

Review Article

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Chemistry and Use of Artificial Intense Sweeteners

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ABSTRACT

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Now a days sugar free food are very much popular because of their less calorie content. So food industry uses various artificial sweeteners which are low in calorie content instead of high calorie sugar. Artificial sweeteners/low calorie sweeteners are synthetic sugar substitutes but may be derived from naturally occurring substances, including herbs or sugar itself. The growing consumer interest in health and its relationship with diet has led to a considerable rise in the demand for low calorie fat products. Artificial sweeteners are also known as intense sweeteners because they are many times sweeter than regular sugar. Therefore, it is very important to understand their chemistry in relation to the stability on processing and storage of food products in which these sweeteners are used.

Introduction

Sweeteners are additives which provide the basic taste of sweetness to a food product. Traditionally sugars are used as sweeteners in food. In addition to sweet taste they provide energy of 4 kcal/g. However, rising obesity rates suggest avoiding over consumption of calories. The growing consumer interest in health and its relationship with diet has led to a considerable rise in the demand for low calorie fat products (Martínez-Cervera *et al.*, 2012). The substances used to replace sugar are called alternative sweeteners or sugar substitute.

These alternative sweeteners could either be from a natural source or artificially derived by chemical synthesis. These artificial sweeteners are chemically very different from the sucrose or other nutritive sweeteners that they are replacing in a food system. Therefore, it very is important to understand their physicochemical properties, taste characteristics and stability for formulation, processing and storage of food products and beverages in which these sweeteners are used (Nelson, 2000).

Aspartame, acesulfame K, advantame, alitame, cyclamate, neotame, saccharin and sucralose are the commonly reported artificial sweeteners. Among the artificial sweeteners saccharin, cyclamate and aspartame are considered as first generation sweeteners, whereas, acesulfame-K, sucralose, alitame, advantame and neotame are new generation sweeteners (DuBois and Prakash, 2012).

History of discovery

The most of the popular artificial sweeteners were discovered by accident, rather than by deduction structural design (Hough, 1993). Saccharin was discovered in 1878 in the laboratory of Ira Remsen at Johns Hopkins University in Maryland by Constantine Fahlberg, a post-doctoral research associate who was trying to oxidize toluene sulfonamides. While working in the lab, he spilled a chemical on his hand. Later while eating dinner, Fahlberg noticed a more sweetness in the bread he was eating. He traced the sweetness back to the chemical, later named saccharin.

Michael Sveda, a graduate student at the University of Illinois discovered the sweet taste of cyclamate in 1937. While working on the synthesis of anti-pyretic (anti-fever) drugs in the laboratory there he was smoking a cigarette. He put his cigarette down on the lab bench and when he put it back in his mouth, he noticed that the cigarette tasted sweet. He realized that the substance he synthesized was on his fingers which imparted the sweet taste to the cigarette (Orphardt, 2003).

Aspartame was discovered in 1965 by James Schlatter, a chemist working at G.D. Searle Pharmaceutical Company while synthesizing aspartame as an intermediate step in generating a tetrapeptide of the hormone, gastrin, for use in assessing an anti-ulcer drug candidate (Walters, 2013). Acesulfame

potassium was developed after accidental discovery of sweet taste of a similar compound (5, 6-dimethyl-1, 2, 3-oxathiazin-4(3H)-one 2, 2-dioxide) in 1967 by Karl Claussat Hoechst AG (DuBois and Prakash, 2012). In 1976 Tate and Lyle, a British sugar company, was looking for ways to use sucrose as a chemical intermediate. In collaboration with Professor Leslie Hough's laboratory at Queen Elizabeth College, halogenated sugars were being synthesized and tested. Hough asked a young Indian graduate student, Shashikant Phadnis to "test" the chlorinated sugar compound. Phadnis misunderstood the instruction and thought that Hough told him to "taste" it, so he tasted the compound. He found that the compound had exceptionally high potency of sweetness. His observation indicated that the selective chlorination of sugar could result in intensely sweet compounds. This discovery led to a series of studies and ultimately identified the compound as 1, 6-dichloro-1, 6-dideoxy- β -D-fructofuranosyl-4-chloro-4-deoxy- α -D-galactopyranoside and named as sucralose (Gold, 2006).

