Nutrición Hospitalaria

Nutr Hosp. 2014;30(Supl. 2):49-55
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Low and no calorie sweeteners (LNCS); myths and realities

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Abstract

Since their introduction in the market, there has been much debate regarding the health effects of low and no calorie sweetners (LNCS). Therefore, through this review, we aim to establish scientific information about the most commonly used LNCS by the food industry. Key questions about uses, safety, and weight control are reviewed. Scientific evidence revised concludes that LNCS available on the market are safe and no epidemiological relationship has been established with the development of non-communicable diseases, including different kind of cancer in humans. Also, LCNS combined with physical activity and a healthy lifestyle can play a significant role in weight loss and the maintenance of a healthy weight. But non nutritive sweeteners will be helpful only as long as people don't eat additional calories later as compensation. Even more, LNCS represent an additional instrument in the dietary treatment of people with diabetes for metabolic control, without avoiding sweet taste.

Nutr Hosp 2014; 30 (Supl. 2): 49-55

Key words: *Low-calorie sweeteners. Non nutritive sweeteners. Low and no calorie sweetners. Safety. Weight. Obesity. Diabetes. Cancer.*

EDULCORANTES HIPOCALÓRICOS; MITOS Y REALIDADES

Resumen

Desde su introducción, ha habido mucho debate acerca de los efectos sobre la salud de los edulcorantes hipocalóricos y sin calorías (LNCS). Por lo tanto, en esta revisión, nuestro objetivo es revisar la información científica disponible acerca de los edulcorantes hipocalóricos y sin calorías más utilizados en la industria alimentaria. Se revisan aspectos clave acerca de los usos, la seguridad y el control del peso.

A partir de la evidencia científica revisada se concluye que los LNCS disponibles en el mercado son seguros, no existe ninguna relación epidemiológica con el desarrollo de enfermedades no transmisibles , incluyendo diferentes tipos de cáncer en humanos. Además, los LCNS, junto con la actividad física y un estilo de vida saludable pueden jugar un papel significativo en la pérdida de peso y en el mantenimiento del peso saludable. Pero los edulcorantes no nutritivos únicamente serán útiles si los usuarios no realizan una compensación, comiendo posteriormente un exceso de calorías. Es más, los LNCS representan un instrumento adicional en el tratamiento dietético de las personas con diabetes para el control metabólico, sin renunciar al sabor dulce.

Nutr Hosp 2014; 30 (Supl. 2): 49-55

Palabras clave: *Edulcorantes bajos en calorías. Edulcorantes no nutritivos. Edulcorantes hipocalóricos y sin calorías. Seguridad. Obesidad. Diabetes. Cáncer.*

Abbreviations

LCS: Low calorie sweeteners.
LNCS: Low and non calorie sweeteners.
NNS: Non nutritive sweetener.
SSB: Sugar sweetened beverages.
BMI: Body Mass Index.
ADI: Acceptable Daily Intake.

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Introduction

Low calorie sweetener (LCS), also named as non nutritive sweetener (NNS), artificial sweeteners or low or no calorie sweeteners (LNCS), is the term used to describe additives 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 to do not increase significantly caloric content. They are widely used in foods and drinks as sugar substitutes to sweeten foods, drinks and medicines throughout the world. Currently, 10 LNCS have been authorized in Europe: acesulfame K (E-950), aspartame (E-951), cyclamate (E-952), sacharine (E-954), sucralose (E-955), thaumatin (E-957), neohesperidine DC (E-959), steviol gicosides (E-960), neotame (E-961)

and aspartame-acesulfame salt (E-962). Some hypocaloric sweetners as polyalcohols (sorbitols, E 420, manitol, E-421, xylitol, E-957, erythritol, E-968) have also been approved. It is mandatory the description and declaration of all these ingredients on product labeling[1]. Stevia, a natural NNS, is a steviol glycoside isolated from the plant Stevia Rebaudiana Bertoni. The stevia leaf contains 11 main glycosides, mainly stevioside and rebaudioside A (Reb A) (together 14-18% of leaf content).). Steviol glycosides are hydrolysed by gut bacteria to release free steviol; once absorbed, undergo glucuronidation in liver and are then excreted. Each steviol glycoside has unique taste and sweetness profile, and can be 150 to 400 times sweeter than sugar.

