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Review

The role of artificial and natural sweeteners in reducing the consumption of table sugar: A narrative review

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SUMMARY

The rapid increase in the prevalence of obesity worldwide has been partially attributed to the overconsumption of added sugars. Recent guidelines call for limiting the consumption of simple sugars to less than 10% of daily caloric consumption. High intensity sweeteners are regulated as food additives and include aspartame, acesulfame-k, neotame, saccharin, sucralose, cyclamate and alitame. Steviol glycosides and Luo Han Guo fruit extracts are high intensity sweeteners that are designated as generally recognized as safe (GRAS). Commonly used non-caloric artificial sweeteners may have unfavorable effect on health including glucose intolerance and failure to cause weight reduction. The nutritive sweeteners include sugar alcohols such as sorbitol, xylitol, lactitol, mannitol, erythritol, trehalose and maltitol. Naturally occurring rare sugars have recently emerged as an alternative category of sweeteners. These monosaccharides and their derivatives are found in nature in small quantities and lack significant calories. This category includes D-allulose (D-psicose), D-tagatose, D-sorbose and D-allose.

Limiting consumption of any sweetener may well be the best health advice. Identifying natural sweeteners that have favorable effects on body weight and metabolism may help achieving the current recommendations of restricting simple sugar consumption.

1. Introduction

Obesity continues to be a major public health issue that lacks an effective and practical intervention [1,2]. The paucity of reliable clinical research has led to substantial confusion as to the optimal mix of diet that can promote healthy living. Low fat diet was the cornerstone of dietary guidelines for decades. Subsequently there was an upsurge of interest in low carbohydrate diet [3,4]. However, professional organizations have not recommended low carbohydrate diets because of concerns of health risks associated with such diets [5]. It is noteworthy that a systematic review concluded that randomized controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983 [6]. Randomized clinical trials have shown that most people (70%) could eat high-cholesterol foods without having elevated serum cholesterol levels. Thus, the recommendation of 300 mg/day of dietary cholesterol has been removed from the 2015 Dietary Guidelines for Americans [7].

The most recent controversy as to the optimal dietary intake revolves around the consumption of simple sugars. The rapid increase in the prevalence of obesity worldwide has been partially attributed to the overconsumption of added sugars. In this communication the evidence supporting the current recommendation of limiting added sugars in the diet will be reviewed and the role of artificial and alternative natural sweeteners in achieving this goal will be discussed.

1.1. Evidence for limiting table sugar in the diet

The consumption of caloric sweeteners has been steadily increasing over the last four decades. The potential health consequences of this practice have been subject to considerable debate. No association of increased consumption of caloric sweeteners and increased risk of diabetes was found in 2 large epidemiological studies while in the Iowa Women's Health Study unexpectedly there was a negative association [8–10]. In a prospective follow-up

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study of 43,960 African American women, higher intake of both sugar-sweetened soft drinks and fruit drinks was associated with increased risk of type 2 diabetes mellitus [11]. This study raises the awareness of the adverse health effects of sugar sweetened fruit drinks in addition to the more widely recognized health concerns attributed to soft drinks [11]. Similar conclusions were drawn from several metanalyses of the available studies [12–27]. The most recent metanalysis of studies in 17 cohorts (38,253 cases/ 10,126,754 person years) indicated that consumption of sugar sweetened beverages was associated with a greater incidence of type 2 diabetes [27]. Artificially sweetened beverages and fruit juice also showed positive associations with incidence of type 2 diabetes. The latter observation may have been biased. Nonetheless, the authors concluded that both artificially sweetened beverages and fruit juice are unlikely to be healthy alternatives to sugar sweetened beverages [27]. The contemporary metanalyses of studies of the metabolic and clinical effects of table sugar, fructose and artificial sweeteners are summarized in Table 1 [12–27].

There is also increasing awareness of the association between the consumption of added sugars and atherogenic lipid profile [28]. In a cross-sectional study among US adults (n = 6113) from the National Health and Nutrition Examination Survey (NHANES) 1999–2006, the mean HDL cholesterol levels were significantly decreased while triglyceride levels increased with increased consumption of sugar. In this population a mean of 15.8% of consumed calories was from added sugars [28]. In contrast, in 1977–1978, added sugars contributed only 10.6% of the calories consumed [29].

The mechanism through which added sugar causes dysmetabolic effects is not completely known. The available evidence suggest that these effects could be mediated by fructose. Sucrose contains 50% fructose and 50% glucose and high fructose corn syrup commonly found in soft drinks contains up to 65% fructose [30].

