REVIEW ARTICLE

Intake of Artificial Sweeteners by Children: Boon or Bane?

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Abstract

Background: Sugar is the main culprit in many health dysfunctions. Excessive sugar intake can negatively affect oral health, precipitate diabetes, and lead to weight gain and obesity. Sucrose is the primary form of sugar, and is strongly correlated with dental caries. Artificial sweeteners are chemically synthesized sugar substitutes that are generally regarded as being low-calorie.

Objective: This review examines the current evidence in the literature for the need for artificial sweeteners and outlines its implications for the health of children. We briefly outline its adverse effects, and concerns regarding their safety.

Review results: Artificial sweeteners are a widely used food additive. Six main artificial sweeteners are approved by the food and drug administration (FDA). The conflicting results and divergent regulatory norms of each sweetener are a constant cause of concern and debate. However, most studies have spotlighted the beneficial effects of artificial sweeteners. Dental caries diminish with the increase in sweetener intake. An increase in appetite and eventually weight gain is observed in individuals consuming artificial sweeteners.

Conclusion: Artificial sweeteners are indeed a bane according to present studies, although more research on recently discovered non-nutritive artificial sweeteners is required. It also has a positive effect on overall health disorders. If one curbs the onset of dental caries, then the eventual rise is highly unlikely.

Clinical significance: Artificial sweeteners' effect on lowering dental caries will help to reduce the caries index in general. Oral hygiene is maintained, and the growth of oral bacterium is depressed. Research on novel sweeteners will help to compare their efficacy in caries prevention compared to existing ones. It is necessary to educate people on artificial sweeteners and its implication as one can use them by being aware of their properties.

Keywords: Artificial sweeteners, Dental caries, Non-nutritive sweeteners, Oral health.

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Introduction

Dental caries is a major public health crisis affecting more than 2.5 billion people across the globe.[1] The worldwide prevalence of dental caries in deciduous teeth is 46.2% and 53.8% in permanent teeth.[2] Dental caries is an interplay of three primary factors: Substrate (diet), host (tooth), and cariogenic microflora. These factors create a state of dysbiosis in the oral biofilm.[3] Time is found to be an additional factor forming the 'caries tetralogy'.[4] The existing body of research on and scientific tenet holds that sugar is the predominant culprit in caries.

Sweet is an inherently pleasurable taste. Sugars are carbohydrates and provide energy. A Higher intake of added sugars is associated with greater energy intake and lower diet quality. Sugar intake is associated with an increased risk of obesity, prediabetes, type 2 diabetes, and cardiovascular disease. In the 20th century, as sugar became recognized as a villain responsible for many health ailments, there was a need for a mass-market sugar substitute. Recognizing the desire for sweet flavors, sugar-free alternatives have been developed as sugar substitutes. Artificial sweeteners are a widely used food additive that occupies a large commercial market share in the production of baked goods, confectionaries, candies, aerated drinks, juices, and energy drinks. They have a higher sweetening intensity per unit weight. Pushed by canny marketers and food gurus as a healthier alternative to sugar, the supporting evidence for the long-term health effects and safety of sugar substitutes remains sparse and debatable. This review examines the current evidence in the literature for the need for artificial sweeteners and outlines its implication on the health of children. We describe popular artificial sweeteners, their adverse effects on health, and concerns regarding their safety.

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Table 1: Classical studies correlating sugar and its effects on dental caries

S. No.	*Classical studies*	*Authors*	*Year*	*Summary*
1.	Stephan plaque PH response	Stephan[11]	1944	Study correlated sugar and dental plaque acidification resulting in dental caries.
2.	Vipeholm study	Gustafsson et al.[12]	1954	Increased frequency of sugar risks the increment in dental caries.
3.	World war II rationing study	Toverud G[13]	1957	Reported there was an alteration in dental caries according to sugar consumed before and after the war.
4.	Hopewood house study	Harris[14]	1963	Vegetarian low sugar diet had fewer dental caries compared to people taking high sugars.
5.	Tristan Da Cunha's population study	Holloway et al.[15]	1963	Changes in diet with an increase in carbohydrates among the given population resulted in higher cases of dental caries.
6.	Turku sugar study	Scheinin et al.[7]	1976	A comparison of sugar and their substitutes showed a lesser prevalence of dental caries among the sugar alternate group.
7.	Experimental caries in man	Geddes et al.[16]	1978	Poor oral hygiene along with increased intake of sucrose solutions for a longer duration-initiated caries.
8.	Hereditary fructose intolerance	Newburn et al.[17]	1980	People having fructose and sucrose in higher content presented with dental caries compared to people having complex carbohydrates.