After the discovery of aspartame, a highly potent dipeptide sweetener was designed from structure activity relationship studies at Pfizer Central Research Inc., utilizing a terminal amide group instead of methyl ester of aspartame. Alitame was patented in 1983 and currently marketed under the brand name Aclame (Hough, 1993). Advantame is a new ultrahigh potency sweetener and flavor enhancer. The sweet taste of advantage was discovered at the Ajinomoto Company where it was subsequently developed and commercialized (Amino *et al.*, 2008; Hazen, 2012). The sweet taste of neotame was discovered in 1992 by Claude Nofre and Jean-Marie Tinti at Universite Claude Bernard in Lyon, France. The French scientists invented neotame from a simple N-alkylation of aspartame (DuBois and Prakash, 2012).

Chemistry and applications

The artificial sweeteners are chemical compounds with a diverse range of chemical structures including sulfonamides, sucrose derivatives, peptides and their derivatives (Seldman, 2010). Due to different physicochemical properties of artificial sweeteners, they used as a stable sweetening agent in a wide range of food products.

Saccharin

Saccharin is chemically known as o-sulfabenzamide (2, 3-dihydro-3-oxobenzisofurazone). It is sulphonamide derivative of toluene and available as acid saccharin, sodium saccharin and calcium saccharin (DuBois and Prakash, 2012). Saccharin (benzoic sulfimide) is a very stable organic acid with a pKa of 1.6 and chemical formula $C_7H_5NO_3S$. It has a molar mass of 183.2 g/mol and a density of 0.83 g/cm³ (Walter, 2013). Saccharin and its sodium and calcium salts are white crystalline solids. The acid form of saccharin is sparingly water soluble (0.2% at 20°C), whereas sodium saccharin (100% at 20°C) and calcium saccharin (37% at 20°C) are readily soluble (Nelson, 2000; DuBois and Prakash, 2012). Saccharin acid is only slightly soluble in water. Sodium saccharin is the most widely used salt because of its high solubility and ease of production.

Calcium saccharin is also used in a variety of food applications. It is interesting to note that the form of saccharin has no effect on its sweetness intensity. In the dry solid form, saccharin and its salts are very stable. In solution it has excellent hydrolytic, thermal, and photo stability. Stability is not affected by temperatures and pH normally encountered in food and beverage manufacturing, including table-top sweeteners, desserts, yoghurt, ice-cream, baked goods, jam, preserves, marmalade, soft drinks, sweets, mustard and

sauces. Because of its stability, saccharin can be used in cooking, baking and canning. The permitted levels of use vary from 100 to 500 mg/kg depending on the food category (Mortensen, 2006).

However, when saccharin is heated to decomposition (380°C), all three saccharin forms emit toxic fumes of nitrogen oxides and sulfur oxides. Although saccharin does not decompose under the conditions encountered during typical food processing, some hydrolysis occurs after prolonged exposure to extreme conditions of temperature or pH, at pH < 2.0 and at extremely high temperatures, hydrolytic decomposition of saccharin to (2-sulfobenzoic acid and 2-sulfamoyl benzoic acid). Neither of these compounds exhibits sweetness (Nelson, 2000).

Cyclamate

Cyclamate is a member of a group of salts of cyclamic acid (*cyclohexylsulfamic acid*). Three different compounds are referred to as cyclamates: cyclamic acid, calcium cyclamate and sodium cyclamate (Mortensen, 2006). The sodium and calcium salts were commonly used as artificial sweetener until. The sodium salt is the most commonly used form. It is a white crystalline salt with good solubility (O'Donnell, 2007). Cyclamate and its sodium and calcium salts are crystalline solids. In its acid form it is a strong acid with pKa of 1.71 and 71 and the pH of a 10% aqueous solution is approximately 0.8–1.6. Although the acid has good water solubility (~13.3% at 20°C), its high acidity results in preference for the very soluble sodium cyclamate (~20% at 20°C) or calcium cyclamate (~25% at 20°C) salts (DuBois and Prakash, 2012). Sodium and calcium cyclamate are strong electrolytes, which are highly ionized in solution, fairly neutral in character, and have little buffering capacity. Both salts exist as white crystals or white

crystalline powders. They are freely soluble in water (1g/5 ml) at concentrations far in excess of those required for normal use, but have limited solubility in oils and nonpolar solvents (Hunt *et al.*, 2012). Sodium and calcium cyclamate decompose at 260°C.

