

ARTIFICIAL SWEETENERS

Most of us love sweets. There isn't much doubt about that. Our palates lust for ice cream, our mouths water at the thought of glazed donuts, our parched throats yearn for soft drinks, while visions of sugar plums dance in our heads. To satisfy these craving, we down about one hundred pounds (45 kg) of sugar per person per year. That's about 120 grams per day. Surprised? Well, the truth is that sugar is not all that sweet. About eight spoonfuls are required to sweeten one can of pop. So much sugar is not exactly ideal for our teeth or for our waistline. There have even been some controversial suggestion that excessive sugar consumption may play a role in certain degenerative diseases. So artificial sweeteners and artificially sweetened products continue to attract increased consumer interest.

The replacement of sugar by artificial sweeteners in the diet may be of importance in weight reduction, in the maintenance of dental health, and in making available a greater variety of foods for diabetics. There are five artificial sweeteners used in Canada today. Aspartame (trade names "Equal" and "NutraSweet") is allowed as an additive in a large number of foods and also as a tabletop sweetener, while cyclamate ("Sweet & Low") and saccharin ("Sucaryl") are allowed only as tabletop sweeteners. Sucralose ("Splenda") is allowed as a tabletop sweetener as well as an additive to a limited number of products, as is acesulfame-K.

In the U.S., cyclamate has been banned since 1970, but saccharin and aspartame can both be used as additives or as tabletop sweeteners. Acesulfame-K is also allowed.

Saccharin, the cyclamates, and aspartame were all discovered through lucky accidents. In 1879, Constantine Fahlberg, a chemist working at John Hopkins University in Baltimore, linked an unusual sweetness in a slice of bread he was eating to a chemical residue on his hands from the lab. Eventually, he traced the sweetness to "benzoyl o-sulfonamide" which was given the name "saccharin". Fahlberg soon became wealthy but his reputation suffered greatly when he applied for patents in secret and refused to give any credit to his research director, Ira Remsen, under whose guidance he was working when the serendipitous discovery was made.

In 1937, Michael Sveda, working on antibacterial substances at the University of Illinois, noted a sweet taste on a cigarette he had placed on a bench top and discovered the sweetening power of cyclamate. Similarly, aspartame was discovered in 1965 when James Schlatter, a researcher at Searle Laboratories, licked his finger while engaged in work on anti-ulcer medications.

Artificial sweeteners are among the most controversial food additives due to allegations of adverse health effects. These allegations include dermatological problems, headaches, mood variations, behaviour changes, respiratory difficulties, seizures, and cancer. A very large number of studies on these substances have been carried out with conclusions ranging from "safe under all conditions" to "unsafe at any dose". Scientists are divided on the issue of artificial sweetener safety, and in many cases researchers seem to arrive at results that confirm their own personal views. In scientific, as well as in lay publications, supporting studies are often widely referenced while the opposing results are de-emphasized or dismissed.

The general conclusion is that artificial sweeteners, when used in moderate amounts, represent a minimal risk. Abusive amounts, which are not rare, are associated with increased but still low risk. Most importantly, however, the risk-benefit ratio of artificial sweeteners is unclear. A number of studies have shown that the use of sweeteners is not associated with weight loss. Apparently, people saving on calories by using artificial sweeteners are so proud of themselves that they indulge on other foods. The elimination of sugar from soft drinks is beneficial in terms of the dental health of children, but it would make more nutritional sense to greatly reduce the over 40 gallons per person per year rate of consumption of soft drinks altogether. One area where artificial sweeteners do afford real benefits is to diabetics, by allowing them to eat foods which otherwise would have to be severely restricted.

Saccharin

Saccharin is about 300 times sweeter than sugar and can be called a true “non-caloric” compound since it is eliminated by the body intact - without undergoing chemical degradation or metabolism. It does have a disagreeable aftertaste which can be minimized by the addition of a small amount of the amino acid, glycine, or by combining it with cyclamate. Sugar contributes not only sweetness but also “body” to a beverage. When sugar is replaced by an artificial sweetener, thickeners such as gum arabic or carboxymethyl cellulose are often used to impart a proper mouthfeel.

