Chapter

Artificial Sweeteners

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Abstract

Nowadays, sugar*free food is very popular because of its low calorie value. So food industries make use of various artificial sweeteners of low calorie as an alternative to high calorie sugars and they provide low glycemic response. The U.S. Food and Drug Administration has approved artificial sweeteners such as saccharin, acesulfame-K, sucralose, aspartame, etc. as per acceptable daily intake value (ADI) value, but these artificial sweeteners that breakdown products during metabolism in turn are known to have health and metabolic effects. Hence, in this work, we will discuss about artificial sweeteners, types, and their metabolic and health effects.

Keywords: artificial sweeteners, adverse effects, potential toxicity

1. Introduction

In the recent scenario, the people are more concerned about health and better quality of life and so they avoid consumption of food rich in sugars, salt or fat so as to protect themselves from obesity and other non-communicable diseases. With the concern of reducing energy intake, food products containing artificial sweeteners other than simple sugars (monosaccharides and disaccharides) have become increasingly popular. Natural sweeteners add to more of nutritional value so they are called nutritive sweeteners. However, synthetic (artificial) sweeteners do not contain nutritional value so they are known as non- nutritive sweeteners On the contrary, artificial sweeteners are gaining very popular because they help reduce calories, control weight, manage diabetes, and prevent cavities. However, their safety has been controversial. In general, artificial sweeteners undergo a safety evaluation to assess their benefits and risks before using them. A health organization such as FDA evaluating all scientific studies and determines the maximum amount that can be eaten on a day without causing any adverse effects for each sweetener. The aim of this paper is to give an idea about the sweeteners, artificial sweetener, their chemical structure and properties and their potential health effects in humans.

2. Sweeteners

A sugar substitute is a food additive that provides a sweet taste like that of sugar is called sweeteners and classification of sweeteners based on calorific value was shown in **Figure 1**.

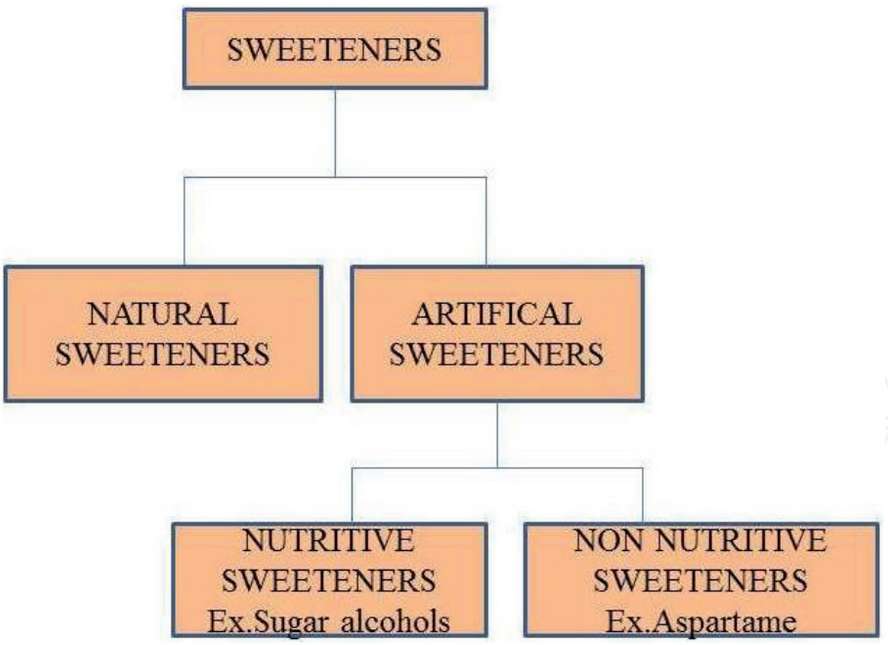

Figure 1.
Classification of sweeteners.

2.1 Nutritive sweeteners

Nutritive sweeteners are otherwise called as carbohydrate sweeteners (caloric). These sweeteners provide high-quality sweet taste and have an acceptable texture and shape and therefore remain as the most popular sweetener. Example for nutritive sweeteners are:

2.1.1 Monosaccharide polyols

Monosaccharide alcohol is the general term for the chain – like polyalcohol obtained by reducing the carboxyl group of sugars.

