A REVIEW ON ARTIFICIAL SWEETENERS

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ABSTRACT

Artificial sweeteners are known to have a magnificent role in controlling the diabetes and obesity. These do not increase the calories more and provide the sweetness as required. Now a days there use has been increased in beverages and other food materials also. These have good acceptability and taste.

KEYWORDS: Sweetener, Acesulfame K, Aspartame, Saccharin, Thaumatin, Cyclamate.

INTRODUCTION

Sweeteners are being categorized as nutritive and non-nutritive sweeteners relying on whether these are the calorie source. Nutritive sweeteners consists mainly the monosaccharide polyols for example sorbitol, mannitol and the disaccharide polyols such as maltitol and lactitol. These are approximately similar in sweetness to sucrose. Non-nutritive sweeteners are regarded as artificial sweeteners and provide about negligible calories Examplified as saccharin, aspartame, sucralose, acesulfame-K, stevioside, cyclamate. The non-nutritive sweeteners are being commonly used in foods such as diet sodas, cereals and sugar-free desserts, and are being recommended for weight loss and for individuals suffering from glucose intolerance and type 2 diabetes mellitus. The artificial sweeteners are to be classified according to the concept of safety levels. Generally, they are designated as food additives which are expressed as accepted daily intake. This will reflect an amount which is hundred times less than the maximum level at which observed adverse effects occur in animal or human studies. The accepted daily intake is usually expressed as mg per kg body weight per day.

