



## Workshop 2013 - Parador of Chinchón - November, 25<sup>th</sup> and 26<sup>th</sup>, 2013 SWEETENERS, HEALTH AND CONSUMERS

### Artículo especial

## Chinchón declaration; decalogue on low- and no-calorie sweeteners (LNCS)

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### Abstract

Multidisciplinary experts in the areas of nutrition and health met in Chinchón, Madrid, on November 25-26, 2013 under the auspices of the Fundación para la Investigación Nutricional (Nutrition Research Foundation) and with the collaboration of the Madrid Regional Government's Health Ministry, the International Sweeteners Association and the Carlos III Health Institute CIBER of Physiopathology of Obesity and Nutrition. They analyzed the current status of scientific knowledge on low- and no-calorie sweeteners (LNCS) and developed a consensus Decalogue on their use; this constitutes the Chinchón Declaration. Sweeteners, including sugar, represent a subject of undeniable interest and are currently a popular topic, although areas relating to their safety and benefits remain unknown to segments of academia and the general public. The nature of LNCS makes them vulnerable to biased and even contradictory information. They are food additives that are broadly used as sugar substitutes to sweeten foods,

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Recibido: 20-II-2014.  
Aceptado: 26-II-2014.

### DECLARACIÓN DE CHINCHÓN; DECÁLOGO SOBRE EDULCORANTES SIN Y BAJOS EN CALORÍAS (ESBC)

### Resumen

Expertos de carácter multidisciplinar de las áreas de conocimiento de la nutrición y la salud reunidos en Chinchón, Madrid, los días 25 y 26 de noviembre de 2013, bajo los auspicios de la Fundación para la Investigación Nutricional y con la colaboración de la Consejería de Sanidad del Gobierno de la Comunidad de Madrid, la International Sweeteners Association y el CIBER de Fisiopatología de la Obesidad y la Nutrición del Instituto de Salud Carlos III, analizaron el estado actual del conocimiento científico en torno a los Edulcorantes sin y bajos en calorías (ESBC) y desarrollaron un Decálogo sobre su uso que constituye la Declaración de Chinchón. Los edulcorantes, incluido el azúcar, constituyen un elemento de indudable interés y actualidad, aunque no exento de desconocimiento por algunos sectores tanto académicos como de la población en general. La propia naturaleza de los ESBC los hace susceptibles de informaciones tergiversadas e incluso contradictorias. Son aditivos alimentarios ampliamente utilizados como sustitutivos del azúcar para endulzar alimentos, medicamentos y complementos alimenticios cuando se persiguen fines no nutritivos. El Decálogo de Chinchón es fruto de una reunión de reflexión y consenso por parte de

medicines and food supplements when non-nutritional or non-caloric alternatives are needed. The Chinchón Decalogue is the outcome of a meeting for reflection and consensus by a group of experts with backgrounds in different scientific disciplines (toxicology, clinical nutrition, community nutrition, physiology, food science, public health, pediatrics, endocrinology and nutrition, nursing, pharmaceutical care and food legislation). The Decalogue includes different aspects of LNCS related to regulation, use, benefits and safety. In general, benefits of LNCS have been traditionally neglected in comparison with the tendency for emphasizing unexisting or unproven possible risks. The need to strengthen research on LNCS in Spain was emphasized, as well as the need to educate both professionals and the public.

(*Nutr Hosp.* 2014;29:719-734)

**DOI:10.3305/nh.2014.29.4.7393**

Keywords: *Low-calorie sweeteners. Non nutritive sweeteners. Safety. Benefits. Consensus.*

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1. LNCS have been used safely by consumers throughout the world for more than a century. In Europe there are ten different authorized LNCS: acesulfame K (E-950), aspartame (E-951), cyclamate (E-952), saccharine (E-954), thaumatococcoside (E-957), neohesperidine DC (E-959), steviol glycosides (E-960), neotame (E-961) and salts of aspartame and acesulfame (E-962). There are also other kinds of low-

calorie sweeteners authorized, such as the polyalcohols (sorbitol: E-420, xylitol: E-967) which are widely used in food products. The description and declaration of all these ingredients on product labeling is mandatory, just as it is for all other additives.

2. All of the no-calorie and low-calorie sweeteners currently used have been subjected to strict safety tests. The LNCS regulatory process is scrupulous and obtaining authorization for a new LNCS is a long and highly scientifically robust procedure; sometimes it can take up to 20 years. All additives have an established Acceptable Daily Intake (ADI) that represents a quantity guideline for health safety purposes. These ADI levels are established by international regulatory bodies [Joint FAO/WHO Expert Committee on Food Additives (JECFA), the European Food Safety Authority (EFSA) and the U.S. Food and Drug Administration (FDA) among others]. They define the ADI as the measurement of the amount of an authorized additive that can be consumed in a person's daily diet (food or drink) over an entire lifetime without any appreciable risk to health.

3. Current scientific evidence indicates that there is no relationship between the consumption of LNCS and the appearance of non-communicable diseases. Very recent studies done with humans have analyzed the possible epidemiological relationship between the consumption of LNCS and different kinds of cancer, without finding any type of relationship or trend. Their consumption was not linked to cardiovascular disease, neurological diseases or with any alterations or effects related to pregnancy. Therefore, their consumption within the quantities indicated, represents no health risk in light of existing scientific evidence.

4. Scientific evidence shows that LNCS do not affect glucose or insulin levels in blood plasma. There-

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Palabras clave: *Edulcorantes bajos en calorías. Edulcorantes no nutritivos. Seguridad. Beneficios. Consenso.*

fore, LNCS represent an additional instrument in the dietary treatment of people with diabetes and obesity and constitute a key element in carbohydrate metabolic control.

5. Scientific research shows that the consumption of foods and drinks in which sugar has been replaced by no-calorie and low-calorie sweeteners combined with physical activity and a healthy lifestyle can play a significant role in weight loss and the maintenance of a healthy weight. Therefore, this is a helpful tool in the prevention of overweight and obesity and of weight management in general. Scientific studies have shown that people who use low and no calorie sweeteners in their diets consume fewer calories than those who have diets with the equivalent caloric products. They also show better energy balance.

6. However, in the face of the uncertainty that is sometimes generated about the impact of LNCS consumption on the eating habits and physical activity of people who consume them, nutrition education and a healthy lifestyle need to be strengthened, with particular emphasis on the promotion of physical activity and exercise. In childhood the use of these types of additives should only be considered as an alternative resource when other preventive strategies have failed, with the exception of the use of chewing gum to prevent tooth decay as well as use in pharmaceutical products.

