International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	SWEETENERS IN THE AGE OF CIVILIZATION DISEASES – A REVIEW OF CURRENT KNOWLEDGE, CONSUMER TRENDS AND THE ROLE OF THE FITNESS INDUSTRY
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3965
RECEIVED	12 August 2025
ACCEPTED	29 September 2025
PUBLISHED	30 September 2025
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SWEETENERS IN THE AGE OF CIVILIZATION DISEASES – A REVIEW OF CURRENT KNOWLEDGE, CONSUMER TRENDS AND THE ROLE OF THE FITNESS INDUSTRY

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ABSTRACT

Introduction: The global rise in obesity, type 2 diabetes, and cardiovascular diseases has intensified the search for dietary strategies to reduce added sugar intake. Low-calorie sweeteners (LCS) have emerged as widely used sugar substitutes, promoted as healthier alternatives. Despite their growing popularity, the long-term health impacts and role of LCS in disease prevention and metabolic regulation remain controversial.
Aim of the study: This review aims to critically analyze the relationship between the increased consumption of LCS and the prevalence of metabolic diseases. Additionally, it explores the influence of the fitness market on the promotion and acceptance of sweeteners and examines global consumption trends and market forecasts.
Materials and methods: A comprehensive literature review was conducted using PubMed and Google Scholar, analyzing recent clinical trials, preclinical studies and researches. The selected studies focus on the metabolic effects of LCS, public health implications, consumer behavior, and market data regarding global sweetener consumption. Attention was given to both synthetic and natural LCS.
Conclusions: Low-calorie sweeteners have become a central component in dietary interventions targeting metabolic health. While some studies support their use as a tool for reducing caloric intake and managing blood glucose levels, others suggest possible adverse metabolic effects. Their widespread adoption, amplified by fitness culture and industry marketing continues to drive global market expansion. Further longitudinal research is essential to assess their safety, efficacy, and role in chronic disease prevention.

KEYWORDS

Low-Calorie Sweeteners, Artificial Sweeteners, Obesity, Type 2 Diabetes, Cardiovascular Diseases, Fitness Market

CITATION

Marcin Ciechański, Edyta Witkowska, Klaudia Wilk, Szymon Cholewiński, Bernadetta Wilk, Piotr Stachura, Piotr Rejman, Katarzyna Pszczoła, Katarzyna Jurkiewicz, Aleksandra Kasprzyk. (2025) Sweeteners in the Age of Civilization Diseases – A Review of Current Knowledge, Consumer Trends and the Role of the Fitness Industry. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3965

Introduction:

A hallmark of the Western diet and the most serious public health challenges

It is well known that high-sugar consumption is a hallmark of the Western diet (Khan et al., 2020). Dietary sugars mainly refer to fructose and glucose which are naturally present in fruits and some vegetables (Ma et al., 2022)(Basaranoglu et al., 2015). The worldwide prevalence of overweight and obesity has nearly tripled over the past four decades, and represents one of the most serious unmet public health challenges of the 21st century. Pooled estimates from population-based studies from across the globe show that the prevalence of obesity increased between 1975 and 2016, from <1% to 6–8% among children, from 3% to >11% among men and from 6% to 15% among women (Bentham et al., 2017). Over 2.1 billion people, or nearly 30% of the global population, have overweight or obesity, giving rise to substantial health, social and economic costs ("Health Effects of Overweight and Obesity in 195 Countries over 25 Years," 2017). Excess weight is the leading risk factor for type 2 diabetes mellitus (T2DM) and can also lead to a number of related chronic conditions, including coronary heart disease (CHD), stroke and many cancers. The global economic effect of obesity is estimated to be ~2 trillion US dollars, or 2.8% of global gross domestic product, which is roughly equivalent to the global economic effect of smoking or armed conflict (*Overcoming Obesity: An Initial Economic Analysis | Sportanddev*, n.d.),(Malik & Hu, 2022).

