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# A Scientific Review on Sweeteners

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**A B S T R A C T**

Sweeteners are food additives that are used to improve the taste of everyday foods. Artificial sweeteners are used in such small quantities that they don't increase calorie intake. However, they react with receptors on the tongue to give people the sensation of tasting something sweet without the calories associated with natural sweeteners, such as table sugar. They are just one type of sugar substitute. Refined white sugar has been linked to dental cavities, increased cholesterol levels, heart disease, hypoglycemia, diabetes, obesity, osteoporosis and nutritional deficiencies; therefore, many people have turned to high-intensity sweeteners like aspartame, sucralose, and saccharin as a way to reduce the risk of these consequences. NAS consumption is considered safe and beneficial, yet scientific data remain sparse and controversial. These low calorie sweeteners are associated with a wide range of adverse health effects too. This review article provides a brief overview on use and effects of sweeteners.

**Keywords:** Acesulfame-K, artificial sweetener, aspartame, neotame, saccharine, Non-caloric artificial sweeteners NAS, sucralose.

## A R T I C L E I N F O

**CONTENTS**



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## 1. Introduction

Sweet taste is universally regarded as the most pleasant experience as human being is actually born with a sweet tooth and preference for sweets, remains with us whole life (1). Recognizing our desire for sweet flavors, the food industry has developed and supplied sugar free alternatives designed to curb our cravings. Sweeteners are food additives that are used to improve the taste of our food. Sugars occur naturally (intrinsic) in all fruit, vegetables, and dairy foods or are it can be added (extrinsic) to foods during processing, or in preparation for consumption by an individual. However, too much of a good thing can lead to problems such as dental cavities, tooth decay, obesity, and the health complications related to being overweight and obese (for example, type 2 diabetes, hypertension, hypertriglyceridemia, and heart disease). Problems such as osteoporosis, vitamin and mineral deficiencies can also occur when high-sugar foods replace more nutritionally balanced foods.

Artificial sweeteners are extensively introduced into our diets with the intention of reducing caloric intake and normalizing blood glucose levels without compromising the human 'sweet tooth'. Do they really help with weight loss or managing blood sugar levels? Or do they actually increase appetite and weight, as some have claimed? What is right? Let's take a look at the different types of sugar substitutes and their role in helping us to manage weight and other medical conditions. Furthermore, artificial sweeteners or low/no calorie sugar substitutes have sparked much controversy and debate. Some have alleged that these sugar substitutes negatively affect behavior and mood, or could even be "toxic."

Sweeteners have been classified as nutritive and non-nutritive depending on difference in the amount of energy or calorie provided.

**Nutritive sweeteners**

a. They act both to provide a sweet taste and to be a source of calories or energy, including the mono-saccharide polyols (e.g., sorbitol, mannitol, and xylitol) and the disaccharide polyols (e.g., maltitol and lactitol)
b. Crystal (Sucrose, Dextrose, Fructose, Glucose, Lactose)
c. Honey
d. Fruits
e. Invert Sugar (by sucrose hydrolisis)
f. Syrups : Glucose, Maple, birch, pine, palm, sugar beet, sorghum, corn, cane, barley malt, molasses, brown rice, etc.
   Their sweetness is approximately equivalent to sucrose.

**Non-Nutritive sweeteners**

The non-nutritive sweeteners, better known as intense sweeteners, sugar substitutes, alternative sweeteners, low calorie sweeteners, sugar-free sweeteners and artificial sweeteners, include substances from several different chemical classes that typically exceed the sweetness of sucrose by a factor of 30 to 13,000 times. They are good alternatives to sugar as they add virtually no calories or insignificant amount to your diet. In addition, you need only a smaller quantity compared with the amount of sugar. Many people use these sweeteners to reduce calories in their diet or in the management of diabetes. The (Food and Drug Administration) FDA has established an acceptable daily intake (ADI) for any food ingredient including each artificial sweetener, at which it can be safely consumed every day over a lifetime.