2.1.1.1 Sorbitol (D-glucitol)

Sorbitol occurs naturally in cherries, plums, apples, many berries, seaweeds and algae. It is moderately sweet, relatively inexpensive and has less shelf life because of hygroscopic property.

2.2 Non-nutritive sweeteners

These are low-calorie sweeteners (referred to as non-nutritive sweeteners, artificial sweeteners or sugar calories) added to foods, yogurt, medicinal preparation, dentifrices, mouthwash and beverages to provide sweetness without adding a calorie. The non-caloric sweeteners are generally much sweeter than sucrose and can, therefore, be used in small amounts.

2.2.1 Requirements for an ideal artificial sweetener

- It should provide sweetness with no unpleasant after taste.
- It should not contain any calories.

- More economical in productivity.
- Should be resistant to heat when cooked.
- It should not be carcinogenic (causing cancer) or mutagenic (change in genetic material in organism)

2.3 Artificial sweeteners

2.3.1 Aspartame

Aspartame is an artificial non saccharide sweetener of molecular formula. $C_{14}H_{18}N_2O_5$ and finds its use in food and beverages as sugar substitute. Aspartame is a methyl ester of aspartic acid/phenylalanine dipeptide and marketed under the name NutraSweet, Equal and Canderel. In 1965, Aspartame was reported and U.S. Food and Drug Administration (FDA) in 1981 approved its use in the food products (**Figure 2**).

2.3.1.1 Metabolism and health aspect

Aspartame is one of the low calorie sweetener used in low, reduced calorie foods and also used in beverages. It is also a low calorie table top sweetener used in gums, breakfast cereals and dry foods. Upon breaking Aspartame produces about 4 calories of energy per gram. On prolonged heating aspartame decomposes and therefore it cannot be used for food items involving cooking and also converts into liquid on storage. The breakdown products upon ingestion are aspartic acid, phenylalanine, methanol and further breakdown products including formaldehyde, formic acid and diketopiperazine. FDA insisted that food products with aspartame should have warning in the label that the person with the rare genetic disorder phenylketonuria should avoid ingesting aspartame. Phenylketonuria is an inborn disease associated with error of metabolism that leads to attenuated metabolism of the amino acid phenylalanine. Phenylketonuria leads to behavioral problems and mental disorders. Peoples suffering from phenylketonuria will have insufficient level of enzyme phenylalanine hydroxylase which is required for the breakdown of phenylalanine [1] and as a result phenyl alanine accumulates in case of people affected with phenylketonuria. The breakdown products of aspartame like methanol, phenylalanine and aspartic acid leads to headache, blurred vision, brain tumors, eye problems, memory loss and nausea [2]. The aspartic acid one of the breakdown products of aspartame leads to excitotoxin. The aspartic acid acts like neurotransmitters

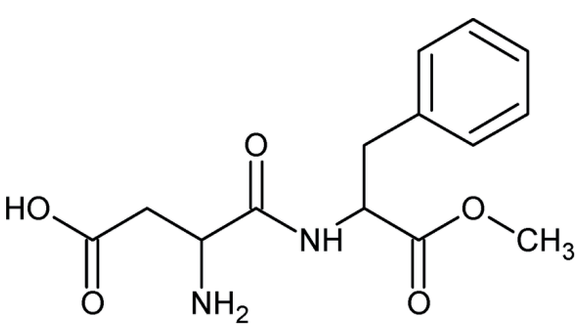

Figure 2.
Structure of aspartame.

stimulating the nerve cells to either damage or kills and may lead to spinal cord injury, stroke and hearing loss [3].

