

Importance of carbohydrate quality: what does it mean and how to measure it?

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List of abbreviations

HDL	High Density Lipoprotein
HEIFA	Healthy Eating Index for Australian Adults
HFCS	High Fructose Corn Syrup
NHANES	National Health and Nutrition Examination Survey
VLDL	Very Low Density Lipoprotein

ORIGINAL UNEDITED MANUSCRIPT

Abstract

Dietary carbohydrates are our main source of energy. Traditionally, they are classified based on the polymer length between simple and complex carbohydrates, which does not necessarily reflect their impact on health. Simple sugars, such as fructose, glucose and lactose, despite having a similar energy efficiency and caloric content have very distinct metabolic effects, leading to increased risk for various chronic diseases when consumed in excess. In addition, beyond the absolute amount of carbohydrate consumed, recent data point out that the food form or processing level can modulate both the energy efficiency and the cardiometabolic risk associated with specific carbohydrates. In order to account for both of these aspects – the quality of carbohydrates as well as its food form – several metrics can be proposed to help identifying carbohydrate-rich food sources and distinguish between those that would favor the development of chronic diseases, of those that may contribute to prevent these. This review summarizes the findings presented during the American Society of Nutrition Satellite symposium on ‘Carbohydrates Quality’, where these different aspects were presented.

Keywords: carbohydrates, nutrient profile, fibres, sugars, dietary surveys

Introduction

The health effects of dietary carbohydrate have been the object of much attention. Until recently, dietary recommendations have mainly specified the proportion of desired carbohydrate in the diet, and partitioned carbohydrate into complex (i.e. starch) and simple (i.e. sugars) carbohydrate. This classification may not adequately address the health effects of sugars, however: prospective observational studies provide overwhelming evidence that sugar-containing foods such as fruits and added sugars, or some starchy foods such as whole grains, pulses, or potatoes, are associated with different effects on the risk of several non-communicable disease. This has led to the concept of “carbohydrate quality”, which aims to address the differing association between carbohydrate from various food sources on health outcomes.

Carbohydrate classification

Carbohydrates constitute one of the three major classes of dietary energy substrates. They are built from basic units of monosaccharide, each containing n atoms of carbons (e.g. pentoses and hexoses containing 5 and 6 carbon atoms respectively) of which $n-1$ carbons carry alcohol residues and 1 carbon an aldehyde or ketone residue. Carbohydrates can further be classified according to their degree of polymerization as mono-, di- and polysaccharides (1).

The most common monosaccharides present in the human diet are glucose and fructose contained in fruits, vegetables, honey and natural syrups (i.e. maple syrup). The most common disaccharides include sucrose (a glucose-fructose dimer present in fruits and vegetables) and lactose (a glucose-galactose dimer present in dairy products). Sucrose can also be extracted and refined in large quantities from sugar-cane or sugar beets. In addition, syrups containing glucose and fructose in various proportions can be produced industrially from starch-containing plants. The most commonly used syrup in the food supply is High Fructose Corn Syrup (HFCS),

which is widely used, mostly in the US (2). Mono- and disaccharides elicit a sweet taste and are commonly referred to as “sugars”. Refined sucrose, HFCS, honey, natural syrups and fruit juice concentrates are generally added to foods during their preparation and are therefore referred to as “added” or “free” sugars, to distinguish them from sugars naturally present in fruits, vegetables and dairy (3). Finally, polysaccharides contain 3 to several thousand monosaccharides. There is a large variety of polysaccharides in plants, however only starches, which are ramified polymers of glucose linked with alpha 1-4 and alpha 1-6 glycosidic bounds, are digestible by human digestive enzymes and are considered dietary carbohydrates. Non-starch polysaccharides, containing mixtures of glucose and other monosaccharides, are not digestible by human enzymes and constitute the major source of dietary fibers. Of note, these compounds can be fermented by colonic bacteria to short-chain fatty acids and lactate, which can secondarily be absorbed in the blood stream and metabolized by the human cells. Ingested mono- and disaccharides and starches deliver approximately 4 kcal/g to the human, while dietary fibers are considered to deliver about 2 kcal/g (4).

