International Sweeteners Association

Low Calorie Sweeteners:
Roles and Benefits

Version • September 2013

This booklet has been developed for healthcare professionals and is designed to provide factual information on low calorie sweeteners, their characteristics, the evidence supporting their safety and how they can help manage calorie intake. It is based on publicly available science, with references and contributions from internationally recognised experts.

International Sweeteners Association

Introduction

Low calorie sweeteners are ingredients used in a growing number of foods and drinks, both in Europe and globally. As humans, we have an innate preference for sweet taste. However, with food plentiful in developed countries and more people leading sedentary lifestyles, this preference for sweetness is something we need to manage more effectively than ever before. High obesity rates show that more people need to focus on active, healthy lifestyles and energy balance – that is, balancing the calories consumed with the calories burned through physical activity.

The health and financial impacts of treating obesity are a cause for concern. In recent years there has been a steady and significant increase in consumer demand for low calorie products. As a result there is growing interest among healthcare professionals and the general public to learn more about low calorie sweeteners, the foods and drinks in which they are found, how they help to reduce calorie intake and contribute to weight management and improved overall health.

Some individuals have claimed that the consumption of one low calorie sweetener in particular, aspartame, is linked to various adverse health effects. These claims have sometimes been amplified by the media, raising concern among some consumers.

Numerous regulatory bodies worldwide, including the European Food Safety Authority (EFSA), have reviewed the extensive science about aspartame and all have concluded these claims are without substance and that it is a safe food ingredient. Nevertheless, many people seek guidance from health experts about whether or not to include low calorie sweeteners in their diet. Written for healthcare professionals, this booklet provides detailed information about low calorie sweeteners, the evidence supporting their safety, and how they can act as an aid to weight reduction and maintenance. It is based on publicly available science, with references provided.

Low calorie sweeteners: Role and Benefits is supported by contributions from a group of eminent scientists and doctors who have undertaken a significant amount of research in the area of low calorie sweeteners, toxicity, epidemiology, appetite/satiety and weight management.

We hope you find this booklet useful and that it will serve as a valuable reference tool in your daily work.

Contributors

Leading scientists and researchers working in the areas of toxicology, epidemiology, satiety and weight management have reviewed the content of this booklet and provided answers to the most frequently asked questions about low calorie sweeteners from their expertise:

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Professor Renwick's work on species differences and human variability in metabolism and kinetics in relation to the safety factors used in risk assessment led to World Health Organisation (WHO) initiatives to develop chemical-specific adjustment factors. In 2002 he received the George H. Scott Memorial Award from the Toxicology Forum. He retired from the University of Southampton in September 2004.

He has published over 160 original research papers and 35 book chapters and other contributions on the metabolic fate of medicines and other foreign chemicals, on what happens to chemicals in the body, on food chemical safety and on low calorie sweeteners. He has served as a member of a number of UK Government Advisory Committees, and he was awarded an Officer of the Order of the British Empire (OBE) in the New Year Honours List in 2000. He was a member of the European Food Safety Authority's (EFSA) Contaminants Panel for 2 years and has attended The Joint Expert Committee on Food Additives (JECFA) as a WHO temporary advisor for the past decade.

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Dr Drewnowski is the Director of the Center for Public Health Nutrition and the University of Washington Center for Obesity Research and a joint member of the Fred Hutchinson Cancer Research Center in Seattle.

Dr Drewnowski develops new methods and measures to explore links between food and diet quality, price, and sustainability. He is the author of the Nutrient Rich Foods Index, which ranks foods based on their nutritional value and helps to identify affordable healthy foods. The Seattle Obesity Study (S.O.S.), led by Dr Drewnowski, applies spatial analyses to survey research in helping to determine who buys what foods, where, why and for how much. Dr Drewnowski has conducted numerous studies on hunger, appetite and satiety to determine how different nutrients and food ingredients can help in the management of body weight.

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Dr La Vecchia received his medical degree from the University of Milan and a Master of Science degree in clinical epidemiology from the University of Oxford, UK. He is recognised worldwide as a leading authority in cancer aetiology and epidemiology with over 1,470 peer-reviewed papers published. Dr La Vecchia serves as an editor for numerous clinical and epidemiologic journals.

Dr La Vecchia is also an Adjunct Professor of Medicine at Vanderbilt Medical Center and the Vanderbilt-Ingram Cancer Center and Adjunct Professor of Epidemiology at the University of Lausanne, Switzerland as well as on the faculty of Medicine at the University of Milan. He is a temporary advisor at the WHO's International Agency for Research on Cancer (IARC) and at the World Health Organisation in Geneva.

Contents

The Development of Sweet Taste

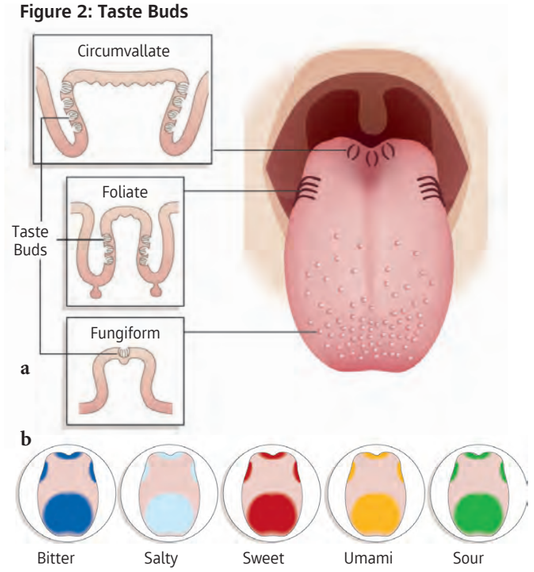
The sense of taste is of immense importance in the lives of animals and humans as it determines food choices and influences the amounts consumed[1]. Taste, in conjunction with other senses, plays a crucial role in decisions about whether a potential food will be accepted or rejected, while ensuring the intake of sufficient nutrients. In humans, taste has the additional value of contributing to the overall pleasure and enjoyment of a food or drink.

There are five basic tastes[2] (Figure 1): **Sweet taste** permits the identification of energy-rich nutrients; **Umami taste** allows the recognition of savoury amino acids (protein-rich foods); **Salty taste** ensures proper dietary electrolyte (mineral) balance; **Sour** or **Bitter tastes** warn against the intake of potentially noxious and/or poisonous substances.

The taste system is complete at birth. Anatomically complete taste buds and olfactory neurons can be identified in the human foetus by the 15th week of gestation, while olfactory neurons are apparently functional by about the 25th week. Although it is difficult to establish at what stage in gestation the foetus actually begins to experience taste and flavour, it has been known for more than 150 years that premature infants respond to some tastes[6].

Figure 1: Five Basic Tastes

Figure 2: Taste Buds



Taste buds across different papillae of the tongue (a), which reveal that there is no 'tongue map' and all five tastes are present in all areas of the tongue (b).

The sensation of taste results from the chemical stimulation of specialised cells called Taste Receptor Cells (TRCs), which are grouped in small clusters called taste buds. Taste buds can be found throughout the oral cavity, but are mainly located on the human tongue. Taste buds are composed of 50-150 TRCs (depending on species) and are distributed across different papillae (Figure 2).

Circumvallate papillae are found at the very back of the tongue and can contain hundreds (for mice) to thousands (for humans) of taste buds. Foliate papillae are present at the posterior lateral edge of the tongue and contain a dozen to hundreds of taste buds. Fungiform papillae contain one or a few taste buds and are found in the anterior two-thirds of the tongue (Figure 2).

It was thought for a long time that different parts of the tongue were sensitive to different tastes. Recent molecular and functional data have revealed that, contrary to popular belief, there is no *'tongue map'*. Responsiveness to the five basic tastes – sweet, salty, sour, bitter and umami – is present in all areas of the tongue[2,5].

From birth, taste and familiarity influence behaviour toward food. Scientists have proven that a liking for sweetness and a dislike for bitterness at birth are innate human traits6, 8. Taste preferences and food aversions develop later in life, through experiences that are influenced by our attitudes, beliefs and expectations[7,8].

Responsiveness to Sweetness

Responsiveness to sweetness is a primitive response, observable even in the simplest of organisms[12]. In humans, sweet taste exerts a profound influence on behaviour[12]. The innate pleasure response to sweet taste, observable at birth, serves to orientate the feeding response and provides a motivation for continued feeding[13].

Scientists believe that our preference for sweetness may be an evolutionary survival mechanism, ensuring the acceptance of breast milk, with its slightly sweet taste from the milk sugar lactose, the primary carbohydrate found in human milk.

The most convincing scientific evidence for this in humans comes from studies of premature and newborn infants that demonstrate conclusively, using a variety of different research techniques, that infants are sensitive to and prefer sweetness on their very first tasting[14,15].

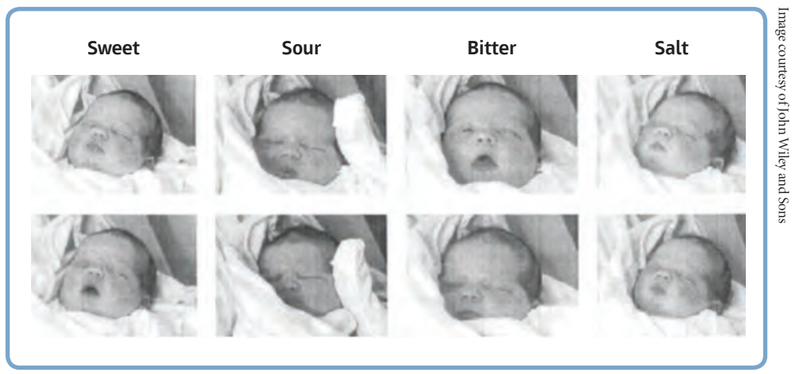
Investigations of newborns' taste responses have uniformly indicated that they respond even to dilute sweet tastes, are able to differentiate varying degrees of sweetness and will consume more of a sweet-tasting sucrose solution when compared to water[9,10,14-17].

Several findings support the conclusion that positive facial expressions elicited by sweet tasting substances are reflex-like. Firstly, single response components, such as tongue movements, can be reliably elicited in newborns by sweet tastes in a concentration dependent manner[16,17].