7. Moreover, LNCS help prevent cavities. In Spain, in barely 20 years, the incidence of dental cavities at 12 years of age has been reduced by 50%. This has demonstrated that factors such as hygienic and dietary measures, surface and systemic fluoride treatments and the use of low- and no-calorie sweeteners that are non-cariogenic (or are even cariostatic, reducing the incidence of cavities)—such as xylitol—have been decisive in this public health success. This could represent

a complementary model for the control of other chronic diseases in the future.

8. Consumer education about these products must be strengthened in a rigorous, objective way, based on the best scientific evidence and regulatory processes. Responsible administrations and scientific societies should disseminate clear, objective information about LNCS on their websites and social networks, and publish educational materials that contribute to the dismissal of doubts and any misinformation that may exist. In this process, the food and pharmaceutical industries should share the information about the content of the sweeteners in their products, for informational and investigative purposes. All of this should reinforce the effort that governments, food safety agencies, professionals and scientists have been making to communicate and strengthen consumers' trust and responsibility with regard to these products.

9. Training provided to primary care and specialized healthcare professionals, dentists and pharmacists should be made a priority in order to make them educational agents on these types of products among the healthy population and in groups with special needs. The training of educators and teachers in primary and secondary schools should also be considered, as well as professionals in general who are linked to diet, nutrition and health.

10. The need to strengthen research on LNCS in Spain was emphasized, to incentivize the monitoring of LNCS intake levels in different population groups and facilitate the execution of multidisciplinary projects on the subject. This is equally applicable to other additives or ingredients or substances present in food products, through Total Diet studies or other methods. Research, in addition to being an engine for knowledge and science, constitutes a fundamental element for training healthcare professionals and for the public's health information and education.

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## The sweet taste across the life stages

Gregorio Varela-Moreiras

Very few of our taste preferences are biologically present. In fact they are linked with some sort of experience. Although there are some genetic factors that cause differences in taste perception, similarities in taste preferences much more commonly reflect similar experiences with types of flavours and foods. The shaping of taste preferences begins in the womb and continues throughout the rest of our lives.

The sensory system is pretty much complete by the time of birth. Taste buds mature by the last trimester of pregnancy. Newly-born babies react to sweet, sour, and bitter tastes - but not so much to salt. It is also believed that prenatal exposure to food odours, derived from

foods consumed by the mother in the course of pregnancy, can influence future food preferences and eating habits.

Babies like sweet and dislike bitter tastes. This can in fact be noted from their facial expressions. A drop of a sweet tasting substance on the tongue makes the infant smile and relaxes. Taste preferences for sweetness are maximal in infancy and childhood and progressively drop during adolescence and adult life. Children adore foods that would be much too sweet for adults. So the basic liking for sweetness is an innate human trait. The preferred level of sweetness is determined first by age and only thereafter by culture. On the other hand, humans equate bitter taste with *dietary danger*.

## Prenatal shaping

Human senses are established in the embryonic phase (weeks 1-8 of gestation) and at the start of the foetal phase, and mature at varying rates. The sense of taste also, forms and matures at an early stage (the first taste buds appear at eight weeks of gestation). Aroma compounds in the amniotic fluid stimulate the foetal taste receptors as soon as the foetus starts swallowing (around 12<sup>th</sup> week of gestation).

Amniotic fluid composition changes along with the development of the foetus. Flavours from the maternal diet reach the amniotic fluid. For newborns, the sense of taste is the most important and most developed of all senses.

## Breast milk shapes preferences

Human breast milk contains numerous aroma compounds that the mother acquires through her diet. The taste of breast milk may impact on the later preferences of the newborn. Children often like foods they have eaten in pleasant situations and reject dishes linked to something negative.

## Infancy

The neophobia effect protects infants from eating harmful or poisonous foods. At an age when children start walking and become more independent in choosing their foods, neophobia may have a certain *survival value*. Older children and adults possess successful means to overcome their innate neophobia. Although the rejection of new foods appears innate, there are individual and gender-specific differences to neophobia, with women seemingly less affected than men. Furthermore, similarities within families hint at a genetic component.

## Teenagers

Older children strive to emulate adults, and will force themselves to ingest things they dislike the taste of, regardless of the flavour. Interestingly, hormones play a key role in how we experience food. Therefore, it has been shown that girls are more sensitive to sweet and sour tastes than boys.

## Ageing

Loss of the sense of taste is common among older people (usually starting at 40 to 50 years in women and 50 in men), but the cause of taste loss is not fully understood. Theories include a decline in gustatory function due to physiological decline in the density of the taste buds and papillae. Alteration in the sense of taste may be due to various central (involvement of the "Taste area" in the temporal lobe) or peripheral (changes in the receptor cell taste buds) functions. Bitter taste is the first to be affected and is the last to be recovered while sweetness is affected later and is the first to be regained. However, true gustatory disorders are rare.

In addition to physiological changes associated with the ageing process, the most common causes of taste disorders are: oral and systemic diseases (7.4 and 6.4%, respectively), drug use (21.7%) and zinc deficiency (14.5%). The main consequence of taste decline and disturbance in the elderly is food-anhedonia (inability to experience pleasure), causing loss of body weight via decreased calorie and nutrient intake. And of course, any change in nutrient intake can lead to malnutrition with its potentially serious consequences. When considering prevention and/or treatment, it is recommended to administrate zinc and/or iron. However the suggestion to use food enhancers or flavours would be appropriate so as to improve dietary intake.

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# History, types of caloric and non caloric sweeteners and intake

Javier Aranceta Bartrina

From the beginning of time there is evidence of the use of sweeteners as nutritious substances and also with a role as gourmet facilitators for the culinary preparation of certain foods. As such, these components are used as preservatives, texturizers and other uses related to the preservation and improvement of the organoleptic qualities of food.

Sweet taste seems to have the most pleasant impact on humankind, possibly as a genetically encoded peculiarity and a survival mechanism. The first food, breast milk, produces the first sensation of sweetness and wellbeing. It is a perception of comfort that can induce a smile in newborns universally.

The term Sweetener is given to any natural or artificial sweetening substance used to provide sweetness to a food or product that would be otherwise bitter, unpleasant or tasteless.

## Sweetening, a historical view

Classical natural sweeteners have also been termed sweeteners. Initially humans used the manna tree, honey or a variety of concentrated grapes such as *defrutum* or *arrope* for this purpose.