This amount is well below the amount that would cause a health risk. The ADI is listed in units of milligram (mg) per kilogram (kg) of body weight. 1 kilogram = about 2.2 pounds. Can sugar, really be that terrible for you? Well, yes. For some time now, eating sugar-sweetened foods and beverages has negative impact on weight and other health outcomes; However, accumulating evidence suggests that frequent consumers of these sugar substitutes may also be at increase risk of overweight or even obesity, type 2 diabetes, metabolic syndrome, hypertension and cardiovascular diseases too [2]. FDA has approved six artificial sweeteners – acesulfame K, aspartame, neotame, saccharin, sucralose, stevia –for use in the U.S. All are chemically manufactured molecules – molecules that do not exist in nature. In case of stevia, it is hard to fit it into one particular category because of what they're made from and how they're made. Although, the FDA has approved highly refined stevia preparations as a novel sweetener. These substitutes are used in one of two ways. They may be used directly in commercially processed foods, or they are mixed with other sweeteners before sale to consumers. Artificial sweeteners are so intensely sweet that dextrose or maltodextrin, or both. Here's we take a look at popular sweeteners and what they mean for your diet.

**Do we know saccharin**

Saccharin was discovered more than 100 years ago, Saccharin, the first artificial sweetener, which makes it, the granddaddy of artificial sweeteners. Its sweetness depends on how it is used, and ranges from 200 to 700 times sweeter than sugar. Saccharin is available commercially as "sodium saccharin" (most common), "calcium saccharin" or "acid saccharin." Saccharin is sold under such brands as Sweet 'N Low, Sweet Twin and Necta Sweet.

**Chemical Composition**

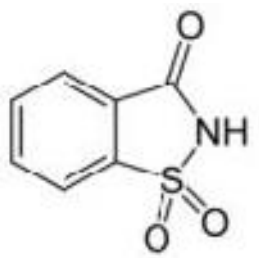



**Figure 1**

Saccharin (benzoic sulfimide) is a very stable organic acid with a pKa of 1.6 and chemical formula $C_7H_5NO_3S$. Its' chemical composition is 45.9% carbon, 2.7% hydrogen,

7.7% nitrogen, 26.2% oxygen, and 17.5% sulfur. It is neither absorbed nor metabolized, whereas it is excreted unchanged through kidneys. It is used in soft drinks, baked goods, jams, chewing gum, canned fruit, candy, dessert toppings, and salad dressings. Saccharin is also used in cosmetic products (e.g., toothpaste, mouthwash, and lip gloss), vitamin, and medications too. In 1977, FDA proposed a ban on use of saccharin because it was reported to be a carcinogen in rats. In 2000, saccharin was removed from the list of carcinogens and the requirement for warning notices was also removed. Now, saccharin is often chosen to be the safest. It has been approved for use in more than 100 countries.

**Aspartame**

Aspartame is also known as Equal, NutraSweet, and Natra Taste. In 1981, it was approved by FDA, in 1983 it received approval for use in beverages, and further in 1996 it was allowed for use in other beverages, baked goods and confections too. It is 160 to 200 times sweeter than sugar, it has been used in more than 6,000 products by hundreds of millions of people in countries all around the world. Aspartame can be found in a wide variety of prepared foods (e.g., carbonated and powdered soft drinks, chewing gum, confections, gelatins, dessert mixes, puddings and fillings, frozen desserts, and yogurt), tabletop sweetener, and some medications (e.g., vitamins and sugar-free cough drops).

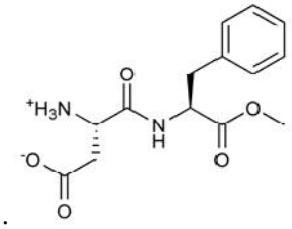


**Figure 2**

**Chemistry**

Aspartame is very widely used in many foods and beverages. But there are controversies about its metabolite which is marked for its toxicity [3]. Aspartame (N-L-alpha-Aspartyl-L-phenylalanine 1-methyl ester) is the methyl ester of the dipeptide of the natural amino acids L-aspartic acid and L-phenylalanine. It has a chemical formula $C_{14}H_{18}N_2O$. Aspartame is broken down in the body to the amino acids aspartic acid and phenylalanine as well as a small amount of methanol. It is a mixture of 40 percent aspartic acid, 50 percent of phenylalanine, and 10 percent of methanol.