In food selection, taste is one of the most important factors, and contributes to the overall pleasure and enjoyment of a food. The sensation of taste results from the chemical stimulation of specialized cells called Taste Receptor Cells, grouped in clusters or taste buds. Each taste bud is composed of 50-150 taste receptor cells, and are mainly located on the tongue, in circumvallate, foliate or fungiform papillae. Sweet taste receptor is an heterodimer of two transmembrane proteins (T1R2, T1R3 and gustducin) has several different binding sites. It is present in lingual taste buds, but also has been discovered in GLP-1 secreting L cells of gut, where it serve as mediator of GLP-1 secretion. It responds to sugars and also to LNCS.

Safety standards for consumption of LNCS

Since their discovery in the early 1900s and introduction into the public market in the 1950s and 1960s, there have been several debates regarding the health effects of LNCS. In the USA, the FDA banned cyclamate, due to its carcinogenic effects in animal studies[2]. Since then, the LNCS industry has come a long way and consumers now have products safe for consumption, even for kids and pregnant women. LNCS currently used have been subjected to strict safety studies. The regulatory process is scrupulous and it is really hard for any additive to be authorized. The Acceptable Daily Intake (ADI) is the amount of a substance that can be consumed daily in the diet, over the course of a lifetime, *without any health problems*. So, setting ADIs is a *guarantee of safety*, a way of ensuring that the actual intake of the LNCS is well below the level that could be considered harmful to health. ADI levels are established by international regulatory Authorities [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]. ADI for aspartame is 40 mg/kg body weight.

LNCS and cancer

The putative role of LNCS in cancer has been widely debated since the 70s, when animal studies found an increased bladder cancer risk in mice treated with extremely high doses of saccharine. An old case-control study including 408 cases[3] showed a 60%increased risk for bladder cancer in men (but not in women) LNCS users. However, other case-control studies of bladder or low urinary tract cancers found no significant association with consumption of sweeteners[4], and the largest case-control study analysing the issue, conducted in the United States, including 3010 cases of bladder cancer, found no relation (odds ratio = 1.01; 95%, confidence interval 0.92-1.11 for ever versus never use)[5]. Another study, including 267 cases of renal cell carcinoma, found no association for lifetime consumption of artificial sweeteners[6]. Although epidemiological studies in humans failed to reproduce these findings[7], and it was shown that saccharine metabolism is species specific[8], these animal data have received widespread attention[9]. The Italian network of cases and control study, performed between 1991 and 2004[10], showed a lack of association between LNCS and the risk of several common neoplasms. Cases were 598 patients with incident, histologically confirmed cancers of the oral cavity and pharynx, 304 of the oesophagus, 1,225 of the colon, 728 of the rectum, 460 of the larynx, 2569 of the breast, 1031 of the ovary, 1,294 of the prostate and 767 of the kidney (renal cell carcinoma). Controls were 7,028 patients admitted to the same hospitals for acute, non-neoplastic disorders. There was a direct association between consumption of sweeteners and laryngeal cancer risk, but also a borderline significant association with sugar was found. And a significant inverse association between sweeteners and ovarian and breast cancer risk. These results are in agreement with a case–control study from Denmark including 1486 breast cancer cases (OR = 0.9; 95% CI 0.7-1.2 for users versus nonusers of artificial sweeteners)[11]. Among the limitations of the study, there is the relatively low frequency of consumption of sweeteners in this Italian population[12], and consequently, despite the large sample size, the relatively limited statistical power. When studying the relation between sweeteners and cancers[13], the role of obesity and sugar on carcinogenesis should be taken into account, since the use of sweeteners is inversely correlated with sugar. And obesity and sugar has been directly associated to the risk of certain cancers. Users of sweeteners were heavier than nonusers (mean body mass index [BMI] 27.0 *versus* 25.7 kg/m^2), but strict allowance was made for BMI in the analyses.

A second study from Italy showed that, after allowance for various confounding factors, the odds ratio for users of sweeteners versus non users were 0.80 (95% CI, 0.45-1.43) for gastric cancer, 0.62 (95% CI, 0.37-1.04) for pancreatic cancer, 0.96 (95% CI, 0.67-1.40) for endometrial cancer[14].

