Quality of Sugars and Sugar-Containing Foods

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ABSTRACT

Dietary sugars are mono- and disaccharides that are naturally present in fruits, vegetables, and natural syrups or are added to foods as refined sucrose or high-fructose corn syrup. Dietary sugars are absorbed in the bloodstream as glucose (indistinguishable from that released from starch), fructose, and galactose. Galactose is converted into glucose, and fructose is converted into glucose, lactate, and fatty acids in splanchnic organs. The main nutritional function of sugars is to provide usable energy to all cells in the human body. The efficiency of usable energy transfer is very high for glucose; lower for galactose, lactose, and sucrose; and lower still for fructose. High dietary sugar intake may be associated with an increased risk for cardiovascular and metabolic diseases. This is especially true for fructose and sucrose, which increase blood lipids and impair hepatic insulin sensitivity when consumed in high doses. The effects of sugar-containing foods vary according to food group: fruit and vegetable consumption significantly protects against cardiovascular and metabolic diseases, while consumption of sugar-sweetened beverages is associated with an increased risk. The quality of sugar-containing foods should be assessed not only based on their sugar content, but also on their overall energy, dietary fiber, and micronutrient contents.

Glucose is a key energy substrate for most cells in the human body and the predominant source of energy for the brain. Blood glucose concentration is normally regulated within relatively narrow limits, and episodes of low blood glucose are associated with acute cognitive dysfunctions, neurological symptoms, fatigue, and decreased exercise performance. In addition to its prominent role in energy homeostasis, glucose is also required for the glycosylation of various lipids and peptides, which play essential roles in cell regulation. Glucose and other monosaccharides, such as galactose and fructose, play key roles in the normal functioning of some cells, such as glycosylation with galactose residues of glycoproteins and glycolipids or energy provision from fructose to sperm cells. However, dietary carbohydrates, which are direct providers of glucose, fructose, and galactose in our diet, are not strictly speaking essential nutrients: glucose can be synthesized endogenously from amino acids or glycerol, while fructose and galactose can be synthesized from glucose. Nonetheless, given the large energy requirements of the human body and the fact that carbohydrates represent a large portion of the energy content of available foods in most regions of the world, most populations rely on the daily intake of substantial amounts of carbohydrate.

Sugar is the generic name used for all mono- and disaccharides. The main dietary sugars are glucose; fructose; sucrose, which is a dimer formed from one glucose and one fructose; and lactose, which is a dimer formed from glucose and galactose. Glucose, fructose and sucrose are found in variable proportions in fruits and vegetables, honey, and natural syrups (e.g., maple and agave syrups). Lactose is present in milk and many dairy products. Galactose is only present in very low amounts in some vegetables and fruits. Modern diets also include variable amounts of crystalline sucrose refined from sugarcane or beet or glucose-fructose syrups industrially prepared from cereals or potatoes. The most commonly used glucose-fructose syrup in North America is high-fructose corn syrup (HFCS) (37).

No universally accepted tool exists for evaluating the quality of a nutrient. Such evaluation would imply assessment of a large number of parameters related to how a nutrient exerts its function(s) in the body, whether it has direct or indirect adverse effects, what the nutritional properties of foods that contain it are, how its consumption affects the consumption of other dietary nutrients, etc. For practical purposes, this article was written following the assumption that the only function of sugars is to transfer usable energy to cells in the body and that different sugars may possibly exert different effects on obesity, cardiovascular, and metabolic risk factors. The quality of sugars, therefore, was addressed in terms of

- How efficient sugars are in exerting their main function, i.e., transferring usable energy.
- How sugars impact the risk of cardiovascular and metabolic diseases.
- How sugars can be qualified as nutrients and how sugar-containing foods can be qualified.

EFFICIENCY OF SUGARS IN TRANSFERRING USABLE ENERGY TO CELLS

Bioavailability of Sugars

Mono- and disaccharides may not be digested by pancreatic enzymes and reach the small intestine, where sucrose and lactose are cleaved into monosaccharides by disaccharidases (sucrase-isomaltase and lactase) located at the luminal surface of the gut (18,36). Disaccharide digestion is a rapid and highly efficient process and is not considered rate-limiting for sugar absorption. Lactase, however, is not expressed in about 25% of adults, resulting in lactose intolerance (36). Glucose and galactose are transported from the gut lumen to the blood by an energy-dependent cotransport with sodium, which allows for their nearly complete intestinal absorption (54). In contrast, fructose is absorbed from the gut by passive diffusion, facilitated by the fructose-specific transporter GLUT5 (27,45). Fructose absorption is markedly increased when it is ingested together with glucose. Gut fructose absorption also increases with chronic fructose intake due to rapid up-regulation of GLUT5 expression (13,14,27).