Table 2: Recent studies correlating sugar and its effects on dental caries

S. No.	*Authors*	*Year*	*Summary*
1.	PJ Moynihan, S Jelly[18]	2014	A systematic review on sugar intake and dental caries showed that there are lifelong effects on dentition due to sugar consumption and dental caries progresses with age.
2.	A Sheiham, WPT James[19]	2015	In the specified study, it explains the pivotal role sugar plays in the spurt of dental caries, thus calling for preventing measures and restricting the consumption of sugars.
3.	Donald L Chi, Scarlett Hopkins, Diane O'Brien et al.[20]	2015	A cross-sectional pilot study among children in Yup'ik population concluded that there is a positive correlation between sugar intake and dental caries.
4.	MA Peres, Sheiham A et al.[21]	2016	A study that investigated the sugar consuming practices and their impact on dental caries from early childhood through adolescents, exhibited that the trajectory of dental caries increases in parallel with sugar increment.
5.	V Skafida, S Chambers[22]	2018	A longitudinal prospective study conducted among children highlighted a positive correlation between dietary habits in early years and their detrimental effect on children's teeth by 5 years of age.
6.	Van Loveren C [23]	2019	A study to device the effect of sugar restriction and its implications on caries prevention emphasized the amount of sugar consumed rather than the frequency will not reduce the caries development in oral cavity.
7.	Kumar D, Gandhi K et al.[24]	2020	A study to evaluate the prevalence of dental caries and its relationship with sugar consumption among children revealed that it is highly significant when the frequency of sugar consumption increases.
8.	Qian Du, Min Fu, Yuan Zhou et al.[25]	2020	An in-vitro study to evaluate sucrose and its effect on dental caries progression revealed a significant disequilibrium in oral microbiota following the consumption of sucrose.
9.	Mahboobi Z, Pakdaman A et al.[26]	2021	A systematic review of the longitudinal studies of dietary sugar and dental caries among children concluded that though their relationship is heterogeneous, a higher frequency of sugary drinks is associated with a higher incidence of dental caries.

Sugarcaries: The Current Evidence

After birth, a child is gradually exposed to external sugar from non-milk products, affecting oral health.[5] In decreasing levels of cariogenicity, sucrose, glucose, and fructose are types of sugar widely implicated in dental caries.[6] *Streptococcus mutants*, a cariogenic bacterium is a microorganism that grows and colonizes dental plaque and is the chief organism playing a role in developing dental caries. Sucrose is the most consumed sugar and promotes the growth of *Streptococcus mutants*. 15 kg/person/year amount of sugar is the upper limit for avoiding dental caries.[6] Often sugar consumption is many times this minimum, causing havoc in human dentition. Overwhelming research has established that sugar plays a central role in dental caries disease. Sucrose acts as a chief dietary source of fermentable carbohydrates that are utilized by the body to break down into acids in the oral cavity, thus enhancing the chances of introduction to dental caries.[7–10] Extensive meta-analyses and reviews have consistently found evidence that sugar intake is related to cardiometabolic problems, weight gain, dental caries, and miscellaneous deleterious health effects. Tables 1 and 2 summarizes the large body of research linking sugar to dental caries.

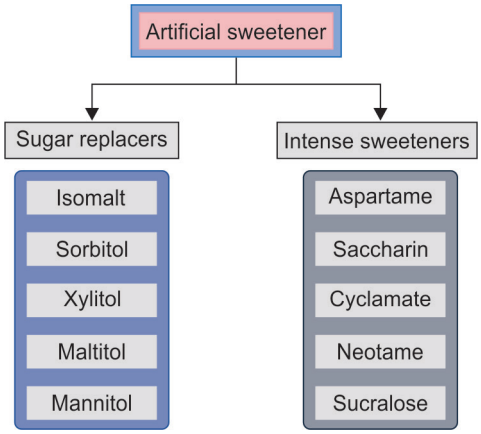
Artificial Sweeteners or Sugar Substitutes

Artificial sweeteners (=high-intensity sweeteners) increasingly become popular in the modern food and services industry, replacing sugar in all areas of prepackaged food from baked goods to beverages.[27] The United States has recently observed a massive increase in sugar substitutes with almost a 200% among children and 54% among adults.[28] Considering the detrimental effects of sugar on oral and general health, sweeteners appear to be a boon in product development, providing lower calories, and texture and reducing caries risk. Artificial sweeteners act as a strategy to tie down the intake of calorific sugar.

