar

Introduction

Over the past few decades, the problem of obesity has become one of the biggest global health epidemics. The World Health Organisation (WHO) notes that the number of overweight and obese people is steadily increasing, in both developed and developing countries. One of the main factors behind this increase is the excessive consumption of sugar, which has become commonplace in the diet of modern humans. Excessive sugar intake can lead to neuro-adaptations in the reward system, which dissociates energy needs from eating behaviour, promoting compulsive overeating. Such consumption is strongly associated with the development of obesity, metabolic syndrome and inflammation, which negatively impacts health. The addictive mechanisms associated with sugar mean that a person may overeat despite a lack of energy need, leading to uncontrolled weight gain. Sugar-rich products, especially sweetened beverages, play a key role in providing empty calories, which leads to excessive energy intake, resulting in weight gain and the development of obesity [4, 5].

Obesity is one of the causes of many serious conditions, including type 2 diabetes, hypertension, cardiovascular disease and non-alcoholic steatohepatitis. In addition, obese people are more likely to suffer from musculoskeletal ailments, such as osteoarthritis, which limits their physical fitness. The consequences of obesity are therefore multidimensional, affecting both physical and mental health, and putting a strain on health systems worldwide [1, 2].

With increasing awareness of the negative effects of excessive sugar consumption, there is growing interest in alternatives such as artificial sweeteners. Substances such as aspartame, sucralose, erythrol or acesulfame offer the possibility of a sweet taste without the extra calories, which could theoretically help with weight control. Artificial sweeteners are commonly used in diet products and ‘light’ drinks to reduce sugar and calorie intake [3].

Although artificial sweeteners may seem like a promising alternative, their health effects and effectiveness in weight control are controversial. The latest WHO 2023 guidelines recommend against the use of artificial sweeteners as a tool for long-term weight control, due to the lack of conclusive evidence for their effectiveness in reducing obesity and potential health risks. Studies indicate that the use of sweeteners may disrupt appetite regulation mechanisms, which paradoxically may lead to excessive calorie intake [4].

Artificial sweeteners offer some benefits in the context of reducing sugar intake, their long-term health effects require further research. In the context of the fight against obesity, these sweeteners can be a helpful tool, but they are not a solution without drawbacks. Therefore, the

search for other strategies to combat the global obesity crisis remains crucial to protect public health [3, 4].

Erythritol

General information

Erythritol is a sweetener belonging to the family of sugar alcohols (polyols) with a molecular formula of C4H10O4 and a mass of 122u. It can also be found under the synonyms meso-erythritol, tetrahydroxybutane, erythritol. This compound occurs naturally in algae, fungi and lichens, among others [6]. According to Commission Regulation (EU) No 231/2012, erythritol is produced by fermentation of a carbohydrate source with Moniliella pollinis or Moniliella megachiliensis, followed by purification and drying. It is characterised by a sweetness of 60-80% that of sucrose [7]. Erythritol is quite easily absorbed, metabolised in a small percentage and then excreted unchanged in the urine [8]. Erythritol and sucralose are the only sugar alcohols that carry no energy value. An important feature of this compound is that it has no effect on the body's glucose and insulin levels (Glycaemic Index of 0.0). This property is particularly important for diabetic patients, as well as those with obesity. Many commonly used sweeteners cause diarrhoea, which does not occur with erythritol [9]. This is due to the relatively good absorption of erythritol. It does not induce osmotic effects and water retention in the intestines and does not ferment causing gas formation [10]. In addition, erythritol exhibits antioxidant activity by scavenging free radicals. It can be found in many commonly available foods or confectionery products. Among others, it is found in chewing gum (does not cause caries), chocolate and candies [9].

Tooth decay

The effects of erythritol on the health and functioning of the body are the subject of much research. Several aspects are worth mentioning here, including the previously mentioned effect on tooth decay. This sweetener definitely has a beneficial effect in this regard. This is due to the inhibition of plaque formation and bacterial growth (osmotic action and, particularly important, passive passage through the cell membrane of bacteria and disruption of growth pathways). These studies referred to both adults and children, with favourable results in both groups [10].

Glycaemia and insulin secretion

Studies have shown that acute doses of erythritol (20-75 g) do not affect blood glucose and insulin levels, with a glycaemic index of 0 and an insulinemic index of 2. A decrease in HbA1c (from 8.5 to 7.5%) was observed in diabetic patients consuming 20 g of erythritol daily for a fortnight, but controlled clinical trials are limited. Erythritol may delay gastric emptying and glucose absorption by increasing intestinal hormones (GLP-1, CCK, PYY), which has been confirmed in animal and human studies. It has been suggested that erythritol may only work under conditions of concomitant ingestion with glucose, which requires further research [10].