In classical times apart from these products, the first artificial sweetener used was lead acetate, also



known as “*lead sugar*”. This substance was utilised both in common recipes and elite cookery books of the time as described in *Apicus*, a Roman cookbook dated in the late fourth century. An average Roman could have about 20 mg of lead per day with wine and other foods.

Sugar cane has been known since 3,000 years before Christ, mainly as an ornamental use. The use of sugar cane in cookery started by the time of King Darius. He referred to it as “*this cane that gives honey without bees*.”

The Crusaders introduced sugar cane to Europe. They found sugar cane plantations in the Arab territories and the plains of Tripoli. Since then, sugar was introduced into Europe, although initially the most common utilisation was limited to use as a drug in pharmacies.

Finally, the Arabs introduced sugar cane culture and the unique use of sugar in gastronomy, especially in pastries as they progressed throughout the Mediterranean basin. Many of these culinary formulas rich in honey, sugar and nuts persist to date across the Spanish geography, in the Maghreb and in other locations.

From its presence in the Iberian Peninsula, sugar cane was also introduced to the islands, such as the Canary Islands, Madeira and the Azores. In 1493 Christopher Columbus brought sugar cane to the Americas.

Traditionally sugar has facilitated the widespread consumption of coffee, tea, pastries and a large number of foods and drinks.

The extraction of sugar from the sugar beet can be attributed to the German scientist Andreas Marggraf, who in 1747 showed that the crystals obtained from beet juice were equivalent to those of sugar cane. During the Napoleonic wars and the British blockade of the French commercial lines in 1811, Napoleon ordered the planting of 32,000 hectares of beets as a supply for the empire. Due to this decision, today almost 90% of the sugar consumed in Europe is obtained from beets. The first sugar beet processing factory was built in Cunern, in Lower Silesia in 1801.

This calm and peaceful relationship with classical sweeteners, especially sugar, was disturbed in the first half of the twentieth century, when a negative role was attributed to sugar in relation to health, viewed as a potential inductor of certain diseases such as diabetes, cardiovascular diseases, dyslipidemia, etc.

This perspective encouraged research driving the development of sweetening products that provide fewer calories, or even zero calories, enabling its use in population groups that need energy restriction or limited glucose intake.

In general, no-calorie and low-calorie sweeteners are used as sugar substitutes in the preparation of a) low calorie foods and drinks, b) non-cariogenic products, c) no sugar added foods that enable better preservation; and d) products for weight control, for diabetic patients or people with reactive hypoglycaemia.

## Artificial sweeteners

*Saccharin*. Known as the oldest artificial sweetener, it is 300 times sweeter than sucrose but has a distinct metallic aftertaste. It was discovered by chance in 1879 by Constantin Fahlberg and Ira Remsem at Johns Hopkins University while doing tests on toluene oxidation. The first commercial use started in 1901 as a soda sweetener and was approved for use in more than 90 countries.

*Cyclamate*. These are sodium and calcium salts of cyclohexyl sulfamic acid having a sweetener potential 30 times stronger than sucrose (E-952). It was discovered in 1937 at the University of Illinois. The European Food Safety Authority (EFSA) supports its use.

*Aspartame*. It was synthesized by Schlatter in 1965 within a research program on peptides for pharmaceutical use. It is formed by the amino acids aspartic acid and phenylalanine in the form of methyl ester. The FDA authorized its use in 1983. It is 200 times sweeter than sucrose, resists heat poorly and is not suitable for people with phenylketonuria. A new report from EFSA showed a favourable evaluation in 2013.

*Acesulfame K*. A sweetener discovered in 1967. It is heat stable and well suited for combining with other sweeteners, enhancing the perception of flavour and freshness. It is not metabolized in the body and contains no sodium. Approved by the FDA and EFSA.

*Sucralose*. Semisynthetic sweetener obtained in 1976 by Tate & Lyle with L. Hough and S. Phadnis at Queen Elizabeth College, London. It is about 400 times sweeter than sucrose, calorie-free, water-soluble and heat stable. It was approved for use in the EU in 2004.

*Advantame* is a new sweetener and flavour enhancer developed by Ajinomoto. It is derived from aspartame and vanillin and is much more potent than aspartame. It is licensed in Australia and New Zealand. In 2013 EFSA declared it as a safe sweetener.

## Non-caloric natural sweeteners

*Steviosides*. These are substances from herbs and shrubs from the sunflower family (*Asteraceae*) originating in South America, Central America and Mexico. They were studied first by the Spanish botanist and physician Petrus Jacobus Stevus (1500-1556). The so-called “*sweet herb*” (*Stevia rebaudiana*) has been used in Paraguay since pre-Columbian times to sweeten mate and confectionery. The leaves are 10 to 15 times sweeter than sugar and stevioside and rebaudioside’s sweetness are about 300 fold that of sugar. The use of these substances was approved in the U.S. in 2008 and in the EU in late 2011.

*Luo Han Guo*. Fruit used in Chinese popular medicine obtained from a perennial plant from the Cucurbitacea plant family (*Grosvenoril Siraitia*). Its sweetening extract is heat stable, non-fermented and doesn’t alter any organoleptic properties of the food.

*Thaumatococcus*. Belongs to a group called sweet proteins. It is extracted from the fruit of *Thaumatococcus Danielli* that grows in West Africa. Its sweetening property was documented by WF Daniell in 1855. It is now used to sweeten and flavour foods and drinks. Thaumatin has a sweetening power 3000 times higher than sugar.

*Monatin*. Also known as ajinomoto, this is a second-generation natural sweetener, 1400 times sweeter than sugar. It is extracted from the root bark of *Schlerochiton Ilicifolius*, a native plant from northern Transvaal in South Africa.

Importantly, there is significant use of low calorie sweeteners such as polyhydric alcohols, sorbitol, mannitol, lactitol, maltitol and xylitol. Along with tagatose and trehalose these are the main natural low-calorie sweeteners.

*Other sweetening substances*: There are many often used substances with sweetening potential, such as *hydrogenated starch hydrolysate*, fructose, coconut sugar, dehydrated date sugar, brown sugar, honey, agave syrup, maple syrup, molasses from rice, barley, corn, wheat, a number of berries or some fruits like apple syrup.

In the field of sweet taste, it is important to find available sweetness enhancing substances and other

components able to modulate flavours of natural or synthetic sweeteners. The *Redpoint Bio* and *Senomyx* are examples of such components that allow reducing by up to 50% the amount of caloric sweetener added or enhancing the sweet taste of stevia or high fructose corn.

