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HEALTH IMPLICATIONS AND SAFETY OF ARTIFICIAL SWEETENERS

ZDRAVSTVENE IMPLIKACIJE I BEZBEDNOST VEŠTAČKIH ZASLAĐIVAČA

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Abstract

Introduction. Non-nutritive sweeteners allow for the enjoyment of sweet-tasting foods with minimal calorie intake. Their growing popularity is driven by increased health awareness and efforts to reduce sugar consumption, particularly among individuals at higher risk of obesity and diabetes. **Results**. Artificial sweeteners vary in chemical structure and mechanisms of action, providing intense sweetness even at low concentrations. Their metabolism in the human body depends on the specific compound, and their safety is rigorously assessed by global regulatory agencies. While most are approved for use and considered safe within recommended intake levels, emerging data suggest potential long-term effects, including alternations in gut microbiota, impaired glucose metabolism, and increased risk of certain diseases. Despite these concerns, sugar substitutes play a significant role in modern nutrition by enabling reduced caloric intake without compromising taste. **Conclusion**. Continued research is essential to fully understand the health benefits and risks of non-nutritive sweeteners, supporting informed choices regarding their inclusion in everyday diets.

Key words: Sweetening Agents; Health Impact Assessment; Safety; Risk Factors; Drug-Related Side Effects and Adverse Reactions; Food Additives

Sažetak

Uvod. Veštački zaslađivači predstavljaju široko korišćene prehrambene aditive koji omogućavaju unos hrane sa slatkim ukusom, uz minimalan unos kalorija. Njihova popularnost raste usled sve veće svesti o zdravlju i potrebe za smanjenjem unosa šećera, posebno kod populacije sa povećanim rizikom od gojaznosti i dijabetesa. **Rezultati.** Veštački zaslađivači poseduju različite hemijske strukture i mehanizme delovanja, koji omogućavaju postizanje intenzivnog slatkog ukusa pri malim koncentracijama. Metabolizam ovih jedinjenja u ljudskom organizmu varira u zavisnosti od vrste zaslađivača, a njihova bezbednost je predmet pažljive procene regulatornih tela na globalnom nivou. Iako su mnogi odobreni za upotrebu i smatraju se bezbednim kada se koriste u preporučenim količinama, dostupni podaci ukazuju na potencijalne dugoročne rizike, uključujući uticaj na mikrobiom creva, metabolizam glukoze i rizik od određenih poremećaja. Veštački zaslađivači imaju značajnu ulogu u modernoj ishrani, omogućavajući smanjenje unosa šećera i kalorija bez kompromisa u pogledu ukusa. **Zaključak.** Ipak, potrebne su dodatne analize kako bi se dodatno razjasnile zdravstvene koristi i rizici, čime bi se omogućilo, uz potpunu informisanost, donošenje odluka o njihovoj upotrebi i integraciji u svakodnevnu ishranu.

Ključne reči: zaslađivači; procena uticaja na zdravlje; sigurnost; faktori rizika; neželjeni efekti i neželjene reakcije na lekove; prehrambeni aditivi

Introduction

Sweetening agents are widely used as sugar substitutes in foods, beverages, pharmaceuticals, and hygiene products across the globe [1]. Research on newborns has demonstrated that human preference for sweet-tasting foods is innate [2].

The U.S. Food and Drug Administration (FDA) has approved several non-nutritive sweeteners (NNS) for consumption within the limits of the acceptable daily intake (ADI). These include acesulfame-K, saccharin, sucralose, neotame, aspartame, and stevia. The ADI represents the quantity of a substance that can be safely consumed daily over a lifetime without posing significant health risks and is expressed in milligrams per kilogram of body weight [3]. Other commonly used sweeteners include alitame – approved for use in South America, China, and Australia – and cyclamate, which is permitted in in 50 countries, though not in the U.S. [4].