Recommendations and demand for sugar reduction

Most food-based dietary guidelines make the sensible and pragmatic suggestion for populations to limit the consumption of foods of low nutrient density, such as foods of low dietary quality that are high in calories, sugar, salt and fat, especially saturated fat. In recent years, many government and health organizations

worldwide have revisited their guidance for dietary sugar intake, particularly in relation to maximum recommended intakes for added or free sugars (Walton et al., 2023).

For free sugars, the World Health Organization (WHO) recommends that all individuals, both adults and children, reduce their intake of free sugars to <10% energy intake and suggest a further conditional recommendation of reduction to <5% energy for further health benefits. This <5% energy value is also proposed by both the UK Scientific Advisory Committee on Nutrition (SACN) (as an average population maximum target) and by the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) (as individual guidance) (Walton et al., 2023; World Health Organization, 2015).

The popularity of low-calorie or non-nutritive sweeteners has risen in recent years in response to consumer demand for sugar reduction or replacement across a wide range of foods and beverages (Sylvetsky & Rother, 2016). There are currently many commercially available sweeteners that are capable of matching the perceived sweetness intensity of sucrose over a range of concentrations, and with fewer calories (Antenucci & Hayes, 2015)(Wee et al., 2018). Many of these sweeteners have advantages as sucrose substitutes such as providing bulk, having an anti-glycemic effect, being low-cost, or supporting a clean label (Clemens et al., 2016)(Lê et al., 2016). Artificial sweeteners have been developed as sugar substitutes. Many of these

have a much stronger sweetness than simple sugar and sucrose and have few calories. Compared to sucrose, artificial sweeteners are hundreds of times sweeter, so the use of various artificial sweeteners together can reduce the amount of sugar used (Iizuka, 2022).

Acesulfame K (ACE K), aspartame, and sucralose are widely used and are well-known as artificial sweeteners and are now being studied by many researchers. ACE K and aspartame are used in soft drinks such as soda and protein drinks(Iizuka, 2022). The use of artificial sweeteners is thought to prevent dental caries and obesity by reducing the use of sugar, and so-called artificially sweetened beverages are sometimes used in place of sugar-laden soft drinks for obese patients with diabetes mellitus(Evert et al., 2019). Therefore, artificial sweeteners are included in many “sweets” and are anticipated to be a “sugar” substitute in patients with diabetes mellitus(Evert et al., 2019). However, substituting sugar-sweetened food and beverages with those that have been artificially sweetened may not be as beneficial as once thought(Nichol et al., 2018). Recently, it was reported that artificial sweeteners can affect glucose tolerance through changes in the microbiota composition(Nichol et al., 2018; Ruiz-Ojeda et al., 2019; Suez et al., 2022). Moreover, artificial sweeteners have side effects in terms of obesity, cardiovascular disease, and mortality(Debras, Chazelas, Sellem, et al., 2022; Debras, Chazelas, Srour, et al., 2022; Mossavar-Rahmani et al., 2019; Yan et al., 2022). In this article, we will take a closer look at them and, based on the available literature, we will try to summarize the effects of their use.

Sweeteners- what are they?

Artificial sweeteners have been developed as sugar substitutes. Many of these have a much stronger sweetness than simple sugar and sucrose and have few calories. Compared to sucrose, artificial sweeteners are hundreds of times sweeter, so the use of various artificial sweeteners together can reduce the amount of sugar used (Iizuka, 2022). Artificial sweeteners (ASs) are the (semi-)synthetic organic compounds with intense sweetness and have been regarded as alternatives to sugar for an extended period of time (Basson et al., 2021). Most ASs, also known as non-nutritive or non-caloric sweeteners, are barely absorbed by the human digestive system and therefore provide few calories (Lohner et al., 2017). Artificial sweeteners are common additives used in the manufacturing of foodstuffs, pharmaceuticals, animal feed, and personal care products (Burh et al., 2021)(Wilk et al., 2022)(Chen et al., 2023).