Body weight

The number of studies evaluating the effect of erythritol on body weight is relatively small and the results are inconclusive. During one clinical trial lasting 7 days, 12 healthy men participated. They consumed 1 g of erythritol per kilogram of body weight per day. Their body weight did not change. Another study lasting 14 days involved patients with type II diabetes. The daily consumption of erythritol was 20g. In this case, body weight changes in several patients, but this was not statistically significant. Available publications also show erythritol-dependent increases in GLP-1, CCK and PYY. Due to the higher osmolality of erythritol compared to other sweeteners, the concentrations of hunger and satiety hormones are altered in the duodenum and consequently hunger is reduced [10].

Cardiovascular diseases

Clinical studies assessing the effect of chronic erythritol consumption on risk factors for cardiometabolic diseases are lacking. One pilot study involving patients with type II diabetes showed improved endothelial function and reduced arterial stiffness, but the lack of a control group limits its reliability. Studies in mice suggest both beneficial effects of erythritol, such as reducing inflammation and improving glucose tolerance, and negative effects in shorter interventions. The results are inconsistent, making it difficult to assess its potential as a healthy sugar substitute. Further clinical studies are needed to clarify its impact on metabolic health [10].

Risk of anaphylactic shock

There are several reported cases of anaphylactic shock caused precisely by erythritol. One of these concerned a 5-year-old boy who ingested a dietary supplement in the form of a

gel containing erythritol as the main ingredient. It is interesting to note the negative spot test with a positive intradermal test in this patient [11]. Another case described was a 36-year-old woman who experienced anaphylactic shock after consuming a drink containing erythritol. The symptoms reported by the patient were dyspnoea and angioedema. The skin spot test was positive [12].

Acesulfame

General information

Acesulfame potassium (ACE K), which belongs to the group of artificial sweeteners, is widely used in the food industry as a food additive with the number E950. Among other things, it is found in table sweeteners, fizzy drinks, cookies, syrups and sauces [6, 14]. It was discovered in 1967 by German scientist Karl Clauss, then in 1988 the US Food and Drug Administration (USFDA) approved the use of ACE K in various foods and beverages [20].

The widespread use of acesulfame potassium is due to a number of beneficial characteristics. ACE K is 200 times sweeter than sucrose. In addition, it shows stability at high temperatures, allowing its use in baking and cooking. It is not metabolised in the body, so it carries no energy value. It is excreted through the kidneys. Acesulfame has a bitter aftertaste, but this is neutralised by mixing it with other sweeteners. The acceptable daily intake is 50 mg/ kg body weight/day [13,14].

Effects on the intestinal microbiota

Acesulfame potassium is a hydrophilic acid derivative that is almost completely absorbed in the small intestine and 99% excreted in the urine and 1% in the faeces. The properties of ACE-K are indicated by the low concentrations that it can reach intestinal bacteria, so the effect of this sweetener on the microbiota is unlikely.

A 2015 study tested the effects of, among other things, acesulfame potassium on the gut microbiota. Seven healthy participants consumed between 1.7 mg and 33.2 mg of ACE-K per day. No changes in BMI values or in the number of gut bacteria were observed in the subjects compared to those who did not consume sweeteners. However, a reduction in the diversity of the gut microbiota was observed [15,23].

Breastfeeding

In a study with breastfeeding women, acesulfame potassium was detected in the milk of mothers who had consumed diet drinks or sweeteners in the last 24 hours. Interestingly, it was also detected in mothers who had not consumed them; this may be due to hidden sources of ACE-K in food. According to the study, the concentration of acesulfame in the mothers' milk ranged from 0.01 to 2.22 mg/l and peaked at 945 mcg/l after 4 hours after consumption of diet drinks. Despite the fact that the concentration of the sweetener in milk does not exceed permissible values, a limited intake during lactation is suggested, due to the unknown effects on infants.

Acesulfame was also detected in the plasma of breastfed infants, with an average concentration of 9.2 mcg/l. Available studies showed that occasional exposure of infants (once a week or less often) to sweeteners increased the risk of vomiting in infants, but that greater exposure did not have a significant effect on their health. There was no association between sweetener intake and infant weight, and no outliers were found in other studies. Further research is still needed to better assess the safety of sweeteners during lactation [16].

Tumour development

Studies conducted to date present inconsistent results regarding genotoxicity and carcinogenicity. Many publications are unreliable due to methodological errors. However, the latest research asserts that there is no evidence of cancer-causing effects from the consumption of sweeteners, including acesulfame potassium. Some studies have suggested a link between sweetener consumption and the risk of developing bladder, pancreatic or haematopoietic cancers. These results were probably a matter of chance, as they have not been confirmed in more publications. The discrepancy in the results across papers is due to different study methodologies and differences in consumption patterns of sweeteners, including acesulfame potassium. These differences make it difficult to draw firm conclusions, but toxicological and epidemiological evidence suggests that there is no reason to reduce the consumption of acesulfame potassium to avoid cancer development [17].