In the European Union, sweetener alternatives are also approved as food additives [5]. Their safety is assessed by national regulatory authorities, the European Food Safety Commission (EFSA), and the Joint FAO/WHO Expert Committee on Food Additives (JECFA), ensuring that only sweet-

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Abbreviations

NNS – non-nutritive sweeteners
FDA – Food and Drug Administration
ADI – acceptable daily intake
EU – European Union
T2D – type 2 diabetes
SCFAs – short-chain fatty acids

eners with established safety profiles are authorized for public use [6].

However, excessive consumption of these additives may lead to adverse effects, and it is essential to raise consumer awareness of potential risks [4]. Studies have associated artificial sweeteners with gastrointestinal disturbances, neurological symptoms (such as headaches and altered taste perception, and an increased risk of cardiovascular disease and type 2 diabetes (T2D) [7].

A large-scale prospective cohort study recently found that individuals with higher consumption of artificial sweeteners had an increased risk of developing T2D compared to non-consumers, with particularly strong association observed for aspartame and acesulfame-K [8].

Due to their widespread used in a dietary, processed, and cosmetic products, complete avoidance of artificial sweeteners is nearly impossible. Nevertheless, certain populations should exercise caution, including children, individuals with diabetes, pregnant or breastfeeding women, and patients with migraines or epilepsy [4].

Children are especially vulnerable, as they tend to consume more food and beverages per kilogram of body weight. The American Dietetic Association advises against the use of artificial sweeteners in children under the age of two years of age and recommends minimal or no consumption during pregnancy and lactation, despite FDA approval. Some evidence also suggests a potential link between sweetener intake during pregnancy and an increased risk of premature birth [9,10].

This study focuses on aspartame and other commonly used FDA-approved sweeteners, which have undergone extensive safety evaluations and are widely incorporated into food and beverage products.

Acesulfame Potassium (E950)

Acesulfame potassium (Ace-K) is a non-caloric artificial sweetener that is over 200 times sweeter than sucrose and is among the most widely used sugar substitutes worldwide [11]. When used alone, Ace-K can produce a slightly bitter aftertaste; therefore, it is often blended with other sweeteners such as sucralose or aspartame. After oral ingestion, Ace-K is rapidly and completely absorbed in the gastrointestinal tract. It is quickly distributed throughout the body and primarily excreted unchanged in the urine, with no evidence of tissue bioaccumulation. At peak plasma concentrations, the highest levels are found in the gastrointestinal tract, bile, kidneys, and bladder [12]. One of the Ace-K's by-products, acetoacetamide, has shown toxic effects in high concentrations. Animal studies demonstrated that a diet containing 1% acetoacetamide over three months induced tumor growth in the thyroid gland. However, human exposure to this compound is considered negligible, and the FDA has concluded that Ace-K is safe for human consumption [13]. The diabetogenic potential of Ace-K has been examined in various studies with findings suggesting a stronger association with impaired glucose metabolism than sucralose. Elevated doses of Ace-K have been linked to disrupted insulin regulation and glucose homeostasis, which could contribute to the development of type 2 diabetes and metabolic disease. One study reported a 36% higher relative risk of developing metabolic syndrome in individuals who consumed Ace-K–sweetened beverages compared to non-consumers [13]. Notably, even low doses of Ace-K (around 1-4% of the ADI) have been associated with earlier onset of puberty in girls [13]. Furthermore, a large cohort study involving 10,388 participants found a significant association between total consumption of artificial sweeteners – specifically Ace-K – and an increased risk of cardiovascular diseases [13]. In animal models, Ace-K has also been shown to alter the composition of the gut microbiota. Mice treated with Ace-K exhibited an increased abundance of the *Bacteroides* genus compared to controls. *Bacteroides* species have are capable of degrading complex glycans and producing short-chain fatty acids (SCFAs), which are vital for host metabolism [14]. Additionally, Ace-K administration led to a significant rise in pyruvate levels, a central metabolite in energy pathways that can serve as a precursor to SCFAs [14].