In 1972, saccharin was removed from the “Generally Recognized as Safe” list in the U.S. when experiments showed a possible link with bladder cancer in rats. This meant that the additive was now subject to the “Delaney Clause”, which had been part of an amendment to the Federal Food, Drug, and Cosmetic Act in 1958. This clause states that any additive which in any dose causes cancer in any species of animal has to be immediately banned. However, the accusatory evidence was judged to be inconclusive and saccharin use was allowed until further research either confirmed or refuted the evidence. Follow up studies on rats, mice, hamsters, and monkeys were negative except for one case in which there was an increased incidence of bladder cancer in male rats fed high lifetime doses of saccharin if, and only if, their parents had also been fed similar high lifetime doses. These doses made up 5% of the rat’s diet and were the equivalent of a human consuming 800 cans of diet drink per day. This, of course, is a very large amount, but the technique of feeding large doses to rats over a short time span is a scientifically accepted method of estimating what might happen in humans exposed to small doses of the substance over a much longer period.

When Canadian studies, in 1977, showed that the bladder cancer was indeed caused by saccharin and not an impurity as some had suggested, the Canadian government banned the use of saccharin as an additive. In the U.S., public and industry pressure forced Congress to pass the “Saccharin Study and Labelling Act”, which put a moratorium on a ban as would have been dictated by the Delaney Clause. This moratorium has been repeatedly extended. Since saccharin costs only about one twentieth as much as sugar, and since it allows for a greater variety of products and hence more shelf space, it is easy to see why the industry would oppose any restriction on the use of this high profit substance.

The cancer case against saccharin is by no means iron clad. A theoretical rationale for the induction of cancer is difficult, since saccharin passes through the body unaltered. The suggestion has been made that saccharin exerts its effects by temporarily attaching to and disrupting certain proteins. As mentioned before, only “double generation” studies in male rats have confirmed bladder cancer and, even in these cases, the incidence of tumours was seen to decline sharply with dose. The really worrisome aspects of carcinogenesis - that is tumours in several animal species, rapid tumour formation, and tumours in various organs - have never been associated with saccharin. Furthermore, human “case-control” studies have examined the lifestyle and dietary intakes of a large number of bladder cancer patients without revealing any link to saccharin. Neither have any studies found increased incidence of tumours among diabetics, a population sub-group which would be expected to be at increased risk due to their extensive use of artificial sweeteners. It is likely then, that any but a vanishingly small effect of saccharin on the incidence of human bladder cancer would have been detected. The possibility exists that saccharin is a “co-carcinogen”, that is, a substance which may initiate cancer in cells which have already been exposed to some other carcinogen. In this context, it should be pointed out that there are many naturally occurring substances in our diet (for example, the amino acid tryptophan) which are known to promote cancer at high doses but represent no risk at all as part of a normal diet. In all likelihood, this is also the case with saccharin. Calculations based on the available animal models show a “worst case scenario” of a one in a million increased risk of bladder cancer due to the consumption of two saccharin sweetened beverages a day over a lifetime.

Cyclamates

Three similar compounds, namely sodium cyclamate, calcium cyclamate, and cyclamic acid, are collectively referred to as the “cyclamates”. They are about thirty times sweeter than sugar and are chemically more stable than saccharin or aspartame. Some of a cyclamate dose is excreted by the body unchanged, but some is converted to a cyclohexylamine, a compound whose safety has been questioned. Like saccharin, cyclamates were granted “Generally Recognized as Safe” status in the U.S. in 1958 based on years of apparent problem free use. This status was rescinded in 1969 when bladder tumours were discovered in rats which had been fed a cyclamate-saccharin (10:1 ratio) mixture. Since saccharin was a minor component of this mixture, cyclamates were implicated in the tumour formation.

The 1969 study by the independent Food and Drug Research Laboratories was widely criticized, and never reproduced with a statistically significant number of animals. In fact, more recent studies on rats, mice, dogs, hamsters, and monkeys, using both cyclamates and their decomposition product, cyclohexylamine, have shown no effect on cancer rates. Indeed, unlike saccharin, the question of whether cyclamates are carcinogenic or co-carcinogenic at all, has not been adequately answered. Neither has the allegation that cyclamates are mutagenic, that is, capable of producing genetic damage which can be inherited, been substantiated.

The only reproducible effect of cyclamates has been testicular atrophy in rats when fed large doses. This problem, which has not been seen in humans, is caused by the metabolic product cyclohexylamine. Taking into account the maximum dose at which no such effect is observed in rats, and building in a hundred-fold safety factor, it is possible to arrive at an “Accepted Daily Intake” of cyclamate which represents an insignificant risk. Accordingly, the Health Protection Branch in Canada allows cyclamate as a tabletop sweetener. The U.S. ban on cyclamates is still in effect, but may be rescinded in light of the fact that the Food and Drug Administration has reviewed the large number of studies submitted to it in the 1980s and has concluded that neither cyclamates nor cyclohexylamine are carcinogens.