Cyclamic acid has a melting point of 169–170°C. They are stable at baking temperatures and during heating in solutions. They have a long shelf life in their dry state and are not hygroscopic. Cyclohexamine, a metabolic breakdown product, is produced from the microflora of the intestine but is not produced during the processing of food systems (Nelson, 2000). Cyclamates are stable in heat and cold and have good shelf-life. The stability and solubility in water facilitate the use of cyclamates in foodstuffs and beverages (Mortensen, 2006). Cyclamate is stable under conditions likely to be encountered in soft drinks, that is, pH range 2–7, pasteurization and UHT treatments (O'Donnell, 2007). Cyclamate solutions are stable to heat, light, and air throughout a wide pH range (Hunt *et al.*, 2012). Cyclamate is stable from pH 2 to 7 and can withstand heat treatments such as pasteurization and UHT (O'Donnell, 2007). Where pasteurization is applied, the HTST method is recommended, whereby more than 90% of the aspartame will remain (Ajinomoto, 2013). Because aspartame may lose its sweetening power upon prolonged exposure to heat, it is not recommended for use in recipes requiring lengthy cooking or baking.

Aspartame

Aspartame consists of three components namely aspartic acid, phenylalanine, and methanol. Aspartame is a dipeptide composed of two amino acids, L-aspartic acid and the methyl ester of L-phenylalanine (Abegaz *et al.*, 2012). The true chemical name is *N*-L- α -aspartyl-L-phenylalanine-1-methyl ester (Nelson, 2000). Aspartame is composed of

57.1% carbon, 6.2% hydrogen, 9.5% nitrogen, and 27.2% oxygen. It has the chemical formula C₁₄H₁₈N₂O, a molar mass of 294.3 g/mol, and a density of 1.3 g/cm³. Aspartame has a melting point between 246-247 °C and will decompose at temperatures above 280 °C. Aspartame has two ionizable groups. Because it is a dipeptide, it is amphoteric, and those sites can dissociate hydrogen ions. The pKa of the two sites are 3.1 and 7.9 at 25°C. The molecule still exhibits sweetness after the sites are dissociated. The isoelectric point for aspartame is 5.2 (Nelson, 2000). Aspartame is slightly soluble in water (approximately 1.0% at 25°C) and is sparingly soluble in alcohol. It is not soluble in fats or oils. Solubility is a function of both temperature and pH. Its solubility is ideal at pH ranges 3.0 to 5.0 (Abegaz *et al.*, 2012). The solubility of aspartame is sufficient for all product applications. In liquid applications such as beverages, typical concentrations are in the range of 0.01% to 0.2%. In water, the solubility is approximately 1% at 20°C and 3% at 50°C. Solubility can be significantly increased if aspartame is dissolved in an acid solution. For example at 20°C, approximately 4% aspartame can be dissolved in a 5% citric acid solution, and about 10% can be dissolved in a 20% citric acid solution. This is helpful when preparing stock solutions (Ajinomoto, 2013).

Its stability is determined by time, temperature, pH and moisture content. Under dry conditions, the stability of aspartame is excellent; it is, however, affected by extremely high temperatures which are not typical for the production of dry food products. At 25°C, the maximum stability is observed at pH ~4.3. Aspartame functions very well over a broad range of pH conditions but is most stable in the weak acidic range in which most foods exist (between pH 3 and pH 5). A frozen dairy dessert may have a pH ranging from 6.5 to more than 7.0 but, due to the frozen state, the rate of reaction is

dramatically reduced. In addition, because of the lower free moisture, the shelf life stability of aspartame exceeds the predicted shelf life stability of these products (Abegaz *et al.*, 2012).

Aspartame can withstand high-temperatures at a short-time and ultra-high temperature processing, such as pasteurization and aseptic processing (Kroger *et al.*, 2006). Where pasteurization is applied, the HTST method is recommended, whereby more than 90% of the aspartame will remain (Ajinomoto, 2013). Because aspartame may lose its sweetening power upon prolonged exposure to heat, it is not recommended for use in recipes requiring lengthy cooking or baking. Aspartame has a free amino group that reacts with carbonyl-containing food ingredients. Aspartame has a peptide that causes it to be susceptible to hydrolysis causing its taste in sweetness to gradually degrade. Being an amine it can react with aldehydes. At elevated temperature under acidic and alkaline pH, aspartame is unstable and rapidly degrades to the rate where sweetness will gradual be lost. For this reason aspartame is not ideal for cooking and baking. The shelf life of aspartame can be prolonged between nine months to a year when used in combination with other non-nutritive sweeteners (e.g. acesulfame K), a more stable sweetener. Aspartame can be encased with fats. An encapsulated version of aspartame is available for use in baked products to enhance its stability properties. The majority is used in soft drinks, which account for more than 70 per cent of aspartame consumption (Anonymous, 2012). As aspartame is approximately 200 times sweeter than sugar, each °Brix of sugar to be replaced requires approximately 50 to 60 mg/l of aspartame. Aspartame is suitable for sweetening many milk products including yogurts, milkshakes, and quark. Frozen desserts are traditionally sweetened with sucrose for its sweetness and

