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REVIEW ARTICLE

Artificial Sweeteners

Dr. Jyoti Bobde

Asst. Professor, Department of Pharmacology, MGM Medical Collage, Aurangabad, India.

Introduction[1–11]

Sweeteners are food substances used to improve the taste and flavor of foods. Major ingredients in natural sweeteners are mono- or disaccharides, thus have nutritional or caloric value.[1] Though it is thought that many factors contribute to obesity, high sugar and fat intake are considered as the leading causes. This thinking has resulted in the increase use of non-nutritive sweeteners (NNSs).[6] In 1885 Constant in Fahlberg produced the first artificial sweetener, saccharin, which surprised scientific establishment due to its extreme sweetness.[4] The artificial sweeteners are synthesized compounds that have high-intensities of sweetness and unlike, natural sweeteners, having no nutritional value.[2] Artificial sweeteners are used in food products to limit caloric intake. Sugar alcohols are natural compounds with varying degrees of sweetness which are often added to boost flavours of products.[3]

Sweet, sour, bitter, salty and umami are the five identified classified categories of taste. Over human evolution, sweetness and bitterness have played a key role to survival. Sweetness provides the means to seek energy source in the form of carbohydrates; and bitterness results in an aversion to potentially deadly substances found in nature, e.g. alkaloids and toxins. Currently six intensely-sweet sugar substitutes have been approved for use by the regulatory authorities. These are stevia, aspartame, sucralose, neotame, acesulfame potassium and saccharin. There is some-ongoing controversy over whether artificial sweetener usage poses health risks.[7–9]

Sweetening compounds are classified into two subcategories, bulk and high-intensity sweeteners. Bulk sweeteners are compounds found in nature, which provide energy, calories and bulk to food. More specifically, the category of caloric bulk sweeteners also known as sugars, includes popular natural carbohydrates. On the other hand, high-intensity sweeteners are primarily synthetic and non caloric, which provide greater sweetness compared to sucrose.[10,11]

Role of Artificial Sweeteners In Nutraceuticals[12,13]

Sugar substitutes are used for a number of reasons, including:

i. To assist in weight loss— artificial sweeteners limit the food energy intake by replacing high-energy sugar food with sweeteners having little or no food energy. This helps to lose weight and avoid other problems associated with excessive caloric intake.

ii. Diabetes mellitus — people with diabetes mellitus and other metabolic conditions have difficulty regulating their blood sugar levels. By limiting their sugar intake with use of artificial sweeteners, they can achieve good glycaemic control.

iii. Dental care — The carbohydrates and sugars consumed usually adheres to the tooth enamel due to which bacteria quickly multiply. As the bacteria feed upon the sugar, they convert it to acid waste leading to decaying of the tooth structure. Artificial sugar substitutes are not fermented by the micro flora of the dental plaque which aids dental health. Artificial sweeteners acts by preventing bacteria from adhering to the tooth surface and preventing plaque formation and eventually decay.

iv. Avoiding processed foods— Many individuals now use artificial sweeteners to prevent the excess calorie intake and metabolic complications.

Individual Sweeteners[14–18]

Acesulfame Potassium[14]

Acesulfame K is 200 times sweeter than sucrose (common sugar), however it has a slightly bitter after-taste, especially at high concentrations.

Mechanism of action[15–17]

Acesulfame is quickly excreted in the urine. It is broken down into aceto acetamide, which can be toxic at high levels but in food and beverages the levels are far below the amount which may be toxic. Tissue samples of animals and humans do not show accumulation after multiple doses of acesulfame.

Acesulfame potassium is stable under heat due to which it is used as a food additive in baking that require a long shelf life. It is also used as a sweetener in protein shakes and pharmaceutical products, especially chewable and liquid medications, as it can make the active ingredients more palatable.

Safety

Several studies of acesulfame on blood glucose levels found that acesulfame has no effect on insulin secretion or blood glucose so it is suggested that acesulfame does not pose a risk to safety concern.

Aspartame[17]

In 1965, a chemist at G. D. Searle while working in the laboratory accidentally found a chemical which was very sweet. This led to the discovery of aspartame.

Mechanism of action[18,19]

Aspartame is hydrolyzed in the intestinal lumen into its components, aspartic acid, phenylalanine and methanol. These components are absorbed into the blood and metabolized.