### Consumption of sugar and sweeteners

According to data published in 2013 by Mercasa, globally some 213,800 thousand tons of sugar beet, 1,339,000 thousand tons of sugar cane and 174,468 thousand tons of refined sugar were produced. In Spain in 2012 the estimated consumption was 189.3 million kilos which represents a per capita consumption of 4.1 kg per year, being lower than the European average. The total estimated consumption of sweeteners is 0.1 kg/per capita/per year. The highest consumption of sugar is detected in La Rioja, Asturias and Galicia and the lowest in Navarra, Castilla La Mancha and Madrid. The individual typology of higher sugar consumption is embodied with more intensity in older, retired people living alone and in those with low income levels.

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## Low- and no-calorie sweeteners; aspects on safety

Arturo Anadón Navarro

### European legislation on food additive sweeteners

Harmonized legislation on sweeteners in foodstuffs was adopted in the European Union (EU) in 1994 [European Parliament and Council Directive 94/35/EC of 30 June 1994 on sweeteners for use in foodstuffs (OJ L 237, 10.9.1994)]; the annex of this Directive indicates the maximum usage levels of each LNCS in a given food category.

Subsequently, the Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives (OJ L 354/16; 31.12.2008) requires that food additives are subject to a safety evaluation by the European Food Safety Authority (EFSA) before they are permitted for use in the EU. In addition, it is foreseen that food additives must be kept under continuous observation and must be re-evaluated by EFSA. For this purpose, a programme for the re-evaluation of food additives that were already permitted in the EU before 20 January 2009 has been set up under Council Regulation (EU) No 257/2010 of 25 March 2010 (OJ L 80/19; 26.3.2010). The re-evaluation of all sweeteners is foreseen to be completed by the end of 2020. However, in 2011 the deadline for the re-evaluation of aspartame was moved forward to May 2013 in light of new scientific information.

All LNCS are subject to comprehensive safety evaluation by regulatory authorities, prior to approval. Scientists evaluate these sweeteners for many attributes including sensory qualities (eg, clean sweet taste, no bitterness, odourless), safety, compatibility with other food ingredients, and stability in different food environments.

### Safety testing of food additive sweeteners

The safety testing of food additive sweeteners requires studies in laboratory animals to determine what effects the compound is capable of producing when administered at high daily doses, or high dietary concentrations. Very high dose levels are used to increase the ability of the study to detect any possible adverse effects.

Table I shows routine procedures for testing the safety of food additives.

For sweeteners, this testing may be expanded to address specific end-points (eg, neurotoxicity and immunotoxicity testings) and effects on humans with relevant conditions (eg, testing sweetener effects on glucose homeostasis in those with diabetes). The neurotoxicity and immunotoxicity responses are based on short-term and subchronic toxicity studies. The previous tests establishes a safety limit of food additive sweet-

**Table I**  
*Toxicology testing for food additives*

<i>Toxicity test</i>	<i>Outputs</i>
Acute toxicity (single dose) (to define extent of toxicity in absence of other data)	Nature of acute effects (overdose); median lethal dose.
Subacute/subchronic toxicity (28-90 days); usually two species (rodent and non-rodent)	Suitable dose levels for chronic toxicity studies; nature of toxicity; target organ(s); dose-response; NOEL (no-observed-effect level); NOAEL (no-observed-adverse effect level); maximum tolerated dose.
Mutagenicity/Clastogenicity (Short-term tests for capacity to interact with DNA and to cause mutations or chromosome changes using a variety of end-points in bacterial and mammalian systems, <i>in vitro</i> and <i>in vivo</i> ).	Evidence of potential genotoxicity.
Chronic toxicity (long-term dietary administration, eg, 6 months to 2 years); provide the data most frequently used in deriving the ADI.	Nature of chronic toxicity; target organ(s); cumulative effects; dose-response characteristics; NOEL/NOAEL.
Carcinogenicity (long-term administration at maximum tolerated dose).	Carcinogenic potential
Reproductive toxicity (single/multiple dose studies during pregnancy; multigenerational studies with dietary administration prior to and during mating, gestation, and suckling); usually involves a multigeneration study in a rodent and developmental toxicity in two species.	Effects on male and female fertility; fetotoxicity; teratogenic potential; effects on lactation and post-natal development.
Metabolism and pharmacokinetic studies	Degree of absorption, distribution in the body, route of metabolism and metabolites, degree and mode of elimination.

eners or conditions of use that are expressed as human intake with negligible risk (or as the estimated amount that a person can safely consume on average every day over a lifetime without risk), which is called the acceptable daily intake (ADI).

Use levels are set to assure that intakes are below the ADI. The regulatory bodies Joint FAO/WHO Expert Committee on Food Additives (JECFA), Scientific Committee on Food (SCF) and European Food Safety Authority (EFSA) monitor estimated daily intakes (EDI) *versus* ADI. If EDI exceed the ADI, there may be limitations on use of the sweetener.

The ADI for a sweetener is not intended to define the maximum dose that would be safe to consume on any given day; it is a guideline for quantity levels, and therefore it is implicit that a person may occasionally consume a sweetener in quantities in excess of the ADI value without adverse effects on health. For instance, there is evidence that children's intake of LNCS is greater than adult consumption, in particular in children with diabetes; however there is no risk for exceeding the ADI values.

The ADI is usually calculated as the NOEL/NOAEL (in mg/kg bw/day) divided by an uncertainty (safety) factor of 100, which is to allow for possible species differences and human variability.

Metabolism data are usually available from studies in humans to support extrapolation of toxicity data from the test animal species to humans. Any human study would have to fulfil criteria of adequate duration, group size, group composition, daily dosage and also investigate the endpoints detected in rats at intake above the NOEL/NOAEL.

### Health-based guidance values for sweeteners

Derivation of a health-based guidance value such as an ADI for food additive sweeteners that produce adverse effects uses information on dose-response relationships. At the risk characterization stage, comparison of the exposure assessment with the health-based guidance values may indicate that additional dose-response assessment may be necessary for the formulation of advice to risk managers. The objective of hazard characterization is to determine the relationship that exists between the magnitude of exposure to a sweetener agent and the severity and/or frequency of associated adverse health effect in experimental animals. This is defined as the dose-response relationship. The dose-response relationship must be established for each toxicological endpoint in each study and aids in the determination of a NOAEL for a particular endpoint in the study. The lowest NOAEL in a study is the study NOAEL. The lowest NOAEL amongst all of the endpoints in all of the studies is often referred to as the critical NOAEL. Health-based guidance values for compounds that are both genotoxic and carcinogenic have not been established using the NOAEL.

