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Artificial Sweeteners: Chemistry, Health Impacts and Regulatory Perspectives

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ABSTRACT

Artificial sweeteners are substances that mimic the taste of sugar but offer negligible or zero calories. Their discovery dates back to the 19th century with saccharin. With the rise in lifestyle diseases like obesity, diabetes etc, their role as sugar alternatives has become increasingly significant. Therefore, food industries use various artificial sweeteners that are used in weight loss, diet planning with no calories or low calorie contents instead of high calorie sugar. These sweeteners are used instead of sucrose to sweeten the product. In recent years, these are used in over 6000 or more products. United States Food and Drug Administration (US FDA) has approved aspartame, acesulfame-K, neotame, sodium cyclamate etc for use as per acceptable daily intake (ADI) value. This paper aims to provide a comprehensive overview about the introduction, structure, possible health benefits and concerns of artificial sweeteners.

Keywords: Artificial sweetener, low calorie sweetener, saccharin, aspartame, acesulfame-K, sucralose, sodium cyclamate, D-tagatose, trehalose, stevia.

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INTRODUCTION

A sugar substitute is a food additive that provides a sweetness like that of sugar while containing significantly less food energy than sugar-based sweeteners, making it a zero-calorie (non-nutritive) or low-calorie sweetener. Artificial sweeteners may be derived through manufacturing of plant extracts or processed by chemical synthesis. Sugar substitute products are commercially available in various forms, such as small pills, powders and packets. Common sugar substitutes include aspartame, saccharin, sucralose, stevia, acesulfame-K(ace-K), and sodium cyclamate.

These sweeteners are a fundamental ingredient in diet drinks to sweeten them without adding calories. Additionally, sugar alcohols such as erythritol, xylitol and sorbitol are derived from sugars. Approved artificial sweeteners have not been shown to cause cancer. Reviews and dietetic professionals have concluded that moderate use of non-nutritive sweeteners as a safe replacement for sugars can help limit energy intake and assist with managing blood glucose and weight. The dietary option that such product provides may be especially helpful in the management of obesity or diabetes mellitus. One group of such sweeteners consists of substances with a very intense sweet taste and is used in small amount to replace the sweetness of a much higher amount of sugar.

The sweeteners of this type currently approved for use in the United States are- Aspartame, Acesulfane-K, Neotame, Saccharin, Sucralose, Cyclamate and Alitame. This review gives the information about the sweeteners such as Saccharin, Aspartame, Acesulfame-K, Sucralose, Sodium Cyclamate, D-tagatose, Trehalose and Stevia.

Types of artificial sweeteners

Artificial sweeteners may be derived through manufacturing of plant extracts or processed by chemical synthesis.

Artificial (Synthetic) Sweeteners

These are chemically synthesized and are much sweeter than sugar but contain little or no calories.

Table 1: Artificial (Synthetic) Sweeteners

S. No.	Name of Sweetener	Brand Names	Sweetness (Compared to Sugar)	Notes
1	Aspartame	Equal, NutraSweet, Sugar Twin	~200x	Not heat-stable, not suitable for cooking
2	Saccharin	Sweet'N Low, Sweet Twin, Necta Sweet	~300-400x	Oldest artificial sweetener, metallic after taste
3	Sucralose	Splenda	~600x	Heat-stable, good for baking
4	Acesulfame-K	Sunett, Sweet One	~200x	Often blended with other sweeteners
5	Neotame	Newtame	~7,000-13,000x	Chemically similar to aspartame but more stable

Sugar Alcohols (Polyols)

These are naturally occurring or synthetic and contain some calories. They are less sweet than sugar.

Table 2: Sugar alcohols (Polyols)

S. No.	Name of Sweetener	Found In	Sweetness (Compared to Sugar)	Notes
1	Xylitol	Chewing gum, toothpaste	~1:1	Tooth-friendly, may cause bloating
2	Sorbitol	Sugar-free candies, syrups	~0.6x	Low glycemic index
3	Maltitol	Baked goods, chocolates	~0.9x	Can cause gas/diarrhea in excess
4	Erythritol	Stevia blends, sugar-free items	~0.7x	Zero calories, no digestive issues in small amounts
5	Mannitol	Medications, gums	~0.5x	Laxative effect in high doses

Natural Non-Nutritive Sweeteners

These are plant-derived and often considered healthier alternatives.