Various artificial sweeteners are described as follows.
Acesulfame K

The sweetness of a dihydrooxathiazinone dioxide was accidentally discovered in 1967 in Germany by K. Clauss and H. Jensen at Hoechst AG while they were carrying out reactions with butyene and flouroisocyanate.\textsuperscript{[4,5]} Analogs of this chemical class were later synthesized and 6-methyl-1,2,3-oxathiazine-4-(3H)-one-2,2-dioxide was found to have the most favorable taste qualities.\textsuperscript{[3]} It is a six-membered heterocyclic system in which oxygen, sulfur, and nitrogen atoms are adjacent to one another. It is about 200 times sweeter than sucrose but has a slight bitter aftertaste. Acesulfame-K has a strong bitter taste to many persons, especially at concentrations greater than 100 ppm.\textsuperscript{[7]} The sweetness may be slightly enhanced in acidic solutions relative to neutral solutions.\textsuperscript{[6]} The sweetness quality of Acesulfame-K is compatible with nutritive sweeteners like sorbitol, xylitol, isomalt and maltitol.\textsuperscript{[6]} The sweetness does not appear to be affected by baking or pasteurization temperatures.\textsuperscript{[8]} Dry form has a very good shelf life under dry conditions at room temperature, independent of exposure to light; aqueous solutions with pH above 2.5-3 show relatively good stability.\textsuperscript{[9,10]} It is heat stable\textsuperscript{[5]} and synergistic with aspartame and cyclamates.\textsuperscript{[5]} However, hydrolytic stability of Acesulfame-K is less than saccharin.\textsuperscript{[11]} Decomposition occurs in extreme conditions and the hydrolytic products are mainly acetone, CO$_2$ ammonium salts, sulfate, and amidosulfonate.\textsuperscript{[6]} Acesulfame-K is readily soluble in water, N, N-dimethylformamide, and dimethyl sulfoxide.\textsuperscript{[12]} It withstands high temperatures, which makes it ideal for use in baked goods.\textsuperscript{[13]} It gets excreted by the kidney in unchanged form. Due to its structural similarity with saccharin it has been alleged as carcinogenic mainly for bladder cancer in male rats, its safety was a big concern. However, a large number of pharmacological and toxicological studies have been conducted and the sweetener has been found to be safe.\textsuperscript{[14]} Acesulfame-K is suitable for low calorie and diabetic beverages, jams and marmalade, confectionary items, sugarless chewing gums, reduced-calorie baked goods, fruit flavored dairy products, oral hygiene products, pharmaceuticals, tobacco products and animal food stuff.\textsuperscript{[6]} In 1988, the FDA approved Acesulfame-K for use in liquid non-alcoholic beverages (soft drinks) on July 6, 1998. A general use approval was granted by the FDA in December of 2003.\textsuperscript{[15]}{calorie control council}
Aspartame
In 1965, Jim Schlatter, working with Dr. Robert Mazur on the synthesis of the C-terminal tetrapeptide of gastrin, discovered the sweet taste of aspartylphenylalanine methyl ester (aspartame). From 1965 to 1970 over 200 analogs of aspartame were synthesized but none was more satisfactory than aspartame itself.\[17, 18\] Aspartame is prepared by two general procedures, named as enzymatic and chemical coupling. These procedures involve coupling of two constituent amino acids, aspartic acid and phenylalanine. In the enzymatic method, carbobenzoxy-L-aspartic acid (Z-Asp) is coupled with L- or DL-phenylalanine methyl ester in the presence of an enzyme under very special conditions. Because the enzyme is specific for the formation of protein – like peptide bonds with L-amino acids, only the alpha-carboxyl of Z-Asp reacts and only with L-Phe-OMe. This gives cleanly Z-L-Asp-L-Phe-OMe which can be catalytically hydrogenated to aspartame. The classical chemical method activates a protected L-aspartic acid by conversion to the anhydride and reaction of the latter with L-Phe or L-Phe-OMe. The Asp protecting group is either formyl or carbobenzoxy. Final purification, after deprotection, usually depends on the lower water solubility of aspartame hydrochloride which is then neutralized to yield aspartame. The chemical synthesis method is less expensive than the enzymatic process.\[19\] At pH 5.2, the isoelectric point, aspartame has a solubility of 1% in water and 0.37% in ethanol at 25°C.\[20,21\] It is more soluble in hot water.\[20\] Aspartame is most stable in solid form and should be stored in an airtight container.\[19\] Under certain moisture, pH, temperature, aspartame hydrolysis. Aspartame is most stable at pH 4.3.\[19, 20\] FDA approval for a heat stable form of aspartame for baking was approved in 1993.\[22\] Products containing aspartame must be labeled to alert persons with phenylketonuria of their need to restrict intake of phenylalanine from all dietary sources.\[23\] Consumption of aspartame has no effect on neurologic function; it does not cause headaches or seizures nor does it alter mood, cognition or behavior.\[17\] Because aspartame, as a high-potency sweetener, does not affect the glucose concentration in the diabetic person, it is useful as a sugar substitute to reduce calorie intake in the Type II diabetic individual for whom weight loss is a goal.\[24\] Aspartame is a noncarcinogenic, and there is some evidence that it may be anti-carcinogenic by inhibition of bacterial growth and/or reduction in plaque formation by streptococcus mutans.\[24\] However, this has not firmly established. In 1974, the FDA approved aspartame for use in dry products including cold breakfast cereals, chewing gum, dry beverage mixes, instant tea and coffee, gelatins, puddings, fillings, dairy product analog toppings, and tabletop sweeteners.\[19\] In addition to the US, aspartame has been approved for use in foods, beverages, and as a tabletop sweetener in over 90 countries.\[18\]
Saccharin
Saccharin was accidently synthesized by the American chemist Constantine Fahlberg, and its potential as a sweetening agent was rapidly utilized commercially.[25] He was working on the synthesis of Toluene derivatives.[26] Saccharin is 300 times sweeter than sucrose and has a slight bitter after taste. Saccharin, as well as the sodium and calcium salts of saccharin, was first listed as GRAS in 1959.[27] In 1972, the FDA removed saccharin and its salts from the GRAS list based on questions of safety raised by the Wisconsin Alumni Research Foundation (WARF) study.[28, 19] Based on a study from the Canadian Health Protection Branch which showed evidence of bladder tumors in second generation male rats fed high doses of saccharin, the FDA proposed to prohibit its use in 1977.[29,30] Saccharin has been the subject of extensive scientific research. It is one the most studied ingredients in food supply. Research conducted over the past 25 years has overwhelmingly demonstrated that saccharin does not cause cancer in humans. Other research indicates that the bladder tumors developed by male rats fed high doses of Sodium saccharin are related to the high doses of sodium salt and not saccharin per se.[16]