Secondly, infants born with severe developmental malformations of the central nervous system react to the sweet taste like a normal term-born infant[17]. Consistent with the above observations for intake and facial expression, infants can express that they perceive and respond positively to sweet stimuli via a variety of other behaviours[11,18-20].

Studies performed in the 1990s using sweet taste solutions of sugar and the low calorie sweetener aspartame showed that they encourage mouthing and sucking movements and hand-to-mouth contacts, both of which are feeding-related behaviours[18,21].

Figure 3: Infant Facial Expressions



Facial expressions, elicited from a 3-day-old infant, which suggest contentment and liking or discomfort and rejection, have been used to assess the newborn's responsiveness to taste stimuli in some of the earliest investigations on human taste development[18].

The innate Human preference for sweetness should be managed with care.

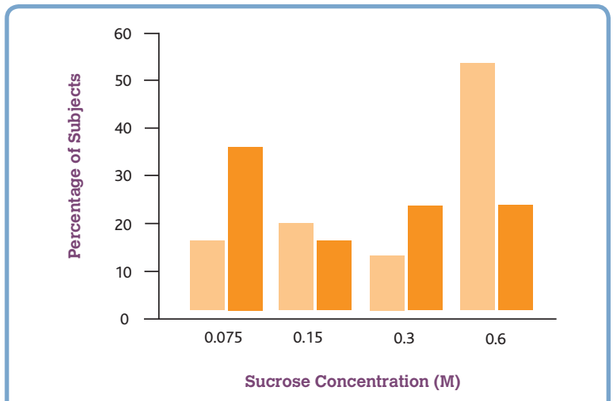
The Preference for Sweetness Beyond Infancy

Sweetness makes foods more appealing and is often used to introduce new foods into children's diets[19,36]. Children learn to accept new tastes and flavours when they are associated with sweetness or with energy-dense nutrients, such as starch[23].

It is important to highlight that preference for very sweet solutions continues during childhood and adolescence[24] and gradually decreases by early adulthood, as shown by both cross-sectional and longitudinal studies[25].

The evidence to date suggests that, on average, children and adolescents prefer higher sucrose (sugar) concentrations in water than adults[24, 25, 26, 27,36].

Figure 4: Preference for Sweetness



Evolution of preference for sweetness with age. Percentage of subjects selecting each concentration of sucrose as their most preferred, when they were 11-15 years old and when they were 19-25 years old [25].

The pleasure reaction to sweet taste is observed across individuals of all ages, races, and cultures

In 1999 De Graaf & Zandstra[26] showed that 9 to 10-year-old children preferred higher concentration levels of sugar in water and lemonade than adolescents (14 to 16-years-old) who, in turn, liked sweetness more than young adults (20 to 25-years-old).

One plausible biological explanation is that children require more energy than adults and that sweetness preferences are a marker for biological growth. In general, sweetness preferences decline once growth is completed[26].

Ageing

Sweet taste preferences persist from birth until old age, although the liking of intensely sweet taste declines substantially between early childhood and adult life. Fewer studies have been conducted on sweet taste preferences in the elderly, although anecdotal reports suggests that the liking for sweetness increases in older people. The evidence suggests that adults have a reduced preference for sweet substances, preferring less intensely sweet foods and drinks compared to children[26, 28-30].

The ability to detect and perceive sweet taste shows remarkable stability across the lifespan. On average, an individual's ability to detect the sweet taste of sugars and to judge taste intensity is little changed between 20 and 80 years of age[28]. By contrast, sensitivity to smell sharply declines with age, robbing some elderly persons of the ability to enjoy the flavour and aroma of foods. Since aroma is a major component of taste, the decline in olfactory ability means that older adults may rely more on sweetness for their enjoyment of foods. However, preferences for sweetness never disappear. Even in old age, sweetness provides the motivation to eat [36].

Q&A

Why do we like sweet tasting foods and drinks?

Dr Adam Drewnowski: The liking of sweet taste is a universal human trait. Infants, children, and teenagers of all races and cultures find sweet foods and drinks highly appealing. By associating pleasant taste sensations with nourishment, nature made sweetness a powerful driver of human eating behaviour. The taste response to sweetness was essential to survival. By contrast, bitter taste, associated with toxic compounds, was nature's signal for dietary danger and led to instant food rejection by the child.

Whereas young children like very sweet tastes, adults do not. Sweet taste preferences typically decline once the child is grown. Adolescents and adults prefer less intensely sweet foods, experiment with other flavours, and even learn to tolerate bitter taste. However, preferences for sweetness never disappear. Even in old age, sweetness provides the motivation to eat.

Sweet Taste and Today's Lifestyles

Our diets and food production have changed significantly since early humans hunted for and gathered food. Today's rigorous food safety standards mean that we no longer need to rely on sweet taste to act as a screening mechanism to identify foods that are safe to eat. In fact, many food and drink delicacies are bitter, salty and sour due to evolving consumer preferences. However, throughout time, one thing has remained constant – our preference for sweetness.

Energy density of the diet is often perceived through the sensation of taste. Sweetness, the traditional sensory indicator of both nutrients and calories[31] adds to the sensory appeal of a given food. Indeed, the concepts of palatability and good taste have long been synonymous with the sweetness of foods.

Given a choice, young children prefer energy-dense foods over those that deliver fewer calories (kcal) per unit weight (g)[32,33]. The main reason is that the presence of sweetness also signals the presence of calories, a major physiological reinforcement for the active, growing child[35]. Energy density and palatability are therefore linked. In general, foods are palatable because their energy density is high[35]. For low energy density foods to be liked, they need to be sweet. In general, sweet fruits are preferred over low energy density foods that are not sweet (e.g. spinach). Sweetened yogurt is preferred over plain yogurt [32,33].

The human preference for sweetness should be managed with care. All foods and drinks can fit into a healthy, active lifestyle that includes a sensible, balanced diet and regular physical activity. However, high obesity rates in children and adults highlight the need for most individuals to balance calories consumed with calories burned during daily activities. While reducing the energy density of foods might seem a logical approach to the prevention of obesity, the fact is that a bulky low-energy diet has low sensory appeal for the consumer. As the energy density of foods decreases, so does palatability.

The modern food industry has managed to provide highly palatable foods and drinks with lower energy density[35]. One of the best examples is the development of food ingredients called low calorie sweeteners. These sweeteners are added to many foods and drinks, but their impact on drinks is potentially the most significant – they can reduce the energy content to zero, while maintaining both palatability and sweetness[35]. Foods and drinks sweetened with low calorie sweeteners represent a growing segment of the food supply.

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The Use and Role of Low Calorie Sweeteners

Low calorie sweetener is the term used to describe compounds that taste sweet and provide few or no calories, or compounds that have such an intensely sweet taste that they can be used in food products at concentrations low enough not to contribute significantly to caloric content[1].

All low calorie sweeteners have a much higher sweetening power than sugar. This offers one major advantage to food and drink manufacturers and ultimately consumers – sweet taste whilst eliminating or substantially reducing the calories in a food or drink.

Low calorie sweeteners are used in a variety of food and drink products including soft drinks, chewing gum, confectionery, frozen desserts, yoghurts, dessert mixes and puddings. They are also widely used in healthcare, making many medicines more palatable. Low calorie sweeteners are clearly labelled on the packaging of food, healthcare and drink products that contain them.

Low calorie sweeteners have been safely used and enjoyed by consumers all over the world for more than a century. The first commonly used low calorie sweetener, saccharin, was discovered in 1879. Since then, a number of other low calorie sweeteners, including acesulfame K (ace-K), aspartame, cyclamate and sucralose, have been discovered and are now in widespread use worldwide[2].

In the European Union (EU), the most frequently used low calorie sweeteners are acesulfame-K, aspartame, cyclamate, saccharin and sucralose. A detailed look at the key characteristics of these low calorie sweeteners can be found on pages 26 and 27.

Each low calorie sweetener used in food and drink production has its own unique taste profile, technical characteristics and benefits. Low calorie sweeteners can be used alone or in combination with each other as a blend. By combining two or more low calorie sweeteners, it is possible for food and drink manufacturers to tailor the taste and characteristics of sweetness to the demands of a product and consumers' tastes, whilst taking into account factors such as stability and cost.

When low calorie sweeteners are combined with each other they continue to be safe. Health authorities around the world have concluded that there is no scientific basis to expect any physiological effects to arise from the use of blends of approved sweeteners[1].

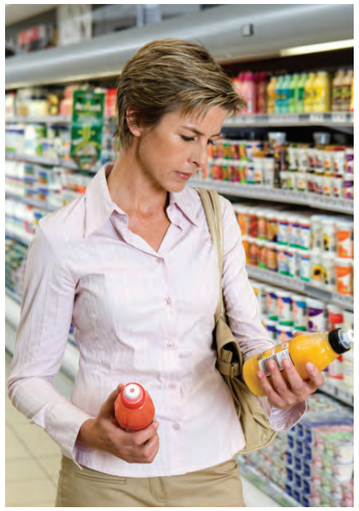
All of the low calorie sweeteners used in food production in Europe today have been subjected to rigorous safety testing [2–4]. This is discussed in more detail in the next section. The regulatory process for low calorie sweeteners is thorough and gaining approval of a new low calorie sweetener is time and cost intensive, with the very stringent approval process often taking from 10 to 20 years.

Today's more sedentary lifestyles and an increased interest in weight management mean that low calorie sweeteners can play an important part in achieving an active, healthy lifestyle. By replacing the equivalent sweetness of sugar without the equivalent calories and increasing palatability of healthy and low calorie foods, low calorie sweeteners, if used consistently to reduce calories, can act as an aid to weight reduction, weight maintenance and oral health. Furthermore, as low calorie sweeteners do not affect insulin levels, they may be used to provide sweet-tasting foods and drinks for people who must carefully monitor carbohydrate intake, such as people with diabetes. These benefits are covered in more detail on pages 16-20.

Low calorie sweeteners, if used consistently to reduce calories, can act as an aid to weight reduction, weight maintenance and oral health.