Sweeteners offer a sweet taste to food and can be classified as carbohydrate (caloric) and noncarbohydrate (noncaloric) sweeteners. Caloric sweeteners include sugar and sugar-alcohols such as erythritol, sorbitol, mannitol, xylitol, maltitol, lactitol, and reducing starch syrup (Gupta, 2018). Noncaloric artificial sweeteners or non-nutritional sweeteners (NNSs) are a heterogeneous group of compounds with different chemical structures, which are popular substitutes for added sugars in foods and beverages due to their low caloric content and sweetness (Fleming-Milici et al., 2022). Non-nutritional sweeteners (NNSs) can be classified into artificial sweeteners when chemically produced in the laboratory, and natural sweeteners (NSs) when directly extracted from plants. ASs include aspartame, saccharin, sucralose, neotame, acesulfame-k, and advantame, and NSs are mainly represented by stevia, made from extracts of the intensely sweet plant *S. Rebaudiana*, but also include hoodia, agavis, and Luo Han Guo Monk fruit extracts (Liauchonak et al., 2019)(Kossiva et al., 2024).

Global consumption growth, fitness market impact and forecasts

In recent years, the global market for low-calorie sweeteners (LCS) has experienced significant growth, driven by increasing health awareness among consumers and the need to reduce sugar intake. In 2024, the market was valued at approximately USD 28.38 billion, with forecasts predicting growth to USD 30.13 billion by 2025, reflecting a compound annual growth rate (CAGR) of 6.2% (*Low-Calorie Sweeteners Market 2025 - Forecast & Trends*, n.d.). Further projections estimate a market value of USD 37.95 billion by 2029, with a CAGR of 5.9% (*Low-Calorie Sweeteners Market Size & Demand 2025-2035*, n.d.). The volume of the 'Artificial Sweeteners' segment of the food market was continuously increasing over the past years. The global volume in the 'Artificial Sweeteners' segment of the food market is forecast to continuously increase between 2025 and 2030 by in total 290.7 thousand tons (+22.97 percent). After the tenth consecutive increasing year, the volume is estimated to reach 1.6 billion kilograms and therefore a new peak in 2030 (*Global: Artificial Sweeteners Volume 2020-2030| Statista*, n.d.). In 2021, the global market revenue of ASs reached approximately $21.3 billion USD and is estimated to rise to $28.9 billion USD by 2026 (*Global: Artificial Sweeteners Market Revenue 2020-2030| Statista*, n.d.).

This growth is fueled by several key factors: health awareness, an increasing number of consumers are seeking sugar alternatives to lower their risk of conditions such as obesity and diabetes, consumer preferences, there is a rising demand for products that use natural sweeteners, such as stevia, contributing to the expansion of the natural LCS segment, food industry innovation, manufacturers are introducing new products containing LCS to meet the demand for healthier food and beverage options (Firoozzare et al., 2024)(Alsubhi et al., 2022).

The impact of artificial sweeteners on selected diseases

Sugar-sweetened beverages (SSBs), artificially sweetened beverages (ASBs), and 100% fruit juices are widely consumed and have been documented to contribute to a significant disease burden. An increase in SSB intake by 250 mL per day was associated with a 4% higher risk of all-cause mortality and an 8% higher risk of mortality from cardiovascular diseases. Similarly, a 250 mL/day increase in ASB consumption was linked to a 4% higher risk of all-cause mortality and a 4% increased risk of death from cardiovascular diseases. However, no significant association was found between the consumption of either SSBs or ASBs and cancer-related mortality. Thus, while increased intake of SSBs and ASBs slightly elevates the risk of all-cause and cardiovascular mortality, it does not appear to significantly affect cancer mortality. The relationship between 100% fruit juice consumption and mortality from cancer or cardiovascular diseases remains uncertain *(Pan et al., 2021).*

Furthermore cohort studies have shown that the consumption of nonnutritive sweeteners was associated with increases in weight and waist circumference, and higher incidence of obesity, hypertension, metabolic syndrome, type 2 diabetes and cardiovascular events. Publication bias was indicated for studies with diabetes as an outcome (Azad et al., 2017).