Table 3: Natural Non-Nutritive Sweeteners

S. No.	Name of Sweetener	Source	Sweetness	Notes
1	Stevia	Stevia plant leaves	~200-300x	Zero-calorie, natural, slightly bitter
2	Monk Fruit Extract (Luo Han Guo)	Monk fruit	~150-250x	No calories, clean taste
3	Thaumatin	Katemfe fruit	~2,000-3,000x	Used as flavor enhancer too

Some Common Artificial Sweeteners

Saccharin (o-sulfobenzimide)

Saccharin is one of the oldest artificial sweeteners, discovered in 1879 and has been used for over a century to sweeten foods and beverages without adding calories. Saccharin has been approved by FDA for use in more than 100 countries. Saccharin has an unpleasant bitter or metallic off taste. As the parent compound is only sparingly soluble in water, the sweetener is usually used as the sodium or calcium salt. Both salts are highly water soluble at room temperature. It is about 300-400 times sweeter than sucrose.

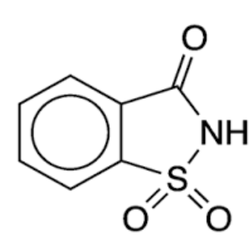

Figure 1: Structure of Saccharin

Aspartame (Methyl L-α-asparthy-L-phenylalaninate)

Aspartame is one of the most debated sweeteners. It has been used in 6000 different products. Aspartame was discovered in 1965 by James Schlatter a chemist. It is an artificial, non-saccharide sweetener, L-aspertyl-L-phenylalanine methyl ester that is a methyl ester of the dipeptide of the amino acids aspartic acid and phenylalanine. It is slightly soluble in water. This sweetener is marketed under a number of trademark names including Equal, Nutrasweet and Candere and has a good clean sweet taste but its time-intensity profile differs from sucrose.

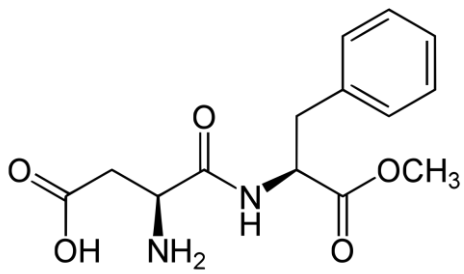

Figure 2: Structure of Aspartame

Acesulfame-K

Acesulfame-Potassium, commonly abbreviated as Ace-K, is a potassium salt of 6-methyl-123-axathiazine-4 (3H)-one 2, 2-dioxide with molecular formula $C_4H_4KNO_4S$ and molecular weight of 201.24 was developed as sweetener by Hoechst. This is a general-purpose sweetener, white crystalline structure, non-nutritive sweetener, non-carcinogenic. It is used in over 4000 products in approximately 90 countries. The “K” refers to the mineral potassium, which is naturally found in our bodies.

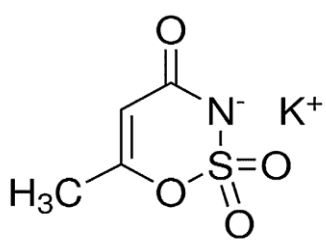

Figure 3: Structure of Acesulfame-K

Sucralose

Sucralose is a sucrose molecule in which three of the hydroxyl groups have been replaced by Cl atoms. Sucralose is also heat stable which quality makes it a superb sweetener for cooking and baking. It retains its sweeteners significantly longer than aspartame. Sucralose was discovered in 1976. This non-nutritive sweetener is made from sucrose by a process that substitutes 3 chloride atoms for 3 hydroxyl groups on the sucrose molecule. Sucralose is 600 times sweeter than sucrose, has a pleasant sweet taste and its quality and time intensity profile is very close to that of sucrose. It has a moderate synergy with other nutritive and non-nutritive sweeteners. It is very much soluble in water and is stable over a wide range of p^H and temperature. It does liberate HCl when stored at high temperature and produce some kind of discoloration.