Fructose promotes de novo hepatic triglyceride synthesis, increases secretion of very low-density lipoproteins and may decrease the peripheral clearance of lipids [31–33]. Some of these changes could be attributed to a decrease in adenosine triphosphate (ATP) content in the liver, decreased cellular binding of insulin and insulin resistance. In addition, fructose induces non-enzymatic glycation, oxidative stress and inflammation [34,35]. Fructose may also increase food consumption [36]. In addition, epigenetic regulation of the intestinal fructose transporter Glut5 during development promotes more efficient absorption of ingested fructose in adulthood thereby further aggravating the potential dire consequences of fructose consumption [37]. The metabolic effects of fructose are summarized in Fig. 1.

It is noteworthy that in observational studies fructose found naturally in fruits and vegetables does not appear to cause harm and indeed may be protective against diabetes and may be associated with reduced mortality [38–40]. The difference in the metabolic consequences of fructose in the fruits compared to fructose in added sugar may be related to the amount of the fructose consumed and the benefits of other nutrients in the fruits [41]. However, fruit juice could be as detrimental as caloric sweetener added beverages [42,43].

Several studies have found an association between calorically sweetened beverages and obesity [11,14,16,23,24,44–48]. The risk of diabetes was 11-fold higher with each 150-kcal per day increase in sugar as compared to 150-kcal per day increase in total calorie availability [48]. Among the sugars, the availability of high-fructose corn syrup has independently predicted greater cardiovascular risk and diabetes prevalence [49,50].

The potential limitations in observational trials and extrapolation of findings from the animal models are well recognized. Interventional trials are more informative but not necessarily free of controversy. Of note is that among trials with partial or total funding from the food industry, 83.3% found insufficient support of a positive association between sugar-sweetened beverage consumption and weight gain, whereas among trials conducted without industry financial support, the same percentage found that sugar-sweetened beverage consumption was a risk factor for weight gain [51]. It can be argued that trials where various sugars and carbohydrates are tested in isocaloric exchanges do not reflect the possibility that people who consume simple sugars especially in beverage form are likely to consume more calories as sugar stimulates increased food intake [52–55]. The differential effects of isocaloric substitution of fructose compared to hypercaloric substitution is observed in several contemporary metanalyses of the literature summarized in Table 1. It is noteworthy that in studies on the health effects of sugar sweetened soft drinks and fruit juices, the amount, type and nutritional composition of these drinks are not always comparable and therefore the conclusions drawn from these studies can be challenged.

1.2. The clinical role of artificial and natural sweeteners

1.2.1. The rationale for alternative sweeteners

Despite the lingering concerns about the consequences of overconsumption of simple sugars, the consumption of added sugar by Americans have increased to the current estimate of 120 lb per person per year [41]. Although the aggressive marketing tactics of the food industry and reformulation of products by manufacturers to increase added sugars in foods and beverages in response to the “low fat” dietary advice is mostly culpable for this trend, it is also likely that human beings have natural or learned craving for sweets. A recent study in twins has shown that at least 30% of the inter-individual variability in craving for sweets is genetically determined [56]. To satisfy this craving without having the risk of increasing the prevalence of obesity and metabolic abnormalities attributed to added sugars, alternative sweeteners have been developed.

It is currently believed that excess sugar consumption is a principal cause of the epidemic of type 2 diabetes. The World Health Organization recommends that added sugars should make up no more than 10% of daily caloric intake, with a proposal to lower this level to 5% or less for optimal health [57]. This restriction is similar to the American Heart Association recommendation to consume no more than 6 table spoon full (24 g, providing 100 calories) of sugar per day for women and 9 table spoon full (36 g, providing 150 calories) of sugar per day for men [31].

1.2.2. Types of sugar substitutes and sweeteners available

Sweeteners are generally divided into two categories as non-caloric high intensity sweeteners and nutritive sweeteners.

High intensity sweeteners are regulated as food additives, unless they are generally recognized as safe (GRAS). Six high-intensity sweeteners are Food and Drug Administration (FDA)-approved as food additives in the United States (Table 2) [58–60]. These non-caloric sweeteners include aspartame, acesulfame-k, neotame, saccharin, sucralose and advantame.

Saccharin is the oldest artificial sweetener that was discovered in 1879. It is 300 times sweeter than sucrose but has a bitter aftertaste.

Aspartame was discovered in 1965 and consists of two amino acids, phenylalanine and aspartate, linked to a methanol backbone. It is about 200 times sweeter than sucrose. Metabolism of aspartame will eventually lead to formation of formaldehyde, formic acid and diketopiperazine [61] and hence its safety has been questioned [62].