Ace-K is currently approved for use in over 50 countries, including Canada, Switzerland, Norway, Japan, the United States, Australia, and various EU member states [15]. The FDA initially approved Ace-K for use in carbonated beverages in 1988, followed by a broader approval for general use in 2003 [16]. The acceptable daily intake (ADI) established by the FDA is 15 mg/kg of body weight [17].

Aspartame (E951)

Aspartame is a low-calorie artificial sweetener approximately 200 times sweeter than sucrose. In Europe, it is approved as a food additive and is widely used to sweeten beverages, desserts, confectionery,

dairy products, chewing gum, low-calorie and weight management products, and as a tabletop sweetener [18]. Chemically, aspartame is a methyl ester composed of two amino acids: L-aspartic acid and L-phenylalanine, combined with methanol through esterification. Upon digestion, these components are released in the following proportions: phenylalanine (50%), aspartic acid (40%), and methanol (10%), all of which are readily absorbed through the intestinal mucosa. While these metabolites are naturally occurring in many foods, in high doses they may exert harmful effects, particularly with chronic consumption [19]. Methanol, once absorbed, is gradually metabolized in the liver into formaldehyde, a known neurotoxin, and subsequently into formic acid via the enzyme alcohol dehydrogenase [12]. Formic acid can inhibit cytochrome oxidase, a critical enzyme in the mitochondrial respiratory chain, leading to increased anaerobic metabolism and lactate accumulation. Elevated plasma levels of phenylalanine – another aspartame metabolite – may inhibit tyrosine hydroxylase and tryptophan hydroxylase, enzymes essential for the synthesis of neurotransmitters such as serotonin and dopamine. These neurotransmitters are involved in regulating mood, cognition, motor activity, appetite, sleep, and cardiovascular function. Therefore, individuals with phenylketonuria – a genetic disorder resulting in the inability to metabolize phenylalanine into tyrosine – must strictly avoid aspartame consumption due to the risk of neurotoxicity [19].

Several studies have suggested a potential link between aspartame intake and disturbances in glucose metabolism, including associations with obesity, insulin resistance, and alterations in the gut microbiota, particularly in animal models [19].

Research has also explored potential neurotoxic effects of aspartame and its breakdown products. Some findings point to a possible association with the pathogenesis of neurodegenerative disorders, including multiple sclerosis, Alzheimer's disease, Parkinson's disease, and brain tumors [19].

In terms of renal safety, frequent high-dose intake of aspartame has demonstrated nephrotoxic effects in experimental studies. Long-term exposure led to a dose-dependent increase in free radical formation in kidney tissues and a significant reduction in the activity of key antioxidant enzymes such as catalase, superoxide dismutase, glutathione reductase, and glutathione peroxidase in both liver and kidney tissues of rats [20].

Aspartame was first approved by the U.S. FDA in 1981 for use as a tabletop sweetener, and in 1996, it received approval for general use in food and beverages [2]. The acceptable daily intake (ADI) of aspartame is 50 mg/kg of body weight per day, as specified by FDA [17].

Saccharin (E954)

Saccharin is an artificial sweetener derivative from toluene sulfonamide, chemically known as osulfabenzamide (2,3-dihydro-3-oxobenzisosulfonazole). It is approximately 200-700 times sweeter than sucrose and is commonly used in combination with other sweeteners such as cyclamate or aspartame to mask its characteristic bitter or metallic aftertaste [15,17]. Saccharin is often employed to enhance the palatability of food, beverages, and pharmaceuticals without increasing their caloric value [15]. Pharmacokinetically, saccharin is not metabolized by the human body and is excreted unchanged in the urine. However, its use is not recommended during pregnancy or breastfeeding due to its potential to cross the placenta barrier and appear in breast milk [2].

