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EFFECTS OF ARTIFICIAL SWEETENERS ON HUMAN HEALTH

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➢ ABSTRACT

The health impacts of artificial sweeteners, which are commonly used as low-calorie sugar alternatives to treat diseases including diabetes and obesity, may be more complicated than previously thought, according to new research. Intriguingly, excessive intake has been linked to a higher risk of metabolic disorders, cardiovascular diseases, some types of cancer, weight gain, unfavourable pregnancy outcomes, and possible hazards for people with low seizure thresholds. Artificially sweetened beverages have been associated in studies, such as the Women's Health Initiative, with an increased risk of stroke, coronary heart disease, and death, regardless of known risk factors. ASs like saccharin have been connected to inflammatory bowel disorders, disruption of the gut microbiota, increased intestinal permeability, and dysbiosis, which can result in metabolic problems like impaired glucose tolerance, insulin resistance, and increased systemic inflammation. These concerns also extend to gut health. The development of metabolic diseases like type 2 diabetes mellitus is further facilitated by these disturbances, which lower the generation of short-chain fatty acids essential for insulin sensitivity. Given these possible health hazards, this review emphasizes the need for careful use, knowledgeable consumer choices, and strict regulatory monitoring. It also highlights the need for additional research to clarify long-term health impacts and create risk-reduction plans.

Keywords: Artificial Sweeteners, Health Risks, Side Effects, Health

➢ INTRODUCTION

Sugar is an essential component of our diet. For centuries, sweeteners have been utilized to enhance the flavour and appeal of food items. Natural-origin sweeteners are either monosaccharides or disaccharides that possess a certain nutritional benefit. (1) It is a fundamental aspect of human nature to enjoy sweet foods. Earlier studies have indicated that new-borns show a preference for sweet-flavoured foods. Consequently, sweeteners have consistently been favoured in artificial food creations.(2) The energy imbalance noted between calorie consumption and its usage, due to the affluent lifestyle accompanying urbanization in the Indian population, is steering them towards obesity. Among the different food sources, sugar-sweetened drinks have been notably emphasized as a contributor to obesity. Lately, the negative impact of excessive sugar consumption is being consistently reported. Conversely, the growing access to databases via internet platforms and media has greatly heightened health awareness among the public in recent years. Consequently, improved options for the current food items are necessary to uphold health and wellness in the community.(3) Some discussed recommendations suggest that high sugar consumption might lead to specific neurodegenerative disorders. With this in consideration, consumers began utilizing artificial sweeteners as an alternative to regular sugar. Several low-calorie products are now on the market as healthier food options. Artificial sweeteners are also categorized as food additives, forming an essential component of the contemporary food industry. They are used worldwide not just for flavor improvement but also for preserving food quality and safety. (4) As indicated by the name, sweeteners are utilized in desserts, drinks, and comparable concoctions. The sweeteners can be either naturally derived or artificially made. Substances that are synthetic, collectively, are referred to as artificial sweeteners.(5) Nonetheless, from a metabolic perspective, artificial sweeteners cannot merely substitute for natural sugars. The natural sweetener's physical traits, including sweetness level, quality, decomposability, and availability in nature, are far better than those of artificial sweeteners. Additionally, they are readily processed in humans. In contrast, artificial sweeteners offer fewer calories since they are not fully metabolized by the human body.(6) This review intends to examine the physical and chemical properties of artificial sweeteners as well as their health effects.

ARTIFICIAL SWEETENING AGENT

Artificial sweeteners are alternatives to sugar, typically non-sugar alternatives. The food sector uses them extensively.[4] Artificial sweeteners are divided into nutritive and non-nutritive categories based on where the calories come from. The nutritive sweeteners that are as sweet as sucrose are called polyols. Known as artificial sweeteners or high-intensity sweeteners, the non-nutritive sweeteners are made up of compounds from different chemical groups that interact with taste receptors. Compared to sucrose, a natural sugar, they are roughly 30–13,000 times sweeter. [7]

1) Saccharin

The first and most traditional artificial sweetener is saccharin.Out of the four sweeteners, its acceptable daily intake (ADI) is the lowest, per the World Health Organization's (WHO) guidelines. Carbonated and noncarbonated drinks, dairy products, tabletop sweeteners, juice, jams, chewing gum, candies, desserts, puddings, and jellies are among the products that include it. [2]

