Review Article

HISTORICAL AND CURRENT PERSPECTIVES ON THE HUMAN CONSUMPTION OF NON-NUTRITIVE SWEETENERS (NNS)

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ABSTRACT

Scientific discovery, consumer preferences, and regulatory concerns mark the trajectory of human introduction to nonnutritive sweeteners (NNS). Since the discovery of Saccharin by chance in the late 19th century, sweeteners such as Aspartame, sucralose, and acesulfame potassium were developed in the 20th century with their unique taste profiles with minimal to no caloric impact. As the demand for sugar alternatives grew, driven by health concerns and dietary considerations, NNS entered various food and beverage products. More recently, Stevia, a natural NNS derived from the leaves of the *Stevia rebaudiana* plant, has further diversified the market. However, debate about their safety and long-term health effects continues to shape research and public discourse. Regulatory bodies worldwide are continually striving to improve guidelines to ensure the safety of these sweeteners. The present review provides historical background, current status, and future outlook on the human consumption of NNS and summarizes their evolution to identify potential research areas.

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INTRODUCTION

Human taste receptors are adept at detecting sweet flavors,a trait that has led to the long-standing and enduring use of sweet substances in our food. These ingredients, derived from sugar cane, include syrups, molasses, and common table sugar. Notably, this inclination towards sweetness is evident even in human infants.[1] Nevertheless, the overconsumption of sugar and its byproducts can have significant negative impacts on human health, as demonstrated by the heightened risk of conditions such as heart disease and Type 2 diabetes mellitus.[2] Consequently, sugar substitutes emerged as a seemingly safer alternative. Sugar free foods are extensively utilized and have gained popularity due to their low-calorie content.[3] While the term 'nonnutritive sweeteners' (NNS) is often used interchangeably with 'artificial sweeteners,' in the present context, the term is used to denote synthetically produced and naturally occurring NNS (Figure 1).

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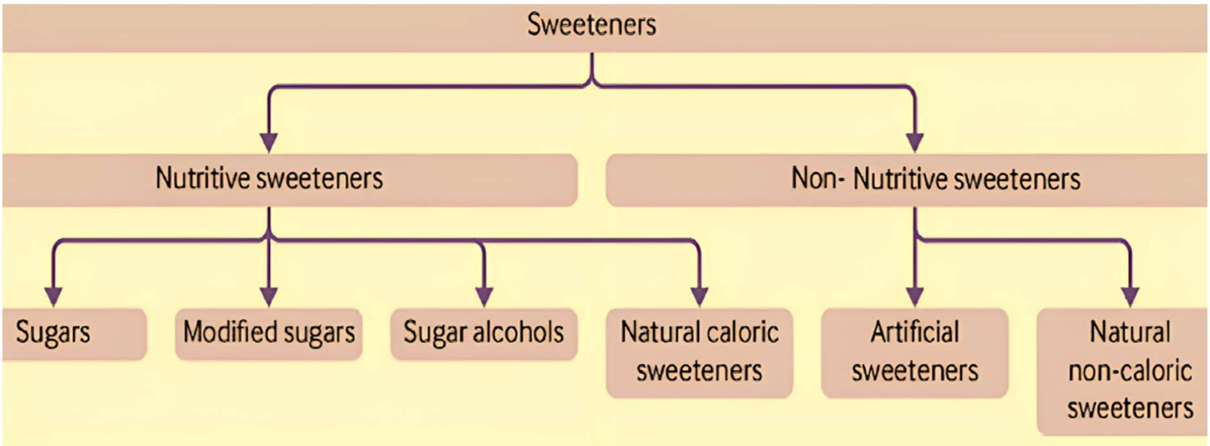