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Metabolism of Monosaccharides Absorbed from the Gut

Once absorbed into the circulation, glucose, either ingested as a monosaccharide or provided from sucrose or starch digestion, is initially delivered into the hepatic portal vein. About 10–20% of a 75 g oral glucose load is retained in the liver to resynthesize the glycogen used between meals, and the rest enters systemic circulation, thus increasing blood glucose concentration, which in turn stimulates insulin secretion. Circulating glucose is then taken up by most of the cells in the body to be used as an energy substrate (3,19).

Galactose present in hepatic portal blood is almost completely extracted in the liver during the first pass. It is metabolized inside the hepatocytes—first to galactose-1-phosphate and then to uridine-diphosphate-glucose, which is a direct precursor for hepatic glycogen synthesis. Galactose, therefore, quickly mixes with the hepatic glucose pool and is subjected to the same regulatory factors as glucose (34,53).

When ingested in very small amounts, most of the fructose appears to be metabolized in small bowel enterocytes, where it is mainly converted into glucose and lactate (23). When consumed in larger amounts, a major portion of the fructose absorbed by enterocytes is released into the hepatic portal blood and then extracted in the liver, where specific fructolytic enzymes (fructokinase, aldolase B) convert it into trioses-phosphate. These compounds then can be metabolized further to lactate, glucose, or fatty acids and triglycerides (31). Based on various experimental studies relying on carbon 13- or deuterium-labeled substrates to trace specific metabolic pathways, it is currently estimated that about 30–50% of an ingested fructose load recirculates as glucose, and about 25% recirculates as lactate within 4–6 hr of eating a meal; a smaller portion is temporarily stored as hepatic glycogen or intrahepatic fat or is secreted in the circulation as triglycerides associated with very low-density lipoproteins (43). Fructolytic enzymes are also expressed in kidney proximal tubular cells and may contribute to the metabolism of fructose that escapes first-pass splanchnic extraction (9).

Fructose metabolism and the effects of dietary fructose on glucose and lipid metabolism differ from those of glucose, because fructolysis, in contrast to glycolysis, is a completely unregulated process. When portal glucose is metabolized in hepatocytes, the glycolytic degradation of glucose carbons occurs until oxidation of trioses-phosphate covers cellular ATP needs, at which point the cellular ATP and citrate levels rise and strongly inhibit glycolysis. In contrast, no such inhibition takes place during fructolysis, and degradation of fructose carbons to trioses-phosphate proceeds as long as fructose is available (31). Even with moderate 20–30 g fructose loads, a portion of the trioses-phosphate is converted into glucose by gluconeogenesis, eventually ending up in glycogen stores or as blood glucose. Trioses-phosphate can also be converted into fatty acids through de novo lipogenesis and, as a result, end up as triglycerides. The amount of fructose converted into triglycerides is generally estimated to be much smaller than that converted into glucose and glycogen but has not been quantified accurately. De novo lipogenesis activity is markedly increased by exposure to high fructose intakes, however, and it is likely that the proportion of fructose converted into lipids is dependent on both daily fructose intake and duration of exposure.

Provision of Energy from Sugars to Cells in the Body

The primary role of dietary carbohydrate is to provide monosaccharides as energy substrates to cells in the human body. In this regard, all digestible carbohydrate contains about 4 kcal/g. However, the amount of energy actually made available to cells may vary according to the number of transformations a monosaccharide undergoes before being delivered as either glucose or fatty acids to cells in the body.

About 80–90% of glucose absorbed from the gut escapes hepatic uptake and reaches systemic circulation, from which it can be directly transported to and oxidized by cells without any prior energy loss. The 10–20% of glucose taken up by the liver is temporarily stored as hepatic glycogen before being subsequently released into the blood as glucose. In this process, about 5% of its energy is used for glycogen synthesis and is lost to heat when glycogen is hydrolyzed back to glucose, thus constituting a "futile cycle" (24). The same 5% energy loss can be extrapolated for galactose, which is initially converted into hepatic glycogen before being released as glucose in the blood. In contrast, fructose absorbed from the gut lumen is first degraded into trioses-phosphate, which subsequently enters either gluconeogenesis or de novo fatty acid synthesis. These two processes use considerable amounts of energy, corresponding to about 8–10% of initial energy from fructose used for glucose/glycogen synthesis and up to 25–30% used for fructose conversion into fatty acids (44).