Historically, saccharin was considered suitable for individuals with diabetes, as it does not undergo metabolic processing and does not elevate blood glucose levels [21]. However, more recent studies have raised concerns about its potential effects on glucose homeostasis. Evidence suggests that saccharin may interfere with glucose regulation, impair insulin sensitivity, and influence glucose absorption, potentially contributing to hyperinsulinemia, insulin resistance, and adipose tissue accumulation [22]. One study demonstrated a positive correlation between saccharin intake and an increased body weight, attributed to the appetite-regulation centers in the brain. In animal studies, saccharin-sweetened water resulted in increased hunger compared to glucose-sweetened water [15]. Furthermore, saccharin and other non-nutritive sweeteners may enhance sweet cravings, thereby promoting overconsumption of high-calorie foods and contributing to weight gain [21]. Artificial sweeteners like saccharin may also induce an insulin response due to their sweet taste, despite the absence of increased blood glucose levels. This mismatch may result in hypoglycemia, which can further stimulate hunger and lead to increased caloric intake. In long-term animal studies, mice fed a mixture of saccharin and cyclamate gradually increased their calorie intake, resulting in weight gain and greater fat deposition [23].

Saccharin is currently approved in over 100 countries and is generally recognized as safe when used within recommended limits. Nonetheless, due to conflicting findings regarding its metabolic effects, caution is advised, particularly in vulnerable populations [24]. The acceptable daily intake (ADI) established by the U.S. FDA is 15 mg/kg of body weight per day [17].

Sucralose (E955)

Sucralose is a synthetic non-nutritive sweetener derived from sucrose through a process that involves substituting three hydroxyl groups with chlorine atoms. This structural modification produces a compound that is approximately 600 times sweeter than sucrose [3,17]. Sensory studies show that sucralose does not have the bitter aftertaste associated with some other non-nutritive sweeteners [25].

The human body does not metabolize sucralose as a carbohydrate, and thus does not provide energy or elevate blood glucose levels. Most of the ingested sucralose passes through the gastrointestinal tract unchanged and is excreted in the feces. A smaller fraction (11–27%) is absorbed and excreted via the urine, without evidence of tissue accumulation [2, 25]. Importantly, sucralose does not cross the placenta or the blood-brain barrier, further supporting its favorable safety profile [25].

However, animal studies have raised concerns regarding the impact of sucralose on gut microbiota. In a study conducted on mice, low-dose sucralose administration led to significant alternations in the microbial composition of the ileum, jejunum, and colon, with a notable increase in pathogenic bacteria [21].

A study involving dietary inclusion of 5% sucralose reported a reduction in thymic weight in animal models. However, further investigation indicated that the observed effect may be attributable to nutritional imbalances rather than sucralose's inherent toxicity [11]. While most clinical studies indicate that sucralose does not significantly alter glucose metabolism, emerging evidence suggest that concurrent intake of sucralose with carbohydrates may impair insulin sensitivity in healthy individuals [21].

The FDA classifies sucralose as safe for human use when consumed in amounts not exceeding the ADI, which is 5 mg/kg body weight [17].

Neotame (E961)

Neotame is the one of the most recent NNS approved for human consumption. It is obtained derivative of aspartame, produced through N-alkylation, resulting in a compound that is chemically similar to aspartimebut significantly more potent [2].

Neotame is approximately 7,000 to 13,000 times sweeter than sucrose, making it one of the most intense sweeteners available. In addition to its use as a non-caloric sweetener, it is also employed as a flavor enhancer, particularly in sour fruit flavors [2].

It is minimally absorbed by the body, does not accumulate in tissues, and is excreted unchanged [11].

In a study involving rats, a reduction in body weight was noted during exposure to neotme. However, this weight loss was not attributed to the toxic effects of neotame, but rather to reduced food intake due to its unpleasant taste at high concentrations [2]. In a separate four-week animal study, neotame exposure was associated with changes in gut microbiota composition, including an increase in *Bacteroides* genus, which is involved in polysaccharide fermemtation, and a decrease in *Lachnospiraceae* and *Ruminococcaceae,* bacterial families known for their production of short-chain fatty acids (SCFAs). SCFAs are crucial for energy homeostasis, lipid and fatty acid absorption, and bile acid metabolism [26]. Human studies have shown that neotame does not raise blood glucose levels. It may cause headaches and loss of appetite, while excessive consumption may affect the liver [27]. Neotame is not metabolized by oral bacteria, which means it does not to contribute to dental caries [28].