A New Low Calorie Sweetener

A new low calorie sweetener was approved for use in the EU in November 2011, called steviol glycosides - or purified stevia extract, derived from the leaves of the Stevia plant (*Stevia Rebaudiana Bertoni*). Native to Paraguay, Stevia belongs to the Chrysanthemum family. Steviol glycosides are 200 - 300 times sweeter than sugar and approved in several South American and Asian countries, with Japan being the highest consumer, followed by China and South Korea. The use of approved steviol glycosides is also permitted in the US. Steviol glycosides were first used in Europe in 2009, when they were approved for use as a sweetener in certain foodstuffs in France. After considering all the data on stability, metabolism and toxicology, the European Food Safety Authority (EFSA) established an Acceptable Daily Intake (ADI) for steviol glycosides, of 0-4 mg/kg bw/day.



In the EU, the most frequently used low calorie sweeteners in foods and drinks are ace-K, aspartame, cyclamate, saccharin and sucralose.

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Q&A

What are low calorie sweeteners?

Prof. Andrew Renwick: Low calorie sweeteners are substances added to foods and drinks to provide sweet taste without calories, or with very few calories. Most low calorie sweeteners are several hundred times sweeter than table sugar, meaning that only small quantities need to be added to achieve a sweetening effect.

Though they are generally referred to as low calorie sweeteners by the scientific community, they are sometimes also referred to as sweeteners, artificial sweeteners, intense sweeteners and non-nutritive sweeteners.

Which foods and drinks contain low calorie sweeteners?

A wide variety of products contain low calorie sweeteners, including soft drinks, dairy products such as yoghurt and ice cream, desserts, chewing gums, condiments such as salad dressing, mustards and sauces and many other products including chewable multivitamins, mouthwashes and cough syrups.

Why do some foods and drinks contain blends of low calorie sweeteners?

Prof. Andrew Renwick: Each low calorie sweetener has its own unique taste profile, characteristics and benefit. By using different blends of low calorie sweeteners, subtle taste options are also available. Food and drink manufacturers choose which low calorie sweetener to use, either on its own or as a blend, based on taste considerations, stability and cost. Blending low calorie sweeteners is safe and the use of a blend reduces the amount of each individual sweetener that would be needed to sweeten foods and drinks.

How do you know if a low calorie sweetener has been added to foods or drinks?

As with any other food ingredient, they are shown on the label and the ingredients list with their full name and other times together with their E number. European legislation requires that foodstuffs and drinks containing a low calorie sweetener must bear the labelling, 'with sweetener(s)'. For the benefit of individuals with Phenylketonuria (PKU), where the low calorie sweetener aspartame is present in food and drinks, the label states that the product 'contains a source of phenylalanine'. Individuals with PKU are diagnosed at birth and have to control the intake of phenylalanine in their diet.

The Safety and Approval of Low Calorie Sweeteners

EU Legislation on Sweeteners

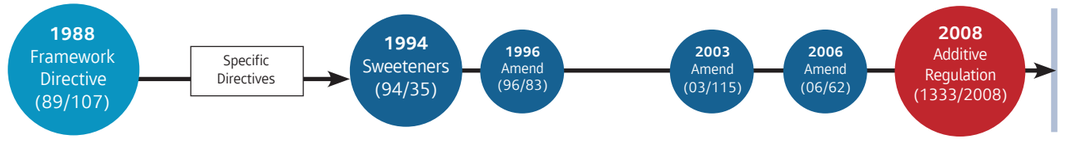
Harmonised legislation on low calorie sweeteners in foodstuffs was adopted in the EU in 1994. This directive is regularly reviewed and has been amended three times to keep pace with technological and scientific developments in the area of sweeteners[2-5]. The legislation on sweeteners and special provisions for the use of sweeteners in foods and drinks provide the purity criteria with which they must comply and determine additional labelling requirements for products containing low calorie sweeteners. The annex of the Directive 94/35 indicates the maximum usage levels of each low calorie sweetener in a given food category[1].

More recently, the European Parliament and the Council adopted a framework regulation Regulation 1333/2008, which consolidates all current authorisations for low calorie sweeteners and other food additives into one legal document.

The Regulatory Bodies Involved

Regulatory approval of low calorie sweeteners in the EU is based on the advice of the European Food Safety Authority (EFSA) and its panel on Food Additives and Nutrient Sources added to food (ANS panel), an independent, transparent panel comprised of members appointed on the basis of proven scientific excellence. The process is explained in more detail on page 12. Previously, the EU relied on the Scientific Committee on Food (SCF). The SCF was the scientific guarantor for the safety of food additives in use within the EU from 1974 to March 2003. Since April 2003, this has been the responsibility of EFSA. At a worldwide level this responsibility rests with the Joint Expert Scientific Committee on Food Additives of the United Nations Food & Agriculture Organisation and the World Health Organisation (JECFA). More details on these organisations can be found in the glossary on page 28.

Figure 1: Chronology of EU Food Additive Law



Within the EU, the 10 low calorie sweeteners currently authorised for use are acesulfame-K (E950), aspartame (E951), aspartame-acesulfame salt (E962), cyclamate (E952), neohesperidine DC (E959), saccharin (E954), sucralose (E955) thaumatin (E957) , neotame (E961) and steviol glycosides (E960).

The ADI is a guarantee of safety, representing the amount of low calorie sweetener that can be safely consumed on a daily basis throughout a person's lifetime.

How a Low Calorie Sweetener is Approved for use in Foods and Drinks in the EU

The authorisation and conditions of use of a low calorie sweetener, like any other food additive, is harmonised at EU level.

EFSA is responsible for the provision of scientific advice and scientific technical support for European Union legislation and policies in all fields that have a direct or indirect impact on food and food safety. Applicants (e.g. ingredient manufacturers) can only apply for approval of a low calorie sweetener after extensive safety tests have been completed and evidence provided of the product's safety and utility. The petition provides technical details about the product and comprehensive data obtained from safety studies.

At a minimum, data is needed to answer the following:

- How the product will be consumed and how much will be consumed?
- Who, including vulnerable groups such as children or pregnant women, will consume the ingredient and how much will each group consume?
- Is the ingredient suitable for food processing use?
- What does the ingredient do, as an additive to food?
- Has the substance been shown not to cause adverse effects or cancer, not to affect reproduction, not to be stored in the body, not to be metabolised into another potentially unsafe substance, and not to cause allergic reactions at a relevant level of intake?
- How and where is the ingredient made and who makes it?

In the approval process, an Acceptable Daily Intake (ADI) is set for each low calorie sweetener by EFSA. The ADI is a guideline quantity that represents the amount of low calorie sweetener that can be safely consumed on a daily basis throughout a person's lifetime without any health problems.

The safety data are then examined by EFSA. At any time, questions raised by EFSA must be answered by the applicant. Sometimes this may require additional studies. Completing and analysing the safety studies may take up to 10 years. Following the publication of a scientific opinion by EFSA, the European Commission drafts a proposal for authorisation of use of the low calorie sweetener in foods and drinks available in European Union countries.

After following the required procedure and only if the regulators are fully satisfied that the product is safe, will approval be given. This means that all of the low calorie sweeteners available in the EU market are safe for human consumption.

How Acceptable Daily Intake (ADI) is Established

The EU evaluation process establishes the ADI of low calorie sweeteners. The ADI is a measure of the amount of an approved additive that can be consumed daily in the diet, over a lifetime, without any health problems.7-10 ADIs are expressed in milligrams (mg) per kilogram (kg) of body weight (bw) per day.

The ADI is usually based on the daily maximum intake that can be given to test animals throughout life without producing any adverse effects, known as the No Observed Adverse Effect Level (NOAEL); the ADI is calculated as the safe intake divided by a 100-fold safety factor to cover species differences and sensitive groups of the population such as children and the elderly. The use of the ADI principle for toxicological evaluation and safety assessment of food additives is accepted by all regulatory bodies worldwide.

Usage levels are set and use is monitored so that consumption does not reach ADI levels. 8-11 As the ADI relates to lifetime use, it provides a safety margin large enough for scientists not to be concerned if an individual's short-term intake exceeds the ADI, as long as the average intake over long periods of time does not exceed it.[7,10,11] The ADI is the most important practical tool for scientists in ensuring the appropriate and safe use of low calorie sweeteners.

Consumption of Low Calorie Sweeteners in Europe

Studies published in this area show that the average intakes of all low calorie sweeteners are well below the ADI values[7-17].

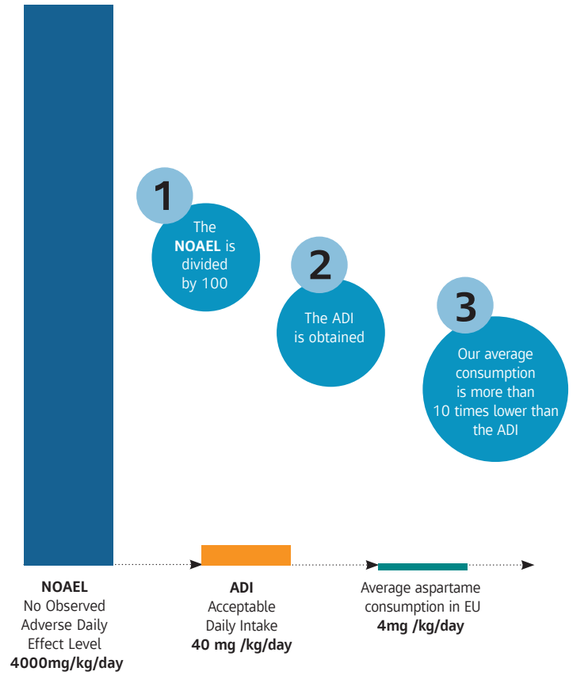
Recent studies have focused on children because of their higher intakes of foods and drinks on a bodyweight basis, and on both children and adults with diabetes, because of their higher potential intakes of low calorie sweeteners [7, 11-16].

Studies published on the intakes of low calorie sweeteners across Europe indicate that the individuals with the highest intakes (90-97.5th percentiles) of acesulfame-K, aspartame, cyclamate and saccharin are well below the relevant ADI values[3].