functional characteristics. Aspartame was sold exclusively by the patent holder and manufacturer (Searle) by the brand names NutraSweet in food products and Equal as a tabletop sweetener (Kroger *et al.*, 2006).

Acesulfame K

Acesulfame is an oxathiazinone dioxide (6-methyl-1, 2, 3-oxathiazine-4(3H)-one-2, 2-dioxide or 3, 4-dihydro-6-methyl-1, 2, 3-oxathiazin-4-one-2, 2-dioxide). Chemically, it bears some structural resemblance to saccharin. The hydrogen atom on the nitrogen is quite acidic (pKa ~2) and it readily forms salts. It is sold as the potassium salt, so it often referred to as "acesulfame-K" (Walters, 2013). Its formula is $C_4H_4NO_4SK$ with a molecular weight of 201.24. It is manufacture by chemical derivation from acetoacetic acid and purified through re-crystallization (O'Donnell, 2007). It is a white, non-hygroscopic crystalline product.

Acesulfame-K does not show a defined melting point although decomposition starts at above 200°C (Nelson, 2000). The density of solid acesulfame-K is 1.81 g/cm³ while that of the commercial acesulfame-K has a range of 1.1-1.3 kg/dm³. Acesulfame K dissolves readily in water, forming a clear solution. Solubility increases with increasing temperature (1300 gm/lit at 100°C). Its crystalline solid has good water solubility (27% at 20°C) (DuBois and Prakash, 2012). It is only slightly soluble in organic solvents such as methanol, ethanol, and glycerol (Nelson, 2000). The shelf life of pure, solid acesulfame K appears to be almost unlimited at room temperature.

Samples kept at room temperature for more than six years and either exposed to or protected from light showed no signs of decomposition or differences in analytical data compared with freshly produced material

(Klug and von Rymon Lipinski, 2012). Acesulfame K is stable in aqueous solutions over a wide range of temperatures, pH levels and light exposure for use in beverage applications (DuBois and Prakash, 2012). At pH <3, acesulfame K is slightly less stable. Acesulfame-K works excellent when foods have a pH of 3 to 7 (Nelson, 2000). Acesulfame K is suitable for low-calorie and diet beverages because of its good stability in aqueous solutions even at low pH typical of diet soft drinks (Klug and von Rymon Lipinski, 2012). Acesulfame K is stable in its dry state, even at high temperatures. Therefore, the sweetener can withstand the temperatures encountered during baking, sterilization, and pasteurization. It is not utilized by microorganisms and is therefore not subject to microbial breakdown (Nelson, 2000). Acesulfame K-containing beverages can be pasteurized under normal pasteurization conditions without loss of sweetness. Pasteurizing for longer periods at lower temperatures is possible, as is short-term pasteurization for a few seconds at high temperatures. Sterilization is possible without losses under normal conditions (i.e., temp. at 100°C for products having lower pH levels and 121°C for products around and >pH 4). Under UHT and microwave treatment, acesulfame K is stable. In baking studies, no indication of decomposition of acesulfame K was found even when biscuits with low water content were baked at high oven temperatures for short periods. This corresponds to the observation that acesulfame K decomposes at temperatures well above 200°C (Klug and von Rymon Lipinski, 2012). It is marketed under the brands Sunett® or SweetOne® (Anonymous, 2012).

