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Consensus statement on benefits of low-calorie sweeteners

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Preference for sweetness is innate and universal, and probably represents a biological response to safe sources of energy such as mother's milk and fruit (Ventura & Mennella 2011). There is some evidence that sweetness preference declines with age, is partly heritable and varies among cultures (Keskitalo *et al*. 2007; Drewnowski *et al*. 2012). Given current concerns about overweight and obesity, low-calorie sweeteners (LCS) are increasingly used to replace sugar and supply sweetness without calories, helping people to moderate their energy intake (Anderson *et al*. 2012). However, some people are confused about the effects of LCS on nutrition and well-being, despite positive statements about safety from regulatory authorities worldwide. This consensus paper summarises current evidence on the benefits of LCS, as reviewed by a panel of independent experts at the International Sweeteners Association Conference in Brussels, in April 2014. The panel included the following scientific experts.

- Prof Adam Drewnowski, Professor of Epidemiology, Director of the University of Washington Center for Obesity Research, University of Washington, USA;
- Prof James Hill, Professor of Pediatrics and Medicine, Executive Director, Anschutz Health and Wellness Center, University of Colorado School of Medicine, USA;
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Definitions

LCS are intensely sweet compounds that contain virtually no calories, and which can be used to replace sugar in food and drinks. Examples are aspartame, acesulfame K, saccharin, sucralose and steviol glycosides.

Hunger, appetite and satiety

Recent studies suggest that LCS neither promote nor suppress appetite (Bellisle & Drewnowski 2007; Renwick & Molinary 2010). Because of their volume, low- and no-calorie beverages may suppress appetite for about an hour, but do not appear to affect food intake at the next meal. By contrast, a caloric beverage will suppress appetite and may or may not reduce energy intake at the next meal. Satiety (fullness after consumption) was similar for children given LCS-containing beverages or sugar-sweetened beverages (SSB) in an 18-month intervention trial (de Ruyter *et al*. 2013), and similar effects have been found among adults (Rolls 1991; Holt *et al*. 2000). For example, in a crossover study, adults given foods sweetened with LCS (290 kcal) or sucrose (490 kcal) before lunch and dinner reported similar hunger and satiety ratings and ate similar amounts at the next meal (Anton *et al*. 2010). A recent meal test study (Maersk *et al*. 2012) showed that after drinking 500 ml of an SSB total energy intake (from the drink

and the following *ad libitum* meal) was higher compared with a diet soft drink or water. It was concluded that the energy provided by SSB was not fully compensated by decreased energy intake at the following meal, emphasizing the risk of generating a positive energy balance by frequent consumption of energy-containing beverages. Furthermore, there were no indications that the artificial sweetener used in this study (aspartame) increased appetite or energy intake, compared with water. More research is needed into possible habituation to the effects of LCS on appetite, satiety and food intake. There is also concern about the generalisability of blinded experimental studies, when cognitive and social factors may have more influence on consumption in real life (Anderson *et al*. 2012).

Energy intake

Studies suggest that food and beverages sweetened with LCS may help reduce energy intake if used in place of more energy-dense food and drinks (Mattes & Popkin 2009). Hence, the benefit of LCS will tend to be greater for drinks (where sugar is the main or only energy source) than for foods (where other macronutrients may be needed to replace sugar and provide bulk). Reviews of randomised controlled trials in which LCS were used in place of sugar or SSB over several days or weeks conclude that *ad libitum* energy intakes are lower with LCS because people only partly compensate for the missing calories (de la Hunty *et al*. 2006; Mattes & Popkin 2009). The degree of compensation of the food or drink is likely to vary depending on the physical form, composition, amount, timescale and individual factors. Variation in design may explain why some studies find a larger energy deficit than others. Such differences may include the type of LCS used, its physical form (food or beverage), the choice of control (*e.g*. SSB, water), the amounts consumed and the caloric context (*ad libitum*, hypercaloric, weight-reducing diet). Although more data from longer-term interventions are needed, it appears that LCS, especially in beverages, can be a useful aid to maintain reduced energy intake (Raben & Richelsen 2012).