The FDA has established an acceptable daily intake (ADI) for neotame of 0.3 mg/kg of body weight [17]. Safety studies have not demonstrated any adverse effects in clinical trials, physical examinations, or histopathological evaluations [11].

Advantame (E969)

Advantame is a non-nutritive artificial sweetener and a chemical derivative of aspartame, composed of 3-hydroxy-4-methoxyphenylpropane, aspartic acid, and the methyl ester of phenylalanine [29]. It has a sweetening power approximately 20,000 times greater than that of sucrose [17]. It does not have a bitter or sour aftertaste [11].

It is suitable for use in iced tea, coffee, and powdered drink mixtures, chewing gums, and yogurts [11].

Toxicological studies have demonstrated that advantame does not exhibit teratogenic potential. Animal toxicity studies and data from human studies have confirmed that it is safe for use in food products [11]. The FDA approved advantame for general use in foods and beverages in 2014. It is considered safe for the population, including individuals with diabetes, as it does not affect blood glucose levels [29]. According to FDA guidelines, the ADI for advantame is 32.8 mg/kg body weight per day [17].

Steviol Glycosides (E960)

Stevia rebaudiana (Asteraceae) is a small perennial herb native to South America, traditionally used to sweeten beverages such as mate tea. Out of approximately 150–300 species of the *Stevia* genus, only 18 possess sweetening properties, with *S. rebaudiana* being

the most potent. The primary sweet components are steviol glycosides, predominantly stevioside (9.1%) and rebaudioside A (3.8%) [30]. Rebaudioside A is approximately 450 times, and stevioside 300 times sweeter than sucrose. Despite their intense sweetness, both stevioside and rebaudioside A may produce a bitter or metallic aftertaste, which is reduced with increased compound purity or when the two are used in combination [15,30]. The European Food Safety Authority (EFSA) has established an acceptable daily intake (ADI) of 4 mg/kg of body weight for steviol glycosides. Clinical evidence indicates that, when consumed within this limit as sweeteners, steviol glycosides exert no significant pharmacological effects. Steviol glycosides are non-caloric, non-cariogenic, non-allergenic, and considered a natural alternative to sucrose [30]. Unlike other artificial sweeteners, they passes through the upper digestive tract unchanged and are fermented only in the large intestine by intestinal microbiota [15]. Preclinical and clinical studies suggest that stevioside lowers blood glucose levels without altering glucagon concentrations. It slows glucose absorption in the small intestine by approximately 40% and suppresses gluconeogenesis by downregulating the gene encoding phosphoenolpyruvate carboxykinase – an enzyme involving hepaticglucose production. These effects are observed only under hyperglycemic conditions [15, 31]. There is evidence of stevioside and rebaudioside A inducing vasodilation, diuresis, and natriuresis, ultimately reducing plasma volume and lowering arterial blood pressure. However, these effects occur only at doses higher than the ADI and are not observed in normotensive individuals [Paucar]. Furthermore, stevia leaf extract has demonstrated antimicrobial and antifungal activities, effectively inhibiting pathogens such as *Staphylococcus aureus, Salmonella typhi, Escherichia coli, Aeromonas hydrophila, Bacillus cereus, Klebsiella pneumoniae* and *Vibrio cholerae,* as well as fungi such as *Penicillium chrysogenum* and *Aspergillus niger* [15]. Additionally, steviol glycosides are non-cariogenic, helping to prevent the development of dental caries [15].