Diabetes

A French prospective cohort study involving 105,588 participants assessed the association between the intake of artificial sweeteners (aspartame, acesulfame-K, and sucralose) from all dietary sources and the risk of developing type 2 diabetes. Compared to non-consumers, individuals with higher intake of artificial sweeteners had an increased risk of developing type 2 diabetes (hazard ratio [HR] 1.69; 95% confidence interval [CI] 1.45–1.97; P for trend < 0.001). Positive associations were also observed for individual sweeteners: aspartame (HR 1.63), acesulfame-K (HR 1.70), and sucralose (HR 1.34). These findings suggest that artificial sweeteners should not be recommended for widespread consumption as a safe alternative to sugar, and instead, efforts should focus on reducing the overall preference for sweet taste in Western diets (Debras et al., 2023).

High intake of artificial sweeteners is associated with an increased risk of metabolic disorders, cardiovascular diseases, certain cancers, and, somewhat paradoxically, weight gain, adverse pregnancy outcomes, and potential risk for individuals with a low seizure threshold. Concerns also extend to gut health, as artificial sweeteners such as saccharin have been linked to inflammatory bowel disease, disturbances in gut microbiota, increased intestinal permeability, and dysbiosis. These changes contribute to metabolic dysfunction, including impaired glucose tolerance, insulin resistance, and enhanced systemic inflammation. Such disruptions reduce the production of short-chain fatty acids, which are critical for insulin sensitivity, thereby further promoting the development of metabolic disorders such as type 2 diabetes (M & Vellapandian, 2024).

Aspartame and sucralose may impair proper insulin function by inducing hyperinsulinemia and insulin resistance through altered expression of glucose transporters and insulin receptor sensitivity. Furthermore,

these sweeteners affect gut microbiota, with saccharin and sucralose shown to induce dysbiosis, glucose intolerance, and systemic inflammation, thereby contributing to the metabolic syndrome (Shon et al., 2023).

Stevia consumption is associated with a significant reduction in blood glucose levels, particularly in individuals with elevated BMI, diabetes, and hypertension. However, stevia does not significantly affect insulin levels or HbA1c. It improves blood glucose control, especially when consumed for less than 120 days (Zare et al., 2024).

In a study comparing the effects of aspartame and sucrose on pancreatic islet cells in mice in vivo, it was observed that high concentrations and prolonged exposure to aspartame may induce caspase-dependent apoptosis of pancreatic islet cells. These results provide evidence of the potential detrimental effects of aspartame on pancreatic tissue (Hu et al., 2024).

Cardiovascular diseases

High nonnutritive sweetener intake was associated with a higher risk of hypertension over 5 to 38 years of follow-up (HR 1.13, 95% CI 1.06 to 1.20; I^2 64%; 5 cohorts; 232 630 participants)(Cohen et al., 2012; Duffey et al., 2012; Nettleton et al., 2009). In addition, high intake of nonnutritive sweetener was associated with a higher risk of stroke (RR 1.14, 95% CI 1.04 to 1.26; I^2 0%; 2 cohorts; 128 176 participants)(Bernstein et al., 2012) and cardiovascular events (RR 1.32; 95% CI 1.15 to 1.52; I^2 0%; 2 cohorts; 62 178 participants),(Gardener et al., 2012; Vyas et al., 2015) whereas there was no significant association with coronary heart disease (RR 0.98; 95% CI 0.90 to 1.07; I^2 0%; 2 cohorts; 131 403 participants) (Azad et al., 2017; De Koning et al., 2012; Fung et al., 2009).

While NNS provide a sweet taste without increasing sugar intake, emerging evidence suggests that maternal consumption of not only nutritive sweeteners (such as fructose) but also NNS may result in adverse effects in offspring, including hypertension. However, data on the impact of maternal NNS intake on offspring blood pressure remain limited, both in human and animal studies. Given the continuous rise in maternal NNS consumption, it is essential to assess their long-term safety and potential implications for offspring health (Tain & Hsu, 2025).

Obesity

Some studies suggest that NNS may stimulate appetite, likely due to their ability to provide a sweet taste without eliciting the metabolic signals typically triggered by digestion, signals that normally communicate with the hypothalamus to suppress hunger. Sucralose, in comparison to sucrose and water, has been shown to increase functional connectivity between the hypothalamus and brain regions involved in motivation and somatosensory processing, including increased blood flow to the hypothalamus and enhanced hunger-related responses. These findings indicate that NNS may influence key hypothalamic mechanisms responsible for appetite regulation (Chakravartti et al., 2025).