The estimated percentage of energy made available to cells in the body is, therefore, about 99% for glucose (assuming 15% cycling in hepatic glycogen), about 95% for galactose, and about 70–92% for fructose. For disaccharides, the percentage of energy made available can be estimated as the average of its constituent monosaccharides, i.e., 97.5% for lactose (assuming no lactase deficiency) and 86–96% for sucrose.

IMPACT OF SUGARS ON RISK OF CARDIOVASCULAR AND METABOLIC DISEASES

Effects on Food Intake

The control of food intake and whole body energy homeostasis is highly complex and still not well understood, but it appears obvious that obesity results from food overconsumption, escaping feedback inhibition from high body energy stores. Schematically, two distinct systems interact to determine food intake in humans: a "homeostatic" food intake control system located in the hypothalamus and brain stem that responds to neuroendocrine signals such as leptin, insulin, and GLP-1, providing information on the level of energy present in the organism, and a "hedonic system," involving mesolimbic dopaminergic brain reward pathways, that qualitatively evaluates foods and promotes the intake of palatable foods.

The effects of sugars on hormones signaling to the homeostatic system differ markedly from those of starch. This difference stems from the fact that starch is entirely absorbed as glucose, while sugars are absorbed as a mixture of monosaccharides, with glucose representing between 0% (as with pure fructose) and 50% (as with sucrose) of the sugar load. Pure glucose ingestion (which can be assumed to be equivalent to isocaloric starch ingestion) stimulates secretion of the anorexigenic peptides GLP-1 and PYY from intestinal endocrine cells and is associated, through mechanisms involving insulin, with increased secretion of the anorexigenic hormone leptin and decreased secretion of the orexigenic hormone ghrelin. These responses are markedly attenuated when fructose (48) or sucrose (40,41) replace glucose, suggesting that fructose and sucrose may have lower satietogenic effects than starch or glucose.

When present in solution in the mouth, all sugars activate the same sweet taste receptor, T1R2-T1R3, but with marked differences in potency. Fructose and sucrose have higher sweetening potency than glucose, and lactose has only a weak sweetening potency (26). Foods with a sweet taste are often evaluated as pleasant, or palatable, when eaten. This is usually associated with activation of the mesolimbic dopaminergic brain reward pathways, and the hedonic tone elicited by ingestion of sweet products is certainly a driver in their overconsumption (10,26). Some authors have also pointed to the fact that sugars activate the same brain reward pathways as cocaine and, therefore, may potentially be addictive (2). This theory remains highly controversial, however.

Effects of High Dietary Sugar Intake on Glucose and Lipid Metabolism

In many countries, energy-dense foods are widely available at affordable prices, and the prevalence of noncommunicable diseases such as obesity, diabetes, and cardiovascular diseases is high. The risk for developing these diseases is markedly determined by nutritional factors, suggesting that identification of the associations between consumption of specific foods or nutrients and incidence of these diseases is of major importance for public health. A brief outline of how dietary sugars may impact the risk for two common noncommunicable diseases—type 2 diabetes mellitus and cardiovascular disease—through alteration of glucose and lipid homeostasis is provided in this section.

Acute Effects of Sugars. The specific effects of individual carbohydrate-containing foods on postprandial glycemia are reflected in their glycemic index. Glycemic index is defined as 100 times the ratio of the postprandial glucose response produced by ingestion of a portion of a food to that produced by ingestion of the same amount of carbohydrate as pure glucose (6). Fructose and galactose both have a glycemic index of about 25%; sucrose has a glycemic index of about 65%. The fact that fructose has a lower glycemic index than many starchy foods may provide an advantage for individuals with diabetes mellitus, for whom blood glucose control is the primary goal of their treatment. Indeed, there is evidence that for individuals with diabetes replacing sucrose with pure fructose actually improves diabetes control (12,17). This beneficial effect may be counterbalanced, however, by the adverse effects of sugars on lipids (discussed in next section). For the general population, however, blood glucose control is not an issue, and there is no evidence supporting beneficial effects of certain sugars due to their low glycemic index.