There is no appreciable risk at intakes below the health-based guidance value. The critical risk assessment issue that should be considered in recommending different health-based guidance values for different population subgroups is whether the most sensitive critical health outcome is irrelevant for a significant part of the whole population. The numerical result of this estimation, the EDI, is then compared with the type and amount of additive residue considered to be

**Table II**  
*Low- and no-calorie sweeteners used in Europe*

<i>Sweetener</i>	<i>Caloric value</i>	<i>Potency (times sweeter than sucrose)</i>	<i>Stability</i>	<i>Uses</i>	<i>ADI (for children and adults)</i>
Acesulfame K (E950) K (E950)	00	200	Heat stable, suitable for cooking and baking	Drinks, foods, table-top sweeteners, oral-care and pharmaceutical products	0-9 mg/kg
Aspartame (E951)	4 kcal/g	200	Looses sweetening properties when exposed to high temperature (not recommended for baking; can be added to foods at the end of cooking cycle)	Drinks, desserts, sweets, dairy, chewing gums, energy-reducing and weight control products and as a table-top sweetener. It is not stable if subjected to prolonged heating, and cannot be used in baking or cooking	0-40 mg/kg
Cyclamate (E952)	Calorie free	30	Good stability at high and low temperatures; can be used in cooking and baking; good solubility.	Table-top sweeteners, drinks, chewing gums, salad dressings and jams	0-7 mg/kg
Saccharin (E954)	Calorie free	300	Heat stable, can be used in cooking and baking	Table-top sweeteners, drinks, desserts and confectionery	0-5 mg/kg
Sucralose (E955)	Calorie free	300	Good stability at very high temperatures; can be used in cooking and baking. Good solubility.	Baked goods, desserts, ice-cream and dairy products, breakfast cereals, and confectionery	0-15 mg/kg
Steviol glycoside (E960)	Calorie free	250-300	Heat stable.	Drinks, desserts, yogurts, confectionary, cakes, biscuits and pastries, sauces, toppings, spread, cereals, canned fruits, and jams among others.	0-4 mg/kg (expr. steviol)

without toxicological hazard for human health, as expressed by the ADI.

The ADI values for the LNCS sweeteners currently approved for use in the EU are expressed in table II.

The use of the ADI principle for toxicological evaluation and safety assessment of food additive sweeteners is accepted worldwide by all regulatory bodies. The E number for LNCS sweeteners assures that they have passed stringent safety tests and are approved for use throughout the EU. In the EU the label on food-stuffs containing sweeteners must state its presence, indicating either its name or its E number.

### **Low- and No-Calorie Sweeteners (LNCS)**

Extensive scientific research has demonstrated the safety of the LNCS (table II). The safety assessment for aspartame, cyclamate and stevia/steviol glycosides are described.

#### *Aspartame*

Aspartame is a low-calorie, intense artificial food additive sweetener authorized in the EU. It is a white, odourless powder. The aspartame molecule consists of two amino acids, phenylalanine and aspartic acid, linked to methanol. Methanol also occurs naturally in foods and is produced by the digestion of other food

constituents. Aspartame itself does not occur naturally. Intestinal esterases hydrolyze aspartame rapidly and completely in the gastrointestinal tract to methanol and the amino acids phenylalanine and aspartic acid.

At a worldwide level the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and at the EU level the Scientific Committee on Food (SCF) delivered several scientific opinions. The first SCF safety assessment was in 1984 and subsequent complementary assessments in 1988, 1997 and 2002. The SCF task was followed from 2003 by the European Food Safety Authority (EFSA) which performed different scientific opinions on the safety of aspartame (E 951). The JECFA (1975, 1980) and SCF committees established an ADI of 0-40 mg/kg bw/day based on chronic toxicity and carcinogenicity studies in rats and applying an uncertainty factor of 100. The available data do not indicate a genotoxic concern for aspartame. The chronic toxicity, reproductive and developmental toxicity, and neurotoxicity were the critical endpoints in the animal database but however it is possible to conclude aspartame is not a carcinogen and it is not associated with reproductive/development and neurobehavioral disorders.

The possibility of developmental toxicity occurring at lower doses than 4000 mg/kg in animals could not be excluded. Based on mode of action (MoA) and weight-of-evidence analysis, the EFSA ANS Panel concluded that developmental toxicity in animals was attributable to phenylalanine. Phenylalanine at high plasma levels



is known to cause developmental toxicity in humans. In addition, EFSA concludes that aspartame and its breakdown products (i.e. phenylalanine, aspartic acid and methanol) pose no safety concern for consumers at current levels of exposure. The current ADI is considered to be safe for the general population and consumer exposure to aspartame is below this ADI. This ADI is not applicable to people who suffer from the hereditary disease phenylketonuria (ie, a homozygous recessive inborn error of metabolism of which affected individuals cannot metabolize phenylalanine), who must strictly limit their intake of phenylalanine. In the EU all products (foods and beverages) containing aspartame must place a statement on the label indicating that the product “contains a source of phenylalanine”.

### Cyclamate

Cyclamate was discovered in 1937. It was used as a low-calorie sweetener in the United States in the 1950s and 1960s. Cyclamate was extensively used during the 1960s, often in a 10:1 blend with saccharin which had a better taste than that of either sweetener alone. In 1969, in immediate response to a study that suggested that cyclamate might cause bladder cancer in rats, the US-FDA announced that cyclamate would be banned; the ban took effect in 1970. Later, extensive further studies in rats, mice, dogs, hamsters, and monkeys did not show any link between cyclamate and cancer. Thus, on the basis of the complete body of evidence, scientists have concluded that cyclamate is not carcinogenic.

The primary concern was that it could be toxic to some individuals who appear to metabolize cyclamate to cyclohexylamine. However, in 1982 the FDA’s Cancer Assessment Committee concluded that it was not carcinogenic in animal experiments and did not present cancer risk in humans. The JECFA and SCF gave a favourable opinion and it is utilised in more than 50 countries worldwide.

It is known that people metabolize cyclamate in different ways. Some people excrete all or practically all of it unchanged, while others convert variable amounts occasionally -as much as 85% of ingested cyclamate- into a metabolite called cyclohexylamine, which has a far greater potential for toxicity than cyclamate itself. Data on the extent to which individuals

convert cyclamate to cyclohexylamine during long-term consumption were supported by the lack of an association between cyclamate and cyclohexylamine and male infertility in humans. The relationship to infertility was of interest because high doses of cyclohexylamine caused testicular atrophy in rats.