A direct correlation between aspartame consumption and the incidence of brain cancer[15] was also suggested, but this hypothesis was not confirmed by studies in animals or humans[16]. In the prospective

NIH-AARP Diet and Health Study, a cohort from the USA, including more than 500,000 subjects, and 315 cases of glioma, no evidence linking aspartame and other low-calorie sweeteners to the risk of brain cancer, either in children or adults[17]. In the same cohort, the possible association between aspartame and hematopoietic malignancies was considered. During follow-up,1888 cases of hematopoietic cancers, 1324 cases of non-Hodgkin lymphoma, 285 multiple myelomas, and 339 leukemia. Again, no association with aspartame-containing beverages, and overall hematopoietic cancers was found (adjusted RR was -0.98 [95% CI: 0.76-1.27] for ≥ 600 mg aspartame/day *versus* none). Authors concluded that aspartame consumption derived from its main source, aspartame-containing beverages, does not raise the risk of hematopoietic or brain malignancies.

In the Nurses' Health Study and Health Professionals Follow-up Study[18], after 22 years follow-up, 1324 cases of non-Hodgkin lymphoma, 285 multiple myeloma, and 339 leukemia were diagnosed. No significant association between soda intake and risks of non-Hodgkin lymphoma and myeloma was seen. Although only in men, 1 daily serving of diet soda was associated with increased risks of NHL and myeloma but the inconsistent sex effects do not permit the ruling out of chance. We agree with Marinovich[19] that scientific evidence indicates that there is no relationship between the consumption of LNCS and the development of non-communicable diseases. So, the low and non calorie sweeteners available on the market are safe and the available epidemiological evidence on LNCS does not support the existence of any consistent association with cancer.

Obesity

With the current obesity epidemic, LNCS have the potential to play an important role in weight control. Even modest reductions in the intake of calories can reduce the risk factors associated with diabetes and cardiovascular disease. So, replacement of sucrose with LNCS could result in a decrease in calorie intake, enough to produce a health benefit. It has been estimated that adults can prevent weight gain by reducing intake by 100 kcal/d. Replacing a regular soda with a diet soda will save about 150 kcal and using a LNCS rather than 2 teaspoons (18 g) of sugar in a cup of coffee, 3 times a day will save about 100 kcal. The question is, do low and non caloric sweeteners actually help to reduce weight? Some data suggest that nonnutritive sweeteners may be used in a structured diet to replace added sugars, and that this substitution may result in modest energy-intake reductions, weight loss, and beneficial effects on related metabolic parameters. In a study by Tordoff, normal weight subjects drank 1,150 g/day soda sweetened with aspartame or high-fructose corn syrup, for 3 weeks and found a 7% decrease in calorie intake when subjects drank aspartame-sweetened soda[20].

Kanders et al measured weight loss, perceived feelings of energy and wellbeing, among 51 free-living obese men and women[21]. At 12 weeks follow-up, sustained weight loss was associated with increased low and non calorie sweetener consumption, a decreased desire for sweets and increased physical activity levels. Although the small sample size prohibits definitive conclusions, the study suggests possible advantages to supplement a balanced deficit diet with aspartame-sweetened foods as part of a multidisciplinary weight loss program.

The first large, randomized, controlled, prospective outpatient clinical trial investigating whether the addition of low and non calorie sweeteners to a multidisciplinary weight control program would improve weight loss included 163 obese women[22]. The aspartame group lost significantly more weight overall ($P = 0.028$) and regained significantly less weight during maintenance and follow-up ($P = 0.046$) than did the no-aspartame group. These data suggest that participation in a multidisciplinary weight-control program that includes aspartame may facilitate the long-term maintenance of reduced body weight. Bellisle et al examined whether reducing the energy density of sweetened drinks and foods through the introduction of low calorie sweeteners can be a useful aid for weight control[23]. In the study by Raben[24], with a parallel design with 2 intervention groups, after 10 weeks, the sucrose group had increases in total energy, sucrose, and carbohydrate intakes and decreases in fat and protein intakes. The sweetener group had small but significant decreases in sucrose intake. Body weight and fat mass increased in the sucrose group (by 1.6 and 1.3 kg, respectively) and decreased in the sweetener group (by 1.0 and 0.3 kg, respectively); the between-group differences were significant at $P < 0.001$ (body weight) and $P < 0.01$ (fat mass). Systolic and diastolic blood pressure increased in the sucrose group (by 3.8 and 4.1 mm Hg, respectively) and decreased in the sweetener group (by 3.1 and 1.2 mm Hg, respectively)