The Aspartic acid which is present in aspartame, is an excitotoxin. An excitotoxin, is a deleterious substance that excites or over-stimulates nerve cells. As it contains phenylalanine, the FDA has mandated packaging that it should be avoided by individuals, with the rare genetic disorder phenylketonuria (PKU) which means they cannot metabolize phenylalanine, a component of aspartame. This substance Phenylalanine is an amino acid used as a building block for proteins. As it is not metabolized due to lack or insufficient amounts of the enzyme phenylalanine hydroxylase (required to breakdown phenylalanine), phenylalanine get accumulated. Phenylalanine buildup can significantly alter human brain function. All children are screened for this rare disorder in the United States. It is common chemical sweetener used in many diet sodas, and it has been suggested by researchers that consuming two diet sodas a day is associated with 500 percent increase in waist size than those of non-users. Furthermore, it is suggested in animal studies that aspartame actually increases blood glucose levels similarly to sugar, which could explain the association between diet soda and diabetes. Chronic exposure to aspartame has been reported to cause many negative effects. There are a few reports on aspartame consumption on various neurological effects that include headache, insomnia and seizures. Headache is the most common adverse side effect attributed to aspartame. Scientific studies have not yet been able to find links to behavioral disorder or brain damage caused by artificial sweeteners (especially aspartame), anecdotal evidence and case studies show that aspartame may, depending on the individual and on the amount of aspartame consumed by the individual, have adverse impact on the neurological system. It was found in University of Liverpool test-tube study that when it is mixed with a common food color ingredient, aspartame actually became toxic to brain cells.

**Acesulfame K**

Acesulfame K, also known as acesulfame potassium or ace K, a white crystalline powder with molecular formula $C_4H_4KNO_4S$, is approximately 200 times sweeter than sugar. It is calorie- free because it's not absorbed by the body. Acesulfame K is sold under the brand names of Sunett, Sweet One, and Sweet & Safe.

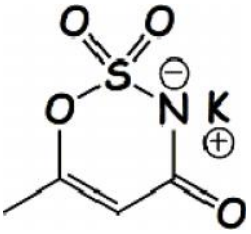


**Figure 3**

It has a slightly bitter aftertaste, so used in combination with other sweeteners, mainly aspartame or sucralose. It is heat stable so suitable for baking and cooking. it can be found in many tabletop sweeteners, desserts, puddings, baked goods, soft drinks, candies (including breath mints, cough drops and lozenges), dairy products, canned foods and alcoholic beverages. An important aspect of Ace-K is, it is stable and retain its sweetness under pasteurizing conditions which often exposes dairy products to a wide variety of temperatures and pH values. Hence, an ideal candidate for 'sugar free' candies and diet drink, as it does not promote tooth decay. It does not influenced blood glucose in diabetic patients.

**Neotame**

Neotame is recently approved artificial sweeteners for general use in the U.S. a derivative of aspartame. The Food and Drug Administration approved neotame as a general purpose sweetener on July 2002. Like aspartame, it is derived from two amino acids aspartic acid and phenylalanine. However, neotame is structurally different which makes it about 40 times sweeter than aspartame, or

approximately 8,000 times sweeter than sugar. Neotame (N-[N-(3,3-dimethylbutyl)+-L-alpha-aspartyl]-L-phenyl alanine 1-methyl ester) is a more stable sweetener molecule made from aspartame. Its' chemical formula is $C_20H_{24}N_2O_5$.

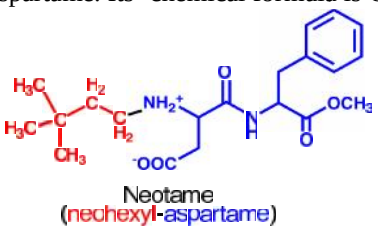



**Figure 4:** Structure of Neotame

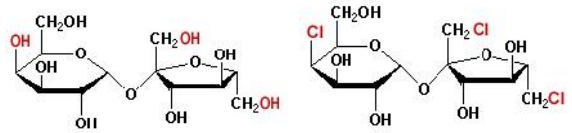
Neotame can be used in the same foods and beverages as both aspartame and acesulfame K. It can be found in baked goods, soft drinks, chewing gum, fro¬zen desserts and novelties, jams, jellies, gelatins, puddings and fillings, processed fruits, toppings, and syrups. In definitive safety studies, no adverse findings related to neotame treatment were found in clinical observations, physical examinations, water consumption, or clinical pa¬thology evaluations.

**Sucralose**

Sucralose is made from sucrose by a multi-step patented manufacturing process. This molecular change makes sucralose 600 times sweeter than sugar. It is marketed as Splenda. It received FDA approval in 1998.

**Chemistry**

Sucralose (1', 4, 6'-Trichloro-galactosucrose) is a chlorinated sugar with chemical formula C12H19Cl3O8 and a molar mass of 397.64 g/mol.