Sucralose

The only non-caloric sweetener prepared from sucrose. Although the name Sucralose ends in -ose, it is not a basic sugar like glucose or

sucrose, so the name is rather misleading. Common brand names of sucralose-based sweeteners include Splenda®. Sucralose is also known as 4, 1', 6'-trichlorosucrose. Sucralose is made from sucrose (common table sugar) by the selective replacement of three hydroxyl groups with chlorine atoms, a process that occurs with inversion of configuration at the 4 position of the galactanalog (Grotz *et al.*, 2012). Its chemical formula is C₁₂H₁₉O₈Cl₃ (MW 397.35) Sucralose is a white, odorless crystalline powder and is readily dispersible and soluble in water, methanol, and ethanol. At 20°C, a 280 g/l solution of sucralose in water is possible. Sucralose presents Newtonian viscosity characteristics, a negligible lowering of surface tension, and no pH effects, and its solubility increases with increasing temperature. In ethanol, the solubility ranges from approximately 110 g/l at 20°C to 220 g/l at 60°C and solubility of sucralose in ethanol facilitates in formulating alcoholic beverages and flavor systems (Nikoleli and Nikolelis, 2012).

It has a negligible effect on the pH of solutions. Sucralose exerts negligible lowering of surface tension (Grotz *et al.*, 2012). Solubility increases with increasing temperature. Sucralose is also soluble over a wide pH range, although solubility decreases slightly with increasing pH (Nelson, 2000). The shelf life of pure dry sucralose is at least two years when stored at 25°C or below. Dry sucralose is, however, sensitive to elevated temperatures. Storage at high temperatures for extended periods can result in color formation. The shelf life can also be affected by packaging materials and container head space, so care should be taken to adhere to the recommended packaging and storage conditions (Grotz *et al.*, 2012). Because of the three substituted sites (at which chlorine replaces a hydroxyl group on the sucrose molecule), the reactivity of sucralose is much

lower than that sucrose. For example, under acidic conditions, sucrose hydrolyzes to its component sugars, glucose and fructose. Sucralose hydrolyzes under highly acidic conditions, and hydrolysis increases with increasing temperatures. However, the rate of hydrolysis is much lower than that of sucrose. Since the primary reaction sites are substituted, sucralose is also less chemically reactive than sucrose. In food systems, sucralose does not interact with other food molecules. In aqueous systems, sucralose is stable over a wide range of pH. At pH 3 or lower, some hydrolysis occurs, but the amount is very small, and at pH 4–7.5, virtually no sucralose is lost when stored at 30°C for a year (Nelson, 2000).

Sucralose is extremely heat stable, even when exposed to high temperature food processing such as pasteurization, sterilization, UHT and baking. The stability of sucralose during food manufacture has been confirmed by a series of processing trials. Sucralose maintains its sweetness and flavour through storage without the development of off-flavours even at low pH. Shelf-life studies have demonstrated that products sweetened with sucralose retain their sweetness throughout extended periods of storage (Anonymous, 2012). The taste, stability and physicochemical properties of sucralose mean that it is a very versatile sweetener suitable for use in a wide variety of food products (Grotz *et al.*, 2012). Sucralose is used in a wide range of food products and beverages. Among these are soft drinks, desserts, ice-cream, confectionery, preserves and sandwich spreads. The permitted levels of use vary from 10 mg/l to 1000 mg/kg depending on the food category. It is sold under the name Splenda (Mortensen, 2006).

Alitame

Alitame is second-generation dipeptide sweetener Alitame is a sweetener formed

from the amino acids L-aspartic acid and D-alanine and a new amine. Alitame is the generic name for L- α -aspartyl-N-(2, 2, 4, 4-tetramethyl - 3- thietanyl)- D-alaninamide hydrate (O'Donnell, 2007). Alitame is formed from the amino acids L-aspartic acid and D-alanine, with a novel C-terminal amide moiety. It is this novel amide (formed from 2, 2, 4, 4-tetramethylthietanylamine) that is the key to the very high sweetness potency of alitame (Auerbach *et al.*, 2012). Incorporation of D-alanine as second amino acid, in place of L-phenylalanine, gives optimum sweetness. Increased steric and lipophilic bulk on small rings led to high sweetness potency with another sulphur derivative, derived from 2, 2, 4, 4-tetramethyl-3-aminothietane proved highly sweet (Hough, 1993). It is a crystalline powder that is odorless and non-hygroscopic. The melting point of alitame is 136–147°C. Alitame is soluble in water and forms clear solutions. Its isoelectric point is 5.7. This is also the pH at which alitame is least soluble (13% at 25°C) (Anonymous, 2012). It is soluble in polar solvents such as methanol, ethanol, and propylene glycol. It is not soluble in nonpolar solvents such as fats, oils, or chloroform. The solubility of alitame increases with increasing temperature and with pH levels greater or less than the isoelectric point (Nelson, 2000). At the isoelectric pH, alitame is very soluble in water.