Mono- di-saccharides and starches are digested by pancreatic and intestinal enzymes in the gut and are absorbed in the blood stream as monosaccharides, i.e. glucose, fructose, galactose. Glucose is a prime energy source for all human cells, and an (almost) exclusive source of energy for the brain. However, it can be synthesized endogenously from amino-acids or glycerol. Monosaccharides are also constituents of mucopolysaccharides and glycosylated proteins in human cells, but the specific monosaccharides required for these processes can be synthesized endogenously. Mono- disaccharides and starches are therefore not be considered as essential nutrients, and their only physiological function is energy provision to the cells (5). However, carbohydrates still represent a major portion of the energy present in available foods, therefore making a major contribution to energy intake when part of a varied diet (6).

Carbohydrate quality in a physiological perspective

The quality of a nutrient from a physiological perspective may be defined: according to the way it fulfills its physiological role, i.e. how efficiently it transfers energy to the cells of the organism; and, according to the absence of adverse health effects, is associated with its intake. The latter is relevant given that cardiovascular and metabolic diseases contribute substantially to the global burden of disease and are primarily driven by environmental factors including nutrition (7). Thus, adverse health effects of a specific nutrient may be unraveled by studying how its consumption influences major cardio-metabolic risk markers such as body weight, glucose homeostasis, insulin sensitivity, or blood lipid profiles.

a) Energy efficiency

Energy efficiency of carbohydrate can be defined as the ratio of the energy used by cells (as chemical or mechanical work), to the energy content of the initial food (pre-digestion) (8). The main factors responsible for lowering this ratio, and hence lowering the energy efficiency of a given carbohydrate include incomplete digestion or absorption, and loss of energy to heat during the process of thermogenesis (9). The monosaccharide glucose does not require digestion and is entirely absorbed from the gut by an energy-requiring sodium-glucose cotransporter. Furthermore, blood glucose is a prime energy substrate readily used by all cells of the organism with little energy loss (needed to initially activate glucose to fructose 1-6 diphosphate prior to further degradation to CO_2 and H_2O) and will be taken as a reference here. The disaccharides sucrose and lactose are normally completely digested by gut disaccharidases and absorbed into the blood stream as glucose, galactose and fructose. In adults, however, lactase deficiency is present in a substantial portion of the population, resulting in incomplete digestion of lactose (10). Galactose is completely absorbed by the same sodium-

glucose cotransporter as glucose. It is however converted to glucose-1-phosphate and glycogen in the liver before being released into the circulation as glucose, leading to an energy loss of approximately 2% (11). In contrast, fructose is absorbed from the gut through simple, facilitated diffusion and is therefore incomplete, particularly when ingested in large amounts (12). It is initially converted into triose-phosphates in the enterocytes and hepatocytes prior to being released into the blood stream as lactate, glucose or triglyceride, and this splanchnic metabolism accounts for the variable losses of energy (ranging from 5% when released as glucose to 25-30% when released as triglycerides) (13)

Although it is expected that the energy efficiency of starch would be similar to that of glucose, being composed of glucose monomers, there are several factors including variation in starch structure according to its plant origin and food processing, that result in differences in its energy availability (14). Furthermore, the digestion of starch is facilitated by swelling of starch granules produced during cooking, that slows digestion and absorption, but this phenomenon varies among various starchy foods, with lesser swelling and slower digestion and absorption of starch from unprocessed cereals than from refined cereal products (15).

b) Effects on cardiometabolic risk factors

A high dietary intake of carbohydrates is associated with an increase in total- and very low density lipoprotein (VLDL)-triglycerides and a decrease in high density lipoproteins (HDL)-cholesterol concentrations (16), which are recognized risk factors for the development of cardiovascular diseases. The adverse effects of a high carbohydrate intake have been attributed to glucose-induced hyperinsulinemia and stimulation of de novo lipogenesis and of VLDL-triglyceride secretion from the liver (16, 17). Compared to dietary starch or glucose, which are only partially metabolized in the liver, fructose is efficiently taken up by hepatocytes, where it stimulates gluconeogenesis and lipogenesis. This is associated with increased intrahepatic fat concentrations, enhanced hepatic VLDL-triglyceride secretion, and impaired suppression of