The information on Sodium saccharin presently available supports the conclusion that sodium saccharin does not pose a bladder cancer risk for humans and that application of safety factor is an appropriate basis for determining the health risk of this additive. The NOEL for sodium saccharin in the male rat according to the findings of Schoenig et al (1985) was a dietary level of 1% or approximately 500mg/kg per day. Applying a safety factor of 100 yields an acceptable daily intake of 5mg/kg/day for humans.[31] Based on US Federal legislation in 2001, products with saccharin no longer need to carry a warning of its use associated with causing cancer in laboratory animals (ADA). The Reproductive and Cancer Hazard Assessment section of the Office of Environmental Protection Agency also removed sodium saccharin from its Proposition 65 list of carcinogens.[32]

Sucralose
During 1970s, a program to develop a new chemical entity from sugar was established at Tate & Lyle.[27] Sucralose, a substituted disaccharide, is a non-nutritive sweetener that is synthesized by selective chlorination of sucrose at three of the primary hydroxyl groups, involving inversion of configuration at carbon-4, from the gluco- to the galacto-analogue.[33] It has been showed that sucralose does not have the bitter aftertaste attributed to some other non-nutritive sweeteners.
The solubility of Sucralose in water ranges from 28.3g/100ml at 20°C to 66g/ml at 60°C. Its solubility in ethanol ranges from 9.5g/100ml at 20°C to 18.9g/100ml at 60°C.\cite{19,34} Sucrose is stable in aqueous solutions with no measurable loss after one year of storage at pH 4.0, 6.0, and 7.5.\cite{35} Sucralose is not susceptible to enzymatic hydrolysis.\cite{35} Sucralose is more stable to heat and acid than sugar, and does not break down under heat conditions used for baked goods.\cite{33} FDA permits Sucralose use as a general purpose sweetener\cite{37}, based not only on the studies designed to directly test the safety of Sucralose, but also on food chemistry studies. Sucralose was approved by the Health Protection Branch in Canada with permission for use in 13 categories as of September 1991. The EEC lists Sucralose as not toxicologically acceptable.\cite{34}

**Cyclamate**

Sodium cyclamate was synthesized in 1937 by Sveda who accidently discovered that it has sweet taste.\cite{19,38,39} Cyclamate is 30-50 times sweetener than Sucrose.\cite{43} After enactment of the food Additive Amendment in 1958, sodium and Calcium cyclamate were classified as GRAS by the US FDA.\cite{19} Cyclamates were first introduced in tablet in the form as a tabletop sweetener for use by diabetics by Abbott Laboratories in the United States in 1951.\cite{19} In UK, Cyclamate was allowed in soft drinks under the 1964 Soft Drink Regulations.\cite{10} Cyclamates are stable in high and low temperature.\cite{40} Sodium cyclamate can be used to mask the bitterness and unpalatable tastes of drugs, especially liquid formulations and chewable tablets.\cite{19,41} Mixtures of cyclamate and saccharin are synergistic and produce sweetness levels that are 10-20% higher than would be expected based on the levels of individual components.\cite{41,19} Cyclamates were prohibited for use as food additives in the U.S.A. and other parts of the world during 1970 because of the fears of carcinogenicity, the appeal made against the decision which led to the lifting of the cyclamate restrictions in Australia in November 1974.\cite{42} The weight of the evidence from metabolic studies, short-term tests, animal bioassays, and epidemiological studies indicates that cyclamate (CHS) is not carcinogenic by itself; however, there is evidence from in vitro and in vivo studies in animals that implies it may have cancer-promoting or co-carcinogenic activity. No epidemiological information exists on the possible associations of these sweeteners and cancers other than those of the urinary tract. It is recommended that (i) no further studies on the metabolism of CHS to evaluate its carcinogenicity are required since no potentially hazardous metabolites have been appreciably detected in humans; (ii) no further animal bioassays to test for the carcinogenicity of CHS by itself are necessary; (iii) the studies in rodents that suggest a
promotional or co-carcinogenic effect of CHS should be repeated because they cannot be ruled out; (iv) because the significance to human health of a positive outcome of such studies is uncertain, additional research aimed at understanding the predictive value for human health of such results and more generic studies to develop well-validated systems that can be relied on in the assessment of cancer-promoting agents are recommended; (v) in populations where CHS continues to be used, epidemiological monitoring should be continued to determine whether there is an increased risk of cancer in humans who are heavy or long-term users or for those observed long after first exposure. In such monitoring, other cancer sites—in addition to the bladder—should be considered. Cyclamate is currently approved for use in foods and beverages in over 50 countries including Australia, but not in Canada or the US. The Acceptable Daily Intake (ADI) for cyclamate has been set at 11mg/kg body weight by JECFA and at 7mg/kg body weight by the SCF. Cyclamate has been approved by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (1982) and by the Scientific Committee on Food (SCF) of the European Commission (2000) - now the European Food Safety Authority (EFSA). The Cancer Assessment Committee of the US Food and Drug Administration confirmed the safety of cyclamate in 1984 and the US National Academy of Sciences did the same in 1985.