Figure 1. General classification of sweeteners

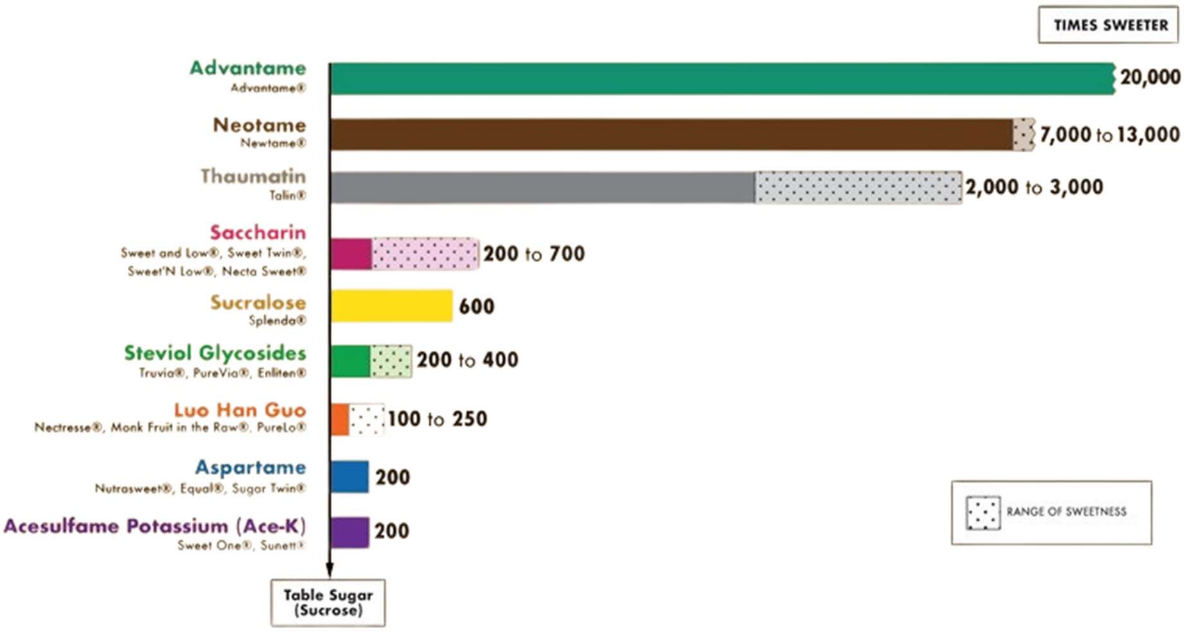

Figure 2. Comparison of sweetness intensities of various NNS and sucrose[4]

Substances with a calorific value of less than 2% that of sucrose per equivalent unit of sweetening capacity are termed NNS, whereas those with greater than 2% are termed nutritive. While the calorie content is negligible or zero, the sweetness intensity of different NNS is typically very high compared to sucrose (Figure 2)

For the present review, a comprehensive literature search was conducted using the keywords - "nonnutritive sweeteners" and "artificial sweeteners" to ensure a targeted exploration from the repositories of PubMed, Google Scholar, FDA (Food and Drug Administration), and dimensions from March 2023 to November 2023. Duplicate and redundant articles were excluded based on their titles. Data extraction following the keyword search was based on individual scrutiny of the retrieved articles from their title, abstracts, and full texts where necessary to identify those articles with historical background and consumption statistics of NNS. The review was synthesized based on the identified articles.

HISTORICAL STANDPOINT

NNS are food additives that provide the same sweet taste as natural sugar but significantly fewer calories, making them a zero or low-calorie alternative. NNS are present in various food items, including ice creams, beverages, chocolates, yogurt, jams, jellies, chewing gums, and salad