This artificial sweetener that can be used for cooking, is the most heat stable of the artificial sweeteners. This property has increased the introduction of sucralose into a broad range of foods and beverages previously sweetened with the other approved general-purpose artificial sweeteners and made it one of the most popular and highly consumed artificial sweeteners. It is used in chewing gum, frozen desserts, fruit juices and gelatins. The alleged symptoms which are associated with sucralose are gastrointestinal problems (bloating, gas, diarrhea, nausea), skin irritations (rash, hives, redness, itching, swelling), wheezing, cough, runny nose, chest pains, palpitations, anxiety, anger, moods swings, depression, and itchy eyes. The only way to be sure of the safety of sucralose is to have long-term studies on human done.

## 2. Stevia

Stevia is also referred to as Rebaudioside A, Reb-A, or rebiana. Truvia, PureVia are names for the brands available in the store, patented by *Coca Cola* and *Pepsi*. Many different forms of Stevia as a sweeteners include: Reb A, Reb B, Reb C, Reb D, *Rebiana*, *Stevioside*, *SunCrystals* and *Enliten*. It is the safest sweetener. All types of stevia are extracted from the leaves of the stevia plant. The stevia plant is native to South America, and today, it can be found growing in many countries including China, Brazil, Argentina, Paraguay, India and South Korea.

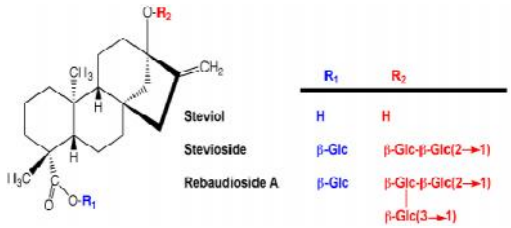
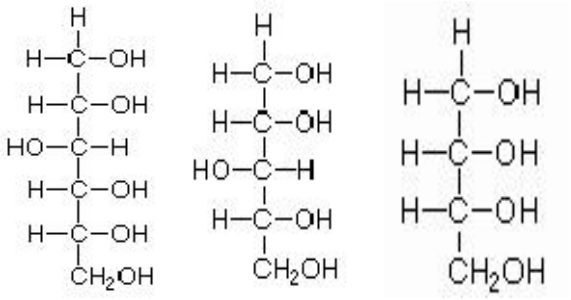



**Figure 5:** Structure of Stevia

Stevioside and rebaudioside are two of the sweet steviol glycosides in the stevia leaf. Stevioside has one beta-D-glucose molecule replacing the bottom hydrogen atom of steviol and two beta-D-glucose molecules replacing the top hydrogen site [4]. It is not absorbed by the body. Studies on the safety, metabolism and intake of food-grade steviol glycosides have demonstrated their safety for all populations. FDA has approved and classified this dietary supplement as "generally recognized as safe" (GRAS) by FDA. Stevia extract is considered to be free of calories, carbohydrates, fats and cholesterol. So, it can be safely used by the diabetic patients. Therefore, the cultivation of stevia with modern agro techniques is gaining importance in India and it has been selected as an alternative crop in many states of India with high return support to the farmers [5].

## 3. Sugar Alcohols

Sugar alcohols (polyols) are carbohydrates that occur naturally in certain fruits and vegetables, but they also can be made commercially. Their chemical structure partially resembles a sugar and partially resembles an alcohol. Sugar alcohols aren't considered caloric free or non-nutritive sweeteners because they contain calories. But they're lower in calories than in regular sugar, making them an attractive alternative. Sugar alcohols produce a lower postprandial glucose response than fructose, sucrose, or glucose. They are commonly used for replacing sucrose in foodstuffs, often in combination with high intensity artificial sweeteners to counter the low sweetness.



**Sorbitol** **Xylitol** **Erythritol**

Popular sugar alcohol sweeteners include xylitol, sorbitol, and erythritol, made through a fermentation process of corn or sugar cane. Sorbitol also known as glucitol, it is obtained by reduction of glucose changing the aldehyde group to an

additional hydroxyl group. It is approximately 60 % as sweet as sucrose. It is commonly used in diet foods, mints, cough syrups and sugar free chewing gums. One of the most common side effect of sorbitol is diarrhea. Mannitol has half the calories of sugar, and is half as sweet. It is poorly absorbed by the body, so it does not raise insulin levels as much as sugar. It does not promote tooth decay. Erythritol is produced commercially by fermentation of glucose with the yeast *Moniliella pollinis*. Xylitol is a five carbon natural sweetener found in fibrous of vegetables and fruit, which offers many health benefits to human. It's sweetness level equals that of sucrose.