In Belgium, a study by WIV (the government's Scientific Institute for Public Health), concluded that low calorie sweeteners do not pose a health risk for adults, or for people with diabetes or for heavy consumers of light/diet products[35]. The study showed that adults who regularly consume products containing low calorie sweeteners only reach a maximum of 25% of the ADI for cyclamate, 17% for acesulfame-K, 5% for aspartame, 11% for saccharin and 7% for sucralose.

In order to reach the established ADI for aspartame (40 milligrams (mg) per kilogram (kg) bodyweight (bw) per day), a woman weighing 60kg would have to consume every day during her lifetime 280 tabletop sweetener tablets or 20 cans of low calorie sweetened soft drinks. See (Figure 2)

Figure 2: Aspartame Consumption Compared with ADI



Q&A

What is the meaning of an E number?

Prof. Andrew Renwick: If a food additive has an E number this is assurance that it has passed stringent safety tests and is approved for use throughout the EU. This approval is monitored, reviewed and amended in the light of new scientific data. In order to be authorised it must be demonstrated that an additive is both harmless and useful.

The 'E' reference for each additive refers to Europe and shows that the additive is authorised and regarded as safe in Europe. In effect, the E is a guarantee of safety. Food additives must be included either by name or by an E number in the ingredient list.

Why is there some speculation and concern over the general safety of low calorie sweeteners?

Dr Carlo La Vecchia: Over the past decades, various reports have claimed that low calorie sweeteners are associated with a range of adverse health effects. However, the evidence for these claims has been reviewed by international agencies, such as EFSA, and they have concluded that such claims are without substance. Much of the potentially frightening misinformation about low calorie sweeteners seems to be based on misunderstandings, data dredging or selective use of information, rather than a balanced view of all the information. The claimed adverse effects have not been found in subsequent studies. Nonetheless, unsubstantiated anecdotal reports have been widely covered in the media and online, leaving some consumers unsure as to whether low calorie sweeteners are safe.

Regulatory agencies, such as EFSA, continue to advise the European Commission that the use of low calorie sweeteners in foods and drinks, consumed within acceptable daily intake allowances, pose no threat to human health.

Is it true that low calorie sweeteners can cause neurological and mood problems?

Prof. Andrew Renwick: Anecdotal reports have suggested that low calorie sweeteners such as aspartame are associated with a range of behavioural and neurological problems such as headaches and epilepsy seizures. But research into aspartame and brain function does not support this. Controlled clinical studies have found no evidence of any neurologic or behavioural effects of aspartame in healthy adults or children[22], no effect of aspartame on cognition or behaviour in children with attention deficit disorder[30] and no association between aspartame and seizures in individuals with seizure disorders[23-24].

Organisations representing the interests of people living with epilepsy, multiple sclerosis, Parkinson's disease and Alzheimer's disease have reviewed these anecdotal claims and concluded that there is no scientific basis to advocate the exclusion of aspartame and other low calorie sweeteners from the diet. This position is also supported by expert scientific committees of European agencies such as EFSA and national food safety agencies including AFSSA, the French Food Safety Agency, which in 2002 concluded that there was no evidence to link aspartame with the occurrence of epileptic seizures[25].

Q&A

Can the consumption of low calorie sweeteners increase the risk of developing certain cancers?

Dr Carlo La Vecchia: No, there is no scientific evidence that links the consumption of low calorie sweeteners to cancer. Silvano Gallus and co-workers from the Institute of Pharmacological Research Mario Negri, published a study that further supports the claim that there is no indication that low calorie sweeteners cause cancer[19, 20].

They studied the intakes of low calorie sweeteners in patients with a range of different cancers. Data were collected over a 13 year period on over 11,000 cases after taking into account various confounding factors (such as smoking), and it was determined that consumers of low calorie sweeteners were not at an increased risk of any of the cancers. Furthermore, when they divided low calorie sweetener use into saccharin, aspartame and other low calorie sweeteners, none of the results suggested a significant increase in any of the cancer forms. A subsequent report in 2009 found no association between low calorie sweeteners and gastric, pancreatic and endometrial cancer[20].

Saccharin

Saccharin safety was questioned after studies conducted in the early 1970s showed that high doses (equivalent to hundreds of cans of diet soft drinks a day for a lifetime) increased the incidence of bladder cancer in male rats[26]. Subsequent laboratory studies demonstrated that this was specific to male rats; investigations in humans determined that there was a species-specific mode of action of saccharin on the male rat bladder. Epidemiology studies have shown there is no association between saccharin consumption and urinary bladder cancer, even in high intake consumers. Thus, research conducted over the past 25 years convincingly demonstrates that saccharin does not cause cancer in humans[19, 20, 26].

Aspartame

A paper published in 2005, by the European Ramazzini Foundation (ERF) claimed that there was a link between aspartame and cancer in rats and mice[18]. However, the data showed no consistent dose-risk relationship had been established, nor was an adequate survival analysis completed. Furthermore, the claimed effects were not found in previous studies conducted according to regulatory guidelines. In response, EFSA's panel on Food Additives and Nutrient Sources (ANS) conducted a detailed review of the ERF data and determined that there were significant flaws in the study, such that it did not provide evidence that aspartame causes cancer. There was therefore, no reason to revise the previously established ADI for aspartame of 40mg/kg bw/day, so aspartame safety was reaffirmed. The ANS panel has recently evaluated a subsequent study performed at the European Ramazzini Foundation (ERF) on mice and concluded that the data does not give reason to reconsider the previous evaluations of aspartame[31-34].

The methodology and conclusions of the ERF's recent and previous studies on aspartame have been dismissed by EFSA and other independent scientific bodies[31 -34]. A statement released in February 2011, by the ANSES (French Food Safety Authority) concluded, "The methodology used (exposure to very high doses over a lifetime) is not used by any other group of researchers and, importantly, does not follow accepted reference methodology (OECD)[34]."

The 2007 review undertaken by Silvano Gallus and co-workers [19, 20] concluded that there is no new evidence that requires a revision of the existing opinions indicating a lack of genotoxic/mutagenic potential of aspartame.

There is extensive evidence to support the safety of aspartame. An epidemiological study from the National Cancer Institute in 2006 concluded that there is no link between aspartame consumption and leukaemias, lymphomas and brain tumours. The study evaluated over 500,000 men and women between the ages of 50 and 69 over a five-year period. The researchers found that there was no evidence of an increased risk of leukaemias, lymphomas and brain tumours among those who used aspartame[21].

Furthermore, a review[13] published in 2007 concluded that suggestions of adverse effects had 'no credible scientific basis'. The review was conducted by a panel of eight eminent experts over an 11-month period. It considered more than 500 studies, articles and reports conducted over the last 25 years, including work that was not published but that was submitted to government bodies as part of the regulatory approval process.

In April 2010, EFSA and its Advisory Forum in cooperation with a group of distinguished European Experts (18 experts from 10 EU countries), reviewed all papers published on aspartame since 2002 (SCF Review 2002) to address any remaining questions raised about the safety of aspartame for use in food[30]. The National Experts concluded that no new evidence had been identified which required a recommendation to EFSA that the previous Opinions of EFSA and the SCF need to be reassessed[30].

Cyclamate

Fewer allegations have been raised about cyclamate, and consequently less epidemiological data are available than for saccharin or aspartame. There is no evidence that cyclamate is associated to elevated risk at any cancer site, and no regulatory agency has raised concern on carcinogenic risk of cyclamate use. There is no evidence of toxicity of cyclamate nor of its carcinogenity in animal experiments[27] nor of cancer risk in humans[29]. Independent scientists of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) have consistently affirmed the safety of cyclamate for use as a sweetener in foods and drinks.

Q&A

What is the meaning of ADI?

Prof. Andrew Renwick: ADI stands for Acceptable Daily Intake. The ADI is an estimate of the amount of an approved additive that can be consumed daily in the diet, over a lifetime, without any health problems. ADIs are expressed in milligrams (mg) per kilogram (kg) of body weight (bw) per day. The ADI is usually based on the daily intake that can be given to test animals throughout life without producing any adverse effects. The ADI is calculated as the safe intake divided by a 100-fold safety factor to cover species differences and sensitive groups of the population such as children and the elderly. The use of the ADI principle for toxicological evaluation and safety assessment of food additives is accepted worldwide by all regulatory bodies.

Who sets the ADI?

Prof. Andrew Renwick: JECFA introduced the concept of the ADI for the safety regulation of all food and drink additives in 1961. Different international scientific authorities such as JECFA, EFSA, and AFSSA (now ANSES) use the same method of deriving the ADI independently, guaranteeing consistency of food safety worldwide.

What if someone exceeds the ADI on any given day?

Prof. Andrew Renwick: The ADI for a food additive is not intended to define the maximum dose that would be safe to consume on any given day – it is a guideline quantity level. It is implicit that a person may occasionally consume an additive in quantities in excess of the ADI without adverse effects on the health.

In that case, why does the ADI matter?

Prof. Andrew Renwick: The ADI provides reassurance that a food additive, in this case a low calorie sweetener, is safe to consume. Setting ADI values and assessing consumption of low calorie sweeteners and other food additives according to their ADIs is a way of ensuring that the actual intake of food additives is well below a level that may be considered harmful to health. The presence of an ADI should not cause alarm, it is actually a guarantee of safety – only when a low calorie sweetener has been found safe by an independent scientific body and approved by the EU is it given an ADI.

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Benefits of Low Calorie Sweeteners for Diet and Health

Low Calorie Sweeteners, Palatability and Calorie Intake

It is clear that to lose weight or to maintain a healthy weight, individuals need to pay careful attention to energy balance. It is important to balance the calories you consume with the calories you burn by maintaining a sensible, balanced diet combined with regular physical activity. In order to lose body weight you need to either burn more calories or consume fewer calories, or both. Energy density (kcal/g) of foods is an important determinant of energy intake in a meal[1, 2] or over the course of the day[3]. By substituting low calorie sweeteners for sugar (kcal/g), it is possible to lower the energy density of foods and drinks. As a result, low calorie sweeteners can eliminate or substantially reduce the calories in some foods and drinks, offering an easy method of reducing calories while maintaining the palatability of the diet.