Excellent solubility is also found in other polar solvents. As expected from the molecule's polar structure, alitame is virtually insoluble in lipophilic solvents. In aqueous solutions, the solubility rapidly increases with temperature and as the pH deviates from the isoelectric pH (Auerbach *et al.*, 2012). Alitame is an amino acid derivative and, therefore, not completely stable. It does hydrolyze in acid conditions, but is more stable than aspartame under certain conditions (O'Donnell, 2007). The unique amide group is in part responsible unique stability

characteristics of alitame compared with those of aspartame. Because of its unique amide group, alitame exhibits superior stability under a variety of conditions. It is less likely to hydrolyze than the methyl ester of aspartame. The half-life of alitame in aqueous solutions at pH 7–8 and 100°C ranges from hours to days. The dipeptide bond of alitame can hydrolyze, forming two final reaction products: aspartic acid and the alanine amide. These end products do not exhibit sweetness.

Alitame is stable in carbonated beverages and can withstand the pH levels typical of soft drinks (pH 2–4). Alitame does not cyclize. At neutral pH under aqueous conditions, it is stable for more than a year (Anonymous, 2012). Because it is stable during heating, alitame can be used in processed foods such as baked goods. In particular, high levels of reducing sugars, such as glucose and lactose, may react with alitame in heated liquid or semiliquid systems, such as baked goods, to form Maillard reaction products. At pH <4, off flavors can form when sodium bisulfite, ascorbic acid, and some caramel colors are also present (Nelson, 2000). Alitame is currently marketed in some countries under the brand name Aclame (Hough, 1993).

Advantame

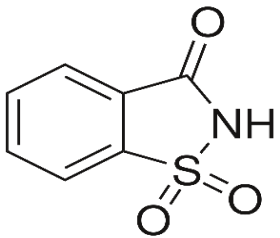
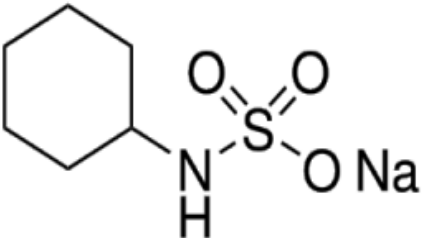
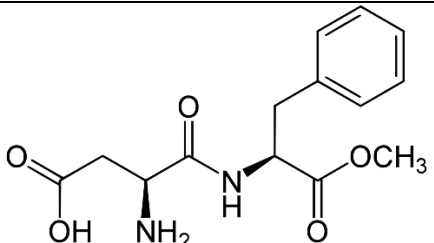
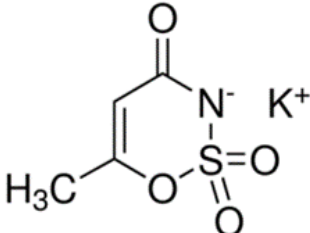
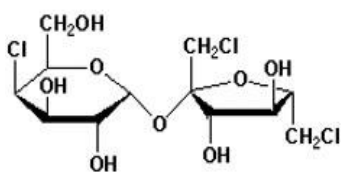
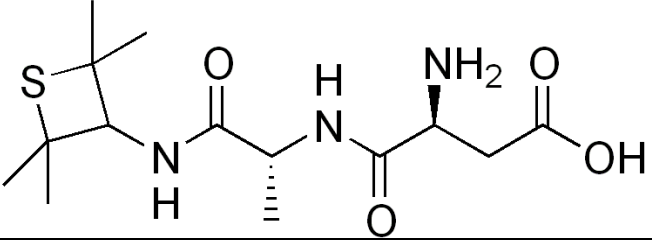
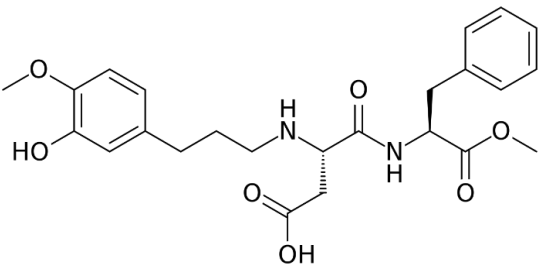
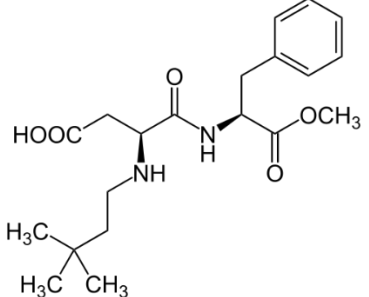
Advantame, one of the latest additions to the group of non-nutritive high-intensity sweeteners is an N substituted (aspartic acid portion) derivative of aspartame that is similar in structure to neotame. Its chemical name is N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-a-aspartyl]-L-phenylalanine 1-methyl ester, monohydrate (Otabe *et al.*, 2011). The starting materials of advantame are aspartame and vanillin. Advantame is synthesized from aspartame and HMPA in a one step process by reductive N-alkylation, carried out with hydrogen in the presence of a platinum