Neotame
Neotame (NTM) is a new high-potency nonnutritive sweetener which is considered as the potential successor of aspartame (APM). Neotame is composed of mainly two amino acids - aspartic acid and phenylalanine, with an additional molecule of 3,3-dimethybutylaldehyde. It is 7,000 to 13,000 times sweeter than Sucrose and 30 to 60 times sweeter than aspartame. It provides no kilojoules and is heat stable during cooking and baking. Neotame has a clean, sweet taste like sucrose and unique flavor enhancement properties. At projected trace levels of use, neotame will provide a full, sweet taste in foods and beverages. Approximately 20% to 30% of ingested neotame is absorbed and rapidly metabolized to demethylated neotame (and methanol) and completely excreted from the body. Neotame ingestion also did not have a significant effect on fasting plasma glucose or insulin levels in those with type 2 diabetes. In human studies, there have been no adverse effects observed following neotame ingestion compared to control subjects. On the basis of a review of 113 preclinical, clinical, and special studies and an additional 32 exploratory and screening studies, the FDA approved neotame as a general-purpose sweetener on July 5, 2002. In 2002, the FDA set the ADI at 18 mg/day. Globally, neotame is approved for use in
multiple countries in North America, South America, Europe, Africa, Asia, and Australia.\textsuperscript{[53]} In June 2003, JECFA confirmed the safety of neotame and granted an ADI of 2 mg/kg bw/day.\textsuperscript{[54]}

**Stevia**

Stevia is a natural and healthy alternative to sugar and artificial sweeteners. Stevia a perennial shrub, belongs to the family Asteraceae, genus stevia and species rebaudiana.\textsuperscript{[55]} In the sixteenth century, Europeans became aware of the herbal sweetener through the Spanish Conquistadors. In the late 1880s, Moises S. Bertoni, director of the College of Agriculture in Asunción, Paraguay, became extremely intrigued by the stevia plant. In 1905, Bertoni published an important article about the incredible sweetening power of the stevia plant, which he considered superior to sugar and extremely marketable.\textsuperscript{[57]} Its ability to sweeten is rated between 70 to 400 times that of white sugar. Typically, it has a mild licorice-like taste and is completely natural in its biochemical profile.\textsuperscript{[57]} It contains sweet tasting glycosides, mainly Stevioside in addition to Rebaudiosides A, B, C, D and E. Stevioside, obtained in the form of a white crystalline compound is 100 to 300 times sweeter than table sugar.\textsuperscript{[57, 58]}