hepatic glucose production. These effects may hypothetically proceed towards the development of non-alcoholic fatty liver disease, insulin resistance and diabetes mellitus, and atherosclerosis (18). Of interest, these deleterious effects of fructose can be blunted when physical activity is performed right after fructose ingestion, by immediately increasing fructose oxidation and decreasing fructose storage (19). This suggests that deleterious effects of fructose and fructose-containing sugars can be compensated by a high whole-body energy output associated to high physical activity level (19). Although the effects of galactose and lactose on these parameters have not been comprehensively studied, a recent study reports that dietary galactose may increase blood triglyceride concentration to the same extent as fructose (20). Finally, it exists some alternative sugars that, although sometimes classified as 'added sugars', may have distinct physiological effects. Isomaltulose, an isomer of sucrose with glucose and fructose linked through an α -1,6 linkage instead of an α -1,2 linkage in sucrose, is digested at a slower rate than sucrose due to lower intestinal enzyme affinity, thus lowering post-prandial glucose response and related inflammatory markers in type 2 diabetic patients (21). Among other rare sugars, allulose is a C3-epimer of D-fructose and tagatose a stereoisomer of D-fructose (22). Due to their different conformation, they are either not metabolized – in the case of allulose – or not absorbed in the case of tagatose, which results in a lower caloric content for both rare sugars. Beyond their lower caloric content, some studies have suggested they may have additional beneficial by decreasing glucose-induced post-prandial glycemia. The postulated mechanism may involve inhibition of α -glucosidase (22). The associations between total dietary carbohydrate intake and health-related outcomes has been intensively studied but remains debated. Recent evidence from the PURE study, which assessed the relationship between self-reported carbohydrate, fat and protein intake from more than 130'000 subjects from 18 countries concluded that high carbohydrate intake was associated with higher risk of total and cardiovascular mortality, whereas total fat and individual types of fat were related to lower risks (23). These conclusions of a negative effect of diet high in carbohydrates are

however not universally applicable. Of note, there is substantial evidence that consumption of a hypocaloric diet results in weight loss proportionate to energy deficit irrespective of the total dietary carbohydrate and fat content (24), suggesting that a high carbohydrate diet may not be a major factor promoting weight gain and associated cardiovascular comorbidity.

Role of processing and food forms

Beyond the absolute amount of carbohydrates consumed, there is now compelling evidence that the associations between carbohydrate intake and health-related outcomes vary according to dietary carbohydrate sources. Systematic reviews and meta-analyses of prospective cohort studies, clearly indicate that carbohydrate from fruits, pulses, or whole grain products are associated with lower mortality and risk of cardiometabolic diseases, whereas refined carbohydrates and added sugars (more specifically from sugar-sweetened beverages) are associated with higher risks (25). These observations are further corroborated by meta-analyses of intervention studies showing decreased risk of cardiometabolic diseases when dietary intake of whole grain (26, 27), pulses (28-31), or fruits (32, 33) are increased.

The underlying mechanisms responsible for differences in health effects across carbohydrate containing foods remain incompletely understood. One possible explanation may be the differences in postprandial blood glucose excursions and insulin responses elicited by different types of carbohydrate. According to this hypothesis, carbohydrates which cause a rapid rise in blood glucose (high glycemic index) may be associated with early postprandial hyperinsulinemia favoring energy storage and late postprandial hypoinsulinemia triggering food intake, while these effects would not be observed with low glycemic index carbohydrate. This hypothesis is supported by prospective cohort studies showing that consumption of a high glycemic index diet is associated with increased incidence of diabetes and cardiovascular diseases(34, 35) (36).

The lower glycemic impact of carbohydrates may be related to a slower rate of intestinal glucose absorption or hepatic first pass metabolism (i.e. fructose or galactose), and

often corresponds to foods high in dietary fiber content. Dietary fibers slow down gastrointestinal transit time and may therefore delay dietary carbohydrate absorption. In addition, they exert beneficial effects on gut microbiota, and are fermented by gut bacteria, thus producing short chain fatty acids. These microbiota-generated metabolites promote beneficial effects on colonocytes' health as well as metabolic health and energy homeostasis (e.g. via satiety signals in the brain) of the host. Systematic reviews of prospective cohort studies indeed indicate that total dietary fiber intake is associated with lower risk of diabetes (37) or cardiovascular diseases (38). Intervention studies also indicate that supplementation with viscous fibers such as beta-glucan, psyllium or guar gum, improve glucose control in subjects with diabetes (39), and lower blood cholesterol (40) and systolic blood pressure (41) in the general population. Finally, the glycaemic impact of carbohydrates is further influenced by its interactions with other macronutrients present in food (e.g. the matrix effect). For example, glucose combined with protein or fat provides differing impacts on glucose and insulin excursions compared to those exhibited when consumed in isolation (42).