2.3.2 Acesulfame-K

Acesulfame potassium also known as Acesulfame-K is a calorie-free sugar substitute (artificial sweetener) marketed as Sunett and Sweet One. Acesulfame potassium is the potassium salt of 6-methyl-1,2,3-oxathiazine-4(3*H*)-one 2,2-dioxide. Acesulfame-K is a white crystalline powder having molecular formula of $C_4H_4KNO_4S$ and molecular weight 201.24 g/mol. It is approximately 120 times sweeter than sucrose and has high water solubility. Acesulfame-K is heat stable and can be used in cooking and baking. Ace-K is often blended with other sweeteners (Sucralose or Aspartame) (**Figure 3**).

2.3.2.1 Metabolism and health aspect

Acesulfame-K is not metabolized in the body and excreted in urine without undergoing any modification and not stored in the body. Pharmaco kinetic studies show that 95% of the consumed sweeteners basically excreted in the urine. It does not influence potassium in take despite of its potassium content. In 1988 UFDA approved to use Ace-K as a general purpose sweetener in a variety of dry products and in alcoholic beverages [4]. The breakdown product of Ace-K is acetoacetamide known to be toxic if consumed in very large doses but human exposure to breakdown products is negligible. Acesulfame-K contains methylene chloride and may lead to headache, depression, nausea, mental confusion, liver and kidney effects [5].

2.3.3 Sucralose

Sucralose is an artificial sweetener and sugar substitute having the molecular formula of $C_{12}H_{19}Cl_3O_8$ and molecular mass 397.64 g/mol. In the European Union it is known with the E number E955 and marketed under the name Splenda. Chlorination of sucrose leads to formation of sucralose. Sucralose is approximately 320–1000 times sweeter than sucrose and three times as sweet as aspartame and acesulfame potassium, and twice than sodium saccharin (**Figure 4**).

2.3.3.1 Metabolism and health aspect

Although sucralose is made from sugar, the human body does not recognize it as a sugar and does not metabolize. It does not produce any calories [6]. Sucralose is responsible for the shrunken thymus glands with diets of 5% sucralose, and also it causes diarrhea and dizziness on prolonged exposure.

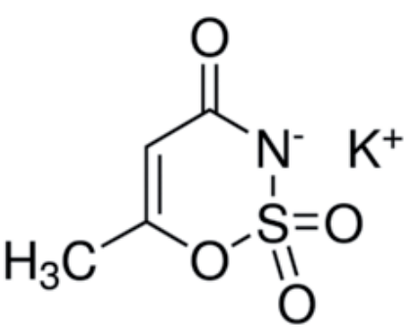

Figure 3.
Structure of Acesulfame-K.

2.3.4 Saccharin

Sodium saccharin of molecular formula $C_7H_5NO_3S$ (benzoic sulfimide) is an artificial sweetener with no calories. It is about 300–400 times as sweet as sucrose but has a bitter after taste at higher amount of intake. Saccharin finds use in products such as drinks, candies, cookies, and medicines. Saccharin is often blended with other artificial sweeteners because of taste purpose and when used in such combinations reduced sugar levels are preferred. In case of oral hygiene products, saccharin masks undesired tastes of other ingredients. Saccharin when used as a starter feed for livestock reduces feed intake after weaning. Besides its applications as an artificial sweetener, saccharin also finds application in electrolytic nickel deposition. Addition of saccharin to the nickel salt solutions increases the hardness and brightness of the nickel plate. This effect is important characteristic feature of saccharin compared to other sweeteners (**Figure 5**).

2.3.4.1 Metabolism and health aspect

The FDA tried to ban saccharin in 1977 because animal studies have revealed that it caused cancer in rat. But there is no supportive evidence to show the carcinogenic effect of saccharin at lower doses. Saccharin is now permitted to use in beverages, processed food and sugar substitutes and level of saccharin is to be indicated in the label [7]. Saccharin causes a headache, breathing difficulties, skin eruptions and diarrhea.