Table 1: Difference in Calorie Content of Foods and Drinks with Sugar or Substituted with Low Calorie Sweeteners

TYPE OF FOOD OR DRINK	CALORIE CONTENT: FOOD OR DRINK WITH SUGAR	CALORIE CONTENT: FOOD OR DRINK WITH LOW CALORIE SWEETENERS
Cola Soft Drink (330ml)	139 kcal	0.7 kcal
Fruit Drink (250ml)	184 kcal	27 kcal
Drinking Yogurt (250ml)	180 kcal	105 kcal
Strawberry Yogurt (125g pot)	118 kcal	84 kcal
Rasberry Jelly (100g)	80 kcal	5 kcal
Orange Squash (250ml)	110 kcal	5 kcal
Tea/Coffee with Sugar or Tabletop Sweetener	16 kcal (1 Teaspoon)	1 kcal (1 Tablet)

Where sugar is the main source of energy, as in soft drinks, low calorie sweeteners help to bring the energy density of drinks close to a negligible calorie content[14].By contrast, sugar is only one of the ingredients of medium or higher energy density foods such as yoghurt or ice cream, with the remaining calories derived from protein or fat[1]. In high energy density foods such as chocolate, replacing sugar with a low calorie sweetener leads to relatively minor reductions in energy[1].

Effect of Low Calorie Sweeteners on Appetite and Food Intake

The influence of low calorie sweeteners on hunger, satiety and energy intake has been addressed in many laboratory studies and reviews[9-14, 41-45].While the use of low calorie sweeteners does not, in itself, result in a rapid weight loss, it may promote long term dietary compliance by improving the diversity, variety and the overall palatability of a reduced energy diet[12-13].

In the 1980s, it was suggested that low calorie sweeteners may stimulate appetite, thereby increasing food intake and promoting weight gain. The appetite stimulation theory first drew attention when in 1986, Blundell and Hill[15] reported that individuals who were consuming highly sweetened solutions perceived themselves to be hungrier than when they were consuming water alone[15].

The study, however, relied only on subjects' hunger ratings and did not measure their actual food intake, which is considered essential by psychologists and obesity experts. Blundell and colleagues conducted a subsequent study using solutions sweetened with several low calorie sweeteners and no increases in actual food intakes were observed[16].

Since then, several studies have examined the acute effects of low calorie sweeteners on hunger and food intake. They concluded that replacing sucrose (sugar) with low calorie sweeteners in foods or drinks does not increase food intake or hunger in children[17-18] nor has it been shown to increase food intake in normal-weight[18-23] or overweight men and women[23-24].

Studies with adults have also shown that familiar low calorie drinks sweetened with aspartame do not affect short-term appetite or food intake when they are consumed before lunch or with meals, compared with the effects of water[19, 24-25]. All of these studies reported either unchanged or reduced motivation to eat regardless of whether the low calorie sweetener was delivered in a solid or liquid medium. For more details, refer to Table 2 on page 18.

Section 4

In 1991, one of the largest literature reviews on the subject was published in the *American Journal of Clinical Nutrition*. Its author was Dr Barbara Rolls, an expert who has studied in detail the effects of low calorie sweeteners and low calorie products on hunger, appetite and food intake[26]. She concluded that: "Preliminary clinical trials suggest that aspartame may be a useful aid in a complete diet-and-exercise program or in weight maintenance. Intense sweeteners have never been found to cause weight gain in humans. In addition, aspartame has not been found to increase food intake; indeed, both short-term and long-term studies have shown that consumption of aspartame-sweetened foods or drinks is associated with either no change or a reduction in food intake"[26].

Low Calorie Sweeteners in Weight Management and Obesity

Strategies to reverse the upward trend in obesity rates need to focus on both reducing energy intake and increasing energy expenditure. The provision of low or reduced calorie foods is one way of helping people to reduce their energy intake and so assist weight maintenance or weight loss. Most studies investigating the role of low calorie sweeteners in weight control have shown that replacing foods and drinks in the diet with light or diet versions as part of a calorie controlled programme can result in an overall reduced caloric intake.

Pioneering work by Porikos and colleagues and by other researchers confirmed the positive effect of low calorie sweeteners on reducing caloric intake. In 1977 to 1984, Porikos *et al.*, showed that lean and obese participants living in a metabolic ward consumed fewer calories overall when all the available sources of sugar in their *ad libitum* diet were replaced with aspartame[27-28].

Research by Tordoff and Alleva[30] found a similar effect and reported that consuming aspartame-sweetened soft drinks significantly reduced energy intake in both males and females eating their normal diet, and significantly decreased the body weight of males over a 3-week period when compared with a no-drink condition.

Further research had revealed that the use of low calorie sweeteners may help increase compliance with longer term weight management control programmes. Kanders *et al.* measured weight loss, perceived feelings of energy and wellbeing, among 59 free-living obese men and women who were knowingly on a weight-control programme for 12 weeks[31]. The experimental group was encouraged to use low calorie sweeteners, whereas the control group were encouraged to avoid all products with low calorie sweeteners. At the one-year follow-up, sustained weight loss was associated with increased low calorie sweetener consumption, a decreased desire for sweets and increased physical activity levels[31].

In addition, Blackburn *et al.*, conducted the first large, randomised, controlled, prospective outpatient clinical trial investigating whether the addition of low calorie sweeteners to a multidisciplinary weight control programme would improve weight loss and long-term control of body weight in 163 obese women. The women were randomly assigned to groups that either consumed or abstained from foods sweetened with aspartame[32-34].

The results indicated that although both groups lost an average of 10% of their initial body weight (~10kg), those who consumed low calorie sweeteners were more successful in keeping the weight off in the long term. After 3 years, the group that consumed food sweetened with aspartame had kept off about half of the lost weight, maintaining a medically significant average weight loss of 5 percent of their initial bodyweight[32-34] while the group that abstained from foods sweetened with aspartame had on average, regained almost all the weight[32-34]. This finding has important clinical implications given the poor long-term success rates of dietary treatments of obesity[35].

A recent review paper by Mattes and Popkin published in the *American Journal of Clinical Nutrition* in 2009 analyzed findings from 224 studies on the effects of low calorie sweeteners on appetite, food intake and weight[36]. They found that longer-term trials consistently indicate that the use of low calorie sweeteners results in slightly lower energy intakes and that if low calorie sweeteners are used as substitutes for higher energy-yielding sweeteners, they have the potential to aid in weight management[36].

A review by Bellisle and Drewnowski published in 2007 examined whether reducing the energy density of sweet drinks and foods through the introduction of low calorie sweeteners can be a useful aid for weight control[1]. Their review of clinical and epidemiological studies concluded that, although they are not a 'silver bullet', low calorie sweeteners can help people reduce their calorie intakes. A review of studies by De la Hunty *et al.*, 2006 demonstrated that, "using foods and drinks sweetened with intense sweeteners instead of sucrose results in a significant reduction in both energy intakes and body weight"[37].

"Intuitively, low calorie sweeteners have the potential to play an important role in helping motivated adults control weight. It has been estimated that adults can prevent weight gain by reducing intake by only 100 kcal per day" [41].

Table 2: Studies Showing an Impact on Hunger, Food Intake or Weight with the Consumption of Low Calorie Sweeteners

AUTHOR	STUDY	CONCLUSION
Rolls et. al (1989)	Healthy body weight; jelly or pudding with aspartame, 2hrs before meal; half aware others not	Reduction of hunger; aspartame helped reduced total kcal intake
Rolls (1987)	Healthy body weight; jelly with sucrose or aspartame	No differences in hunger; no compensation; ate same wt. of food
Rolls et. al, (1990)	Healthy body weight; 8-16 oz of lemonade (sucrose or aspartame) or water	No difference in hunger or intake
Mattes (1990)	Healthy body weight ; cereal with unsweetened cereal, or cereal with aspartame or sucrose; some aware others not	No difference in hunger or food intake
Chanty et. al, (1991)	Healthy body weight ; 7 oz of water or soda with saccharine., aspartame or sucrose (after breakfast, 1 hr. before lunch)	No increase in hunger ratings; No difference in kcal intake
Porikos et.al, (1984)	Obese; calories diluted with low calorie sweetener Healthy wt; calories diluted with low calorie sweeteners	kcals reduced by 16%
Kanders et. al, (1988)	Obese men and women, 12 weeks LCS group were given, in addition to weight loss diet, low-calorie, aspartame sweetened puddings or milkshakes and encouraged to use diet drinks	LCS group sustained weight loss at 1 yr follow-up
Tordoff and Alleva (1990)	30 non-obese men and women 3 weeks. subjects were given 1150ml of soft drink (~4 cans) sweetened with either aspartame or high-fructose corn syrup (HFCS) or no soft drink in a crossover study	LCS group (men and women) overall kcals reduced. LCS male group achieved weight reduction over the 3 –weeks
Kanders, Blackburn et al (1993, 1994)*	163 Obese women -19 weeks, weight loss programme groups that either consumed or abstained from foods sweetened with aspartame.	Both groups had 10% (~10kg) weight reduction. LCS group more successful in keeping the weight off in the long term.
Blackburn et. al (1997)*	Obese women, +3 year study. Intervention group were given, in addition to weight loss diet, aspartame-sweetened puddings or milkshakes and encouraged to use other aspartame-sweetened products	LCS group had sign. better weight maintenance (5% of weight loss) at +3yr follow-up.
De Ruyter et al (2012)	A 18-month trial involving 641 normal-weight children 5-12 years of age. Each child was given daily either 250 mL [100 calories (kcals)] non-carbonated sugar-sweetened beverage (SSB) or 250 mL non-carbonated sugar-free beverage sweetened with sucralose and acesulfame potassium (Low Calorie Sweeteners). The provided beverage was given to replace their usual serving of SSB per day.	Average body weight was lower by 1 kg (2.2 lbs.) in the LCS group. When adjusted for differences in height, body weight in the LCS group was lower by 0.82 kg (1.8 lbs.). Children in the LCS group also gained less body fat (0.55 – 0.57 kg). All of these results were statistically significant.
Piernas et al (2013)	Data derived from the CHOICE study. A sub-analysis evaluating the effect of water vs. diet beverages (DB) in a 6-month (total length) weight loss intervention, with analysis at 3 and 6 months. [water groups: n = 106 (94% women); DB group: n = 104 (82% women)].	The DB group decreased energy from all beverages more than the water group did only at month 3. The DB group had a greater reduction in dessert intake than the water group did at month 6.