Safety

Aspartame has been the most controversial artificial sweetener because of its potential toxicity. Shankar et al. in a systematic review, reported that aspartame may cause headaches, Alzheimer's disease, attention deficit disorders, birth defects, cancer, diabetes and lupus. Aspartame remains controversial but still is the most frequently used in non-nutritional sweeteners.

Cyclamate[20]

In 1937 at the University of Illinois Michael Sveda, a graduate student, while working in the laboratory on synthesis of anti-fever medication accidentally put his cigarette down on the laboratory bench and, when he put the cigarette back to his mouth, he discovered the sweet taste of cyclamate which lead to its discovery.

Cyclamate is 30–50 times sweeter than sucrose (table sugar),due to which it is the least potent of the commercially used artificial sweeteners. It is often used with other artificial sweeteners like saccharin to mask the off-tastes of both sweeteners. It is less expensive than other sweeteners and is stable under heating process.

Safety[21,22]

In a 1969 study it was found that the common 10:1 cyclamate: saccharin mixture caused increase in the incidence of bladder cancer in rats. The released study concluded that at levels of humans ingesting 350 cans of diet soda per day, could develop risk of bladder tumors.

Neotame[23,24]

Neotame is the newest artificial sweetener which is a derivative of aspartame. It is 7,000 to 13,000 times sweeter than sugar. The FDA approved neotame in 2002 as a sweetener for use in baked goods, soft drinks, chewing gum, frosting, frozen desserts, jams, jellies, gelatins, puddings, processed fruits, toppings and syrups.

Mechanism of action[25,26]

Neotame is rapidly metabolized by hydrolysis of the methyl ester by esterases present throughout the body. The de-esterified neotame is the major metabolite, and an insignificant amount of methanol is also produced. Neotame and de-esterified neotame are rapidly cleared from the plasma and completely eliminated from the body in urine and feces within 72 hours.

Safety

Studies of neotame reveal changes in body weight, body weight gain and food consumption.

Saccharin[27,28]

In 1879, Constantine Fahlberg was researching the oxidation mechanisms of toluene sulfonamide while working at Johns Hopkins University in the laboratory of Ira Remsen. During his research, a substance accidentally splashed on his finger which he later licked and noticed the substance had a sweet taste which lead to discovery of saccharin. Later a number of compounds have been discovered and used as food additives for their sweetener properties. Saccharin has been in use since 1900 and obtained FDA approval in 1970.

Mechanism of action[29,30]

Saccharin is formed by an initial reaction between toluene and chloro sulfonic acid which is then converted to a sulfonamide with ammonia, which is then oxidized to a benzoic acid and heated to form the cyclicimide. Saccharin is not absorbed or metabolized and is excreted, unchanged, through the kidneys.

ADR studies[31–33]

A study by Fukushima et al. (1983) showed an increase in bladder neoplasms. Another case study of the hepatotoxicity of saccharin was published in 1994 by Negro et al. where patient presented with elevated serum concentrations of liver enzymes after the oral administration of three different drugs, of which saccharin was the only common constituent. Re-exposure to pure saccharin supported its role in pathogenesis of the liver damage.

This led to ban of sachharin in USA which was withdrawn in 1991, but foods containing saccharin were required to carry a warning to indicate "saccharin is a potential cancer causing agent." Future research on the safety of this product led to this decision being overturned in 2000 but a ban on saccharin still exists in Canada.

Sucralose[34,35]

Sucralose was accidentally discovered in 1976 when Tate and Lyle, a British sugar company, was looking for ways to use sucrose as a chemical intermediate. Sucralose is 600 times sweeter than sugar and contains no calories. Sucralose was approved by the FDA in 1998 for use in 15 food categories.

Mechanism of action[36,37]

It is poorly absorbed by the human body. About 85% of sucralose is unabsorbed and excreted unchanged. The absorbed sucralose is circulated throughout the body. However, there is no active transport across the blood-brain barrier, placenta or into human milk. It does not bind to proteins. The remaining 2–3% of consumed sucralose is converted to water soluble solute that is non-toxic.

Safety[38]

Cases studies have been reported on sucralose consumption causes increased incidence of deleterious effects like migraines triggered by sucralose.