Type 2 diabetes

A cohort study published in 2023. on the relationship between the consumption of artificial sweeteners (including acesulfame potassium) and the risk of type 2 diabetes involved 105,588 people. 79.2% of these were women and the average age was 42.5 years. Those who

consumed higher amounts of acesulfame potassium had a 70% higher risk of developing type 2 diabetes compared to those who did not consume it (HR 1.70 [1.42-2.04], P -trend <0.001). The analysis performed took into account confounding factors; nevertheless, reverse causality cannot be excluded. The results suggest that the consumption of acesulfame potassium as a sugar substitute is dangerous in terms of the risk of developing type 2 diabetes [18].

Cardiovascular disease

The NutriNet-Santé study on a large sample group showed that the consumption of acesulfame potassium was associated with a higher risk of developing cerebrovascular disease, particularly coronary heart disease (1.40, 1.06 to 1.84, P=0.02; incidence rates 167 and 164). The risk was particularly high for sweeteners from beverages and solid foods. The analyses show that consumption of artificial sweeteners may increase the risk of cardiac problems, but does not reduce the risk compared to sugar. The studies point to the need for caution in their consumption and suggest that artificial sweeteners may negatively affect cardiovascular health (the mechanism is not yet fully understood). In conclusion, the health benefits of replacing sugar with artificial sweeteners in a cardiovascular context have not been demonstrated [19, 20].

Sucralose

General information

Sucralose is a popular food additive numbered E955, and is widely used to impart a sweet taste to foods with minimal impact on calories. Sucralose accounts for 30% of the sweetener market worldwide in the US, and its presence in more than 4,500 food and beverage products indicates its key role in the food industry. Sucralose was discovered in 1976 and is an artificial sweetener derived from sucrose by halogenation, the addition of three chlorine atoms in place of hydroxyl groups to sucrose, which alters the way it is absorbed in the body [21].

Initially used mainly in the diets of people with obesity and diabetes, sucralose has gained popularity among a wide range of consumers due to its unique properties, such as stability under various conditions and lack of effect on tooth decay. It is approximately 600 times sweeter than sugar, and its consumption has been deemed safe by the FDA and the WHO, who have set the acceptable daily intake at 15 mg/kg body weight. Despite previous assurances of its safety, recent studies suggest that excessive consumption of sucralose may be linked to health problems such as inflammation and metabolic diseases [21].

Comparison with sucrose

When comparing sucralose and sucrose, although both are sweeteners, they differ in many ways, from their origin to their effects on the body. Sucralose is an artificial sweetener, while sucrose (commonly known as sugar) comes from nature. The sucralose molecule is hydrophobic, meaning that it does not dissolve easily in water, unlike sucrose, which is hydrophilic and dissolves well [21].

In terms of its ability to bind to T1R3 taste receptors in the taste buds, sucralose is much more intensely absorbed, making it perceived as extremely sweet. In fact, sucralose is approximately 600 times sweeter than sucrose [21].

In terms of calorie intake, sucralose has a significant advantage because it is virtually calorie-free. Sucrose, on the other hand, provides a high amount of calories, making it a source of energy, but also one of the factors contributing to weight gain. The differences between these substances can also be seen in the effect on blood sugar levels. Sucralose has long been considered a sweetener with no major effect on glycaemia, but recent studies are prompting a reassessment of this aspect. Sucrose, on the other hand, directly raises blood glucose levels, which is particularly important for people with metabolic problems [21].

In terms of metabolism, as much as 84% of sucralose is not absorbed by the body and its metabolites are excreted. In contrast, sucrose is fully metabolised to glucose and fructose, which are used by the body as energy sources [21].

Effects on the microbiome

The results of studies on the effects of sucralose on the microbiome are inconclusive. A 2019 and 2020 study in which participants consumed 780 mg sucralose per day for seven days and 0.136g per day for two weeks, respectively, showed no significant changes in the gut microbiome [23]. In 2022, a study involving 47 healthy subjects was conducted. The results of the clinical trial showed that daily intake of 48 mg sucralose for ten weeks led to intestinal dysbiosis, increasing Blautia coccoides and decreasing Lactobacillus acidophilus. This is one of the first studies to suggest that sucralose doses significantly lower than the recommended ADI can affect the balance of the gut microbiome [22].

Pregnancy and breastfeeding

Sucralose can persist in the blood for more than 18 hours after ingestion, which means it can reach the placenta and fetus during pregnancy, and is also detected in breast milk. This raises concerns about its impact on the baby's health. Studies suggest that regular consumption of artificial sweeteners by pregnant women can lead to higher BMI in their children. Specifically, maternal consumption of sucralose has been linked to later weight gain, obesity and insulin resistance in offspring, especially boys. In addition, studies in cellular models and adipose tissue of the offspring showed increased expression of genes responsible for adipose tissue development, suggesting that sucralose may directly affect adipose development [24].