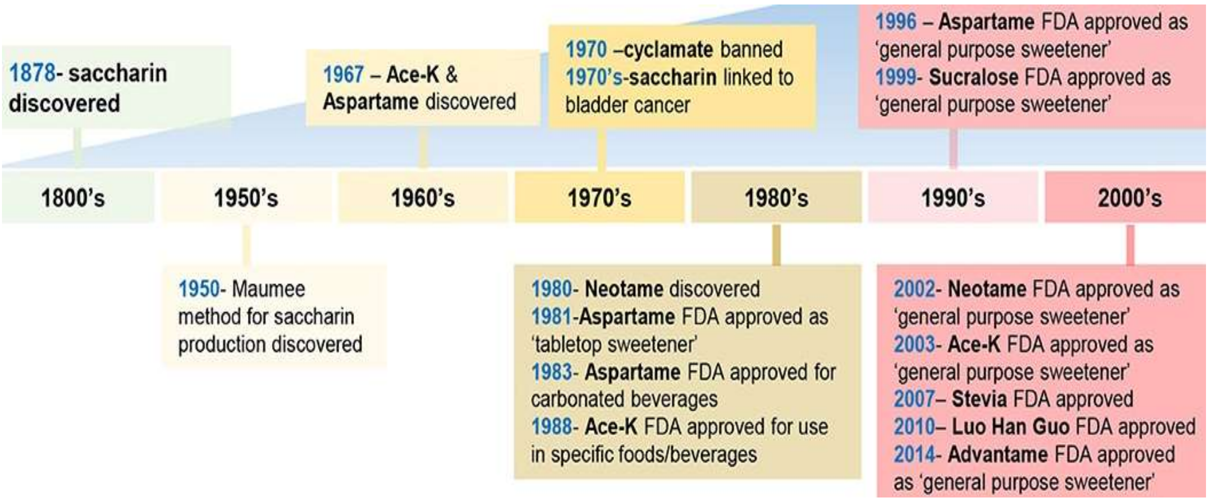

Figure 3. Discovery and approval timeline of NNS[5]

dressings. While NNS such as Alitame and cyclamate are utilized in some countries, the U.S Food and Drug Administration (FDA) has currently authorized the use of Saccharin, Sucralose, Aspartame, Acesulfame Potassium, Neotame, and Advantame. In contrast, the natural NNS, steviol glycosides, monk fruit (also known as Luo Han Guo), and thaumatin are 'generally recognized as safe' (GRAS).[4] The incorporation of NNS into the food industry began in the early 1800s, and that has continued to date with the addition of new entrants (Figure 3)

Saccharin was first discovered in 1879 during an experiment conducted by Constantine Fahlberg. Fahlberg was studying the oxidation mechanisms of toluene-sulfonamide when a splash accidentally landed on his finger. The sweet flavor he tasted upon licking his finger unveiled its potential as an alternative to sugar. Saccharin received FDA approval in 1970 and was widely used in soft drinks, chewing gums, toothpaste, mouthwash, and cosmetics.[6] However, certain studies conducted on rat models pointed to the potential development of bladder cancer linked to Saccharin use, prompting a prohibition on its use in Canada and a proposed ban in the USA.[7,8] Consequently, products containing Saccharin were mandated to carry a warning label in the USA for a period. Subsequent research into Saccharin's safety in humans led to the reversal of this decision by the USA in 2000. Health Canada also rescinded its ban on Saccharin in 2014, permitting its use in specific products.[9]

Aspartame was discovered accidentally in 1965 by James M. Schlatter during his research on anti-ulcer drugs. The FDA approved it as a table sweetener in 1981, and it received general-purpose sweetener approval in 1996. Aspartame has been the subject of extensive research as an additive in human food, and the FDA persistently reviews new scientific literature for updated information on Aspartame.[10] Acesulfame-K (acesulfame-potassium) was first discovered in 1967 by chemist Karl Clauss. It received FDA approval as a beverage sweetener in 1998 and later received generic approval in 2003. It is currently the most highly consumed NNS in diet soft drinks, dairy products, frozen desserts, and candy.[11] The British sugar company discovered Sucralose 'Tate & Lyle' in 1976 while searching for a chemical intermediate of sugar to use as a sweetener. The FDA granted it limited use approval in 1998, which was upgraded to general use in 1999.[12] Neotame, a derivative of Aspartame, was approved in 2002 as a general-purpose sweetener. Because of its heat-stable properties, neotame is an effective alternative to sugar for baking purposes.[13] Advantame is a relatively new entrant to the list of NNS and was approved by the FDA for use as a general-purpose sweetener in 2014. Like Neotame, Advantame is also heat-stable and is used in sugar-free baked products.[14]