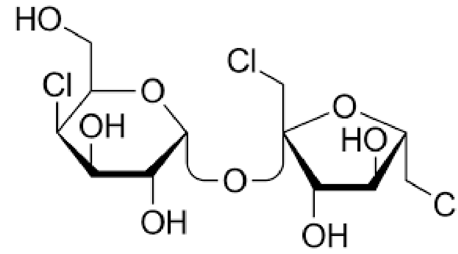

Figure 4: Structure of Sucralose

Sodium Cyclamate

Cyclamate was discovered in 1937. It was used as a low calorie sweetener in the United States in the 1950s and 1960s. It is a salt of cyclo hexyl sulfamic acid. Sodium cyclamate is used as none nutritive sweetener and the analogous calcium salt used specially in low sodium diets. Cyclamate is 30 times sweeter than sucrose. It has a bitter off taste, but has good sweetness synergy with saccharin. It is soluble in water, and its solubility can be increased by preparing the sodium or calcium salt.

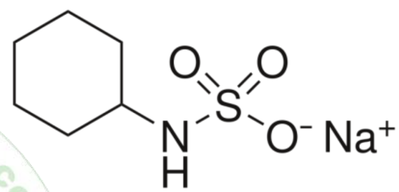

Figure 5: Structure of Sodium Cyclamate

D-tagatose

The ketohexose D-tagatose is structurally similar to D-fructose except for an inverted optically active center. Because of its excellent taste and bulk properties, combined with a possibly very low energy value, D-tagatose has potential for use as a sweetener.

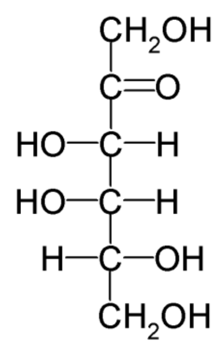

Figure 6: Structure of D-tagatose

Trehalose

Trehalose is a non-reducing disaccharide that consists of two glucose units linked by a 1,1-glycosidic bond. It is with a relative sweetness of 40-45% that of sucrose. Trehalose is produced directly from starch by a multienzymatic process. This disaccharide is enzymatically hydrolyzed by the enzyme trehalase in the small intestine into two glucose subunits which are subsequently absorbed and metabolized in a manner similar to maltose. Trehalose is approved in Japan, Korea, Taiwan, and UK.

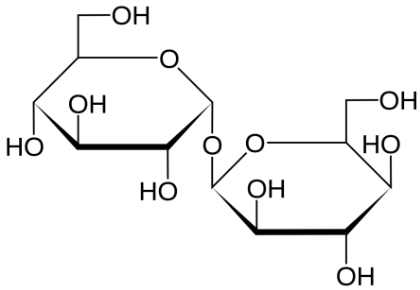

Figure 7: Structure of Trehalose

Stevia

Stevia is a natural herb sourced from the leaves of the Stevia rebaudiana. This zero calorie sweetener mainly contains steviol glycoside which is 200-300 times sweeter than sucrose. Human body does not metabolize these sweet glycosides, so obtains no calories from stevia. Unlike artificial sweetener, the sweet glycoside does not break down in heat which makes stevia an excellent sweetener for cooking and baking. Studies have indicated that stevia tends to lower the elevated blood pressure. It also significantly improves nutritional status of diabetic patients.

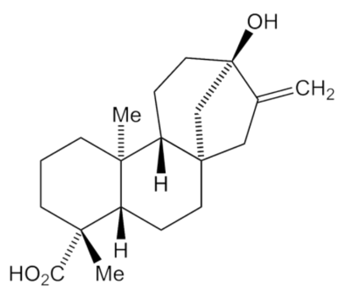

Figure 8: Structure of Stevia

Possible Health Benefits of Artificial Sweeteners

Weight Management

Artificial sweeteners provide little to no calories, which can help reduce overall calorie intake. They may support weight loss or weight maintenance in individuals trying to manage their weight.

Blood Sugar Control

Most artificial sweeteners do not raise blood glucose levels, making them suitable for people with diabetes. They help in managing glycemic response when replacing sugar in the diet.