Effects on the reward system

A California study published in 2021 found that obesity and gender affect neurobehavioral responses after consuming sucralose. In 74 healthy adults, brain activity (using MRI), metabolic responses and eating behavior were studied after consuming beverages containing sucrose, sucralose or water. Obese participants and especially women showed stronger neural responses to images of food in areas of the brain associated with the reward system and also consumed more calories after drinking a beverage with sucralose. This suggests that ingestion of artificial sweeteners may impair the brain's response to food, which may negatively affect eating behavior and metabolism, especially in women; however, much more research is needed to prove this thesis [25].

Aspartame

Aspartame is an artificial sweetener that was developed as an alternative to sucrose. It was discovered by James M. Schlatter in 1965. It is about 180-200 times sweeter than sugar, which was thought to help fight obesity in developing countries and treat diabetes. Aspartame is widely used in the production of soft drinks, candy and medicines. Despite its widespread use, the safety of aspartame consumption is controversial. It came to market in 1981 under the name NutraSweet, initially without raising concerns about possible carcinogenic effects. According to FDA guidelines, the acceptable daily intake of aspartame is 40 mg per kg of body weight in Europe and 50 mg per kg in the US, for both adults and children. Products containing aspartame must have an appropriate statement that it is not suitable for cooking or baking. Aspartame consists of two amino acids - L-phenylalanine and L-aspartic acid, which are broken down in the digestive tract by esterases and peptidases. During digestion, three substances are

released: methanol (10%), aspartic acid (40%) and phenylalanine (50%). The use of aspartame in food production is limited due to its instability, especially in solutions when the temperature is high or the pH exceeds 6 [26].

Effects on caloric intake

Two studies were conducted that analyzed the effects of drinking water and aspartame- and sucrose-sweetened carbonated beverages on the amount of food consumed and feelings of hunger in 11 men and 14 women who followed a food restriction diet. At the end of the day, total energy intake was similar in all test conditions in both the male and female groups. Therefore, low-calorie/low-sugar drinks did not help reduce total energy intake during the day. In addition, an increase in caloric intake was observed in the women's group on the following day. There are suggestions that the taste of beverages sweetened with both sugar and artificial sweeteners may intensify feelings of hunger, resulting in greater caloric intake and potential weight gain. However, these issues require further research [26, 27].

Inflammation

A study was conducted to evaluate the effects of a diet rich in sucrose and artificial sweeteners, including aspartame, on inflammatory markers such as CRP, haptoglobin and transferrin in overweight individuals. Participants in the study, both men and women, consumed beverages containing sucrose or artificial sweeteners for an average of 10 weeks. The results showed that in the sucrose group, haptoglobin, transferrin and CRP concentrations increased by 13%, 5% and 6%, while in the artificial sweetener group, these concentrations decreased by, respectively: 16%, 2% i 26% [28].

Damage to the cerebral cortex

Through a study on 19 rats, it was found that oral ingestion of aspartame can lead to damage to the cerebral cortex in these animals, as manifested by reduced survival of pyramidal cells and glial astrocytes. Possible mechanisms for this effect include decreased levels of brain-derived neurotrophic factor (BDNF), increased oxidative stress, inhibition of antioxidant capacity, blocked mitochondrial biogenesis, and increased expression of apoptosis-related proteins such as Bax and caspase-3. In addition, elevated levels of pro-inflammatory cytokines and increased inflammatory responses, including PGE2 and COX-2, have been observed [29].

Cancer Development

Conducted in Spain between 2008 and 2013, the study aimed to identify etiological factors of common cancers. Individuals between the ages of 20 and 85 who were diagnosed with histologically confirmed cancer were invited to participate. This study analyzed the association between consumption of products containing aspartame and other artificial sweeteners and cancer risk. No association was found between consumption of artificial sweeteners and cancer risk in the study group. However, in people with diabetes, the results indicated that consumption of products containing aspartame and other artificial sweeteners may have been associated with a higher risk of gastric cancer, and high consumption of other sweeteners may have been associated with colorectal cancer [30].

Conclusions

Sweeteners can be an effective substitute for sugar, especially for those concerned about the caloric content of their diets or those battling diabetes. Natural substances such as stevia and erythritol are prized for their safety of use, while synthetic sweeteners such as aspartame are still somewhat controversial. Research on their health effects is inconclusive, especially in the context of the gut microbiome and long-term use. Nevertheless, they are considered safe at certain doses. A key finding is the need to educate consumers on the informed choice of sweeteners and their moderation in the diet. Sweeteners can support a reduction in sugar intake, but they are not a one-size-fits-all solution. Further research can help better understand their effects on the body and enable the development of safer sweeteners.

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