Steviol glycosides, found in the leaves of the Stevia rebaudiana (Bertoni) plant, native to certain regions of South America and commonly referred to as Stevia, are natural sweeteners. High-purity stevia derived sweeteners such as Rebaudioside A, Stevioside, and Rebaudioside D are considered safe by the FDA.[15] However, using stevia leaf and unrefined extracts is not deemed GRAS, and their distribution in the U.S. as sweeteners is prohibited.[16] Thaumatin is a collection of highly sweet basic proteins extracted from the Thermococcus Danielle fruit, also known as the West African Katemfe fruit. Thaumatin has food additive authorization in the European Union (E.U.). It is used as a sweetening agent in various such as jams, ice cream, baked goods, potato-based snacks, and breakfast cereals; the plant known as Siraitia grosvenorii (Swingle), more commonly referred to as Luo Han Guo or monk fruit originates from Southern China. The China Food and Drug Administration (CFDA) approved its use as a food sweetener in the 1990s. Extracts derived from this fruit are typically used as sweeteners for general purposes and also as tabletop sweeteners.[17]

GLOBAL CONSUMPTION OF NNS

In recent years, there has been a significant surge in the consumption of NNS. An examination of Euromonitor sales data over 12 years from 2007 to 2019 revealed a 36% rise in the per capita quantities of NNS sold through beverages globally.[18] In the USA, data from the National Health and Nutrition Examination Survey (NHANES), collected from 1999 to 2008, reveals that consuming beverages containing NNS rose from 18.7% to 24.1% among adults and from 6.1% to 12.5% among children.[19] A similar study using NHANES data from 2003 to 2010 also found an increase in NNS consumption, with adults consuming NNS containing beverages rising from 21.1% to 24.9% and children increasing from 7.8% to 18.9%. In the same study, data collected from Neilsen Homescan (Neilsen Co.) between 2000 and 2010 revealed a rise in purchases for products containing low-caloric sweeteners, particularly in households with children.[20] As of the year 2019, beverages continue to be a concerning source of NNS intake for children in the U.S., with over 70% of drinks advertised to children containing NNS.[21] While NNS are used globally, dependable estimates of the prevalence of NNS consumption at the national level are primarily restricted to data from the United States. In 2023, the worldwide sweeteners market was valued at USD 102.2 billion. It is projected to reach approximately USD 144.86 billion in a decade (Figure 4), with a compound annual growth rate (CAGR) of 3.6% from 2023 to 2032.[22]

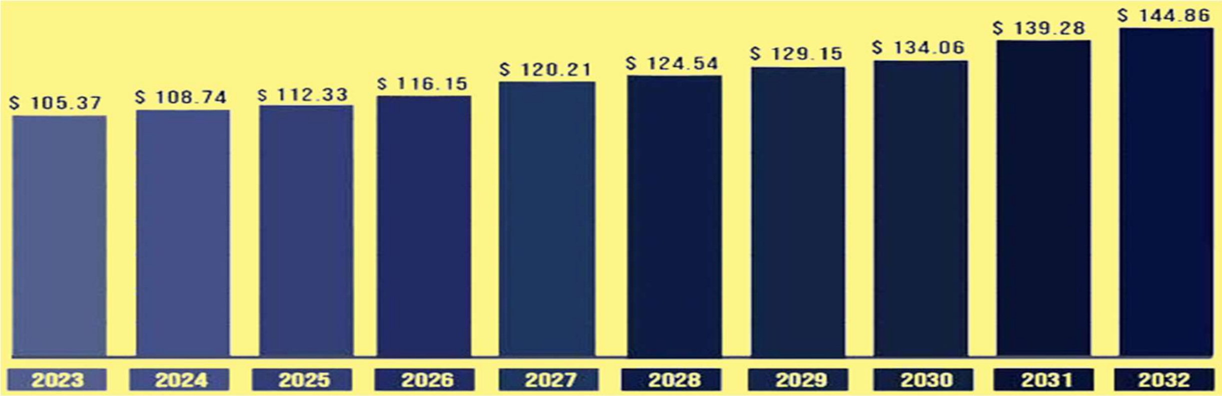

Figure 4. The projected global market value of nonnutritive sweeteners[22]