Aspartame

Aspartame can not be considered a “non-caloric” sweetener since it is broken down in the digestive tract into its components which are absorbed and metabolized. These components, aspartic acid, phenylalanine, and methanol, account for the 4 Calories per gram energy rating of aspartame. However, since the substance is about 180 times sweeter than sugar, very little needs to be used in foods and beverages to achieve a satisfactory degree of sweetness. Diet drinks normally contain about 60 milligrams per 100 millilitres. Which translates to roughly 200 milligrams per serving. The average total consumption is about 500 milligrams per day - replacing 90 grams of sugar intake and reducing calories to 2 Cal from 360 Cal. Aspartame can not be used in cooked or baked foods since it breaks down into its components and loses its sweetening power.

Aspartame is the most widely researched food additive to have ever come on the market. As with any other newly introduced substance, reports of adverse reactions were expected since no amount of testing can preclude idiosyncratic reactions in a small minority of the population. In reality, the number of such reports has been unusually small. Over 70 million people in North America use aspartame on a regular basis, yet the number of reported complaints average only around three hundred per year. The majority of these complaints (67%) refer to headaches, dizziness, visual difficulties, and mood alterations. Gastrointestinal problems (24%) and allergic symptoms such as hives, rashes, and swelling of tissues (15%) have also been reported. On occasion, seizures have been linked with aspartame exposure. In most instances, these difficulties were noted only with amounts of aspartame exceeding normal use.

Double blind challenges have been carried out with aspartame. At Duke University, in one of the best designed of these study, the effects of a single large dose of aspartame in people who had claimed to be sensitive to the substance was investigated. The results showed no difference in headache frequency, blood pressure, or blood histamine concentrations (a measure of the allergenic potential) between the experimental and control groups.

In another study which involved diabetics, at the University of Illinois, subjects in the placebo group actually had more reactions than those in the aspartame group. On the other hand, surveys by physicians in headache clinics reveal that aspartame precipitates headaches about 8% of the time. This kind of conflicting data is characteristic of the research on the possible side effects of aspartame. Reported anecdotal experiences are not confirmed by carefully controlled scientific studies. This, of course, does not mean that the problems are not real, but it does imply that in many cases the symptoms may not be caused by aspartame itself. People get headaches, upset stomachs, aches, and pains of all kinds on a regular basis for no easily discernible reason. If they recall having consumed aspartame when one of these ailments strikes, the sweetener may be judged to be guilty by association. This is even more likely if people are familiar with some of the adverse publicity that aspartame has received.

At least one study has, however, confirmed allergic symptoms such as hives and swelling in sensitive individuals. It is unclear how the allergy comes about, since none of the components of aspartame are believed to be capable of producing allergic reactions. It has been suggested that diketopiperazine, a compound which forms when aspartame decomposes, may be responsible.

A number of theoretical possibilities have been advanced to account for aspartame associated problems. The three breakdown products of aspartame are all toxic in high doses. Phenylalanine is an essential amino acid which must be included in the diet for normal growth and maintenance, but sustained high blood levels can lead to brain damage. This is of major concern to the one out of roughly twenty thousand children who are born with an inherited condition called "phenylketonurea" or PKU. These children can not metabolize phenylalanine, which then builds up to dangerous levels in their brains. The condition, therefore, necessitates a severe curtailment of phenylalanine intake for at least the first six years of life. This means that aspartame, due to its phenylalanine content, is not suitable for PKU sufferers and consequently requires a warning to that effect on products in which it is an ingredient.

In the general population, the amount of phenylalanine in the blood after aspartame ingestion is in the same range as after eating any protein containing food. Even at abusive amounts, equivalent to a child swallowing 100 sweetener tablets, levels do not rise above those which are considered to be safe in children afflicted with PKU. Dr. Richard Wurtman, a noted MIT researcher, has suggested that some of the untoward effects of aspartame may be caused by a sudden increase in brain phenylalanine levels, especially when the sweetener is consumed along with foods high in carbohydrates. Carbohydrates trigger insulin release into the bloodstream which, in turn, makes it easier for phenylalanine to be absorbed by the brain. According to Wurtman, such a sudden increase in brain phenylalanine levels can cause depression, sleep problems, headaches, and even seizures. These ideas have not been confirmed in human studies and Wurtman, who uses aspartame moderately himself, feels the problem is only significant when consumption of aspartame is unnecessarily high.