Artificial sweeteners are from 20 to 20,000 times more potent than sucrose. Sweeteners used in combination show greater potency. Some sweeteners are obtained naturally whereas others are chemically synthesized.[29] They can be broadly divided into sugar replacers and intense sweeteners (Flowchart 1). Numerable natural sweeteners have been discovered among which widely used xylitol and sorbitol have proved their positive effect on the oral cavity.[30] An ideal sucrose substitute should not be an energy source metabolized by oral bacteria to produce acids. It should not act as a substrate for the synthesis of glucan by oral bacteria but should inhibit glucan synthesis of sucrose.[31]

Currently, sweeteners are termed as high potency/bulk sweeteners and low caloric artificial sweeteners, among which six artificial sweeteners are approved by FDA for regular use. Numerous other sweeteners are currently used in countries other than the United States, such as cyclamate, alitame, and glycosides (Table 3).

Flowchart 1: Two major categories of sweeteners



Saccharin

Saccharin is 300 times sweeter than sucrose and other forms of sugar. It is mainly approved for cooking and a table use of various processed foods.[32] Saccharin is often used with a combination of other artificial sweeteners such as aspartame and cyclamate, as it is slightly acidic in taste.[27] Saccharin at higher doses produced tumors in the bladder of male rats.[33] Studies suggest that it does not get accumulated in the body tissues and is excreted in urine and feces unchanged.[34] The percentage of the dose recovered from human feces is around 3% (2 g/person) after normal and high doses. According to Agren and Bock, saccharin binds reversibly with the plasma protein. The metabolism, pharmacokinetics, and excretion of saccharin are similar in both rats and humans.[35] Exposure studies indicate that saccharin has the potential to induce cancer in rats, dogs, and humans. Rats exposed to 5–7.5% of saccharin from the time of conception till death showed evidence of carcinogenicity with an increased frequency of urinary bladder cancer and also suppresses the production of humoral antibodies in rats. It has also been reported to cause hepatotoxicity.[36]

Aspartame

Aspartame is a non-nutritive sweetener popularly added to dairy products. Distributed in the market by the name of NutraSweet in dry food, frozen and processed food, and ice creams. Aspartame is unstable in prolonged heat and hence not advisable for cooking

Table 3: Artificial sweeteners approved by FDI

Year	*Approved by FDA*	*Artificial sweeteners*	*Brand names*	*Chemical structure*	*No. of times sweeter than sucrose*	*Stability*	*Acceptable daily intake (mg/kg body weight/day)*
1878	1958	Saccharin	Sweet'N Low®, Sweet Twin®, Necta Sweet®	1,2-benzisothiazol-3-one-1, 1-dioxide	300	Heat resistant	5
1967	1988	Acesulfame potassium (Ace-K)	Sunett®, Sweet One®	6-methyl-1,2,3-oxathiazine-4(3H)-one2, 2-dioxide	200	Heat stable	50
1967	1981	Aspartame	Equal®, Sugar Sweet®, Sugar Twin®	N-L-α-aspartyl-L-phenylalanine1-methyl ester	180–200	Heat stable	40
1980	2002	Neotame	Newtame®	N-[N-(3,3-dimethybutyl)-l-aspartyl]-L-phenylalanine 1-methyl ester)	7,000–13,000	Moderate Heat stable	18
1999	1999	Sucrolose	Splenda®	1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl-4-chloro-4-deoxy- α-D-glucopyranoside)	600	Heat stable	5
2014		Advantame		N-[N-[3-(3-hydroxy-4-methoxyphenyl)prpyl]-α-aspartyl]-L-phenyalanine 1-methyl ester, monohydrate	20,000	Heat stable	5

or baking. Animal studies have revealed the antipyretic, analgesic, and anti-inflammatory effects after regular use of aspartame.[37,38] Research conducted by Ramsland et al. expressed the joint effect of aspartame and rheumatoid factor which eventually leads to the elimination of pain following a chronic inflammatory condition.[39] Aspartame is widely used across 75 countries owing to its sweet and accepting taste among people.[40] Orally administered aspartame either gets hydrolyzed in the intestinal lumen to aspartate, phenylalanine, and methanol by several proteolytic and hydrolytic enzymes or after demethylation in the lumen, it yields dipeptide aspartyl-phenylalanine and methanol. Studies indicate that in neonatal mice administration of high doses of aspartate resulted in elevated plasma aspartate concentration and hypothalamic neural necrosis.[41]