2.3.5 Sodium cyclamate

Sodium cyclamate is an artificial sweetener of molecular formula $C_6H_{12}NNaO_3S$. It is 30–50 times sweeter than sucrose (table sugar) and because of this it is least potent of the commercially used artificial sweeteners. It is always blended with

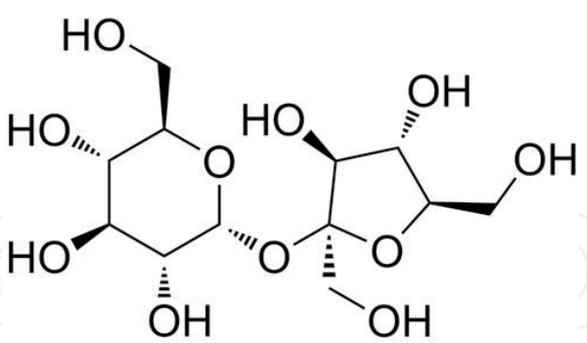

Figure 4.
Structure of sucralose.

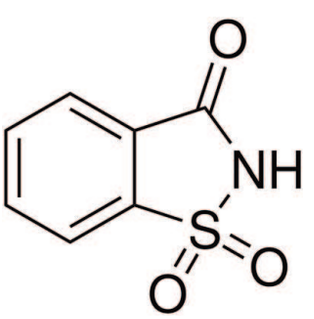

Figure 5.
Structure of saccharin.

other artificial sweeteners; especially saccharin in the ratio of 10:1 that is 10 parts of cyclamate to 1 part of saccharin. It is less expensive than most sweeteners including sucralose and stable under heat. Cyclamates are being banned in the United States and other countries due to safety reasons. But European Union considers them as safe (**Figure 6**).

2.3.5.1 Metabolism and health aspects

Cyclamate itself shows very slow toxicity but it is metabolized to cyclohexylamine which shows greater toxicity because of the nature of the cyclamate metabolism [8]. The possible exposure to cyclahexylamine from cyclamate metabolism in humans over a period is relevant to the establishment of ADI for cyclamate.

2.3.6 Neotame

Neotame is the low calorie artificial sweetener of molecular formula $C_{20}H_{30}N_2O_5$ and molecular mass 378.469 g mol^{-1} and it is the derivative of aspartame. A t-butyl group is added to the free amine group of aspartic acid. It is 8000 times sweetener than sucrose. It can be used alone or often blended with other sweeteners especially saccharin. Neotame is used in carbonated soft drinks, cakes, drink powders, table top sweetener and bubble gums. The neotame was approved in 2002 as a general purpose sweetener, excluding in meat and poultry by FDA (**Figure** 7).

2.3.6.1 Metabolism and health aspects

Neotame is rapidly metabolized by esterase present throughout the body into methyl ester and also forms a minor amount of methanol. This metabolic process yields de-esterified neotame which is completely eliminated from the body in urine and feces within 72 h. It is safer to use with people suffering from phenylketonuria because t-butyl group is added to the free amine group of aspartic acid breaks the peptide bond between the aspartic acid and phenylalanine, thus reduce the availability of phenylalanine which is responsible for phenylketonuria [9]. Neotame causes some of the toxic effects at high doses in the human such as it to reveal changes in body weight and food consumption and headache.

2.3.7 Alitame

Alitame of molecular formula $C_{14}H_{25}N_3O_4S$ is an aspartic acid-containing dipeptide sweetener. It was developed by Pfizer in the early 1980s and currently marketed in some countries under the brand name Aclame. It is an intense sweetener with sweetness potency 200 times greater than that of sucrose (**Figure 8**).

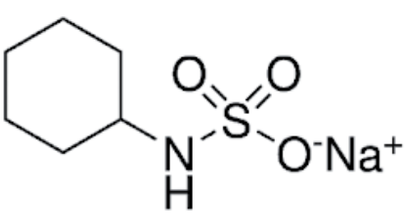

Figure 6.
Structure of sodium cyclamate.