HEALTH IMPACT AND FUTURE OUTLOOK

NNS has been shown to exhibit clinical benefits, particularly in weight management and glycemic control. By imparting sweetness without affecting the caloric content of food, NNS is a productive tool for individuals requiring weight management. This attribute is particularly relevant for populations contending with obesity and diabetes. Furthermore, NNS offers individuals with specific dietary constraints, such as those who have diabetes, the opportunity to indulge in sweetened products without potentially compromising glycemic equilibrium.[23] However, the current clinical utilization of NNS is not devoid of complexities, and research on NNS continues to be dynamic, revolving around the long-term health effects of NNS consumption.[24] Despite being considered safe by regulatory authorities, there is an ongoing interest in understanding their impact on metabolic health, gut microbiota, and potential links to chronic conditions.[25] The development of novel NNS formulations, seeking alternatives that mimic sugar's taste and sensory experience without compromising health, is another area under exploration. The environmental implications of widespread NNS use, such as their production processes and disposal, are also worth assessing in the context of sustainability. Likewise, behavioral studies examining consumer perceptions, preferences and adoption of NNS is another avenue for research.[26-28]

CONCLUSION

In conclusion, the historical development and contemporary consumption patterns of NNS from the accidental discovery of Saccharin in the late 19th century to the modern diversification with alternatives like Aspartame, sucralose, acesulfame potassium, and Stevia, these sweeteners have become ubiquitous in the realm of sugar substitutes. The ever-growing demand for healthier alternatives has driven their integration into many food and beverage products. However, as consumption patterns rise, so do concerns about safety and long-term impacts. In this context, the regulatory landscape is pivotal in establishing guidelines on using NNS to safeguard public health. A multifaceted approach is required to comprehensively understand NNS, addressing both the scientific and societal dimensions of their use.

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AUTHOR CONTRIBUTION

SIAS: Conceived the review, reviewed & finalized the manuscript

HN: Conducted the literature search, revised the draft, reviewed & finalized the manuscript

NN: Conducted the literature search, wrote the first draft of the manuscript, reviewed & finalized the manuscript.