Chronic Effects of Sugars. A study by Johnston et al. (25) found that replacement of starch with an isocaloric amount of glucose in the diet of healthy volunteers for 2 weeks did not significantly alter blood glucose and triglyceride concentrations. It also did not alter intrahepatic lipid concentration (25). This is not surprising, because ingestion of isocaloric amounts of starch or glucose is expected to result in the absorption of the same amount of glucose in the blood. Consumption of a hypercaloric (about 130% of energy requirements), high-glucose (25–30% of total energy) diet did not change fasting blood glucose and insulin, nor insulin sensitivity, compared with a baseline weight-maintaining diet (25,42). Some studies, however, have reported an increase in blood triglycerides and intrahepatic fat concentrations (25,33). To my knowledge, no study has addressed the effects of a high-galactose or high-lactose diet on glucose or lipid metabolism in humans. This can be explained by the fact that total dietary galactose intake from dairy products and vegetables represents only a minor portion of total energy intake.

Many studies have assessed the effects of high-fructose diets in normal weight and obese volunteers over periods ranging from a few days to 6 months. Fructose typically contributed 15–30% of total energy intake and, hence, largely exceeded the current recommendations of a maximal added-sugar intake of ≤10% total energy. These studies have consistently reported that fructose, consumed as part of a hypercaloric diet, produces a modest, yet significant, increase in fasting insulin concentration. Studies that used dynamic tests to assess glucose homeostasis have reported that hepatic insulin sensitivity decreased and postprandial blood glucose responses significantly increased with high daily fructose intake. In contrast, whole body insulin-mediated glucose disposal, which mainly reflects muscle insulin sensitivity, was not altered (49).

High intakes of fructose, sucrose, or HFCS also consistently increased fasting and postprandial blood triglyceride concentration. This effect is mainly related to an increase in triglycerides associated with very low-density lipoproteins, suggesting that their origin is hepatic. This is mainly observed when fructose is consumed together with excess total energy (11), but some studies also have reported stimulation of hepatic de novo lipogenesis and an increase in blood triglycerides when fructose isocalorically replaced starch (15,38). In addition, many studies have reported that consumption of a hypercaloric, high-fructose diet increased intrahepatic fat concentration in normal weight and obese volunteers (25,42). Some studies, however, have reported similar effects with high-glucose and high-fat diets (25, 33), raising the possibility that increased intrahepatic fat concentration is due to excess energy intake rather than to a specific effect of sugars.

Effects of Sugar-Containing Foods on Cardiometabolic Risk

The most commonly consumed sugar-containing food groups in the United States and Europe are sugar-sweetened beverages (SSBs) and fruit juices, fruits and vegetables, grain products (e.g., breakfast cereals, cookies), dairy products with added sugar, and sweets and desserts (e.g., chocolate, candies, ice-cream, etc.) (1,29,30,51). Although epidemiological studies indicate that total sugar consumption is associated with adverse health effects, the relative contribution of sugars from various food groups is still debated. Prospective cohort studies show strong positive associations between SSB intake and body weight gain and between SSB intake and total energy intake (50). Addition of SSBs to the diet of adults or children has been shown to cause a significant increase in body weight (46). This strongly suggests that SSB consumption may contribute to the development of obesity by increasing total energy intake. The same conclusions were reached when assessing the effects of sugar-sweetened fruit juices, whereas the effects of 100% fruit juices with no added sugar remain controversial (22,35). SSB intake was also positively associated with increased blood lipids and increased risk for diabetes, but this was mediated, in part, by its effect on adiposity (47).

In contrast, high-fruit and -vegetable intake has been shown to provide protective effects against obesity (8,32,39), dyslipidemia, and risk for diabetes and cardiovascular diseases (7,20, 21,55). The intake of vegetables, which have lower sugar con-