catalyst (Amino *et al.*, 2008). Advantame has a molecular weight of 476.52 g/mol and the monohydrate has a melting point of 101.5°C. Advantame is a crystalline solid with solubility in water of approximately 0.10% at 25°C (DuBois and Prakash, 2012). Considering the ultrahigh potency of advantame, its solubility in water, ethanol and ethyl acetate is more than sufficient for the required functionality (Bishay and Bursey, 2012). Advantame is more stable than aspartame under higher temperature and higher-pH conditions." In general, 4.5 is considered a higher pH condition, but he notes all formulations are unique (Hazen, 2012). Advantame is stable under dry conditions.

In aqueous food systems, its stability is similar to aspartame with greater stability predicted at higher and neutral pH, as well as higher temperature conditions (e.g., baking and other prolonged heating processes) and in yogurt. The stability of advantame is dependent upon pH, moisture, and temperature. Advantame in dry applications, such as tabletop or powdered soft drinks, is very stable and maintains its functionality during normal storage and handling conditions. Advantame gives stability in carbonated soft drinks. Advantame is also stable in tabletop mix, when stored at 25°C and 60% relative humidity (RH). Under these conditions, advantame displays the same stability profile as aspartame indicating that both sweeteners follow the same degradation mechanism (Bishay and Bursey, 2012). Advantame was demonstrated to perform very well as a sweetener in coffee (hot and warm), iced tea, powdered beverage formulations, and as a flavor enhancer in beverages, chewing gum and yogurt. These properties make advantame a high-intensity sweetener in a variety of products (Otabe *et al.*, 2011).

Table.1 Sweetness potency of intense artificial sweeteners

Sweetener	Potency (More times compared to sucrose)
Cyclamate	30
Aspartame	180
Acesulfame K	200
Saccharin	300
Sucralose	600
Alitame	2000
Neotame	8000
Advantame	20000

	
Saccharin	Cyclamate
	
Aspartame	Acesulfame K
	
Sucralose	Alitame
	
Advantame	Neotame
Chemical structure of artificial sweeteners	

Allowable levels of advantame in food products are: 2 ppm in nonalcoholic beverages; 1 ppm in milk products, 1 ppm in frozen dairy products and 50 ppm in chewing gum (Hazen, 2012).

Neotame

Neotame is a new high-potency nonnutritive sweetener which is considered as the potential successor of aspartame. It is a derivative of aspartame, produced by adding a 6-carbon (neohexyl) group to the amine nitrogen of aspartame (O'Donnell, 2007). Its chemical name is N-[N-(3, 3-dimethylbutyl)-L- α -aspartyl]-L-phenylalanine 1-methyl ester. Its chemical formula is $C_{20}H_{24}N_2O_5$ and it has a molar mass of 378.46 g/mol (Boone, 2009). The solubility in water of neotame is 12.6 g/l at 25°C (Nofre and Tinti, 2000). The solubility of neotame in water, ethyl acetate and ethanol at a range of temperatures illustrates how neotame behaves in various food matrices. Neotame is very soluble in ethanol at all temperatures tested. The solubility of neotame increases in both water and ethyl acetate with increasing temperature. This solubility may create opportunities for food and beverage manufacturers to use neotame in a wide range of liquid systems (Mayhew *et al.*, 2012). As a dry ingredient, neotame has excellent stability and will function well in finished dry products such as powdered soft drinks and dessert mixes. In food where moisture is present, the stability of neotame will be influenced by pH, temperature and time. In solution, it shows highest stability at pH 4.5. At low pH, neotame a dipeptide methyl ester, hydrolyzes to the dipeptide carboxylic acid, the non-sweet major metabolite of neotame in humans (BFNE, 2010; Nofre and Tinti, 2000).