Sucralose

Sucralose is an inexpensive non-caloric artificial sweetener. Sucralose in its free form is an odorless white powder that is intensely sweet and highly soluble in water. It is extensively used in food, commercial confectionery products, and dairy products from milk to ice creams. Another property of sucralose is that it is stable in an acidic condition contrary to aspartame's property thus, sucralose is extensively used in drinks.[31] Studies were conducted to analyze the effect of sucralose in baking products at varying temperatures, which revealed that sucralose remained uncompromised as an artificial sweetener.[42] Case studies reported increased migraine incidents due to sucralose according to Bigal and Krymchantowski.[36] Mclean Baird et al. reported that it is not absorbed in the body completely and is released unchanged in feces. He also reported that it does not have any adverse effect on the gastrointestinal tract. In rodents treated with gavage acute toxicity was observed for extremely high doses. Kille et al. revealed that sucralose was not found to be teratogenic in rabbits.[43]

Neotame

Neotame is a flavor-enhancing, clean, moderately heat-stable compound that has the potential to be used in all tabletop sweeteners, frozen and processed food, and dairy products.[44] It is widely used and approved in the USA, Mexico, Russia, Australia, New Zealand, China, the Philippines, and many more.[44] Sucralose belongs to the category of synthetic organochlorine sweeteners. Chloropropanols generated after cooking sucralose at high temperatures are potentially toxic compounds. Several rodent and human studies demonstrate that sucralose may alter glucose, insulin, and glucagon-like peptide one level.[45] The metabolization of neotame in the human body is by esterase enzyme into de-esterified neotame and methanol, it is eliminated within 72 hours in urine and feces. It has been reported that chronic consumption of neotame has been related to low body weight and low weight gain.[46]

Studies reveal that no adverse findings in neotame treatment were found nor were there organ toxicity, morbidity, or mortality according to different post-mortem findings. (Mayhew, Cornel, and Stargel, 2003).[36] It has been reported that neotame does not affect blood glucose levels. Excess consumption of neotame can cause liver toxicity. Nofre reported that it can cause mild headaches and loss of appetite.[47]

Acesulfame Potassium

Acesulfame potassium is a high-intensity sweetener developed by Hoechst. It is a white crystalline powder with high solubility in water. Acesulfame potassium is not metabolized in the human body nor is metabolized by bacteria.[48] Its sweetness is similar to aspartame and is non-toxic in evidence.[49] Acesulfame potassium has been reported to increase body weight in male but not in female mice, fecal metabolite changes were also observed in both male and female mice. Acesulfame potassium has a strong gender-dependent effect on the gut microbiome.[50]

Advantame

Advantame is a sweetener that was developed by a chemical reaction between vanillin and aspartame. It is 90–120 times sweeter than aspartame and is used in several fermentable food items like cocoa products, dairy products like milk, and beverages. Its approval has extended to Japan, New Zealand, Australia, and European Union.[51] Advantame after being hydrolyzed is absorbed rapidly in the body and is converted into ANS980-acid in the plasma. It is excreted mainly through feces and minorly through the urinary route. Clinical trials on the human body reveal that it is well tolerated in single doses up to 0.5 mg/kg body weight.[52]

Cyclamate

Cyclamate was used as a table-top sweetener and in liquid form in the USA, Brazil, Spain, Japan, Taiwan, and Germany too incorporated as an additive.[53] It is generally 30–50 times sweeter than sucrose and thus among the least potent artificial sweetener. It leads to a bitter aftertaste that reduced its popularity. It was banned in the United States owing to its potential carcinogenic effects. Evidence of rodents on cyclamate developing testicular atrophy and seminal vesicle dysfunction has caused an impact on the male reproduction system.[54] Studies conducted by Gottinger, Hagmuller et al. revealed that when 0.5–2% of sodium cyclamate was added to the drinking water of the male guinea pigs mortality rate was high. Glutamic-pyruvate transaminase and lactic dehydrogenase were elevated in the 2% cyclamate group. Nephrosis and increased nephritis were observed in chronic studies.[55]