2) Sucrose

Sucralose is produced by replacing the sucrose molecule's three hydroxyl groups with chloride atoms. [3] Sucralose has no calories but is 600 times sweeter than sugar. Since the FDA approved it in 1998, it has been sold under the registered name Splenda. In baked goods, it serves as a sweetening agent. Sucralose can also be found in gelatine, dairy products, sweets, jams, pie fillings, juices, frozen desserts, and other processed foods. The FDA expanded sucralose's use as a tabletop sweetener in all food products in 1999. [8] According to recent research, thymus gland shrinkage occurs when 5% sucralose is consumed daily. However, a thorough review of the documentation and particular immunotoxicity tests clearly dispelled the myth, demonstrating that the thymus gland's involution process was mostly caused by a nutritional deficiency [9] Increased sucralose consumption has been linked to migraine attacks [10] According to tolerance tests and a comprehensive animal safety database, frequent or prolonged use of sucralose at the maximum amount recommended for ingestion does not have any negative effects on human health. [11] It was persuasively shown that increasing sucralose intake led to a sequential decrease in food intake, which in turn decreased body weight increase and food conversion efficiency. [12]

3) Aspartame

Aspartame is a dipeptide consisting of the amino acids phenylalanine and aspartic acid, which are connected by a methyl ester (L-aspartyl-L phenylalanine methyl ester). In acidic or alkaline environments, it hydrolyzes to produce methanol. Under harsh circumstances, the peptide bonds hydrolyze, producing phenylalanine and aspartic acid. It dissolves a little in water. Aspartame's solubility is correlated with both pH and temperature. At a pH of 4.3, aspartame is most stable. Individuals who have phenylketonuria (PKU), a genetic disorder, are susceptible to phenylalanine, an aspartame metabolite [13] Aspartame is not a nutritional sweetener because of its low calorie content. After being absorbed by the body, aspartame breaks down into natural components such phenylalanine, aspartic acid, and methanol, which then further simplify into products such as formic acid, formaldehyde, and diketopiperazine. [13]

4) Cyclamate

Cyclamate is a salt of cyclohexylsulfamic acid. One non-nutritive sweetener that is used is sodium cyclamate.Particularly in low-sodium diets, its equivalent calcium salt is employed. Compared to sucrose, cyclamate is thirty times sweeter. It's utilized in diet drinks, low-calorie foods, and as a tabletop sweetener. Moreover, many medications utilize cyclamate to improve their flavor. [4,7]

5) Neotame

Aspartame is N-alkylated to form neotame, a derivative. Its level of sweetness fluctuates according to the type of food and the makeup of the blend. Compared to sugar and aspartame, it is 7000–13,000 times sweeter and roughly 30–60 times sweeter, respectively. There are no calories in it. It is used as a sweetener in beverages, baked goods, gelatines, chewing gum, jams, jellies, and many other foods as a flavor enhancer since the FDA approved it in 2002. Neotame powder is white to grey-white and odorless. It is marginally soluble in water and easily soluble in alcohols. With a pH of 5.8, the 0.5% neotame aqueous solution is slightly acidic. [8]

6) Alitame.

Alitame is readily absorbed and quickly metabolized in the gastrointestinal (GI) tract before being eliminated. It

disintegrates into alanine amide and aspartic acid, its two main components.[14] Alanine amide experiences minor metabolic changes, but aspartic acid is readily processed. In humans, the main urine metabolite is the glucoronic derivative of D-alanine tetramethyl thietane amide. Four Adverse Reactions The gut microbiome, gastrointestinal motility, intestinal absorption and permeability, and the structure of the gastrointestinal tract are among the many gastrointestinal system activities that are impacted by artificial sweeterns.

- **SIDE EFFECTS**

1) **Gastrointestinal:** ASs impact various functions of the gastrointestinal system, including the gut microbiome, gastrointestinal motility, intestinal absorption and permeability, and the anatomy of the gastrointestinal tract.