### *Stevia/steviol glycosides*

Steviol glycosides are natural sweet tasting constituents of *Stevia rebaudiana*, a South American shrub of the *Chrysanthemum* family that is commonly called stevia, and contains intensely sweet substances that are 250 to 300 times sweeter than sugar. Steviol glycoside preparations usually contain the glycosides Stevioside (no less 95%) and Rebaudioside A as the major components. Stevioside was evaluated by the SCF (1999). JECFA (2009) reviewed its safety and established an ADI for steviol glycosides (expressed as steviol equivalents) of 0-4 mg/kg bw/day. The EFSA ANS Panel (2010) concluded that steviol glycosides are not carcinogenic, genotoxic or associated with any reproductive/developmental toxicity. The ANS Panel established an ADI for steviol glycosides (expressed as steviol equivalents) of 4 mg/kg bw/day based on the application of a 100-fold uncertainty factor (ie, this safety factor covers species differences and sensitivity groups of the population such as children and the elderly) to the NOAEL in the 2-year carcinogenicity study in rats given 2.5% stevioside in the diet (corresponding to approx. 388 mg steviol equivalents/kg bw/day). Conservative estimates of steviol glycoside exposures both in adults and in children suggest that it is likely that the ADI would be exceeded at the maximum proposed use levels.

Stevia has a very low acute toxicity, and no allergic reactions to it seem to exist. However, several studies in animals have suggested that steviol glycosides may have adverse effects on the male reproductive system. These studies, some of which have never been published in English, were reviewed in detail by the European SCF, which declined to approve stevioside as a sweetener (SCF, 1999). Of course, the mere fact that high doses of a substance can produce an adverse effect in experimental animals does not necessarily mean that the substance would be harmful when consumed in far smaller amounts by humans.

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## Low- and no-calorie sweeteners and obesity

Carmen Gómez-Candela, María Martín Fuentes, Samara Palma Milla

There are more than 1 billion adults in the world who are overweight and at least 300 million that are clinically obese. Currently the total calorie value of our diet has increased, physical activity has declined and most of the population is sedentary.

The relationship between sugar and body weight is controversial. Barclay et al demonstrated that in the Australian population, there was a substantial decline in refined sugar intake over the same timeframe that obesity had increased. Mattes et al concluded that the

current evidence does not conclusively demonstrate that nutritive sweetened beverages have uniquely contributed to obesity or that reducing consumption will reduce BMI levels in general.

Low and no calorie sweeteners (LNCS), otherwise referred to as non nutritive sweeteners (NNS), artificial sweeteners or non caloric sweeteners, 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 to not contribute significantly to caloric content.

LNCS are used by adults to limit or reduce daily energy intake and are thus a tool in weight management. However earlier perceptions held that LNCS can increase hunger and possibly cause weight gain.

Although excessive and disordered eating are factors in the development of obesity, there is no evidence that sugars or LNCS themselves trigger overeating. Several studies have examined the acute effects of low calorie sweeteners on hunger and food intake and they concluded that replacing sucrose (sugar) with low calorie sweeteners in foods or drinks does not increase food intake or hunger.

There is a proliferation of studies related to LNCS consumption and weight gain.

Kanders et al. measured weight loss, perceived feelings of energy and wellbeing among 59 free-living obese men and women. At 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.

Kanders et al. also conducted the first large, randomized 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 results indicated that those who consumed low calorie sweeteners were more successful in keeping the weight off in the long term. Bellisle et al examined whether reducing the energy density of sweet drinks and foods through the introduction of low calorie sweeteners could be a useful aid for weight control. Mattes and Popkin 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.

In conclusion the bulk of epidemiologic studies, but not all, reported a positive association between body weight, weight gain and LNCS use. However, it was noted that such findings do not prove causality. In addition, available intervention studies do not show that LNCS use increases body weight.

In the “Workshop about LNCS, Appetite and Weight Control”, they concluded that current knowledge in this area is modest at best and does not yet permit an informed view of how the ingestion of energy-containing sugars and LNCS affects overall mechanisms of energy balance and thus influences body weight.

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## Non-caloric sweeteners and dental health; review

Reina García-Closas

Dental caries and periodontal diseases constitute a Public Health problem due to their prevalence and socioeconomic consequences. In Spain, 36.6% of 5-6 year-old children, 45% of 12 year-old children and 92-94% of 35-74 year-old adults have caries.

In the period 1993-2000, prevalence decreased 40% for permanent teeth in 12 year-olds, and the ICAOD12 decreased from 4.2 in 1983 to 1.12 in 2000. In the last 10 years, caries indicators have not changed. Sixteen to 30% of Spanish adults have periodontitis. In the period 1993-2010, periodontitis decreased by half.

Dental decay results from a complex interaction between host susceptibility, oral microflora and environmental factors (diet, hygiene, use of fluorides). The caries process only takes place when dental plaque bacteria are capable of metabolising fermentable carbohydrates into organic acids.

The role of sugars in the etiopathogenesis of dental caries has been established in epidemiological studies. Sugar consumption frequency is more important than

the quantity of sugar intake. The most cariogenic sugar is saccharose, and foods rich in processed starches and sugars are especially cariogenic. Sugars are frequently added to foods (pastry, snacks, cookies, breakfast cereals, chewing-gum, milk products, sauces, bread, processed foods, etc) and beverages. Those hidden sugars are the main source of sugar intake in developed countries.

Sugar consumption has increased during the last 50 years, especially from processed foods with low nutrient density, which contributes to dental caries and possibly obesity. Sacarose, high-fructose corn syrup, fructose and maltose are the most common sugars added to foods and beverages. Non-nutritive sweeteners are non cariogenic since they cannot be metabolized by oral bacteria. To date, of these, aspartame is the most frequently added to non-caloric beverages, yogurts and snacks. Saccharine, in combination with cyclamate and/or acesulfame K- is also widespread in beverages. Sucralose is progressively substituting

other NCS, and the recently approved neotame is promising. Stevia is non-cariogenic and seems to inhibit bacterial metabolism.

Xylitol has been widely used in chewing-gums and candies. Clinical studies have shown that xylitol is effective and safe as a sugar substitute for the control of dental decay. Frequent consumption of xylitol (in chewing-gums and candies) has shown to interfere in bacterial growth and to reduce dental caries incidence. Xylitol is associated with the remineralization of caries lesions and it reduces cariogenic bacteria transmission from mother to children in comparison to chlorhexidine and fluoride. Moreover, xylitol can prevent gingivitis and periodontitis. The combination of xylitol and erythritol could be specially anticariogenic. The deter-

rents of xylitol use are cost, caloric content (x0.6 energy density of sugar), and that it can be partially fermented by intestinal bacteria, thus producing bloating and diarrhea. Other sugar alcohols (sorbitol) do not have an important effect on plaque mass and bacteria growth.