The effects of aspartic acid, another aspartame breakdown product, has also been rigorously examined. Administration of extremely large amounts to non human primates produced no damage even though blood levels were greatly elevated. In humans, even high doses are quickly eliminated. Most significantly, aspartic acid levels in the blood are not increased after eating aspartame containing foods or when drinking sweetened beverages even at the rate of three drinks in four hours.

Perhaps the most unscientific accusations levelled at aspartame have involved its methanol content. It is a fact that in large doses, methanol can lead to blindness and even to death. Alarmists have therefore referred to the methanol which is released from aspartame as an "unsafe" substance. It must be remembered, however, that there are no safe substances, only safe doses. The amount of methanol which can be released from aspartame is inconsequential in the context of the overall diet. Methanol occurs naturally in foods. In fact, the "natural" methanol content of fruit juice is about 2.5 times higher than from aspartame sweetened drinks. Even at the 99th percentile level of 34 mg per kg of body weight consumed per day, blood levels of methanol are undetectable.

A study published in 1996, claiming that a 10% increase in brain tumours noted in the 1980s was associated with the introduction of aspartame, received a great deal of publicity. The suggestion was that aspartame or its diketopiperazine breakdown product may combine with nitrites in the diet to form nitrosated

compounds. Nitrosoureas are indeed known to produce brain tumours in animals. But the manufacturer of aspartame (The NutraSweet Co.) points out that while aspartame use has increase dramatically since the 1980s, brain tumour rates have not experienced a corresponding increase. Furthermore, they say, the increase in brain tumours noted in the earl 1980s occurred before aspartame was introduced. Still, a number of objective scientists are calling for a review of the safety of aspartame, especially when noting that most of the studies showing aspartame to be safe were industry funded. By contrast, none of the studies that raised concerns were funded by the industry.

Sucralose

They tortured that poor molecule. They heated it, they froze it, they dissolved it in acid, they baked it into cakes, they fed it to rodents, and they stuffed it into people's mouths. They even made it radioactive so they could follow its path through an animals' body. Then they extracted it from the rodents' excrement to see how it fared. And it fared well. In fact, it passed every indignity with flying colours. As a result, we now have a new artificial sweetener trying to grab its share of the market. Sucralose, or "Splenda" as it is known in the trade, is ready to sugar coat our lives, but without actually using sugar.

The classic problem, facing any of the other artificial sweeteners, is that none have measured up in a completely satisfactory way to sugar. Aspartame is not stable in acidic conditions or when heated. This represents a significant problem for diet drink manufacturers and for baking. Saccharin and the cyclamates are sweet enough but leave an after taste. And then there are the lingering health concerns.

As described above, aspartame can not be used by consumers who have an inherited condition called "phenylketonurea" because of their body's inability to metabolize phenylalanine, one of the breakdown products of the sweetener. Saccharin and the cyclamates, in turn, have had to cope with the shadow of cancer. Some studies, probably of no relevance to humans, have suggested a slightly elevated risk of the dreaded disease when test animals were fed massive amounts of the sweeteners. In any case, the nutritional world was primed for a new sweetener.

The compound was created in a laboratory at Queen Elizabeth College, University of London, in 1976. The researchers studying the chemical reactions of ordinary table sugar, or sucrose, certainly did not have artificial sweeteners on their minds. But when the managed to incorporate three chlorine atoms into a sucrose molecule, they aroused a sugar company's interest.

A company representative called one of the researchers to ask for a sample to be tested. As luck would have it, the young foreign chemist misunderstood and thought the request was for a sample to be "tasted:. So, with some bravado, he popped some of the chlorinated sugar into his mouth. He told his supervisor about the sweet experience, who then quickly seized the moment and redirected the laboratory's research efforts in this new direction. Sucralose, as the new compound came to be called, turned out to be six hundred times sweeter than sugar.

However, may years of testing faced the excited chemists before the new product could be brought to market. Their enthusiasm increased when sucralose turned out to be water soluble as well as stable to heat and acid. This meant that it could easily be used in diet drinks and baked goods. Then came the all important safety tests. For fifteen years, sucralose was subjected to a battery of both short and long term animal feeding studies. The results are conclusive. Sucralose simply was excreted unchanged. Every bit the animals were fed could be recovered in their excreta. Any concerns about storage in the body or interference with metabolic pathways now essentially evaporated. However, while our bodies can no break down sucralose, microorganisms in water and soil readily do so. In other words, the stuff is biodegradable and poses no environmental hazard. The results look good and you can rest assured that they haven't been "fudged", because that is the one thing that sucralose is not good for - making fudge. It comes out much too liquidy. But in every other area, sucralose seems to hold great promise.