Dental Health

Unlike sugar, artificial sweeteners do not contribute to tooth decay or cavities. Some sweeteners, like xylitol, may even inhibit the growth of bacteria that cause dental caries.

Reduced Risk of Metabolic Syndrome

Substituting sugar with non-caloric sweeteners may reduce risk factors such as high blood pressure, high triglycerides, obesity, and insulin resistance.

Suitable for Special Diets

Artificial sweeteners are often safe for individuals following special diets, such as ketogenic or low-sugar diets. People with conditions like phenylketonuria (PKU) should avoid specific sweeteners like aspartame.

Support for Healthy Lifestyle Transitions

Artificial sweeteners can help individuals transition from a high-sugar diet to one with better sugar moderation. They may also help reduce sugar cravings over time.

Possible Health Concern of Artificial Sweeteners

Metabolic Effects

Some studies suggest artificial sweeteners may alter gut bacteria, leading to impaired glucose metabolism and increased risk of insulin resistance. Despite being calorie-free, some research links artificial sweeteners (especially aspartame and saccharin) to increased appetite or weight gain due to disrupted hunger signals.

Gut Microbiota Alteration

Artificial sweeteners like sucralose and saccharin may negatively affect gut bacteria diversity, potentially leading to inflammation, metabolic disorders and digestive issues.

Increased Cravings for Sweet Foods

Regular consumption may increase preference for overly sweet foods, which can lead to poor diet quality and increase sugar intake from other sources.

Headaches and Mood Disorders

Aspartame has been reported to trigger headaches, dizziness, and mood changes in sensitive individuals. Some people also report anxiety or depression-like symptoms, though evidence is not consistent.

Potential Cancer Risk

Earlier studies (especially in animals) linked artificial sweeteners to cancer risk, but: modern reviews by FDA, EFSA, and WHO generally conclude approved sweeteners are safe in moderation. However, IARC (2023) classified aspartame as 'possibly carcinogenic' based on limited evidence in humans.

Allergic Reactions

Rare cases of allergic reactions or intolerance have been reported, especially to saccharin, acesulfame K, or aspartame.

Impact on Children and Pregnant Women

The long-term safety of artificial sweeteners in children and pregnant women is not fully established. Caution is advised due to potential developmental and metabolic effects.

Regulatory and Safety Evaluation

Regulatory bodies such as the FDA, EFSA and FSSAI have approved artificial sweeteners after extensive testing. Each has an Acceptable Daily Intake (ADI).

United States- Food and Drug Administration (FDA)

- Regulates sweeteners under the Food Additives Amendment of 1958
- Must be generally recognized as safe or approved via food additive petitions
- Safety assessment includes toxicology data, carcinogenicity, EDI, and ADI

Europe – European Food Safety Authority (EFSA)

- Conducts risk assessments and sets ADI values
- Evaluations follow international guidelines, including OECD protocols

World Health Organization (WHO) & Joint Expert Committee on Food Additives (JECFA)

JECFA evaluates global safety data and determines ADI based on NOAEL from animal studies

India- Food Safety and Standards Authority of India (FSSAI)

- Approves sweeteners under the regulation 3.1 of the Food Products Standards & Food Additives Regulations, 2011
- Currently permits a defined list of five major artificial sweeteners, with strict maximum levels for each category of food items.

Safety Assessment Methodologies

- Toxicological Testing: Acute, sub-chronic and chronic toxicity
- Carcinogenicity Studies: Long-term studies
- Metabolism Studies: ADME profile
- Human Clinical Trials: Effects on insulin, weight and gut microbiota

Recent Developments

- Development of next-gen sweeteners like allulose and monk fruit extracts.
- Advances in biotechnology to create tailored sweet proteins (e.g., brazzein, thaumatin).
- Studies exploring combination sweeteners for improved taste and safety.

CONCLUSION

Artificial sweeteners are a double-edged sword, offering benefits in calorie control and disease management, yet accompanied by ongoing scientific scrutiny. Responsible consumption, guided by current research and regulatory guidelines, is the key to their safe use. So, research is required to make natural sugars having the desired quantities of sweetness, low caloric value and least observed physiological effects.

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Conflicts of interest

Authors have no conflict of interest to declare.

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