Cyclamate has low-order acute oral toxicity (10–20 gm/kg) and even in an animal when cyclamate is administered it induces few pathophysiological changes. If the dose is raised high enough it has been reported that in all animal species including man development of soft stools takes place as a result of the osmotic activity of unabsorbed cyclamate. In rats, chronic ingestion of food consisting of 5% sodium or calcium cyclamate leads to testicular atrophy and nephrocalcinosis.[55]

Effect of Artificial Sweeteners on Dental Caries

According to Matte et al. the consumption of artificial sweeteners in food and beverages has increased across all age groups.[56] Children ingest a higher amount of artificial sweetener in comparison to their body weight due to their smaller size and intake of beverages.[57] A systematic review of children observed that there is a 4–18% intake of carbonated beverages[58] whereas 15% was the probable intake in the American population above 2 years of age.[56] National health and nutrition examination survey (NHANES) research over a period has shown that there is a doubling in taking beverages by children compared to adults.[59]

Saccharin is profoundly studied for its effect on the prevention of dental caries, and it is highly disputed. Another readily available alternative is polyalcohol since they are anti-cariogenic.[30] An evaluation of saccharin deduced that it cannot be fermented by

oral microorganisms.[60] Tanzer et al. in their a study proved that saccharin inhibits caries in rats thus showing significant inhibition of streptococcal mutants growth.[61] Imfeld et al. determined that saccharin is non-acidogenic in *in-situ* plaque pH measurement. It does not present with cariogenicity in man or animal.[62] However, these presentations were contradicted by several research.[48,63] Saccharin has reduced plaque accumulation properties when used as a table-top sweetener and decreases the incidence of developing caries when mixed in dietary drinks.[40]

Several in vitro studies have investigated the potential effect of aspartame on dental health and they concluded by stating no increased cariogenic effect is visible on teeth.[63–68] In vivo investigations by Reussner et al. and Tanzer et al. have also studied the potential of aspartame on dental caries prevention and had promising results.[61,69] Aspartame does not ferment the dental plaque thus showing no effect on oral health.[70] An *in vivo* study by Das S et al. confirmed the lower growth of *S. mutants* while consuming aspartame alone in comparison with sucrose and sucrose, thus indicating the relevance of aspartame in caries prevention.[71]

Acesulfame potassium in a study has been shown to hinder the growth of *S. mutants*, while other studies have reported that it decreases the acid formation compared to sucrose.[62,72] A study by Siebert et al. revealed that acesulfame potassium alone showed no effect on the development of dental caries but in combination with other sweeteners like saccharine and cyclamate, it impeded the progress of the dental caries.

It is proposed that sucralose may enhance the tooth surface recalcification which is affected by dental caries.[73] Research conducted on oral bacterial metabolism, animal models caries experiment, and the effect of sucralose-containing solutions on human plaque summed up to demonstrate that sucralose is non-cariogenic in nature.[74] A study conducted by Young et al. have proved the effect of sucralose in stopping the growth of several oral bacterial species. Other research have confirmed that *S. sobrinus* glucosyltransferase (GTase) and *S. salivarius* fructosyltransferase (FTase) inhibit the synthesis of glucan and fructan by sucrose, respectively.[31,75] Cyclamate, a sweetener used in Europe, was observed to have less dental plaque in the cyclamate group in contrast to the sucrose group.[49]

Thus, it was gathered from the research done across different countries and age groups that artificial sweeteners act as a majority help to maintain good oral health.[36] Though positive results are observed most studies are ascertained by sugar alcohols like sorbitol, xylitol, or naturally obtained sweeteners like stevia moreover these are conducted on relatively restricted measures hence its clinical relevance by a regular customer in optimum quantity is warranted for investigation.[40] Studies on dental health after consumption of sucralose have shown no negative effects.[76] The health effects of artificial sweeteners are depicted in (Fig. 1).