**Uses of sugar alcohols**

They are found in many processed foods and other products, including chocolate, candy, frozen desserts, chewing gum, toothpaste, mouthwash, baked foods, fruit spreads and medicine industries.

**Honey:** Honey is a natural sweetener. It is a sweet food made by certain insects using nectar from flowers mainly by bees.

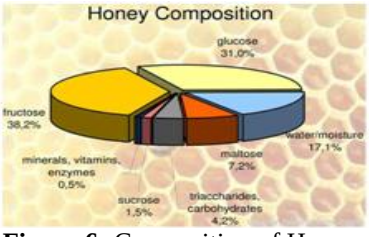



**Figure 6:** Composition of Honey

Honey is a mixture of sugars and other compounds. It is a combination of fructose, glucose, and water. With respect to carbohydrates, it does boast higher fructose levels (about 38.2%) and glucose (about 31.0%) other carbohydrates include maltose, sucrose, and other complex carbohydrates. The specific composition of honey depends on the flowers available to the bees that produced it. The pH of honey is commonly between 3.2 and 4.5 and this acidic pH level prevents the growth of many bacteria and makes honey a natural antiseptic. It is also proven to be low in calories and contains a lot of sugar and minerals. Because honey contains very low calories, it is suitable to be used as a sweetener for obese, diabetics and heart patients. . It also contains a bounty of cancer-defending antioxidants, and local honey has been said to help alleviate allergy symptoms too. Honey also has a low glycemic index, so adding it to your tea or yogurt won't lead to energy-busting blood sugar drops later in the day.

**Blackstrap molasses:** Molasses is the syrupy by-product of the process that turns sugar cane or sugar beet into refined white table sugar. The quality of molasses depends on the maturity of the sugar cane or sugar beet, the amount of sugar extracted, and the method of extraction.

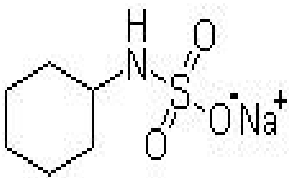


**Figure 7:** Chemical Structure of Molasses

Molecular formula of molasses is $C_6H_{12}NNaO_3S$. Molasses contains the following substances: sucrose 35.9 %, fructose 5.6 %, nitrogen 1.01 %, reducing substances 11.5 %, glucose 2.6 %, and sulfur 0.78 %. Sugar cane juice is boiled three times to concentrate, extract the crystallized sugar, first light molasses are created, then a dark molasses is created, and finally, third boiling makes nutrient-rich blackstrap molasses. They are rich in iron, potassium, magnesium and calcium. Cane molasses is different from molasses that creates from the sugar beet. As compare to nutritionally defunct artificial sweeteners or even regular refined sugar, blackstrap molasses are healthier choice. In fact, one tablespoon of blackstrap molasses provides more iron but fewer calories and fat.

**Health Benefits from Artificial Sweeteners**

Artificial sweeteners have been the subject of intense scrutiny for decades. These sweeteners were extensively introduced into our diets with the intention of reducing caloric intake and normalizing blood glucose levels without compromising our ‘sweet tooth’. A key question is whether replacement of sugar-sweetened products with those containing artificial sweeteners is truly beneficial. There have been sporadic claims that low calorie sweeteners are associated with a range of adverse health effects.

- Nutritive sweeteners need not necessarily be restricted, but, if consumed, they should be substituted for other carbohydrate sources
- Nonnutritive sweeteners can be used by diabetics, as they do not affect glycemic response
- Polyols have a lower glycemic response than fructose, glucose or sucrose, most likely because of their incomplete absorption however, the amount of polyols consumed may need to be limited, as they possess laxative effect.