But non randomized prospective cohort studies found positive correlation between LNCS use and weight. The potential for LNCS consumption to promote weight gain drew attention in 1986 based on findings from an American Cancer Society survey conducted over one year with 78,694 women 50–69 years of age. After controlling for initial body weight, those who used LNCS were significantly more likely to gain weight than non-users. However, mean weight changes differed by less than 0.5 kg between users and non-users. However, hypothesis generated considerable debate and suggested that LNCS cause people to compensate for the energy they are saving by increasing appetite, hunger, or food intake or inducing cravings for sweets. Even more, in the San Antonio Heart Study long-term weight gain was increased in low caloric sweetened beverage users[25], and suggested that LNCS consumption might be fueling the obesity epidemic instead of fighting it.

In the MESA study[26], 6814 adults, 45-84 years were followed and intake was assessed with a frequency food questionnaire at baseline (2000-2002). Daily consumption of diet soda was associated with 36% greater risk of metabolic syndrome and 67% greater relative risk of type 2 diabetes compared with non consumption. Potential mechanisms blamed for these findings were that dissociating sweetness from calories, LNCS could interfere with physiological responses that control homeostasis and facilitate any compensation. Also, LNCS could affect the microbiota and trigger inflammatory processes associated with metabolic disorders. Interacting with sweet-taste receptors in gut, LNCS could activate gut sweet-taste pathways that control incretin release and up-regulate glucose transporters. But the results should be interpreted with caution. These were observational studies, not clinical trials and the potential confounding of LNCS use for weight control could not be ruled out. The positive associations could be due to possible mediating factors, such as BMI.

In a systematic review and meta-analysis[27], 15 studies were included, 3 trials with obese using LNCS showed effectiveness of foods and drinks sweetened with non-nutritive sweeteners compared with sucrose: Energy intake was reduced by about 10% and mean weight loss by 0.2 kg/week.

A second systematic review and meta-analysis by Mattes[28], addressing nutritively sweetened beverages and body weight, included only trials of at least 3 weeks duration. Reducing or replacing sugar in beverages (long term studies) did show no overall effect on BMI. But in sub-group analysis, just considering three studies in overweight subjects, replacing sugar by LNCS did show a benefit in weight.

More recent trials probably tilt the balance in favour of a beneficial effect of LNCS. In the CHOICE study[29], a prospective randomized control trial, participants were randomized to 3 groups: control, water (n = 106) or diet beverages (DB) (n = 104) group, for 6 months. Both intervention groups lost weight and reduced waist circumference, and reduced intakes of total daily energy, carbohydrates, fat, protein, saturated fat, total sugar, added sugar and had positive changes in energy intakes and dietary pattern. DB group reduced more desserts than the water group. No evidence to suggest that consumption of diet bevereages, compared with water, increases preferences for sweet foods and beverages was observed. LNCS users (vs. no users) were more likely to be females, white, older, educated, higher socioeconomic status; Reported similar energy intakes but higher intakes of fruits, vegetables, calcium and magnesium, lower intakes of fat, added sugars, and saturated fats and report reading labels. So, LNCS users had a better diet quality.

The DRINK trial[30] was a prospective, randomized, double blind trial with 641 normal weight children, 4-12 years old, given 250 ml/day of a sugar-containing beverage 104 kcal or a diet drink for 18 months. The DRINK trial tried to overcome the behavioural factors that affect compensation by designing two study drinks, which tasted and looked the same. Group 1 (n = 322) received 10% sugar-containing lemonade, with 104 kcal. Group 2 (n = 319) received sugar free lemonade, sweetened with non nutritive sweeteners, and thus contained zero calories. The sugar-free beverages contained 34 mg of sucralose and 12 mg of accesulfame potassium per can. This 'masked' replacement of sugar-containing beverages with non-caloric beverages significantly reduced weight gain and fat accumulation in normal-weight children over the period of the trial. The authors did not measure energy intake and could not calculate compensation but a plausible explanation for the observed reduction in body fat is that the removal of liquid sugar was not sensed by satiating mechanisms and was incompletely compensated for by the increased consumption of other foods.