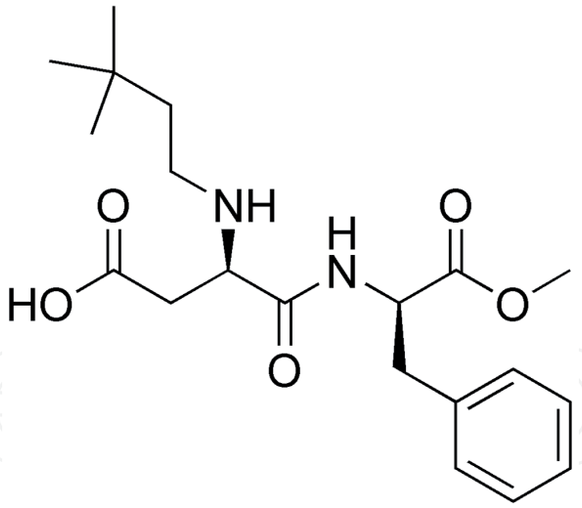

Figure 7.
Structure of neotame.

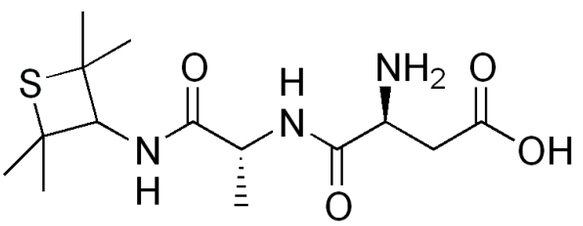

Figure 8.
Structure of alitame.

2.3.7.1 Metabolism and health aspects

Alitame is readily absorbed in gastrointestinal tract and then rapidly metabolized and excreted [10]. Alitame consists of two main components namely aspartic acid and alanine amide. The aspartic acid component is metabolized normally and alanine amide passes through the body with minimal changes.

3. Conclusion

The increased concern about obesity and the associated metabolic comorbidities have led to a reduced consumption of simple sugars and an increase in the intake of artificial sweeteners. These sweeteners, which appear as sugar alternatives, have been critically evaluated by the FDA and EFSA. Artificial sweeteners are not carbohydrates and so they will not increase blood sugar levels leading to diabetics but instead every gram of table sugar contains four calories and contributes to obesity [11]. The artificial sweeteners like saccharin, acesulfame-K and aspartame induces DNA damage in human peripheral lymphocytes [11]. The degradation products of acesulfame-K under basic conditions such as acetoacetic acid and acetoacetamide-N-sulfonic acid may cause DNA strand breaks [5]. Aspartame leads to gastrointestinal problems. The toxic potential of various artificial sweeteners for the human body was shown in **Table 1**. Therefore artificial sweeteners provide some potential health benefits. In addition they are toxic at high concentrations for the long time exposure. Artificial sweeteners consumption has been shown to cause mild to serious side effects including life threatening brain damages at high concentrations. But however low concentrations of these sweeteners does not cause threat to human health.

Common name	Brand names	FDA approval	Number of times sweeter than sucrose	kcal/g	Commercial uses
Acesulfame-K	Sunett, Sweet One	1988—tabletop	200	0	Baked goods, frozen desserts, candies, beverages, cough drops, breath mints
		1993—beverages			
		2003—general use, but not in meat or poultry			
Alitame	Aclame	Pending	2000	1.4	Baked goods, hot and cold beverages, milk products, frozen desserts and mixes, fruit preparations, chewing gums and candies, tabletop sweeteners, toiletries, pharmaceuticals
Aspartame	NutraSweet, Equal	1981—tabletop	200	4	General-purpose foods
		1996—general purpose			
Cyclamate	SugarTwin, Sucaryl	GRAS until banned in 1970	30	0	Tabletop sweetener, beverages
Neotame		2002	7000–13,000	0	Baked goods, soft drinks, chewing gum, frosting, frozen desserts, jams, jellies, gelatins, puddings, processed fruit and fruit juices, toppings, syrups
Saccharin	Sweet'N Low, Sweet Twin, Necta Sweet	GRAS	200–700	0	Tabletop sweetener, baked goods, soft drinks, jams, chewing gum
Sucralose	Splenda	1998—in 15 food categories	~600	0	Tabletop sweetener, beverages, chewing gum, frozen desserts, fruit juices, gelatins
		1999—general-purpose sweetener			

FDA, Food and Drug Administration; GRAS, generally recognized as safe.

Table 1.
List of few artificial sweeteners, ADI value and uses.

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