Artificial sweeteners are present in many foods consumed by Americans. Their use is beneficial in that they provide sweetness, increasing the palatability of foods without the added sugar and resulting calories, an important adjunct to weight loss and diet regimens. Most artificial sweeteners are not metabolized by the body and are therefore considered safe. However, scientists disagree about safety because the metabolites of the “non-metabolized” compounds have been shown to produce deleterious effects in mice, rats, and dogs. It has been reported by researchers that artificial sweeteners may disrupt the body’s ability to control blood sugar, causing metabolic changes that can be a precursor to diabetes. Appetite may be increased due the dissociation of the sensation of sweet taste from caloric intake, which may lead to greater food consumption and weight gain. In addition, increased consumption of added caloric sweeteners has been associated with lower diet quality in children, perhaps by altering taste preferences toward sweetened foods in place of more healthful foods, such as fruits and vegetables; this mechanism could apply to artificial sweeteners as well. According to many researchers artificial sweeteners may interfere with the body's natural ability to count calories based on a food's

sweetness and make people prone to overindulging in other sweet foods and beverages.

**Artificial Sweeteners and Metabolism**

As would be expected that drinks with non-caloric sweeteners would promote weight loss, but epidemiological studies have found that consumption of diet soda is associated with the development of metabolic syndrome (4). Several recent studies have focused on the effects of artificial sweeteners on metabolic systems, especially in individuals with diabetes. In a study carried out by Weizmann Institute of Science and published in *Nature*, it was showed that artificial sweeteners have a direct impact on the body's ability to utilize glucose, they observed significant intolerance to glucose when mice was given water lacing with the artificial sweeteners. This glucose intolerance is often a precursor to larger illnesses, such as type 2 diabetes or metabolic syndrome. Not only this study, a series of experiments suggests artificial sweeteners can cause glucose intolerance in mice, and perhaps in humans, they achieve this by altering composition and function of the intestinal microflora; the substantial population of microbiome residing in our gut. Sweeteners actually hasten the development of glucose intolerance and metabolic disease. Over a 9 years of follow-up study it was found that middle-aged men and women consuming $\geq$1 servings of diet soft drinks per day had >30% higher risk of developing metabolic syndrome [6]. In other study researchers found that artificial sweeteners alter metabolic pathways associated with metabolic disease. Decreased function was observed in pathways associated with the transport of sugar in the body. Artificial sweeteners, while they are low caloric and are not metabolized much within the human body; they also found to induce gut dysbiosis and glucose intolerance in otherwise healthy people. Among the various artificial sweeteners, saccharin (Sweet'N Low) had the strongest impact, followed by sucralose and aspartame. Glucose intolerance is a well-known precursor to type 2 diabetes, as mentioned above, but it also plays a role in obesity, because the excess sugar in your blood ends up being stored in your fat cells. Earlier research also suggests people who eat large amounts of artificial sweeteners have higher incidences of obesity and diabetes.

**Artificial sweeteners and genotoxicity**

Many researchers have reported that consistent ingestion of food additives may have toxic, genotoxic and carcinogenic effects (7, 8, 9). These food additives induced DNA damage depends upon their transport across cell membranes/ nuclear membranes, the activation or inactivation of intracellular enzyme mechanisms, the levels of antioxidants and the repair mechanism in target cells. Geno toxicity pertains to all types of DNA damage. Genotoxins are agents those who reacts with DNA and or associated cellular components or enzymes (10). In the similar study it was demonstrated that acesulfame-k, aspartame, saccharin and sorbitol cause DNA damage and may be toxic when they are chronically use in high concentrations. Therefore there should be extensive investigation on the effect of sweeteners, mainly when they are used at high concentrations.

**Artificial Sweeteners and dental health**

Cavities occur when bacteria in dental plaque break down starches and sugars to form acids, which destroy tooth enamel. Low calorie sweeteners, cannot be metabolized by oral bacteria to form acids. Therefore, they may reduce risk for dental caries. To decrease dental erosion, we have to limit the amount and frequency of soft drinks and juices.

**Can everyone consume artificial sweeteners**

Susceptible populations for the potential deleterious effects of artificial sweeteners include diabetics, children, pregnant women, women of childbearing age, breastfeeding mothers, individuals with low seizure thresholds, and individuals at risk for migraines.

## 4. Conclusion

Taken together, it is suggested from all studies that consuming artificial sweeteners is just as bad for you as sugar and these artificial sweeteners may even exacerbate the negative effects of sugar. Well it can be say to make life easier for everyone, this is one instance where you may want to follow the "better safe than sorry" principle. The sweetest advice is to use "natural" sugar substitutes like honey and maple syrup in moderation, or just turn to fruit to soothe your sweet tooth - it's high in nutrients, fibers and phytochemicals, and is broken down more slowly than any kind of refined sugar.

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