Conclusion

In contemporary diets, non-nutritive sweeteners play essential key role in reducing calorie and sugar intake – an essential strategy for the prevention and management of obesity and metabolic disorders. Their ability to provide intense sweetness without contributing to caloric intake makes them an appealing option for health-conscious consumers. However, despite approval from regulatory agencies, the long-term safety and health implications of artificial sweeteners remain incompletely understood, warranting further investigation.

Emerging evidence suggests that certain artificial sweeteners may be associated with adverse health outcomes, including alterations in glucose metabolism, modulation in the gut microbiota, enhanced appetite, and potential neurodegenerative changes.

Use of artificial sweeteners is particularly prevalent among specific population groups, notably women, individuals with higher body mass index, and those with higher education and income levels. These compounds are most commonly found in dietary beverages, sugar-free chewing gums, low-calorie dairy products, and tabletop sweeteners. Consumption trends show increasing use of sweeteners such as sucralose and saccharin, while the use of others, like cyclamate, has declined due to shifting consumer preferences and regulatory guidance.

Public education is vital in promoting informed choices regarding artificial sweeteners. Consumers must be made aware of potential individual sensitivities, such as phenylketonuria, and the need for special caution in vulnerable populations, including children, pregnant women, and individuals with chronic health conditions. Enhancing food literacy, particularly in the interpretation of nutrition labels, can empower consumers to make healthier dietary choices and better understand the potential effects of artificial sweeteners on overall health.

References

1. Weihrauch MR, Diehl V. Artificial sweeteners--do they bear a carcinogenic risk? Ann Oncol. 2004;15(10):1460-5.

2. Ižaković M, Ačkar Đ, Šubarić D. Commonly used artificial sweeteners in Europe. Food in Health and Disease, scientific-professional journal of nutrition and dietetics. 2021;10(1):24-34.

3. Sardarodiyan M, Hakimzadeh V. Artificial sweeteners. International Journal of PharmTech Research. 2016;9(4):357-63.

4. Sharma A, Amarnath S, Thulasimani M, Ramaswamy S. Artificial sweeteners as a sugar substitute: are they really safe? Indian J Pharmacol. 2016;48(3):237-40.

5. Novaković B, Torović Lj, editors. Bromatologija. Novi Sad: Medicinski fakultet; 2014.

6. Mortensen A. Sweeteners permitted in the European Union: safety aspects. Scandinavian Journal of Food and Nutrition. 2006;50(3):104-16.

7. Ghusn W, Naik R, Yibirin M. The impact of artificial sweeteners on human health and cancer association: a comprehensive clinical review. Cureus. 2023;15(12):e51299.

8. Okoro FO, Markus V. Artificial sweeteners and type 2 diabetes mellitus: a review of current developments and future research directions. J Diabetes Complications. 2025;39(2):108954.

9. Englund-Ögge L, Brantsæter AL, Haugen M, Sengpiel V, Khatibi A, Myhre R, et al. Association between intake of artificially sweetened and sugar-sweetened beverages and preterm

delivery: a large prospective cohort study. Am J Clin Nutr. 2012; 96(3):552-9.

10. Mao D, Lin M, Zeng Z, Mo D, Hu KL, Li R. Artificial sweetener and the risk of adverse pregnancy outcomes: a Mendelian randomization study. Nutrients. 2024;16(19):3366.

11. More TA, Sheikh Z, Ali A. Artificial sweeteners and their health implications: a review. Biosciences Biotechnology Research Asia. 2021;18(2):227-37.

12. Volz M, Christ O, Eckert HG, Herok J, Kellner HM, Rupp W. Kinetics and biotransformation of acesulfame-K. In: Mayer DG, Kemper FH, editors. Acesulfame-K [Internet]. New York: Marcel Dekker; 1991 [cited 2025 Apr 3]. p. 7-26. Available from: https://books.google.rs/books?hl=en&lr=&id=BTD6o22FXbYC&oi=fnd&pg=PA7&dq=Kinetics+and+biotransformation+of+acesulfame-K&ots=nNy8IRZH8V&sig=3h-ekaNVFVC-MxrvPc-R9gI-LC20&redir_esc=y#v=onepage&q=Kinetics%20and%20biotransformation%20of%20acesulfame-K&f=false

13. Xu X. The review: effects of acesulfame K on human health. International Journal of Agriculture and Food Sciences Research. 2024;1(1):64-70.