In the BASH study, a prospective randomized trial, 224 overweight adolescents from Boston were delivered either SSB or diet drinks for 1 year[31]. The increase in BMI was smaller in the experimental group than in the control group after a 1-year intervention, but not at the 2-year follow-up.

Of course, sweeteners will be helpful only as long as people do not eat additional calories. It has been said that LNCS may not promote satiety and therefore compensatory eating occurs at the next meal. Compensation is the difference between expected "theoretical" energy intake and actual intake. Compensation can take two forms: physiological, where the body might be expecting more calories and so the individual may be hungrier and therefore may eat more; and psychological, where the person thinks he is allowed to eat more sugar-rich food because they consumed a diet food or beverage. Possible mechanisms considered for compensation after LNCS intake are: i) LNCS may over-stimulate taste receptors and increase cravings for sweetness. ii) NNS may provoke hunger and cause overeating. The degree of compensation depends on the form of the food/drink and how they are being used by the consumer. Compensation is less likely when these sweeteners are consumed in beverages as opposed to solid food. So it appears that there is more room for beneficial effects of these sweeteners when used in beverages. Again, the key is how much compensation is induced? If there is only partial compensation, then the balance is still in favor of fewer calories. Even allowing for compensation, an energy reduction of 100 kcal per day could be achieved by replacing 1 can soft drink per day with 1 can sweetened with LNCS.

However, in a study specifically designed to evaluate the degree of compensation[32] participants did not compensate (food intake at subsequent meals was not increased) by eating more at either their lunch or dinner meal when they consumed lower calorie preloads containing stevia or aspartame compared to when they consumed higher calorie preloads containing sucrose. In other words, even after a lower calorie preload, food intake at subsequent lunch and dinner meals was not in-

creased and discretionary food intake did not differ between the conditions.

A recent randomized trial[33] compared the efficacy of non-nutritive sweetened beverages versus water for weight loss during a 12-week behavioral weight loss treatment program. The LNCS beverage treatment group lost significantly more weight compared to the water group (5.95 kg *versus* 4.09 kg; $P < 0.0001$) after 12 weeks. Even more, participants in the LNCS beverage group reported significantly greater reductions in subjective feelings of hunger than those in the water group during 12 weeks. The authors concluded that water is not superior to LNCS beverages for weight loss during a comprehensive behavioral weight loss program. The study demonstrates that LNCS beverages can be part of an effective weight loss strategy and individuals who desire to consume them should not be discouraged from doing. A longer term follow-up of this randomized cohort, is now underway, could clarify the utility of LNCS beverages in weight loss maintenance.

In children, 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[34].

So, although mixed results are shown, likely due to different levels of compensation, we can conclude that the use of LNCS in food and beverages may lead to reduced energy intake and body weight reduction, especially in overweight people. But it must be combined with physical activity and a healthy lifestyle to achieve weight loss and to maintain a healthy weight. A concern, though, is that just replacing sugar with artificial sweeteners leaves a person, especially children, conditioned to high levels of sweetness, which is likely to influence their food choices adversely.

Diabetes

Some associations were found between LCNS consumption and increased diabetes risk in the French prospective Etude Epidémiologique auprès des femmes de la Mutuelle Générale de l'Education Nationale-European Prospective Investigation into Cancer and Nutrition cohort, after 14 years of follow-up, but in absence of a consistent trend in both sugar and artificially sweetened beverages consumption. A total of 66,118 women were followed from 1993, and 1369 incident cases of type 2 diabetes were diagnosed during the follow-up. Compared with non consumers, women in the highest quartil of consumption of sugar sweetened beverages (SSB) and low and non calorie sweetened beverages had an increased risk of diabetes. These associations were partly mediated by BMI, although there was still a strong significant independent effect. But it is known that people also tend to consume LCNS when they have prediabetic conditions, such as obesity. Other factors responsible for the association with diabetes could not be ruled out. So, the positive association between low calorie sweetened beverages and diabetes risk has been told to be due to reverse causation[36].

However, in the Nurse's Health Study and the Health Professionals Follow-up cohorts, there was an association of type 2 diabetes with sugar sweetened bevereages, but not with low-calorie ones[37]. Another putative mechanism that might explain the positive relation between LCNS with obesity and diabetes risk have been said to be an appetite enhancement, previously described as "compensation".