According to new tentative specifications prepared at 63rd meeting in 2004 of JECFA, published in FNP52 and ADD12 (2004); Steviol glycosides are functionally designated as sweetener not as a food additive.\textsuperscript{[55]} The metabolism of stevioside is discussed in relation with the possible formation of steviol. Different mutagenicity studies as well as studies on carcinogenicity are discussed. Acute and subacute toxicity studies revealed a very low toxicity of Stevia and stevioside. Fertility and teratogenicity studies are discussed as well as the effects on the bio-availability of other nutrients in the diet. The conclusion is that Stevia and stevioside are safe when used as a sweetener. It is suited for both diabetics, and PKU patients, as well as for obese persons intending to lose weight by avoiding sugar supplements in the diet. No allergic reactions to it seem to exist.\textsuperscript{[59]} USFDA has approved Stevia as a dietary supplement or an herb but not as a sweetener.\textsuperscript{[60]} They are thermostable even at temperatures of up to 200\textsuperscript{0}C, making them suitable for use in cooked foods.\textsuperscript{[58]} Until recently, stevia sweeteners were only available as dietary supplements in the U.S. and were not permitted in foods and beverages. However, in December 2008, the U.S. Food and Drug Administration (FDA) issued a “letter of no questions” that stated it does not question the conclusion that highly purified stevia sweeteners (also known as steviol glycoside extracts) are generally recognized as safe (GRAS) as general purpose sweeteners.\textsuperscript{[62]}
Neohesperidine DC
It was discovered in 1963 by Horowitz and Gentili. Neohesperidine DC (INS 959, E 959) is a low-calorie sweetener and flavor modifier which may be produced by hydrogenation of neohesperidine, a flavonoid occurring naturally in bitter oranges. It offers foods and beverages a liquorice flavor and can enhance the mouthfeel of beverages. In the United States, neohesperidine dihydrochalcone is GRAS as a flavor ingredient but not as a sweetener. Neohesperidine DC is stable in solid form and in aqueous solutions of pH 1-7 (t½ > 1 year, 20°C). It is heat stable and can therefore be used in foods requiring pasteurization or UHT processes. Neohesperidine DC does not promote tooth decay and may be used in products for diabetics. The safety of neohesperidine DC was confirmed in 1988 by the Scientific Committee on Food (SCF) of the European Commission - now the European Food Safety Authority (EFSA). EU countries have authorized the use of this sweetener in a range of energy-controlled products.

Thaumatin
Thaumatin is a natural product from the fruit of Thaumatococcus daniellii, a plant that grows abundantly in the rain forest belt of West Africa, primarily in Ghana, Ivory Coast, Togo, and Sierra Leone. After the fruit is collected, the arils are removed, frozen and transported to the UK for processing. The details of the extraction and purification process are proprietary, but basically, a solely aqueous extraction process using filtration and ultra filtration are used. The sweetness of the red, pyramid-shaped fruit of the tropical plant was first described in the literature by British physician- amateur botanist W.F. Daniell in 1855. John Joseph Bennett, F.R.S. first classified the plant as from the species Phrynium danielli but it was later classified as Thaumatococcus. Thaumatin’s flavor profile indicates a delay in perceiving the sweetness, a slow buildup to maximum intensity, and a long, lingering sweet aftertaste without any unpleasant aftertaste. The protein (thaumatin) molecule is most stable to heat between pH 2.7 and 6.0, with an optimum around 2.8-3.0. At higher pH values, Thaumatin protein becomes less stable to heat but at ambient temperatures is stable at pH up to 8-9. It can be pasteurized or sterilized at ultrahigh temperatures. Because Thaumatin protein stability is enhanced at lower pH levels, it can be heated at 100°C for several hours without sweetness loss, thus making it suitable for typical soft drinks, which have pH 2.8 -3.5. Thaumatin is extremely soluble in water. It has good solubility in aqueous alcohols, propylene glycol and in higher alcohols such as sorbitol. It is used in chewing gum in the US and Europe. Talin has been permitted as a natural protein in Japan since 1979, with recommended codes of...
practice and specification/analysis published by the Japanese Food Additive Federation. A petition for its use in medicines is under consideration. In the UK, the Thaumatin protein has been listed as a safe excipient in medicines when accompanied by the appropriate product license as determined by the UK Committee on the Safety of Medicines in 1981. In 1982 the Food Additive and Contaminants Committee agreed to regulate Thaumatin protein as a sweetener. The Sweeteners in Food Regulations took effect in 1983 permitting the use of Talin protein in foods, drinks, and dietary products with the sole exception of baby foods.\textsuperscript{[65]} In the United States the Flavor Extract Manufacturers Association (FEMA) has designated Thaumatin protein as GRAS (generally regarded as safe) as a flavor adjunct in chewing gum.\textsuperscript{[65]} The FAO/WHO JECFA set specifications in 1983; in 1985 they agreed it was safe for food use and designated at ADI of "not specified" in its 29th Report. Petitions are pending in various other countries for use of Thaumatin protein as a flavor enhancer and sweetener.