Neotame is stable enough in heat that it can be used for baking and cooking unlike Aspartame which easily degrades when

heated. As a dry ingredient Neotame is stable enough for storage of at least five years, in temperatures between 15° and 30°C and at relative humidity between 35% and 60% when the inner bag is sealed. However, when in a system of moisture the rate of degradation of Neotame becomes a function of pH, temperature, and time.

When used as a sweetener in carbonated soft drinks and ready-to-drink beverages (pH 2.9-4.5), if these products are properly stored and handled, Neotame remains stable adequately for the normal shelf life. For baked goods Neotame exhibits high stability. In one study only 15% of Neotame was lost (85% retained) during baking and only 19% was lost (81% retained) after 5 days of storage at room temperature. In dairy products such as yogurt only 1% of Neotame was lost after ultra-high temperature (UHT) pasteurization. There was no noticeable degradation after fermentation followed by 5 weeks in refrigerated storage (Anonymous, 2006). The high potency of neotame allows it to maintain a highly competitive relative cost (cost per sucrose equivalent). Therefore it is possible to achieve a cost reduction in almost any given sweetener blend BFNE (2010).

Regulatory aspects

Food ingredients are evaluated and/or regulated by numerous national and international bodies. International groups that evaluate use of sweeteners include expert scientific committees such as the Scientific Committee on Food (SCF) of the European commission (EC), the Joint Expert Committee of Food Additions (JECFA) of the United Nations Food and Agricultural Organization (FAO) and the World Health Organization (WHO) (Nabors, 2001). In India Saccharin, Aspartame, Acesulfame k, Sucralose are permitted under FSSAI, 2011.

Sweetness characteristics

Sucrose is the standard sweetener to which all other sweeteners are compared. The relative sweetness of sucrose is set to 1 or 100%. A growing number of alternative sweeteners exist on the market; all with somewhat different sweetness compared to sucrose. Each high-intensity sweetener has its own characteristics. Using the right sweetener or combination of sweeteners is the key in product success.

The potency of an intense sweetener is an important basic characteristic, due to its impact on a variety of issues including relative cost and amounts consumed (the latter impacting safety considerations). Different artificial sweeteners provide different sweetness potency, which is presented in Table below.

In reality the potency is affected by many factors such as temperature, viscosity, pH and medium in which the sweetener is used. The presence of other sweeteners (both intense and nutritive sweeteners) may have impact on the potency of the sweetener as well as other sensory attributes (Bakal and Cash, 2006).

Health hazards

The artificial sweeteners are a mix of laboratory chemicals used to create a 'sweet' taste. The accumulating evidence suggests that frequent consumers of these sugar substitutes may also be at increased risk of excessive weight gain (Swithers and Davidson, 2008; Davidson and Swithers, 2004; Fowler *et al.*, 2008), metabolic syndrome (Yang, 2010), type 2 diabetes (Brown *et al.*, 2010; Swithers *et al.*, 2013), cancer (Soffritti *et al.*, 2006; Howe *et al.*, 1977; Andreatta *et al.*, 2008), hypertension (Swithers *et al.*, 2013) and cardiovascular disease (Jang *et al.*, 2011). In addition to these

health related general concerns of artificial sweeteners, there are several other sweetener specific health risks (Williams *et al.*, 2008; Takayama *et al.*, 2000; Mann *et al.*, 2000; Boone, 2009; Van Stempvoort *et al.*, 2011; Buerge *et al.*, 2009). Therefore, usefulness of the artificial sweeteners for purpose of their use and safety has become questionable.

Because of increasing consumer desire for products that deliver great taste with fewer calories, the need for improved zero- and reduced-calorie sweetener technologies will continue. Eight artificial sweeteners are used worldwide. Those are acesulfame-K, advantame, alitame, aspartame, cyclamate, neotame, saccharin and sucralose. However, the main barrier in using any intense sweetener is technical one. It is never easy to replicate the mouth feel and taste of a full sugar product.

It requires the careful blending of sweeteners, alongside the use of flavour and texture enhancing ingredients, to optimize the sensory characteristics and to bring a low/zero calorie product in to line with the 'full-sugar' version. Moreover, the usefulness of the artificial sweeteners for the purpose they are used and their safety is doubtful.

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