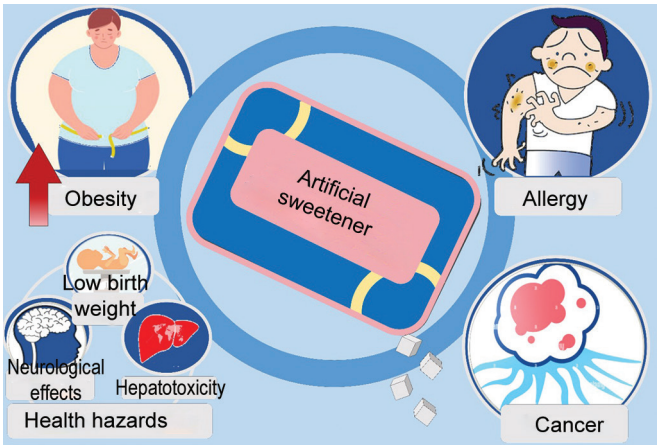


Fig. 1: Health effects of artificial sweeteners

Adverse Effects of Artificial Sweeteners Consumption on Health

Weight Changes/Obesity

Data from large-scale epidemiologic studies support the existence of an association between There is a constant debate on the potentially harmful effects on health. Studies that are conducted on animals have exhibited the effects of artificial sweeteners on human body weight gain. Another interesting observation was that as these substitutes have a sweet taste it enables an insulin response which indirectly causes the blood sugar to accumulate in tissues without it realistically increasing, resulting in hypoglycemia as well as an increase in food intake causing weight gain.[77–79] Over three decades in the United States, there is a gradual increase in obesity in individuals on artificial sweeteners.[80] Two cross-sectional studies on schoolchildren and adolescents have implicated a positive correlation between the consumption of artificial sweeteners and BMI.[81,82] However, a contrasting result was suggested in a study conducted among the 2–5 year age group.[83] Another study showed minimal relevance among obese and overweight individuals to artificial sweeteners except for antidotally.[30]

Diabetes

Since the time artificial sweeteners are researched, there is a constant emphasis on their effect on our physiological system, weight, glucose metabolism, and metabolic diseases.[84–87] Saccharin, unlike sucrose or glucose, cannot be metabolized nor does it produces food energy, hence it is a sweetener of high value among diabetic patients.[88] However, its effect on blood insulin is controversial. Whitehouse et al. in the animal study revealed that saccharin does not affect blood insulin levels through their lifetime however Ionescu et al. contradict it.[36,88] Rosenman, in his study, derived the inference of that artificial sweeteners does not affect dietary adherence.[30]

Sucralose's study on human tolerance tests did not affect plasma insulin, thus concluding its safe use in diabetic patients.[89] This was substantiated by another research which suggested that people with diabetes have fluctuations in blood sugar consuming artificial sweeteners compared to sucrose thus helping in creating stability in blood sugar levels.[90]

Allergic Reaction

Aspartame has confirmed allergic reactions in sensitive patients such as hives and swellings. A possible explanation is that while aspartame decomposes, the diketopiperazine compound that is formed may be responsible.[91,92]

Cancer

The breakdown products of aspartame such as aspartic acid and diketopiperazine have been extensively studied, with the latter showing deleterious effects while combining with nitrates in the diet to form nitrosated compounds that have the potential to

develop brain tumors.[79] A study by Olney et al. in 1996 verified this finding by claiming a 10% increase in brain tumors after the introduction of aspartame.[93]

The FDA and the federal agency of the United States Department of Health and Human Services (DHHS) have declared saccharin to be a safe artificial sweetener.[94] The Joint FAO/WHO Expert Committee on Food Additives (JECFA), European Union, Japan, France, China, and India have approved the acceptable daily intake of saccharin at 5 mg/kg body weight. However, a study in the 1960s feared the introduction of bladder cancer in rats having saccharin. These subsequently asked countries like Canada to ban the consumption of saccharin. Nevertheless, later studies proved that cancer-forming cells were specific to animal studies and not relevant to humans.[95]

Sucralose under various research on mutagenicity and carcinogenicity represented no mutagenic hazard to humans.[89]

Neurological and Mental Health

Aspartame is generally asked to avoid in patients with phenylketonuria, a rare genetic disorder that creates difficulty in metabolizing phenylalanine. Aspartame is generally one of the safest artificial sweeteners however potential behavior effects and altered cognitive functions have been extensively studied in healthy, hyperactive, and sugar- sensitive children.[96] A dangerous risk of increased consumption of aspartame shows a seizure activity in animal models, however, it is negated by human trials, with minimal difference between aspartame-consuming and placebo-acquired patients.[97,98] Thus it is suggested to avoid the use of aspartame in mood disorder individuals.[99]

Electron microscopy studies of sucralose and its hydrolysis products conducted on mice had no pathological changes in the central nervous system. Along with other studies' findings, it was concluded that sucralose lacked neurotoxic properties.[89]