Stevia[39]

The plant Stevia rebaudiana has been used for more than 1,500 years by the Guaraní peoples of South America. The leaves have been used traditionally for hundreds of years in both Brazil and Paraguay to sweeten local teas and medicines so termed as a "sweet treat". The genus was classified by Spanish botanist and physician Petrus Jacobus. Stevus was a professor in botany at the University of Valencia in whose memory the name stevia is given.

Mechanism of action[40]

In the digestive tract, rebaudiosides are metabolised into stevioside. This stevioside is broken down into glucose and steviol. The glucose released by this process is used by bacteria in the colon but is not absorbed into the bloodstream. Steviol is not further digested and is excreted.

Japan is the largest consumer of stevia leaves and uses the plant to sweeten foods, such as soy sauce, confections and soft drinks, and as a replacement for aspartame and saccharin.

ADR studies

Stevia is not mutagenic or genotoxic. Stevioside is found to be nontoxic in acute toxicity studies in a variety of laboratory animals. Chronic administration of stevia to male rats has no effect in fertility in control studies. Stevioside has no toxic effects when given to rats at dose up to 2,000 mg/kg/day for 90 days proving it to be a safe artificial sweetener.

Controversies about Artificial Sweeteners and its Metabolism[41]

Several recent studies have focused on the effects of artificial sweeteners on metabolic systems, especially in individuals with diabetes. In 2007, Ferland et al. investigated the effects of aspartame on plasma glucose and insulin levels during acute exercise in 14 men with type 2 diabetes. Contrary to all expectation, the aspartame breakfast also induced a similar rise in glucose and insulin levels at baseline as the sucrose meal.

Populations Susceptible to Side-Effects[42]

Susceptible populations are at risk for the potential deleterious effects of artificial sweeteners which include diabetics, children, pregnant women, women of childbearing age, breast feeding mothers, individuals with low seizure thresholds and individuals at risk for migraines. More studies are required for these susceptible populations to determine its safety and efficacy.

Because artificial sweeteners are in more than 6,000 products, including foods, medications and cosmetics, it is impossible to completely eradicate them from daily encounters. Replication studies and long-term assays are

required to decrease fear resulting from the limited research that currently exists.

Alternatives to Artificial Sweeteners[43]

Various natural sweeteners can be used instead of artificial sweeteners. Many of these include added benefits of being rich in minerals and vitamins. These include honey, coconut nectar, fruits, coconut sugar, maple syrup, molasses, sugar alcohols, stevia, dates, agave nectar, apple sauce and others.

Honey is considered as the best alternative to table sugar and artificial sweeteners. It contains probiotics which aid in improving the health of the digestive system. Fruits are another source of healthy and naturally available sugar as they contain fructose which is packed with fiber and minerals.[44]

Coconut nectar is derived from the coconut tree blossoms is rich in vitamin C and amino acids. Sugar alcohols like sorbitol, xylitol, mannitol, erythritol and isomalt occur naturally in many fruits and vegetables. Though these are carbohydrates that are not calorie free but have fewer calories than white sugar, and due to this fact, they offer no nutritional benefit. However they can cause bloating, gas and diarrhoea if taken in large amounts.[45]

Summary and Conclusion

Review of many scientific journal articles on the health effects of artificial sweeteners has shown that while artificial sweeteners may not be linked to cancer, but they certainly do have an effect on obesity and the micro flora of the human gastrointestinal tract. Also, it has been found that while scientific studies have not yet been able to find links to behavioural disorder or brain damage caused by artificial sweeteners case studies show that aspartame may have adverse impact on the neurological system.

Saccharin and aspartame have been the major artificial sweeteners accused of being carcinogenic. Research shows that artificial sweeteners do, however, have an effect on obesity. Though they do not directly cause obesity (obviously because they are low in calories), however it is postulated that consuming artificial sweeteners has been shown to impair the brain's ability to "count" calories based on the sweetness profile of food.

The use of artificial sweeteners remains controversial. Their consumption has been shown to cause mild to serious side effects. Healthcare providers should be aware of current research surrounding the use of artificial sweeteners and inform patients of the potential risks associated with their use.

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Learn as if you were to live forever."
— Mahatma Gandhi