tents, is particularly effective in this regard, but intake of fruits exerts the same effect, in spite of their higher sugar contents. The beneficial effects of eating fruits are unlikely to be due to their sugar being "natural" as opposed to "industrial," because sugars in fruits are chemically identical to their refined, industrial counterparts. Rather, the beneficial effects of fruits versus other sugar-containing foods may be due to their low sugar content by portion relative to other sugar-containing foods. An average fruit portion is 100–150 g, and the sugar contents of apples, peaches, and pineapples are about 9, 8, and 10 g/100 g, respectively, which is significantly lower than the sugar content of a can of sugar-sweetened soda (about 30 g) (5). Due to the relatively low sugar content of whole fruits, their consumption is unlikely to be associated with a daily intake of fructose higher than 50 g, which is the minimal dose at which some adverse metabolic effects are observed (4,28). In addition, fruits do not contain significant amounts of fat or protein and, hence, have a low caloric content compared with other sugar-containing foods. Finally, many fruits have a high dietary fiber content, which may induce satiety through a bulking effect and, as a result, may prevent overfeeding. These key properties of whole fruits (i.e., low sugar intake per portion and high fiber content, most likely contributing to reduced food intake) may not be retained in fruit juices, however. A 3 dL portion of unsweetened orange or apple juice contains 24–30 g of sugar (i.e., similar to that of a can of sugar-sweetened soda), and a 3 dL portion of grape juice contains about 48 g of sugar. In contrast, the dietary fiber to sugar (g/g) ratio decreases from 0.28 in a whole orange and 0.15 in a whole apple to only 0.01–0.02 in orange or apple juice (5).

Other sugar-containing foods constitute a very inhomogeneous group with wide variations in their macro- and micronutrient contents. For example, some candies contain no or very few nutrients other than sugar, whereas sugar-sweetened dairy products or breakfast cereals may also contain proteins, fat, calcium, dietary fibers, and many other micronutrients. Unfortunately, the available scientific literature does not allow an evaluation of the associations between consumption of each of these subgroups and health-related outcomes.

HOW TO QUALIFY SUGARS AS NUTRIENTS AND HOW TO QUALIFY SUGAR-CONTAINING FOODS

The "quality" of a food depends on how adequately it meets one or several nutritional requirements, while at the same time being associated with the lowest possible risk for noncommunicable diseases.

The only known nutritional function of sugars is to provide energy, and their quality, therefore, may be assessed based on how efficiently they provide usable energy to support the needs of all the cells in the human body. However, there is also strong evidence that a high sugar intake may alter glucose and lipid homeostasis in ways that may predispose a person to develop metabolic and cardiovascular diseases or negatively impact their evolution in individuals with these diseases. Finally, although refined sugars do not contain other nutrients of interest they are mainly consumed in foods and beverages that do contain other nutrients that are important for health. Sugar quality, therefore, may also be assessed based on the group of sugar-containing foods from which it is obtained (i.e., fruits versus grain products versus beverages, etc.).

Most of the dietary glucose reaches cells in the body unchanged, with only minimal energy loss due to hepatic glycogen cycling and, hence, is highly efficient in transferring usable energy to cells. All other sugars require preliminary (mainly hepatic) transformations, with small losses of energy for sucrose and galactose and moderate to large losses for fructose (Fig. 1A).