REFERENCES

1. Maone TR, Mattes RD, Bernbaum JC, Beauchamp GK. A new method for delivering a taste without fluids to preterm and term infants. Developmental Psychobiology: J Int Soc Dev. Psycho. 1990 Mar;23(2):179-91. https://doi.org/10.1002/dev.420230208
2. Howard BV, Wylie-Rosett J. Sugar and cardiovascular disease: A statement for healthcare professionals from the Committee on Nutrition of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association. Circulation. 2002 Jul 23;106(4):523-7. https://doi.org/10.1161/01.
3. Chattopadhyay S, Raychaudhuri U, Chakraborty R. Artificial sweeteners–a review. JFST 2014 Apr;51:611-21. https://doi.org/10.1007/s13197-011-0571-1.
4. USFDA. Aspartame and other sweeteners in food USA: U.S. Food and Drug Administration; 2023 [17th December 2023]. Available from: https://www.fda.gov/food/food-additives-petitions/aspartame-and-other-sweeteners-food.
5. Basson AR, Rodriguez-Palacios A, Cominelli F. Artificial sweeteners: history and new concepts on inflammation. Front. nutr. 2021 Sep 24;8:746247. https://doi.org/10.3389/fnut.2021.746247
6. De la Peña CT. Empty pleasures: The story of artificial sweeteners from Saccharin to Splenda. Univ of North Carolina Press; 2010.
7. Arnold DL. Two-generation saccharin bioassays. EHP 1983 Apr;50:27-36. https://doi.org/10.1289/ehp.83502.
8. Lepkowski W. The Saccharin Debate: Regulation and the Public Taste. Hastings Center Report. 1977 Dec 1:5-7.
9. CSPI. Saccharin Washington DC, USA: Center for Science in the Public Interest; 2022 [cited 2023 15th December 2023]. Available from: https://www.cspinet.org/article/saccharin
10. C Czarnecka K, Pilarz A, Rogut A, Maj P, Szymańska J, Olejnik Ł, Szymański P. Aspartame - true or false? Narrative review of safety analysis of general use in products. Nutrients. 2021 Jun 7;13(6):1957. https://doi.org/10.3390/nu13061957
11. Wu HT, Chiang CC, Wang CT, Chen YH, Hsu SY, Chen YC. Consumption of the nonnutritive sweetener acesulfame potassium increases central precocious puberty risk. J Hazard Mater. 2024 Jan 5;461:132529. https://doi.org/10.1016/j.jhazmat.2023.132529.
12. Mitchell H, editor. Sweeteners and sugar alternatives in food technology. John Wiley & Sons; 2008 Apr 15.
13. Prakash I, Corliss G, Ponakala R, Ishikawa G. Neotame: the next-generation sweetener. Food technology (Chicago). 2002;56(7):36-40.
14. CSPI. Advantame Washington DC, USA: Center for Science in the Public Interest; 2023 [cited 2023 17th December 2023]. Available from: https://www.cspinet.org/article/advantame.
15. Ashwell M. Stevia, nature's zero-calorie sustainable sweetener: A new player in the fight against obesity. Nutrition today. 2015 May;50(3):129. doi: 10.1097/NT.0000000000000094
16. EFSA Panel on Food Additives and Flavourings (FAF), Younes M, Aquilina G, Castle L, Engel KH, Fowler P, Frutos Fernandez MJ, Fürst P, Gürtler R, Gundert-Remy U, Husøy T. Re-evaluation of thaumatin (E 957) as food additive. EFSA Journal. 2021

Nov;19(11):e06884. https://doi.org/10.2903/j.efsa.2021.6884
17. Gong X, Chen N, Ren K, Jia J, Wei K, Zhang L, Lv Y, Wang J, Li M. The fruits of Siraitia grosvenorii: a review of a Chinese food-medicine. Front Pharmacol . 2019 Nov 22;10:1400. https://doi.org/10.3389/fphar.2019.01400
18. Russell C, Baker P, Grimes C, Lindberg R, Lawrence MA. Global trends in added sugars and nonnutritive sweetener use in the packaged food supply: drivers and implications for public health. Public Health Nutr . 2023 May;26(5):952-64. doi:10.1017/S1368980022001598
19. Sylvetsky AC, Welsh JA, Brown RJ, Vos MB. Low-calorie sweetener consumption is increasing in the United States. AJCN. 2012 Sep 1;96(3):640-6. doi: 10.3945/ajcn.112.034751
20. Piernas C, Ng SW, Popkin B. Trends in purchases and intake of foods and beverages containing caloric and low-calorie sweeteners over the last decade in the United States. Pediatric obesity. 2013 Aug;8(4):294-306. https://doi.org/10.1111/j.2047-6310.2013.00153.x
21. Choi YY, Andreyeva T, Fleming-Milici F, Harris JL. U.S. Households' Children's Drink Purchases: 2006–2017 Trends and Associations With Marketing. Am. J. Prev. Med. 2022 Jan 1;62(1):9-17. https://doi.org/10.1016/j.amepre.2021.06.013
22. Sylvetsky AC, Rother KI. Nonnutritive sweeteners in weight management and chronic disease: a review. Obesity. 2018 Apr;26(4):635-40. https://doi.org/10.1002/oby.22139
23. Shah I. Nonnutritive Sweeteners: Too Sweet to be True?. JUCMD 2023:7-. https://doi.org/10.51846/jucmd.v2i1.2169
24. Nieuwdorp M, Herrema H. Non-nutritive sweeteners too sweet to be wholesome?. Nature Reviews Endocrinology. 2022 Dec;18(12):719-20. https://doi.org/10.1038/s41574-022-00758-4