14. Bian X, Chi L, Gao B, Tu P, Ru H, Lu K. The artificial sweetener acesulfame potassium affects the gut microbiome and body weight gain in CD-1 mice. PloS One. 2017;12(6):e0178426.

15. Antonik N, Janda K, Jakubczyk K. Characteristics of sweeteners used in foods and their effects on human health. Pomeranian J Life Sci. 2020;66(3):57-65.

16. Saulo AA. Sugars and sweeteners in foods. Honolulu: Cooperative Extension Service, College of Tropical Agriculture and Human Resources, University of Hawai'i at Mānoa; 2005. p. 1-7.

17. U.S. Food and Drug Administration. Aspartame and other sweeteners in food [Internet]. 2024 [cited 2025 Mar 31]. Available from: http://www.fda.gov/food/food-additives-petitions/aspartame-and-other-sweeteners-food

18. European Food Safety Authority (EFSA). Aspartame [Internet]. 2023 [cited 2025 Apr 3]. Available from: https://www.efsa.europa.eu/en/topics/topic/aspartame

19. Czarnecka K, Pilarz A, Rogut A, Maj P, Szymańska J, Olejnik Ł, et al. Aspartame-true or false? Narrative review of safety analysis of general use in products. Nutrients. 2021;13(6):1957.

20. Shaher SAA, Mihailescu DF, Amuzescu B. Aspartame safety as a food sweetener and related health hazards. Nutrients. 2023;15(16):3627.

21. Yin J. Artificial sweeteners: current discoveries, healthy effects and future developments. MedScien. 2024;1(1 issue 3):1-6.

22. Karagöz MF, Sağdiçoğlu-Celep AG. Saccharin by nutritional metabolism perspective. EC Nutrition. 2020;15(3):1-5.

23. Hasan HM, Alkass SY, de Oliveira DSP. Impact of long-term cyclamate and saccharin consumption on biochemical parameters in healthy individuals and type 2 diabetes mellitus patients. Medicina (Kaunas). 2023;59(4):698.

24. Mahmood AA, Al-Juboori SB. A review: saccharin discovery, synthesis, and applications. Ibn AL-Haitham Journal For Pure and Applied Sciences. 2020;33(2):43-61.

25. Grotz VL, Munro IC. An overview of the safety of sucralose. Regul Toxicol Pharmacol. 2009;55(1):1-5.

26. Chi L, Bian X, Gao B, Tu P, Lai Y, Ru H, et al. Effects of the artificial sweetener neotame on the gut microbiome and fecal metabolites in mice. Molecules. 2018;23(2):367.

27. Patil S, Jalal RAS, Albar DH, Bansal SJ, Patil S, Nagaral S, et al. Intake of artificial sweeteners by children: boon or bane? J Contemp Dent Pract. 2023;24(2):137-45.

28. O'Donnell K. Aspartame, neotame and advantame. In: O'Donnell K, Kearsley MW, editors. Sweeteners and sugar alternatives in food technology. 2nd ed. Chichester: Wiley-Blackwell; 2012. p. 117-36.

29. Khan R, Aroulmoji V. Low calorie high-intensity sweeteners. International Journal of Advanced Science and Engineering. 2018;5(2):934.

30. Orellana-Paucar AM. Steviol glycosides from Stevia rebaudiana: an updated overview of their sweetening activity, pharmacological properties, and safety aspects. Molecules. 2023;28(3):1258.

31. Vujašević M, Lalić N, Jotić A, Miličić T, Maćešić M, Lukić L. Assessment of cardiovascular risk in patients with type 2 diabetes and albuminuric diabetic kidney disease phenotype. Med Pregl. 2024;77(1-2):25-30.

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