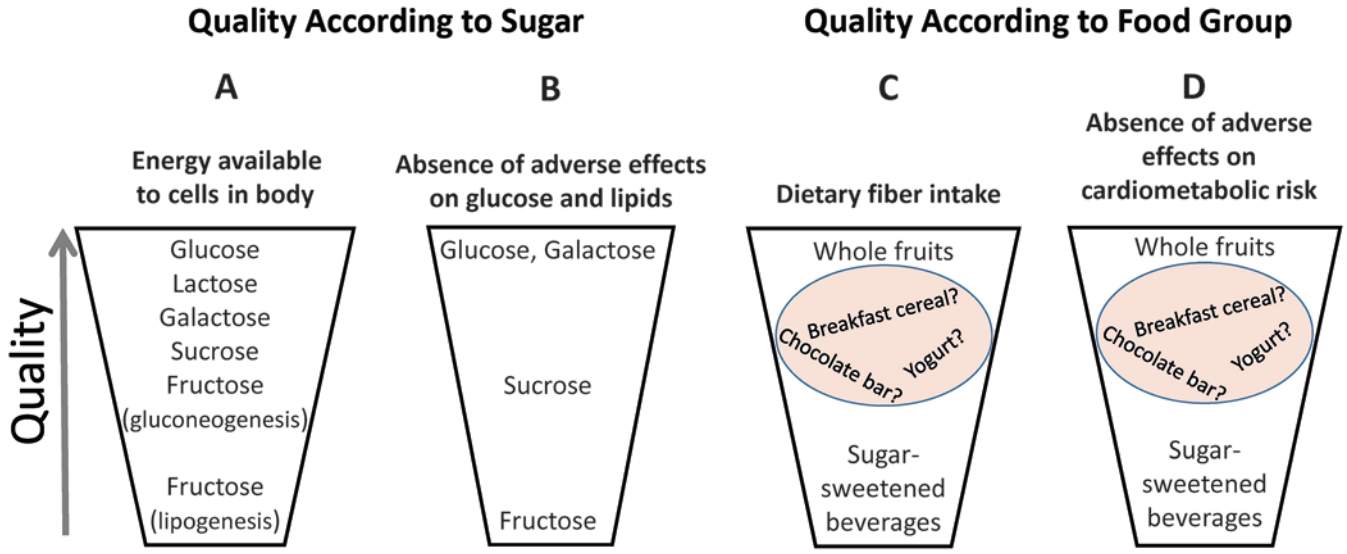

Fig. 1. Illustration of how the quality of sugars may be evaluated based on several complementary criteria. **A** and **B** depict quality of sugars as nutrients; **C** and **D,** depict quality of sugar-containing foods, which depends on sugar and other nutrient contents beneficial for health. **A,** Sugar quality ranked in terms of efficiency of usable energy transfer to cells in the body. Between-sugar variations are explained by specific metabolic pathways for individual monosaccharides. **B,** Sugar quality ranked in term of potential adverse effects associated with equimolar amounts of sugars. Adverse effects are represented as changes in cardiometabolic risk factors. Between-sugar variations are explained, as for **A**, by specific metabolic pathways for individual monosaccharides. **C,** Sugar-containing food quality ranked in terms of fiber content per gram of sugar; similar representation may be used for other nutrients. Whole fruits have a high fiber to sugar content ratio and, hence, a high nutritional quality compared with sugar-sweetened beverages. **D,** Sugar-containing food quality ranked in term of potential adverse effects (per gram of sugar). Unlike for **B**, between-food variations are not due to sugar content but to other food-related nutritional factors. Whole fruits are strongly associated with low and sugar-sweetened beverages are strongly associated with high cardiometabolic disease risk. Effects of other sugar-containing foods remain to be evaluated.

Ingestion of fructose and sucrose has a greater impact on hepatic insulin sensitivity and blood lipids than does ingestion of isocaloric amounts of glucose. These effects are mainly observed when fructose and sucrose are included in a diet that also provides an excess of total energy. Such effects have not been documented for lactose and galactose but are very unlikely to occur at the level of intake observed in common dietary patterns. This implies that the quality of dietary sugars is inversely proportional to their fructose content due to the potential adverse metabolic effects of fructose (Fig. 1B).

High consumption of fruits and vegetables is strongly associated with lower risk and SSB consumption with increased risk of metabolic and cardiovascular diseases. It may be inferred from this that fruits and vegetables have higher nutritional quality (most likely unrelated to the quality of their sugars). Currently, there is insufficient information to evaluate the risk associated with other sugar-containing foods (Fig. 1C). Nonetheless, the observation that consumption of fruits, which contain sugars, is associated with beneficial health effects, whereas consumption of total sugar, particularly SSBs, is associated with adverse health effects, has led many agencies to provide recommendations to reduce the consumption of sugar that is not associated with fruits and vegetables. Sugars not associated with fruits or vegetables are defined as "added" or "free" sugars, i.e., all monosaccharides and disaccharides added to foods by the manufacturer, cook, or consumer (16). Free and added sugars include honey and natural syrups (e.g., agave syrup, maple syrup). Unsweetened, 100% fruit juice remains an area of controversy and is included in the definition of free sugars, but not in that of added sugars. Most national and international dietary recommendations propose the specific limitation of consumption of free or added sugars.

The impact of sugar-containing foods on health goes beyond energy production and cardiometabolic risk, because balanced nutritional intake implies that one consumes a variety of foods that covers not only basic energy requirements, but also provides a sufficient supply of essential macro- and micronutrients. At similar energy contents, foods containing high levels of these nutrients would, therefore, have higher overall quality compared with foods that are devoid of them. Fruits and vegetables have low energy densities but have high fiber, vitamin, and antioxidant contents, whereas most sodas contain sugars, but no micronutrients or fiber. As a result, fruits and vegetables have higher overall nutritional quality than sodas (Fig. 1D). No system for assessing the overall nutritional quality of other sugar-containing foods has been agreed on; some breakfast cereals may provide a large quantity of fiber and micronutrients relative to their caloric content and, therefore, may have a high nutritional quality; the same may be true for some sugar-containing dairy products with a high calcium versus calorie content.