**Longest trial to date on low calorie sweeteners and weight management*

The Academy of Nutrition and Dietetics (formerly the American Dietetic Association) updated its position paper on nutritive and non-nutritive sweeteners in 2012 and concluded that "there is good evidence to support the use of aspartame and aspartame-sweetened products as part of a comprehensive weight loss or maintenance program by individuals may be associated with greater weight loss and may assist individuals with weight maintenance over time" [42].

Low calorie sweeteners allow a more versatile approach to weight management and may even encourage compliance with a diet. Even modest amounts of weight loss have been shown to contribute significantly to a reduction in risks associated with obesity and overweight, such as diabetes and heart disease.

A paper by Raben and Richelsen (2012)[45] concludes that low calorie sweeteners can be a helpful tool to reduce energy intake and body weight and thereby risk for diabetes and cardiovascular diseases (CVD). Considering the challenge of increasing rates of obesity and diabetes low calorie sweeteners can provide an important alternative to caloric sweeteners.

Low Calorie Sweeteners and Diabetes

Diabetes is recognised as a group of heterogeneous disorders with the common elements of hyperglycaemia and glucose intolerance, due to insulin deficiency, impaired effectiveness of insulin action, or both[38].

Diabetes is a chronic disease that occurs when a person's body 1) can no longer make insulin, or 2) can no longer make enough insulin, or 3) cannot use insulin properly. Insulin is produced by the pancreas [39].

The importance of low calorie sweeteners in the diet of people with diabetes is undisputed. People with diabetes may, however, consume moderate amounts of sugar. If the sugar contained in food products stays for a longer time in the stomach and intestines (as is the case, for example, with chocolate), then people with diabetes may also enjoy some of these products.

Low calorie sweeteners offer people with diabetes broader food choices by providing the pleasure of the sweet taste without raising blood glucose. As low calorie sweeteners have no impact on insulin and blood sugar levels and do not provide calories, they can also have a role in weight loss and weight control for people with type II diabetes. Furthermore, in 2012 the American Heart Association (AHA) and the American Diabetes Association (ADA) issued a joint scientific statement on low calorie sweeteners and their potential usefulness in helping people achieve and maintain a healthy body weight and help people with diabetes to control their glucose level. More details on diabetes can be found on page 23.

Low calorie sweeteners also help people with diabetes or those on calorie restricted diets to feel less alienated because of their dietary requirements.

Q&A

How can low calorie sweeteners benefit people with diabetes?

Dr Adam Drewnowski: The dietary control of blood glucose involves avoiding or sharply limiting foods that contain quick-release carbohydrates or simple sugars. Diabetic patients are advised to seek out sugar-free foods and drinks, and to select low-glycaemic index foods wherever possible. However, a sugarless diet of fibre and whole grains can lack in sensory appeal and may be hard to follow for long periods of time. Low calorie sweeteners offer an ideal way to preserve eating pleasure and promote dietary compliance. Replacing sugar in drinks with low calorie sweeteners maintains sweet taste and glycaemic control. Low calorie sweeteners can improve the quality of life of the diabetic patient.

Do low calorie sweeteners have an impact on appetite and food intake?

Dr Adam Drewnowski: Human appetite is influenced by both calories and volume of the just-consumed food or drink. A high calorie drink will suppress appetite and may reduce the amount of food eaten at the next meal. A zero calorie drink will suppress appetite for about an hour but will not affect the amount of food eaten in the next meal. Suggestions that low calorie sweeteners promote appetite and can result in overeating are incorrect. Numerous laboratory studies have shown no difference in appetite or satiety between drinks and yogurts that were plain and those that were sweetened with low calorie sweeteners.

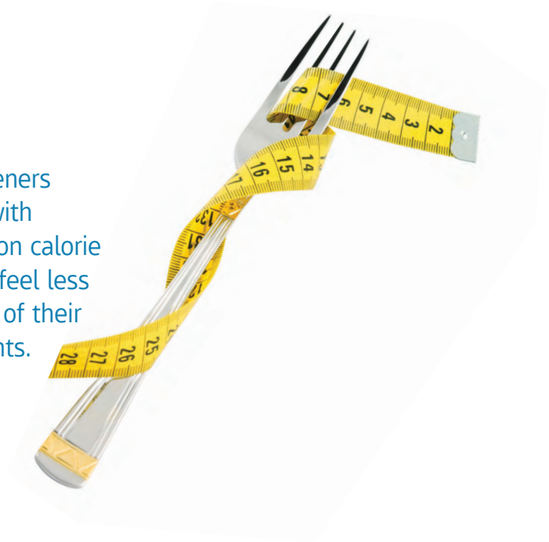
Can low calorie sweeteners help people reduce their calorie intake and lose weight?

Dr Adam Drewnowski: Substituting sugar calories in a sugar-sweetened drink with a low calorie sweetener leads to a saving of some 150 kcal and reduces the energy density of the drink from 0.4 kcal per gram down to zero. Zero calorie drinks, in turn, help to bring down the energy density of the diet. Low energy density diets have been linked with higher nutrient density and with better management of body weight. In principle, a calorie saving of 150 kcal/day should lead to a substantial weight loss. However, it must be noted that low calorie sweeteners are most helpful when used in the context of an active, healthy lifestyle that includes a sensible, balanced diet and regular physical activity. Using low calorie sweeteners does not give permission to eat.

Low Calorie Sweeteners Provide Dental Health Benefits

When sugar-sweetened foods and drinks are consumed, the bacteria present in the mouth converts the sugar to acid. If this acid is not removed by teeth cleaning, it can wear away the surface enamel, eventually causing cavities to form. Low calorie sweeteners are not fermentable, and do not contribute to tooth decay[40] . By improving palatability, low calorie sweeteners can also encourage the use of toothpastes, mouthwashes and fluoride supplements that assist dental hygiene.

Low calorie sweeteners also help people with diabetes or those on calorie restricted diets to feel less alienated because of their dietary requirements.



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Low Calorie Sweeteners and Special Health Considerations

Though the general population may not have any specific health concerns relating to the consumption of low calorie sweeteners, they may decide to seek the advice of a healthcare professional on whether they should or could include low calorie sweeteners in their diet. This section discusses the use of low calorie sweeteners by those sectors of the population with special health considerations: children, pregnant women, people with diabetes, or those suffering from the rare, inherited condition phenylketonuria (PKU).

Low Calorie Sweeteners and Children

Low calorie sweeteners are not approved for use in foods for infants and young children. These foods are generally known as 'baby foods' and include foods specially formulated for infants and young children who are in good health, and foods for those whose digestive processes or metabolism is disturbed[15,16]. 'Infants' are defined as children under the age of 12 months and 'young children' as children aged between one and three years[15,16].

The consumption of low calorie sweeteners by children is sometimes questioned for two main reasons – because of their physical size and relatively high food and drink intakes compared with adults. However, studies undertaken in this area indicate that children can safely consume low calorie sweeteners.

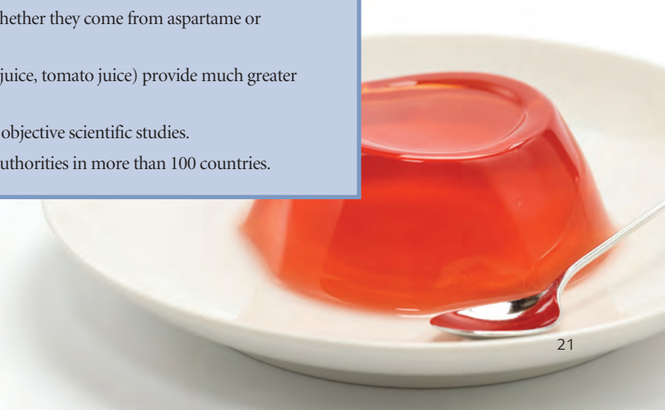
In comparison to adults, children tend to have the highest intake of low calorie sweeteners as calculated as milligrams (mg) of intake per kilogram (kg) of bodyweight (bw) per day. Though there is evidence that children's intake of low calorie sweeteners is indeed greater than adult consumption, particularly within children with diabetes, there is no risk of exceeding the ADI levels[2,3]. In December 2002, European regulators stated that in the numerous studies focusing on the intake of aspartame by children in Europe, all found that even the highest consumption is well below the ADI[1].

In the past, questions have been raised about whether low calorie sweeteners and specifically aspartame have behavioural effects on children. Studies conducted in this area demonstrate that aspartame has not been found to show behaviour effects. Controlled studies found no evidence of any neurologic or behavioural effects of aspartame in healthy adults or children,[4] no effect of aspartame on cognition or behaviour in children with attention deficit disorder,[5] and no association between aspartame and seizures in individuals with seizure disorders[6].

Though there is evidence that children's intake of low calorie sweeteners is indeed greater than adult consumption, particularly within children with diabetes, there is no risk of exceeding ADI levels[2-3].

Key Facts About the Most Widely Used Low Calorie Sweetener – Aspartame

- Aspartame is made from two amino acids (building blocks of protein) aspartic acid and phenylalanine (as the methyl ester).
- The two amino acids in aspartame are found in mother's milk and occur naturally in foods such as meats, milk, fruits and vegetables.
- When aspartame is digested, it is broken down to common dietary components, including a small amount of methanol. More methanol is released by the metabolism of pectin in fruit juices, than is formed from a similar volume of an aspartame sweetened drink.
- The body uses these components in exactly the same way whether they come from aspartame or common foods.
- The foods we consume every day (e.g. chicken, milk, grape juice, tomato juice) provide much greater amounts of these components than aspartame does.
- Aspartame's safety has been documented in more than 200 objective scientific studies.
- The safety of aspartame has been confirmed by regulatory authorities in more than 100 countries.