**Xylitol**

Xylitol is found naturally in small amounts in a variety of fruits and vegetables. It is also formed naturally in the body as an intermediate in glucose metabolism through the glucuronate cycle in the liver.\textsuperscript{[66, 12]} It was first synthesized and described by Emil Fischer and his associates in 1891.\textsuperscript{[66]} Xylitol is produced synthetically by chemical conversion of xylan which has been extracted from birchwood, almond shells, straw, corn cobs, or wastes from the pulp and paper industries. Xylan is first hydrolyzed to xylose which is then hydrogenated to xylitol in the presence of a nickel catalyst.\textsuperscript{[19]} Xylitol is more chemically inert than sucrose and thus pharmaceutical preparations made with xylitol have good shelf life because they neither ferment nor mold. Xylitol is a good carrier for tablets because of its low melting point (92-96°C). Stable at 120°C and under normal food processing conditions with no caramelization; caramelization occurs if heated for several minutes near boiling point of 216°C (760 mmHg).\textsuperscript{[66]} Xylitol has been used in an aspartame:xylitol mixture 2.4 : 97.6 to provide a taste more like that of sucrose and to improve the stability of aspartame.\textsuperscript{[9]} Solid dispersions of some drugs with xylitol showed a faster release than micronized drugs. Xylitol is also used in parenteral nutrition because it has little effect on insulin and thus does not suppress lipolysis.\textsuperscript{[66]} Xylitol is not fermented by most oral microorganisms and plaque pH is not reduced upon exposure to xylitol.\textsuperscript{[19]} Xylitol is generally considered noncariogenic and may be anticariogenic. Under certain conditions, it reduces the cariogenic potential of sucrose.\textsuperscript{[67]} Xylitol taken orally does not increase blood glucose or insulin levels, probably because conversion of xylitol to glucose is very slow.\textsuperscript{[66]} It may affect mineral absorption and
Xylitol has been found to have low acute toxicity by all routes of administration. It is not embryotoxic, teratogenic, mutagenic, or clastogenic. Xylitol is used as a sweetener in non cariogenic confectionery such as chewing gum, candies, chocolate and gum drops, and in foods for diabetics. It is also used in pharmaceutical preparations, including tablets, throat lozenges, multivitamin tablets, cough syrup and toothpaste. The JECFA assigned an ADI of “not specified” in its 27th report in 1983. For xylitol, label designation E 967, the proposed level is quantum satis. In the United States, it is approved as a food additive for special dietary or nutritional uses as long as the amount used does not exceed that needed to produce the intended effect.