Some studies have indicated that the source of dietary fibers may play a role in the prevention of chronic diseases, with cereal fibers showing the strongest association with risk reduction of type 2 diabetes and cardiovascular diseases (43, 44). Beyond the food sources, and similarly to starch, there is also evidence that the degree of processing can alter the fiber's beneficial effects on health (45). Harsh mechanical and/or thermal treatments used in some food processing can disrupt the fiber network and physico-chemical structures, thus modifying the way they interact with digestible carbohydrates present in whole-foods (46).

Pragmatic metrics to help define carbohydrate quality

Based on physiological considerations and on human prospective and intervention studies, there is clear evidence that carbohydrate quality differs across various foods and has highly relevant importance for human health. It can be readily communicated for traditional, un- or

minimally-processed foods such as whole grains, fresh fruits, pulses, sugars, etc. (39). When it comes to packaged or ready-to-eat foods, however, a clear, multidimensional definition of carbohydrate quality is required.

A recent article, reporting on several meta-analyses from prospective cohort studies and intervention studies, identified whole grains and dietary fiber as major food components related to beneficial health outcomes (25). Whole grain and products made from it are defined by the Oldways Whole Grain Council as products containing “all the essential parts and naturally-occurring nutrients of the entire grain seed in their original proportions” (47). There are however various alternative definitions of whole grain which may lead to some degree of confusion (48). In addition, consumption of added or free sugars is increasingly recognized as being associated with adverse health effects (49). It appears therefore that a high dietary fiber content together with a low added sugar content would be key descriptors of carbohydrate quality. The WHO dietary guidelines indeed recommend daily consumption of > 25 g dietary fiber and that free sugars represent less than 10% of total energy (49). These recommendations are only met by a minority of the Australian population (50-52). In the US population, according to National Health and Nutrition Examination Survey (NHANES) 2015-2016, carbohydrates account for approximately 52% of total daily energy intake. Of these, only 9% are from high quality carbohydrates such as whole grain, fruits and pulses, while the vast majority was from refined grain, starchy vegetables, added sugars and sweet beverages (53).

From a practical point of view, one major challenge imposed on nutritionists is how to communicate to the general population the best and simplest way of identifying high quality carbohydrates. This is particularly relevant for industrial products, the composition of which is not immediately apparent to the consumer. Based on the associations observed between added sugar and dietary fiber intakes and health outcomes, several empirical indexes reflecting carbohydrate quality of carbohydrate-rich, packaged food products have been proposed. The

simplest one is a total carbohydrate to dietary fiber ratio of less than 10:1 to target fiber rich carbohydrate products. Modified forms of this index, including a total carbohydrate (g) to dietary fiber (g) ratio of less than 10:1, together with a total carbohydrate (g) to added sugar of less than 10:1 or 10:2 have therefore been developed (Table1) (54).

A recent study calculated the composition of carbohydrates containing products meeting the 10:1 carb:fiber ratio consumed by urban residents of Sao Paulo, Brazil. These products contained less added sugar and saturated fat and more dietary fiber and protein per serving than products with carb:fiber ratio $> 10:1$. In addition they also containing more micronutrients (potassium, magnesium, selenium, zinc) per serving. Furthermore, in this population, consumption of food products meeting the 10:1 carb:fiber ratio was associated with decreased blood triglyceride concentration, lower fasting insulin concentration, and better indexes of insulin sensitivity. Application of the $\leq 10:1$ carbohydrate to fiber ratio was shown to identify healthy grain foods and its association with cardiometabolic risk factors (55). In Australia, according to the 2013-2016 nutrition survey, the 10:1 ratio was attained by 50% of products consumed by adults and by 29 % those consumed by children, while the modified 10:1:2 ratio were attained in only 33 and 19% and the dual ratio in 41 and 22% respectively (56). Products meeting any of these indexes of quality contained on average more energy, protein, unsaturated fat, B-vitamins (with the exception of vitamin B12), iron, magnesium, and zinc and less total carbohydrate, added sugars and sodium than products which did not meet any index of quality, indicating a globally higher nutritional value (51). Interestingly, a recent study showed that the 10:1 ratio prove to be applicable to beverages, showing that increasing the fibre content allows to differentiate the more nutritious products with higher content of proteins, dietary fibres, and lower caloric content, added sugars, cholesterol and sodium (57). These results demonstrated that this metric serves as an effective method to identify foods with a better nutritional quality. This is further supported by a recent study which confirmed that these metrics are associated