2) **Gastrointestinal motility:** The main indirect mechanism by which ASs may affect gastrointestinal motility is through their effects on serotonin and incretin hormone production. It has been discovered that a number of ASs cause increases in the levels of gastric inhibitory polypeptide, which may slow stomach emptying, and cholecystokinin, which delays stomach emptying. Additionally, ASs have been shown to raise peptide YY (PYY), which can cause a delay in intestinal transit, and glucagon-like-peptide-1 (GLP-1), which has been shown to decrease motility in the antro-duodeno-jejunal area and suppress the migrating motility complex in both people with and without gastrointestinal disorders [16–20].

3) **Gastrointestinal anatomy:** ASs have been shown to cause hyperkeratosis, papillomas, ulcers in rats' glandular stomachs,[22] DNA damage in the stomach and colon, [22]and an osmotic impact [21] that raises the water content of stool. Colon histopathologic observations include scarring of the epithelial tissue, a modest decrease in the number of goblet cells, and lymphocyte infiltration into the epithelium. Rabbits given high dosages of ASs (750–1,000 mg/kg/day) experienced signs of cecal hypertrophy and perianal soiling.[24]

4) **Permeability and intestinal absorption:** Little is known about how ASs affect these processes. Although it was not observed, the investigations seem to prevent the passive transfer of sugar across the basolateral membrane.

5) **Neurological manifestations:** Aspartame research account for the majority of reports on how AS affects neurological manifestations. AS and aspartame will be used interchangeably in this section. More specifically, aspartame has been widely linked to headaches. Aspartame is also linked to neuropsychological symptoms such anxiety, sadness, sleeplessness, and seizures.

6) **Headaches and migraines:** Aspartame is composed of 45% aspartate and 55% phenylalanine. Unlike dietary protein, aspartame ingestion can raise aspartic acid and phenylalanine levels in the brain. These substances have the ability to prevent the production and release of dopamine, norepinephrine, serotonin, and other known neurophysiological activity regulators. Aspartame raises plasma cortisol levels and causes an excess of free radicals, which makes it a chemical stressor. The brain may be more vulnerable to oxidative stress due to elevated cortisol and extra free radicals, which could have a negative impact on neurobehavioral health. [27]

7) **Taste alteration:** There is some evidence to suggest that exposure to non-nutritive sweeteners (NNS) may change how people perceive taste, though this is not known. Blood oxygen level-dependent reactions in the insula and amygdala to sucrose are inversely correlated with NNS use [52]. The reduced afferent signaling and perceived intensity of sweet stimuli may therefore be the cause of the altered activity in these
areas of heavy NNS consumers. [28]

8) **Allergic reaction:** Some sweeteners, such as erythritol, xylitol, and aspartame, have been linked to allergic reactions. Skin rashes and contact dermatitis are among the systemic reactions caused by formaldehyde, which is produced during the metabolism of aspartame [29–31]. Skin responses and severe allergies, including oral ulcers, have been linked to xylitol [32]

9) **Diabetes mellitus type 2 :** Recent years have seen a significant rise in the prevalence of diabetes mellitus, which is mostly attributable to our sedentary lifestyles and food choices. [33] An increased risk of type 2 diabetes mellitus (T2DM) was linked to AS use in a recent large population-based cohort research that included 105,588 French people. Aspartame, acesulfame-K, sucralose, and total sweeteners were among the sweeteners for which favorable relationships were found. [2]

10) **Risk for Cancer:** To evaluate the possible connection between AS and cancer risk, numerous investigations have been carried out. The 1977 study, which showed a link between ASs and bladder cancer, was one of the first to raise concerns about ASs. According to a case-control research by However bladder cancer risk was 1.6 times higher for every AS user than for those who had never used these sweeteners [34]

➢ CONCLUSION

The usage of ASs has been steadily rising in the last several years. Numerous studies have reported a number of adverse consequences linked to the usage of ASs, despite their diverse applications. As we show in our thorough research, ASs can affect a number of cardiovascular, neurological, and gastrointestinal system processes. The majority of contemporary research data, including systematic reviews and meta-analyses, do not associate the use of ASs with an increased risk of cancer, despite the fact that several studies do. Nevertheless, additional long-term prospective research is required to more accurately describe how ASs affect human health.

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