HFCS

HFCS is a carbohydrate sugar. It provides 4 calories (17 kilojoules) per gram. HFCS is made from corn and is used to sweeten most caloric sparkling beverages in the United States and some other countries. High fructose Corn Syrup (HFCS 55, Isoglucose) contains both fructose and glucose, commonly in a ratio of 55% fructose to 45% glucose. Fructose and glucose both have the molecular formula \( C_6H_{12}O_6 \), although the atoms are in different arrangements. High fructose corn syrup is a viscous liquid. Because of the fructose content, high fructose corn syrup does not tend to form crystals, as sucrose syrups do. The level of sweetness depends on the extent to which glucose has been converted to fructose: glucose is less sweet than sucrose (table sugar), and fructose is sweeter. The 55:45 ratios create a sweetness that is about equal to that of sucrose. High fructose corn syrup is produced from corn starch. Starch is a polymer made of glucose molecules linked into long chains. Corn starch is first treated with the enzymes alpha-amylase and glucoamylase. These break the starch down to glucose. The glucose is then treated with another enzyme, glucose isomerase that can reversibly convert glucose to fructose. At the end of this step, the mixture usually contains about 42% fructose and 58% glucose. A separation step produces syrup containing about 90% fructose, and this can be blended with the 42% fructose material to make the 55% fructose syrup that is widely used in beverage manufacture. Corn syrup is primarily used as a food product. In the United States, its production and use falls under the control of the federal Food and Drug Administration (FDA) that sets rigid quality standards. The corn refiners, working through the Corn Refiners Association, have developed comprehensive analytical procedures for testing the properties of corn products, including corn syrup. Some of the important properties of corn syrup are dextrose or fructose content, carbohydrate composition, solids content, sweetness, solubility, viscosity, and acidity. In addition to
monitoring the materials and processes used to make corn syrup, manufacturers also take frequent samples of the finished product for analysis.\(^{[77]}\) A pilot study reported that some high-fructose corn syrup manufactured in the U.S. in 2005 contained trace amounts of mercury. The mercury appeared to come from caustic soda and hydrochloric acid, two chemicals used in the manufacture of high-fructose corn syrup. It has been found that caustic soda used by HFCS has been produced in industrial chlorine chlor-alkali plants using the mercury cell Castner-Kellner process, and can contain traces of mercury. Mercury concentrations in the samples testing positive ranged from 0.012 μg/g to 0.570 μg. Of 55 major brands with high fructose corn syrup as a main ingredient, 1 in 3 tested positive for mercury. With the average U.S. citizen consuming 28.5 kg of HFCS annually, health effects are an obvious concern.\(^{[77]}\)

When it comes to satisfying your appetite, HFCS is as effective as table sugar. In fact, two 2007 studies comparing sparkling beverages sweetened with HFCS or sugar showed no difference in hunger, satiety or short-term energy intake.\(^{[78, 79]}\) The American Medical Association recently confirmed that HFCS is no more likely to contribute to obesity than table sugar or other full-calorie sweeteners.\(^{[80]}\)

**Sorbitol**

Sorbitol was first isolated in 1872 from the berries of the mountain ash tree by French chemist Joseph Brussingault. Sorbitol is widely distributed in nature.\(^{[81]}\) Sorbitol is more heat stable than the corresponding mono- and disaccharides and is more resistant to microbial degradation than the sugars. It does not caramelize due to the absence of free carbonyl groups.\(^{[19]}\) Sorbitol is very hygroscopic. It is stable at high temperatures with a melting point of 96-97°C.\(^{[81]}\) It is stable to sterilization by autoclaving.\(^{[20]}\) Sorbitol is more heat stable than the corresponding mono- and disaccharides and is more resistant to microbial degradation than the sugars.\(^{[70]}\) It does not caramelize due to the absence of free carbonyl groups. Sorbitol is very hygroscopic. It is stable at high temperatures with a melting point of 96-97°C.\(^{[81]}\) Sorbitol is slowly absorbed from the gastrointestinal tract by passive diffusion. Part is oxidized, mainly in the liver, to fructose, catalyzed by sorbitol dehydrogenase.\(^{[20, 81, 82]}\) The fructose is then converted to fructose-1-phosphate, catalyzed by fructokinase in a step that is not dependent on or regulated by insulin. The fructose-1-phosphate is metabolized in the liver to dihydroxyacetone phosphate and glyceraldehyde. The dihydroxyacetone phosphate is metabolized either to pyruvate or to glucose and glycogen, depending on the metabolic state.
of the person.\[81]\) Some sorbitol can undergo direct conversion to glucose in the presence of the enzyme aldose reductase.\[81, 82]\) The portion that reaches the distal intestine is partially or completely fermented by the intestinal flora to short-chain volatile fatty acids which are then absorbed from the gut and metabolized.\[82]\) The presence of sorbitol in the small intestine can result in osmotic diarrhea, especially in large amounts.

CONCLUSION
The artificial sweeteners are to be used as per their sweetness criteria and safety levels, there are useful in many cases but precaution should be taken for their use.

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