Anton et al[38] studied the effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels. They showed that aspartame, generates a similar body response in terms of postprandial glucose and insulin concentrations to those induced by sucrose. Indeed, in their study, which included 31 subjects, there was no significant difference in glucose and insulin concentrations 30 min after ingestion of a load of aspartame compared with after a similar ingestion of sucrose. However, participants who ingested preloads of stevia had significantly reduced insulin concentrations 30 and 60 min after the test meal compared with those of participants who ingested aspartame preloads.

The effect of artificial sweeteners on glucose, insulin, and glucagon-like peptide (GLP)-1 in humans was studied in 22 healthy volunteers[39]. Subjects drank 240 ml of diet soda or carbonated water, in randomized order, 10 min prior to an oral glucose tolerance test, with frequent measurements of glucose, insulin, and GLP-1. Glucose excursions were similar after ingestion of carbonated water and diet soda. Serum insulin levels tended to be higher after diet soda, without statistical significance. GLP-1 peak and area under the curve (AUC) were significantly higher with diet soda. So, LNCS synergize with glucose to enhance GLP-1 release in humans. This increase in GLP-1 secretion may be mediated via stimulation of sweet-taste receptors on L-cells by artificial sweetener. But the effect must be specific because sucralose given by intragastric infusion does not stimulate GLP-1 or GIP release in humans or slow gastric emptying[40]. This implies that it may have no therapeutic benefit in the dietary management of diabetes, other than as a substitute for carbohydrate.

The American Heart Association and the American Diabetes Association have issued a joint scientific statement giving a cautious recommendation to the use of nonnutritive sweeteners to help people maintain a healthy body weight and for diabetics to aid glucose control[41]. The statement, published in both *Circulation* and *Diabetes Care* warns, however, that non nutritive sweeteners will be helpful only as long as people don't eat additional calories later as compensation. It adds that scientific evidence is limited and inconclusive about whether this strategy is effective in the long run for reducing calorie and added-sugars consumption.

Vascular diseases

Information on sugar and non nutritive sweetened beverage consumption and the risk of coronary heart disease was provided from the Nurse's Health Study. After follow-up, 423 cases of coronary heart disease among daily users of low and no calorie beverages, and 301 among daily users of sugar sweetened beverages, have been diagnosed[42]. The relative risks were 1.07 (95% confidence interval 0.96-1.20) for low and no calorie beverages and 1.59 (95% confidence interval 0.92-2.74) for sugar-sweetened beverages. But data from the Northern Manhattan Study showed an association, of borderline significance, between both diet and sugar sweetened soft drinks and combined vascular events (myocardial infarction, stroke or vascular death combined), with hazard ratios for daily consumption of 1.59 (95% confidence interval 0.92-2.74) for diet soft beverages and of 1.57 (95% confidence interval 1.05-2.35) for sugar-sweetened beverages[43]. These estimates were based on 15 combined events only for diet soft beverages daily users, and 41 combined events for sugar sweetened beverages daily users. The continuous HRs were 1.03 (95% 1.00-1.07) for diet soft beverages and 1.02 (95% CI 0.99-1.04) for sugar sweetened beverages. Since diet beverages tend to be more frequently used by subjects who are prone to weight gain to control body weight[44], reverse causation may partly or largely account for the modest and non-significant association between diet soft beverages and vascular disease observed in this study.

Conclusions

In conclusion, LNCS have been used safely by consumers throughout the world for more than a century and have been subjected to strict safety tests. Current scientific evidence indicates that there is no relationship between the consumption of LNCS and the appearance of non-communicable diseases, including different kinds of cancer, or cardiovascular disease. Therefore, their consumption represents no health risk in light of existing scientific evidence. Also, it is a helpful tool in the prevention of overweight and in weight control as sientific research shows that the consumption of foods and drinks in which sugar has been replaced by LNCS combined with physical activity and a healthy lifestyle can play a significant role in weight loss and the maintenance of a healthy weight. But non nutritive sweeteners will be helpful only as long as people don't eat additional calories later as compensation. Even more, LNCS represent an additional instrument in the dietary treatment of people with diabetes for metabolic control. Anyways, consumption of a heathy diet and promotion of physical activity and exercise must be strengthen, as well as consumer education based on the best scientific evidence.

Still, more research on LNCS is highly recommended to more definitively determine the benefits and risks of frequent LNCS consumption.

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