Low Calorie Sweeteners and Pregnancy

The consumption of approved low calorie sweeteners within the ADI is safe during pregnancy.

Scientific communities around the world, including in Europe, have conducted safety evaluations in this area, focusing on the possible effects of low calorie sweeteners on pregnant women as well as any effects on the developing foetus. No evidence has been found to indicate that there is any risk to the mother or the foetus[2,7].

The above is also reaffirmed by the position of the Academy of Nutrition and Dietetics published in 2012 which states: "Pregnancy is a time of special concern because the focus is on maternal and fetal health. All FDA-approved low calorie sweeteners are approved for use by the general public, which includes pregnant and lactating women. The position of the Academy is that use of low calorie sweeteners is acceptable during pregnancy. Any low calorie sweetener that was found to be unsafe at any stage of life would not be approved for use" [18].

In the case of aspartame, a sweetener made from two amino acids, further evaluation of safety in pregnancy has been conducted to evaluate foetal exposure to the components of aspartame: aspartic acid, phenylalanine or methanol. Unlike other approved low calorie sweeteners, aspartame is metabolised in the human body. Enzymes in the digestive tract break aspartame down into its components, each of which is then metabolised just as it would be if derived from other dietary sources. All three of the metabolites of aspartame are present in many foods consumed as part of a normal diet. As a result of these studies, it was concluded that, like other low calorie sweeteners, it is safe to consume aspartame within the ADI during pregnancy[8].

A recent allegation, made by a group of Danish researchers,[13] that the intake of low calorie sweeteners increases the risk of preterm delivery is not consistent with the extensive body of scientific evidence that shows these products are safe.

The authors suggested that methanol formed from aspartame could be responsible for the association. However, the main human exposure to methanol arises from the digestion of pectin, which is present in high concentrations in fruit juices (300-600mg/day). There is more methanol released from the digestion of fruit juice than from an equal volume of a low calorie sweetened carbonated drink. In addition a recent statement on the effects of chronic dietary exposure to methanol, released in March 2011, by the UK –COT (Committee On Toxicity Of Chemicals In Food, Consumer Products And The Environment) concluded that the exposure to methanol at the levels found in the diet both naturally occurring and from currently permitted levels of aspartame would not be expected to result in any adverse effects[17].

The use of low calorie sweeteners has been very well studied both in humans and in animals. This research has shown no adverse effects on the mother or the developing baby related to the use of low calorie sweeteners[12].

There are many factors that increase the risk of premature births, including being overweight or obese, smoking, diabetes, poor nutrition, anaemia, stress, depression and many more. At a time when the consequences of obesity, including in pregnancy, pose a significant challenge to public health, unsettling potentially sensitive population groups about choices that help them control their weight is particularly irresponsible.

In February 2011, EFSA reviewed and dismissed the recent publications by Danish[13] researchers (Halldorsson *et al.*, 2010) alleging that low calorie sweeteners may be unsafe.

EFSA Panel concluded that, "there is no evidence available to support a causal relationship between the consumption of low-calorie sweetened soft drinks and preterm delivery"[14].

Aspartame and People with Phenylketonuria

Phenylketonuria (PKU) is a rare inherited condition affecting 1 in 10,000 people. Those who have it lack the enzyme that converts phenylalanine into the amino acid tyrosine. Phenylalanine is an essential amino acid and is a building block of protein. It is also a component of aspartame. For those with PKU, consuming protein-containing food leads to a build up of phenylalanine in the body. People with PKU must limit their intake of phenylalanine to prevent it reaching toxic levels in their blood and other tissues.

Figure 1: Example of a Drink Label Carrying a Statement Indicating that the Product Contains Phenylalanine

Ingredients: Water, Orange Fruit from Concentrate (11%), Citric Acid, Acidity Regulator (Sodium Citrate), Preservatives (Potassium Sorbate, Sodium Metabisulphite), Sweeteners (Aspartame, Saccharin), Flavourings, Stabiliser (Cellulose Gum), Colour (Beta-Carotene). **Contains a Source of Phenylalanine.**

Management of PKU requires a low phenylalanine diet. This means that high protein foods such as meat, cheese, poultry, eggs, milk/diary products and nuts are not permitted. Instead the diet is supplemented with artificial protein which contains a low level of phenylalanine.

For the benefit of individuals with PKU, foods, drinks and healthcare products that contain the low calorie sweetener aspartame must legally carry a label statement indicating that the product contains phenylalanine. (Figure 1).

Throughout most of Europe, PKU is screened for shortly after birth.

Low Calorie Sweeteners and People with Diabetes

Based on the latest figures released by the International Diabetes Federation11 it was estimated that, in Europe in 2010, 55.2 million people between 20-79 years of age were suffering from diabetes. By 2030, it is estimated that this number will increase to 66.2 million.

Type I Diabetes Mellitus:

Sometimes called insulin-dependent diabetes, type I diabetes is caused by destruction of the insulin producing cells of the pancreas, typically due to an auto-immune reaction, where these cells are attacked by the body's defence system. The beta cells of the pancreas therefore produce little or no insulin, the hormone that allows glucose to enter body cells (Figure 2). The disease can affect people of any age, but usually occurs in children or young adults. People with type I diabetes need injections of insulin every day in order to control the levels of glucose in their blood.

Type II Diabetes Mellitus:

Characterised by insulin resistance and relative insulin deficiency, either of which may be present at the time that diabetes becomes clinically manifest. The diagnosis of type II diabetes usually occurs after the age of 40 years but could occur earlier, especially in populations with high diabetes prevalence and/or in individuals who are overweight or obese. There are increasing reports of children developing type II diabetes. Type II diabetes is often, but not always, associated with obesity, which itself can cause insulin resistance and lead to elevated blood glucose levels.

As low calorie sweeteners have no impact on insulin and blood glucose levels, their importance in the diets of people with diabetes is undisputed. Low calorie sweeteners offer people with diabetes the pleasure of sweet tasting foods and drinks without raising blood glucose. Food and drink products prepared with low calorie sweeteners are suitable for people with diabetes9. Scientists have also concluded that low calorie sweeteners help people with type II diabetes in the important and often challenging task of controlling their weight[10].

In 2012, the American Heart Association (AHA) and the American Diabetes Association (ADA) issued a joint scientific statement on low calorie sweeteners and their potential usefulness in helping people achieve and maintain a healthy body weight and in helping people with diabetes to control their blood glucose levels [19].
The statement highlights that:

- Substituting low calorie sweeteners for sugars added to foods and beverages may help people reach and maintain a healthy body weight – as long as the substitution doesn't lead to eating additional calories later as "compensation."
- For people with diabetes, low calorie sweeteners used alone or in foods and beverages remain an option and when used appropriately can aid in glucose control.

Figure 2: Illustration Explaining Type I Diabetes

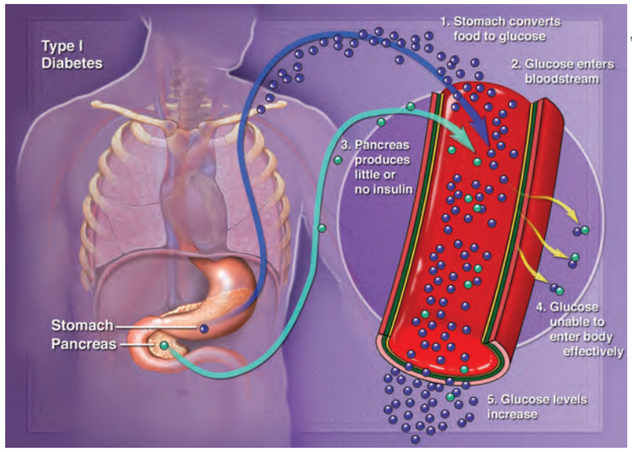
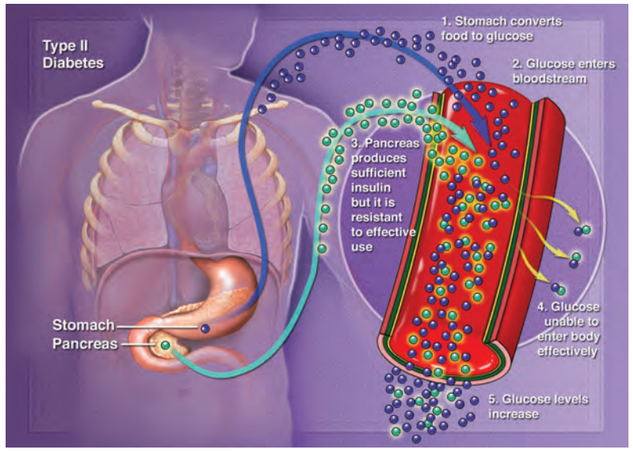


Figure 3: Illustration Explaining Type II Diabetes



Q&A

Should pregnant women avoid consuming products with low calorie sweeteners?

Dr Carlo La Vecchia: Women do not need to avoid or be concerned about consuming low calorie sweeteners whilst pregnant. Consumption of low calorie sweeteners, within the ADI set by EFSA, is safe during pregnancy, because all low calorie sweeteners have been subject to appropriate testing. The variety of foods and drinks sweetened with low calorie sweeteners can help satisfy a pregnant woman's taste for sweetness while adding few or no calories. In any case, pregnant and breastfeeding women need to consume adequate calories to nourish the foetus or infant and should consult with a physician about their nutritional needs. It is important to remember that weight control remains a priority, particularly in pregnancy.

Should children be consuming products containing low calorie sweeteners?

Dr Carlo La Vecchia: Low calorie sweeteners are also safe for children, but it is important to keep in mind that children, particularly young children, need ample calories for rapid growth and development.

Are people with diabetes at risk of overconsumption of low calorie sweeteners in their diet?

Prof. Andrew Renwick: No, people with diabetes are not at risk of overconsumption of low calorie sweeteners. Overconsumption would require an individual to exceed the ADI. As low calorie sweeteners are very beneficial for people with diabetes and are regularly included in the diet, the consumption of low calorie sweeteners by people with diabetes has been carefully monitored by the scientific community. Studies have shown that the intakes of low calorie sweeteners across Europe are well below the ADI, including within people with diabetes. Even within children with diabetes, the group with the highest potential for intakes, various studies have shown that the intakes are still below the ADI[3].