Finally, one key issue regarding the role of sugar in the pathogenesis of cardiovascular and metabolic diseases may be that consumption of sugar-containing foods is often associated with a high energy intake, which promotes obesity (50,52). This may be due to lower satiety signals produced with sugars than with other macronutrients, but also to the fact that sugar combined with other nutrients, such as starches and fats, may confer a strong hedonic tone to foods. The latter remains difficult to evaluate in terms of quality because the preparation of foods that people enjoy eating is a key factor in gastronomy and nutrition.

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Conflicts of Interests

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Luc Tappy obtained his M.D. degree at Lausanne University in 1981 and his medical training in the Department of Internal Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, and in the Diabetes section, Temple University Hospital, Philadelphia, PA. He then joined the Department of Physiology at Lausanne University, Faculty of Biology and Medicine, as an independent researcher in 1988 and was awarded a Foundation Max Cloëtta fellowship (1991–1997) to pursue his research projects in the field of human metabolism. In 2002, Luc was appointed a full professor of physiology. He has also been an invited professor at the Centre Hospitalier Sart Tilman in Liège, Belgium (1998–2001) and in the Department of Nutrition at the University of California at Berkeley (1995). Since 2015, he has held a part-time appointment with the Metabolic Center of the Intercantonal Hospital of Broye, Estavayer-le-lac, Switzerland. Research projects conducted in of Luc's laboratory have addressed various aspects of nutrition, physical exercise, and metabolism in healthy individuals and in patients with diabetes, obesity, and acute critical illnesses. His current research is essentially focused on the environmental factors involved in the pathogenesis of obesity and type 2 diabetes. He has conducted several studies to evaluate the role of dietary sugars in the development of obesity and insulin resistance, the role of sport and physical activity in the prevention of metabolic disorders, and the metabolic effects of bariatric surgery.

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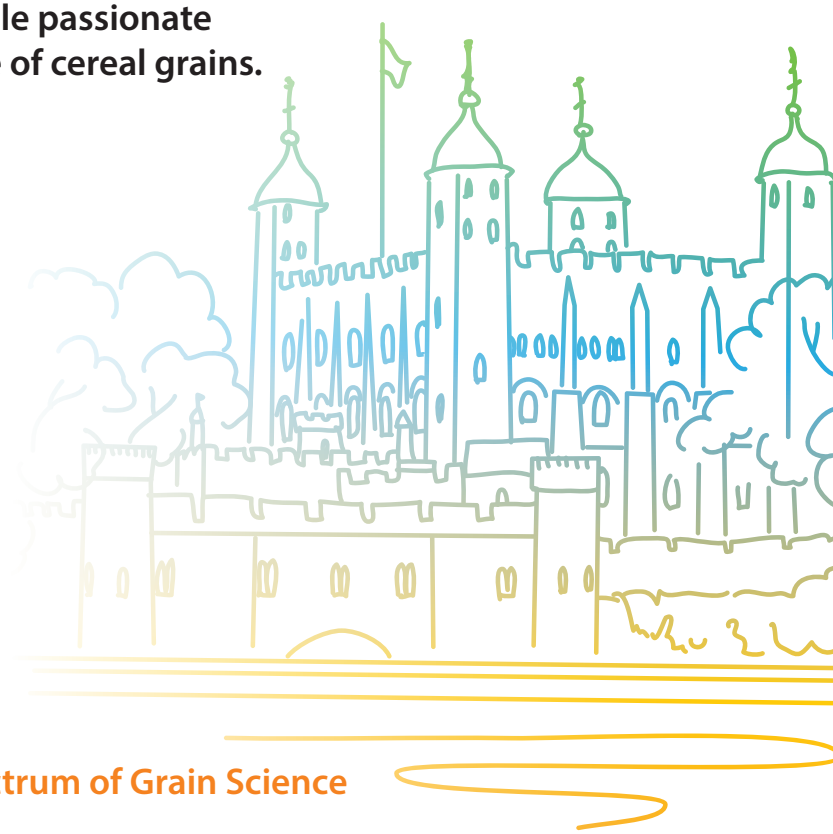

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