Conversely, a study assessing the efficacy and safety of stevia (a natural sweetener) used as a table-top sweetener among overweight individuals with normoglycemia and those with prediabetes demonstrated that substituting dietary sugar with a stevia-based table-top sweetener, combined with a physical activity program, supported weight loss and waist circumference reduction in both groups (Raghavan et al., 2023).

It is noteworthy that many NNS can cross the placenta and have been detected in amniotic fluid and breast milk, pointing to potential risks in developmental programming of offspring health. Analysis from certain birth cohort studies indicated that high intake (at least one serving per day) of beverages containing NNS during pregnancy is associated with an increased risk of preterm birth and elevated body weight or BMI in male offspring, independent of maternal weight. Interestingly, this effect appears to be mitigated by breastfeeding for at least six months (Kearns & Reynolds, 2024).

Cancers

A review study evaluating the relationship between sweetener consumption and the risk of endometrial cancer classified sweeteners into nutritive sweeteners (typically referring to sugars such as sucrose and glucose) and non-nutritive sweeteners (generally artificial sweeteners like saccharin and aspartame). The findings indicated that the intake of nutritive sweeteners may be associated with an increased risk of endometrial cancer, whereas no significant association was found between non-nutritive sweetener consumption and the incidence of this malignancy (Kearns & Reynolds, 2024).

A Spanish study assessed the relationship between aspartame and other artificial sweeteners and cancer risk. It included a total of 1881 colorectal cancer cases, 1510 breast cancer cases, 972 prostate cancer cases,

351 gastric cancer cases, and 109 chronic lymphocytic leukemia (CLL) cases, alongside 3629 control participants from the MCC-Spain case-control study. Overall, no general associations were observed between the consumption of aspartame or other artificial sweeteners and cancer. However, an elevated risk of gastric and colorectal cancer was noted in individuals with diabetes who had a high intake of aspartame and other sweeteners. Conversely, a reduced risk of breast cancer was reported, although the small number of cases limits the reliability of these findings (Palomar-Cros et al., 2023).

Another study explored the relationship between three natural sweeteners (steviol glycosides, glycyrrhizin, and neohesperidin dihydrochalcone) and two synthetic sweeteners (saccharin and sucralose) in relation to the gut microbiome. The research also discussed the effects of these five sweeteners and their metabolites on signaling pathways associated with gastrointestinal cancers. The gut microbiota plays a key role in metabolizing certain sweeteners, which may be relevant for overall health. Beneficial effects of sweetener consumption on cancer-related pathways in the gastrointestinal tract, such as induction of apoptosis and cell cycle arrest were observed.

Overall, the involvement of the gut microbiome in sweetener metabolism presents a promising avenue for future anticancer therapies, particularly in conjunction with existing treatment modalities (AL-Ishaq et al., 2023).

Conclusions

Evidence does not clearly support the intended benefits of nonnutritive sweeteners for weight management. In contrast, observational data suggest that routine consumption of nonnutritive sweeteners may be associated with a long-term increase in BMI and elevated risk of cardiometabolic disease; however, these associations have not been confirmed in experimental studies and may be influenced by publication bias. New studies are needed to compare different types and formulations of nonnutritive sweeteners, and to evaluate effect of substituting nonnutritive sweeteners for sugar. Given the widespread and increasing use of nonnutritive sweeteners, caution is warranted until the long-term risks and benefits of these products are fully characterized.

Disclosure

Author's contribution:

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All authors have read and agreed with the published version of the manuscript.

Funding Statement: The study did not receive special funding.
Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data Availability Statement: Not applicable.
Acknowledgments: Not applicable.
Conflict of Interest: The authors declare no conflict of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process

In preparing this work, the author(s) used ChatGPT for the purpose of improving language and readability. After using this tool/service, the author(s) have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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