In 2010, an estimated 55.2 million people in Europe between 20-79 years of age were suffering from diabetes. By 2030 it is estimated that this number will increase to 66.2 million[11].

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The Role of Media in Food Safety Scares

In the next two decades, World Health Organisation experts predict that there will be in excess of 334 million people living with diabetes globally. Figures highlight that overeating and our sedentary lifestyles are contributing to significant weight gain, with more than 1 billion adults currently overweight globally and 300 million of these obese. These statistics demonstrate how for many people, low calorie sweeteners could play a key role in the modern diet, and their importance and use looks set to grow.

But in many ways, low calorie sweeteners are victims of their own success. Though European regulatory bodies have confirmed that low calorie sweeteners permitted for use in the EU are safe for consumption, they continue to be some of the most researched, scrutinised and misrepresented ingredients in the food supply. Public health issues and, more specifically, issues that affect the food we eat will always capture the attention of the general public and garner media headlines – particularly when the focus is an ingredient that most of us consume at one time or another.

Undoubtedly there will be further research published that challenges the safety and the benefits of including low calorie sweeteners in the diet. What is less clear however is how the general public can determine the credibility of that research – when is a scare genuinely something to worry about?

In his paper '*Risk Communication, Media Amplification and the Aspartame Scare*,' risk expert Ragnar Lofstedt discusses "pseudo-scares based on non peer-reviewed science". Before the internet, scientific findings were filtered by credible scientific authorities, whereas nowadays, scientific findings can reach the public in a matter of seconds via the lens of the media and online commentators. In the case of low calorie sweeteners for example, the European Ramazzini Foundation (ERF) findings, which were widely considered a pseudo-scare on aspartame as they were based on non peer-reviewed science, gained widespread global media coverage. This coverage may have caused some consumers to question their consumption of aspartame and raised concern in some healthcare professional communities too.

So how do we address these issues? This question is one that Lofstedt considers in a recently published article in the *Journal of Risk Research*. He calls for "better integration of communications between scientists, regulators, industry and NGOs." He argues that "one way to start this integration process would be the development of a media communication checklist that could help journalists better differentiate between risk, uncertainty, science and pure lobbying".

But the reality is that a pseudo-scare sells newspapers, and because of this we may be a while yet from implementation and large scale adoption of such a media communication checklist. In the interim, what can the health professional community do in order to help provide reassurance to consumers around the safety of low calorie sweeteners?

A starting point could be to help consumers understand how the results of a scientific study are communicated, and what the indicators are to highlight whether they are credible or not (Table 1). In addition, it may be helpful to direct them to a few sources of credible further information to ensure that they feel they are getting a balanced view from a wide variety of sources.

Low calorie sweeteners have been used for generations, with saccharin now well over a century old, and many more with a safety profile spanning decades. New and innovative low calorie sweeteners, such as steviol glycosides (stevia extract) continue to keep these ingredients at the forefront of food science. Regardless of media speculation and the publication of non peer reviewed science, we can expect low calorie sweeteners to continue to play an important role in the European diet for generations to come.

Table 1: How Science Results are Communicated and Disseminated (Code of Conduct)

Credible practices	Non-credible practices*
Share data with regulators	Kept data secret
Dialogue with regulators	Little dialogue with regulators
Openness regarding funders	Secrecy regarding funders
Few if any press conferences	Many press conferences
Publish in best scientific peer-review journals	Many non peer-review journals and general media
Proper risk communication	Faulty risk communication

*based on ERF case study

Courtesy of:
Ragnar E. L. Lofstedt, King's Centre for Risk Management, King's College London, UK: *Risk Communication, Media Amplification and the Aspartame Scare.*

Characteristics of Low Calorie Sweeteners Commonly Used in Europe

	ACESULFAME POTASSIUM (Ace-K) E950	ASPARTAME E951	CYCLAMATE E952	SACCHARIN E954	SUCRALOSE E955	STEVIOL GYLCOSIDES E960
Composition	A combination of an organic acid and potassium	Aspartame is made from two amino acids aspartic acid and phenylalanine. These are found naturally in the diet.	Cyclamic acid (an organic acid), sodium- or calcium salt	Saccharin (an organic acid), sodium or calcium salt	Derived from sugar in a process that selectively substitutes three atoms of chlorine for three hydroxyl groups on the sugar molecule	Steviol glycosides are natural sweet tasting constituents of *Stevia rebaudiana*, a plant native to South America. Steviol glycoside preparations usually contain as the major components the glycosides Stevioside and Rebaudioside A.
Acceptable Daily Intake ADI (for Children & Adults)	0-9 mg/kg	0-40 mg/kg	0-7 mg/kg	0-5 mg/kg	0-15 mg/kg	0-4 mg/kg (expressed as Steviol)
Sweetening Power Compared to Table Sugar (Sucrose)	c. 200 times sweeter	c. 200 times sweeter	c. 50 times sweeter	c. 500 times sweeter	c. 600 times sweeter	c. 200 to 300 times sweeter depending on the glycoside
Year Discovered	1967	1969	1937	1879	1976	1931 (first isolated)
Metabolic and Physiological Properties	Not metabolised by the human body and excreted unchanged	Digested like other proteins to its components all of which occur in the diet in greater quantities.	Generally not metabolised and excreted unchanged	Not metabolised and excreted unchanged	Not metabolised and excreted unchanged	Steviol glycosides are broken down to steviol in the gut. Steviol is excreted in the urine as steviol glucuronide.
Caloric Value	Calorie free	4kcal/g (used in very small amounts)	Calorie free	Calorie free	Calorie free	Calorie free
Stability	Heat stable, suitable for cooking and baking Readily soluble	Loses sweetening properties when exposed to high temperature, therefore not recommended for baking Can be added to foods at the end of cooking cycle	Good stability at high and low temperatures, can be used in cooking and baking Good solubility	Heat stable Can be used in cooking and baking	Good stability in very high temperatures. Can be used in cooking and baking Good solubility	Steviol glycosides are heat stable
Uses	Used in drinks, foods, table-top sweeteners, oral-care and pharmaceutical products	Widely used in beverages, dairy products, table-top sweeteners and confectionery incl. chewing gum, due to its sweet taste profile.	Used in table-top sweeteners, drinks, chewing gums, salad dressings and jams	Used in table-top sweeteners, drinks, desserts, confectionery and also in pharmaceutical products	Used in baked goods, desserts, table-top sweeteners, ice-cream and dairy products, breakfast cereals and confectionery	Used in foods, drinks and table-top sweeteners

Glossary

ADI: ADI stands for Acceptable Daily Intake. The ADI is a measure of the amount of an approved additive that can be consumed daily in the diet, over a lifetime, without any health problems. ADIs are expressed in milligrams (mg) per kilogram (kg) of body weight (bw) per day. The ADI is usually based on the daily intake that can be given to test animals throughout life without producing any adverse effects and is calculated as the safe intake divided by a 100-fold safety factor to cover species differences and sensitive groups of the population such as children and the elderly. The use of the ADI principle for toxicological evaluation and safety assessment of food additives is accepted worldwide by all regulatory bodies.

ANSES (French Food Safety Agency): An independent public institution created by a merger of AFSSA and AFSSET which, through its monitoring and research activities, contributes to the improvement of public health, animal health and welfare, and plant and environmental health. **www.anses.fr**

EFSA (The European Food Safety Authority): EFSA is an independent agency funded by the European Union which was established in 2002 to improve food safety in the European Union and to help ensure a high level of consumer protection and consumer confidence in the EU food supply. EFSA has a number of Scientific Committees and Panels that review and assess food safety, nutrition, animal health and welfare, plant protection and plant health. Its role is to assess and communicate all risks associated with the food chain and its independent scientific advice supports European food policy and legislation. **www.efsa.europa.eu**

FSA (Food Standards Agency): An independent UK Government agency set up by an Act of Parliament in 2000 to protect the public's health and consumer interests in relation to food. **www.food.gov.uk**

JECFA (The Joint Expert Committee on Food Additives of the United Nations Food and Agricultural Organisation and World Health Organisation.): JECFA is responsible for implementing the joint FAO / WHO programme on food additives which evaluates substances and provides advice to member states on the control of additives and related health aspects. It carries out risk assessments of food additives by reviewing available safety and technical data, and endorses substances for use in foods and allocates Acceptable Daily Intake levels (ADI). **ttp://jecfa.ilsi.org/**

Low calorie sweetener: The term used to describe compounds that taste sweet and provide no calories or compounds that have such an intensely sweet taste that they can be used in food products at concentrations low enough not to contribute significantly to calorific content.

SCF (The Scientific Committee on Food of the Commission of the European Union):
The SCF was established in 1974 and reformed in 1997. It advised the Commission of the European Union (EU) on issues relating to the protection of Health and Safety of persons arising from the consumption of food. It was responsible for risk assessment of food additives until establishment of the EFSA. **http://ec.europa.eu/food/fs/sc/scf/index_en.html**

Sugar: Sugars are the naturally-occurring nutrients that make food taste sweet. Sucrose (also referred to as table sugar) is a crystalline or powdered substance, white when pure, consisting of sucrose obtained mainly from sugar cane and sugar beets and used in many foods, drinks, and medicines to improve their taste. There are a number of other different sugars including glucose and fructose, found in fruit and vegetables, milk sugar is known as lactose, and maltose is found in malted drinks and beer. All types of sugar have the same nutritional value, 4 kilocalories per gram.

The European Food Safety Authority's ANS Panel:
The panel on food additives and nutrient sources added to food (ANS) deals with questions of safety in the use of food additives, nutrient sources and other substances deliberately added to food, excluding flavourings and enzymes. EFSA's panels are composed of independent experts appointed on the basis of proven scientific excellence.

International Sweeteners Association

The International Sweeteners Association is a non-profit making, industry funded organisation representing manufacturers and users of low calorie sweeteners. The ISA is recognised by the European Commission, national and international regulatory authorities, and the World Health Organisation, and has Non-Government Observer status with the Codex Alimentarius Commission which establishes international food standards. **www.sweeteners.org**