Inflammation and Gut

Artificial sweeteners may have various effects on organ systems depending on the dose, compound, and host genetics. Artificial sweeteners are reported to cause antibiotic-like alteration of gut microbiota.[84] In the research conducted by Basson et al. it explained that in conditions like chronic digestive inflammatory disorders, there are visible pro-inflammatory changes in the bacterial gut and immune reaction to the gut wall. Thus, it affects negatively chronic inflammatory conditions.[27]

Other Health Hazards

Neotame can result in headaches, and lower birth rates, and hepatoxicity is warranted. Headache, dry mouth, dizziness, nausea, vomiting, thrombocytopenia, and mood swings are the side effects visible with the consumption of aspartame.[36]

Sims et al. reported that consumption of sucralose regularly can shrink the thymus glands, and cause diarrhea and giddiness.[100] Recent evidence suggests that polyol sweeteners such as erythritol are associated with an increased risk of major adverse cardiovascular events.[101]

Four commonly used artificial sweeteners (saccharin, sucralose, aspartame, and acesulfame potassium) are suspected of promoting the transfer of antibiotic resistance genes, enabling competent bacterial species to evolve as resistance bacteria. This has grave implications for public health and environmental risk.[102]

Some artificial sweeteners like saccharin, acesulfame potassium, and aspartame have properties that involve a change in genetic composition, especially in the DNA of lymphatic cells and mat eventually called the breakage in DNA strands with the help of its by-products, distorting the metabolic properties in human. Nevertheless, more studies are required in this regard.

Safety

Clinical safety data is sufficient to analyze the safety factor of artificial sweeteners. Enumerable safety tests and data on genetic testing, teratogenicity, cariogenicity, carcinogenicity, obesity, and metabolic effects of sucralose have stated that it is indeed safe to be widely used as a food additive.[89] The U.S. Food and Drug Administration (USFDA) has performed over 50 scientific studies on safety issues on consuming acesulfame potassium for food and beverages before it was approved in dry fruit products.[29] Health regulations vary from country over 90 countries have approved the use of acesulfame potassium following the extensive research findings by the European Food Safety Authority over 15 years. Currently, the EU has directives regarding the maximum allowable levels of specific artificial sweeteners as food additives including acesulfame K, aspartame, cyclamate, saccharin, sucralose, xylitol, mannitol, and neotame. Legal and regulatory aspects need to be reviewed consistently and continually based on newer scientific updates and advances. Risk factors relating to excretion and the effect of intermediate metabolites, allergic reaction, hypersensitivity, tissue accumulation, and effects of normal intestinal flora are of concern.

In 1996, USFDA approved aspartame as a safe artificial sweetener to be used in the diet. Aspartame is unstable when heated and thus should be avoided in baking or cooking. Hence an information label stating it will enable people to use it accordingly. Another important safety measure to be followed is the phenylalanine label of warning especially, for phenylketonuria patients. Aspartame was tested among several groups for its safe use, such as a study among children, and was accepted for use.[103,104] Further studies are necessary to delineate their metabolic effects, strengths, weaknesses, and possible threats.

Lauded by its supporters and marketers as the answer to everything from diabetes to weight gain and demonized by its detractors, artificial sweeteners remain enigmatic. For a comprehensive safety assessment, an international database consisting of regulatory information should be created. It must incorporate results from animal and laboratory studies, toxicological testing, and human subjects in the context of dosage, purity, and synergistic effects. Future long-term studies are required for the interpretation of risk appraisal for artificial sweeteners.

Conclusion

Although artificial sweeteners have been cast as a healthy alternative to sugar, the scientific evidence supporting unconditional use and safety for newer generation sweeteners remains scarce.

Recommendations by American Pediatric Association have implied that nutritive and non-nutritive sweeteners can be used in the diet daily according to the Dietary Guidelines of Americans.[57] According to the literature available, we can conclude:

- Artificial sweetener is currently an asset in our diet.
- As minimal studies are conducted on newly discovered sweeteners like advantage and neotame on dental health, there is a need to explore this regard.

- If one is cautious in taking artificial sweeteners and maintains their permissible guidelines it can benefit several health conditions.
- Though contradictory studies are prevalent, dental caries are indicated to decline in individuals having artificial sweeteners.
- Hence the push can be given dental practitioners in spreading awareness among people and recommending the use of artificial sweeteners in rampant caries cases. Though the stress on optimum use cannot be over-emphasized.

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