In conclusion, public health policies and dietary counselling should be oriented to reduce consumption of foods high in refined starches and sugars and in sugar sweetened beverages, particularly in high-risk population groups. The substitution of sugars by non-nutritive and non-cariogenic sweeteners (or anticariogenic) could be an important tool in the prevention of dental caries and should be included in preventive programmes based on fluoride use and hygiene.

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## Low-calorie sweeteners, cancer and selected other diseases; epidemiological evidence

Carlo La Vecchia

The role of low-calorie sweeteners on cancer risk has been widely debated since the 70s, when animal studies found an excess bladder cancer risk in more than one generation of rodents treated with extremely high doses of saccharin, and a few earlier epidemiological studies found inconsistent associations with bladder cancer risk in humans. This was however not confirmed in subsequent studies, and mechanistic data showed different saccharin metabolism in rodents and humans. To provide information on the role of low calorie sweeteners on the risk of cancer at several sites, we considered data from an integrated network of case-control studies that were conducted in Italy between 1991 and 2008. Cases were 598 incident, histologically confirmed cancers of the oral cavity and pharynx, 304 of the oesophagus, 1,953 of the colorectum, 460 of the larynx, 2,569 of the breast, 1,031 of the ovary, 1,294 of the prostate, and 767 of the kidney. Controls were 7,028 patients (3,301 men and 3,727 women) admitted to the same network of general and teaching hospitals, for acute non-neoplastic diseases. We also considered 230 patients with cancers of the stomach and 547 controls, 326 of the pancreas and 652 controls, and 454 of the endometrium and 908 controls. ORs were obtained from multiple logistic regression analyses, including allowance for total energy, as well as major recognized risk factors for each neoplasm. The ORs for an increase of one sachet-day of low calorie sweeteners were 0.81 for cancers of the oral cavity and pharynx, 1.09 for oesophagus, 0.96 for colon, 0.94 for rectum, 1.16 for larynx, 0.94 for breast, 0.87 for ovary, 1.03 for prostate, and 0.99 for kidney cancer. There was no material difference in risk for saccharin vs other low calorie sweeteners. After allowance for various confounding factors, the ORs for ever users of sweeteners versus nonusers were 0.80 (95% CI, 0.45-1.43) for gastric cancer, 0.62

(95% CI, 0.37-1.04) for pancreatic cancer, and 0.96 (95% CI, 0.67-1.40) for endometrial cancer. Corresponding ORs for saccharin were 0.65, 0.19, and 0.71, and for other sweeteners were 0.86, 1.16, and 1.07, respectively. This is the first comprehensive dataset on the relation between sweeteners, digestive tract and selected other major cancers. Other data on brain and haematopoietic neoplasms also showed no association. Thus, there is now convincing epidemiologic evidence of the absence of association between saccharin, aspartame and other sweeteners, and the risk of several common neoplasms.

With reference to cardiovascular disease, the pooled RR from the two studies —obtained combining the study estimates by meta-analytic methods— was 1.19 (95% CI 0.84-1.67) for regular ( $\geq 1$  times per day) consumption of low-calorie beverages as compared to non users, and 1.29 (95% CI 1.13-1.48) for regular consumption of sugar-sweetened beverages. Available epidemiologic data thus indicate that, while use of sugar-sweetened beverages appears to be related to increased risk of cardiovascular disease, consumption of low-calorie beverages is not significantly related.

With reference to preterm delivery, when the main findings of the two studies were pooled, the RR was 1.25 (95% CI 1.09-1.43) for  $\geq 4$  servings/day of low-calorie beverages. However, for lower levels of consumption risk estimates were close to unity and, most importantly, similar risk estimates were found for sugar-sweetened beverages (RR = 1.23, 95% CI 1.06-1.42 for  $\geq 4$  servings/day). Thus, the two studies, Hall-dorsson et al., and Englund-Ogge et al, show no evidence that low-calorie beverages have an impact on preterm delivery at any variance from that of sugar sweetened beverages.

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# Identification and control of sweeteners in food products

Eladia Franco Vargas

Food additives are quite an unknown topic within the food consumption field, as well as being an issue that consumers are deeply concerned about. Despite the fact that they are associated to modern times, food additives have been used for centuries. They have been used since mankind learned how to preserve food. Thanks to the development that food science and technology have achieved in the past 50 years, several new substances providing some benefits have been discovered, such as certain sweeteners used in low-calorie products, non-cariogenic food, etc.

For the identification and control of table top sweeteners and those used in foodstuffs the European Union legal framework must be taken into account, which includes their conditions of use, specifications, authorization procedure, evaluation and re-evaluation programs. In addition the Official Control food law must be taken in to account.

The use of additives is strongly regulated, and the criteria used for their approval are: that there is a reasonable technological need, that they are safe, and that they do not mislead consumers.

All food additives must have a demonstrated useful purpose and must undergo a rigorous and comprehensive Scientific Assessment to assure their safety before their use is authorized. At the level of the European Union the risk assessment of food additives is the responsibility of the European Food Safety Authority (EFSA). At the international level, the Joint Expert Committee on Food Additives (JECFA), which works under the auspices of the United Nations Food and Agriculture Organization (FAO) and the World Health Organization (WHO), is responsible for the evaluation and risk assessment of Food Additives.

One element of the legislation about additives in the EU is the Regulation (EC) 1333/2008 that provides harmonized lists of authorized food additives (Annexes II and III), their conditions of use, including the additives used in additives, enzymes and flavors, as well as their labeling legal requirements.

The European Union defines 26 functional classes according to the technological activity, and sweeteners are included as one of those.

For most of the additives that are authorized there is a minimum level necessary to achieve the desired effect. This level takes into account the acceptable daily intake (from the Additive and from any other sources) and the possible daily intake even for the most sensitive consumers. However, there is the

possibility to use additives without complying with maximum levels and following the principle “quantum satis”, which means the use of the minimum amount required to obtain the desired effect. The presence of additives in intermediate products is also permitted.

The principle of transfer allows the presence of an unauthorised additive in a particular food, as long as it has been used in any of the ingredients contained in it, or by being part of another additive, flavors and/or enzyme.