Weight management

Several reviews of epidemiological and clinical studies have concluded that reducing or replacing SSB with low- or no-calorie alternatives has beneficial effects on bodyweight (Dennis *et al*. 2009; Malik *et al*. 2013; Ebbeling 2014), but evidence that using LCS results in weight loss has been limited (Shankar *et al*. 2013). In 2011, the European Food Safety Authority (EFSA) rejected a claim for non-nutritive sweeteners in weight loss, partly on the grounds that a cause and effect relationship between sugar intake and obesity had not been proven and partly because some of the evidence cited related to beverages rather than LCS-containing products in general (EFSA NDA 2011). However, evidence is steadily accruing from randomized controlled trials, and recent reviews have concluded that using LCS to replace sugars results in (modest) weight loss (<1 kg over several weeks) (Te Morenga *et al*. 2013) and a reduction in fat mass and waist circumference (Miller & Perez 2014). However, many studies included large amounts of sugars or SSB as the control, while others found significant effects only in subgroups, for example, overweight subjects or Hispanics. Such data indicate that additional research is needed to understand variation in response and mechanisms (Kaiser *et al*. 2013; Ebbeling 2014). In general, evidence supports the conclusion that substituting energy-free beverages or water in place of SSB facilitates weight management (Dennis *et al*. 2009). However, few studies have compared the impact of consuming LCS-containing beverages versus water, which would address whether LCS-containing beverages facilitate dietary adherence and weight loss because of their sweet taste and palatability, as opposed to merely substituting for sugar calories. This question was investigated in a recently published randomized controlled trial from the United States, which has indicated that LCS-containing beverages produce greater weight loss over 3 months compared with water (Peters *et al*. 2014). In this study, subjects were randomly assigned to consume either LCS-containing beverages or water (at least 710 ml/day) while participating in a 12-week behavioural weight loss programme, comprising weekly group sessions covering topics such as weight loss strategies, food labels, portion control and physical activity. Those assigned to the LCS group lost 5.95 kg, which was significantly greater than the average of 4.09 kg lost by those in the water-only group ($P < 0.0001$).

Prevention of weight gain is also important for public health and it has been hypothesised that an energy deficit of 100 kcal/day may be sufficient to prevent progressive weight gain in 90% of the adult population (Hill *et al*. 2003). A 100 kcal/day reduction in liquid calories was associated with a small weight loss (0.25 kg) over 6 months in the *PREMIER* prospective study (Chen *et al*. 2009); this deficit is equivalent to the energy in a 250-ml SSB or six teaspoons of sugar added to tea or coffee during the day. A high proportion of American adults who are trying to maintain their weight

use LCS as part of that strategy and also follow other healthy eating and lifestyle behaviours (Drewnowski 2013). Phelan *et al.* (2009) found that weight loss maintainers consumed more artificially sweetened soft drinks and used more fat- and sugar-modified foods than normal weight controls (Phelan *et al.* 2009). Similarly, participants in the US National Weight Control Registry consume three times as much LCS as normal weight controls. The other behaviours associated with successful weight loss maintenance in this cohort include calorie counting, consistent dietary restraint, self-weighing, eating breakfast and taking exercise (Wing & Hill 2001).

Diabetes and insulin

Diabetes has different forms, but all feature abnormal glucose metabolism because of insulin deficiency and/or impaired insulin effects. People with diabetes are encouraged to follow a healthy diet, with around 50% of energy from carbohydrates, which can include a small amount of added sugar. There is evidence that LCS can provide sweetness without raising blood sugar or affecting insulin or gut peptide release in any way (Grotz *et al.* 2003; Ma *et al.* 2009, 2010), in contrast to high sucrose/high-energy diets, which normally tend to increase post-prandial glycaemia, insulinaemia and lipidaemia (Raben *et al.* 2011). Equally, when consumed with glucose, LCS do not appear to modulate the glycaemic response (Bryant *et al.* 2014). LCS have been declared safe for people with diabetes, and EFSA has recently approved the health claim that LCS help reduce post-prandial glycaemic response (EFSA NDA 2011). Maintaining a healthy bodyweight is central to good control of diabetes, so LCS may also benefit people with diabetes by facilitating weight control, if consumed in the context of a calorie-controlled diet and healthy lifestyle. More research is needed into their role in long-term blood glucose control.

Oral and dental health

LCS are non-cariogenic, which means that they are not fermented by oral bacteria and do not cause tooth decay (Grenby 1991). However, LCS-containing foods are not necessarily 'tooth-friendly' if they contain fermentable carbohydrates or food acids with an erosive effect. Hence, the tooth-friendly property depends upon the food's overall composition and characteristics. EFSA has published a positive opinion on the claim that sweeteners may decrease the rate of tooth demineralization (EFSA NDA 2011).

Conclusions

(1). LCS do not increase appetite and have no discernible effect on satiety.
(2). LCS help to reduce energy when used in place of higher energy ingredients.
(3). LCS can enhance weight loss under real-life conditions when used as part of a behavioural weight loss programme.
(4). LCS may have a beneficial effect on post-prandial glucose and insulin in healthy individuals and in people with diabetes.
(5). LCS have dental benefits when used in food, beverages, toothpaste and medications, provided other constituents are also non-cariogenic and non-erosive.

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Conflict of interest

Consensus panel experts were: Prof Adam Drewnowski, Prof James Hill, Prof Anne Raben, Prof Hely Tuorila, Prof Eeva Widstrom. An independent nutritionist (Sigrid Gibson) was responsible for literature research, drafting the preliminary document and revising for publication. All authors agreed the final version.

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