There is a common authorization procedure applicable for the 28 countries of the European Union established in the Regulation (EC) 1331/2008. There is an application that shall be submitted by the MMSE or the interested party to the European Commission (EC), and the EC requests EFSA to conduct the risk assessment. The dossier shall include the documentation required in the regulation that is mandatory for both the risk and management assessment.

The European Commission established a Re-evaluation of Additives program for the additives approved before 2009. The priority for re-evaluation takes into account: exposure assessment to consumers, the elapsed time since the last risk assessment, the availability of new scientific evidences and the level of use of the additive. Dyes, which had old SCF assessments, were prioritized. The evaluation of sweeteners that is the most recent and will be reevaluated at the end of the program.

Official Control covers companies and products. The activities included in official controls are: inspection, supervision of HACCP's stakeholder programs, sampling and analysis. They are undertaken by the competent authorities at any stage of production, processing and/or distribution. For the effectiveness of these operations they have to comply with the provisions in the Regulation (EC) 882/2004, in terms of procedures, training of control authorities, auditing controls, etc.

The Community of Madrid has two programs in place that provide the official controls described above: «Food Inspection Program and Control and Program Monitoring and Control of Contaminants and Residues in Food». They aim to control companies that process, pack, storage and / or distribute foodstuffs, including sweeteners.

The companies in the additives sector are considered in the categories of A and B of lower risk given the conformity of the official controls obtained during past years.



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# Sweeteners, nutrition and medicine; what do we do in primary care?

M.<sup>a</sup> Luisa López Díaz-Ufano

Health protection has been constant throughout history, although it is true that all the health aspects have centred on the concept of illness during the XIX century and great part of the XX century. In the International Congress on Primary Health Care of Alma-Ata, health was defined as a state of complete physical, social and mental well-being, and not just simply a lack of illness. The fundamental pillars of primary care are prevention and health promotion, as well as the way to manage any health problem subject to being attended to within the primary care setting.

The Portfolio of Primary Care's Standard Services of the Community of Madrid is defined as *"the offer of benefits and special monitoring services for the citizens, prioritized depending on the health problems and needs of the population of Madrid, that are subject to being attended by the first level of care, and in which, according to the standards established, have the purpose of guaranteeing the quality of care"*.

Health education is a process that approaches not only how health information is transmitted, but also helps to foment motivation, personal abilities and the self-esteem necessary to adopt measures destined to improve health.

Through the Service Portfolio and a series of periodic recommendations, preventive methods are put into action based on scientific evidence. Of all the services that it encompasses we will refer to: Pregnant women care, The promotion of childhood health habits, Overweight children care, The promotion of health in adolescence, Childhood oral hygiene and The promotion of healthy lifestyles for adults.

There is vast evidence of the correlation between specific health lifestyles and the decrease of the main chronic diseases. Many interventions have been based

on the behaviourism model, suggesting different ways of acting depending on the person's state. This model has limitations when it comes to complex behaviours (physical activity or eating behaviour). International recommendations suggest that consulting and advice interventions be based on the 5 A's model created by the USTSTF. And last of all the Institute for Clinical Systems Improvement (ICSI) advises to carry out a personalized intervention adequate to the risk presented, increasing the person's awareness and motivating him/her to change.

With the SWOT analysis we can reach the following conclusions:

1. Training health professionals. The lack of knowledge on behalf of health professionals about differential features between different sweeteners in order to give advice and/or select a determined sweeteners based on its properties (weakness).
2. Commitment with the Administration. There are few solid studies based on humans that confirm their possible benefits (weakness).
3. Patient training. The use and abuse of "evidence" provided by the media leads to lack of information for the patient (threat).
4. An increasing interest of the population and health professionals in nutraceutical products with sweetening properties, which could take us to the creation of coordinated applications related to their use and interaction with medication and/or foods (strength).
5. A common message when it comes to preventing chronic diseases with health promotion, the growing culture of caring for one's body and achieving an optimum health state (opportunity).

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## Sweeteners and food; view of the health administration

Jesús Vázquez Castro

Each year 2.8 million adult people die of overweight and obesity. 11% of the Spanish population is diabetic. Between 92-94% of people aged 35 years and over suffer from tooth decay.

In the Community of Madrid the prevalence of obesity in those aged 6-18 years is 7.4% and is 21.7% in adults (30-74 years old). According to other communities the Community of Madrid is situated at a medium-low level.

The significant observed increase in the consumption of sugar sweetened beverages may contribute to obesity.

For these reasons, the aim of the administration in the Autonomous Community of Madrid was to improve the professional knowledge of Primary Care professionals and citizens in relation to sweeteners and food. A SWOT (Strength, Weakness, Opportunities, Threats) analysis was administered to Primary Care professionals in the Community of Madrid to measure their knowledge of sweeteners. The results are shown in table III.

In conclusion, the following recommendations can be made:

**Table III**  
Sweeteners. SWOT

Weakness	Threats
<ul style="list-style-type: none"> <li>• Lack of robust studies in humans.</li> <li>• Little information on nutrition labels of consumer products which contain sweeteners.</li> </ul>	<ul style="list-style-type: none"> <li>• No existence of data about the use of sweeteners in the long term.</li> <li>• No knowledge of the specific amounts of dose-response.</li> <li>• Doubts about the risk of use.</li> </ul>
Strength	Opportunities
<ul style="list-style-type: none"> <li>• The increased interest in these products.</li> <li>• Beneficial effects.</li> <li>• Sweet taste without calorie inputs.</li> <li>• They are safe if consumption corresponds to the level of daily intake established by regulatory agencies.</li> </ul>	<ul style="list-style-type: none"> <li>• The information on the nutritional label should include sweeteners.</li> <li>• It is necessary to be aware of the dose-response amount to clarify the effects of use at the metabolic level.</li> <li>• Include studies with specific pathologies (diabetes) or special groups (pregnant women or children).</li> </ul>

- The actions should improve the influence of food and nutrition knowledge on health and cover it throughout all of the life cycle.
- The information about the use of sweeteners should be transmitted in diabetic education and obesity sessions.
- We should have nutritional information about consumer products that contain sweeteners.
- It is necessary to have evidence based information to formulate consumption recommendations.

- It is important to inform and train Primary Care professionals on nutrition, dietetic aspects, the use of sweeteners and the interactions of drugs with food, as well as assuring that protocols and dietary prescriptions are unified.
- The key is to have designated units that inform professionals and citizens to encourage consumer co-responsibility and to increase their knowledge base.

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