with improved diet quality (58). Diets meeting the original validated 10:1 carb:fiber ratio, the modified 10:1:2 carb:fiber:added sugars ratio and dual ratio 10:1 & 1:2 carb:fiber & fiber:added sugars ratio 10:1 had lower energy, total sugars and saturated fat intakes but higher protein, monounsaturated and polyunsaturated fatty acids, and dietary fiber compared to those that did not meet the ratios. Furthermore, diets meeting the target ratios were characterized by higher daily intakes of several micronutrients (B-vitamins, vitamin E, folate, iron, magnesium, zinc) and higher Healthy Eating Index for Australian Adults (HEIFA-2013) with lower intakes of discretionary foods/beverages (high in saturated fat and/or added sugars, added salt, or alcohol), and higher intakes of vegetables, fruits, grains, meat, water, fat, sodium and added sugars. The same report also describes a novel dietary modelling analysis examining the impact of consuming foods that satisfy the carbohydrate ratios on estimated nutrient intakes. The authors replaced in the model each carbohydrate-based food that did not satisfy a ratio with the closest foods that met the carbohydrate ratio. This substitution analysis resulted in an increased energy, protein, total fat, mono- and polyunsaturated fatty acids and dietary fiber intake, but less total carbohydrate, added and free sugar. Intake of micronutrients increased with diet modelling analysis, but interestingly did not improve the intakes of folate and vitamin B12. A possible explanation provided by the authors may be local fortification rules.

Existing markers of carbohydrates quality in a product include the glycemic index, whole-grain claims and avoidance of added sugar. While the glycemic index is well recognized in a limited number of countries (e.g. Nordic countries and Italy), its use beyond these countries is presently limited, and requires clinical tests to determine its value (59). Presence of whole-grain claim in a food ensures that a minimum requirement for whole-grain content is met, but as mentioned above, does not guarantee that the product meets other basics nutrition requirements, such as an upper limit for added sugars (48). The ratio mentioned in the present paper can to some extent overcome these issues and provide a complementary approach, as it can be easily

assessed from nutritional facts, and ensures in most cases that the food products has superior nutritional quality (Figure 1). With respect to added sugar, there are currently limitations of developing food databases with information on added sugar and front-of-package labels indicating added sugar content remain scarce (60). The ratio has been primarily developed to help discriminate the nutritional quality of cereal-based products (54) (61). This was initially thought to provide some guardrail for the application of the ratio to pure sugar-based confectionary products for example, where the addition of fibres may not be enough to qualify such products as 'healthy', or products primarily high in proteins or fat, for which such ratio may not be relevant. However, it may be considered to extend the use of such ratio beyond cereals, to legume-, nuts and seed-based products, as these foods are of high nutritional value, and can positively contribute to reaching the ratio by providing a good fibre source.

Despite the fact that this approach based on total carbohydrate to dietary fiber and added sugars ratios is empirical and based only on three nutrients, it allows to discriminate food products of higher nutritional value. The beneficial effects of foods may not be only linked to their fiber and/or total sugar content, however, but also to presence of other compounds present in whole grains, pulses and fruits, such as vitamins, micronutrients, or polyphenols. As such, these different ratios based on total carbs, added sugars and dietary fibers may indirectly reflect foods' global nutrients content, and hence nutritional value.

Conclusions

There is increasing evidence that the effects of carbohydrate-containing foods on health-related outcomes vary widely according to the food sources, a phenomenon referred to as "carbohydrate quality". There is strong evidence that consumption of whole grain products and a high dietary fiber intake are associated with benefits, while consumption of added sugars and refined carbohydrates are linked with adverse health outcomes. Based on these observations,

various empirical indexes based on the ratio of total carbohydrate to dietary fiber and added sugar contents reflecting carbohydrate quality have been proposed. Among these, a simple ratio of total carbohydrate: dietary fiber < 10:1 appears to be the best suited in promoting the choice of healthier carbohydrate sources. All these indexes identified products with higher protein, vitamins, and micronutrient contents, and hence with higher overall nutritional qualities. Future studies are still needed to test the use of these ratios for consumer messaging or policy actions, e.g. as part of Front-of-Package Labeling Systems, Nutrition Facts, and/or nutrition targets for industry.

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VC and KAL designed the manuscript outline based on the content presented during the American Society of Nutrition annual 2020 meeting; LT, VC and KAL wrote the paper; All authors have read and approved the final manuscript.

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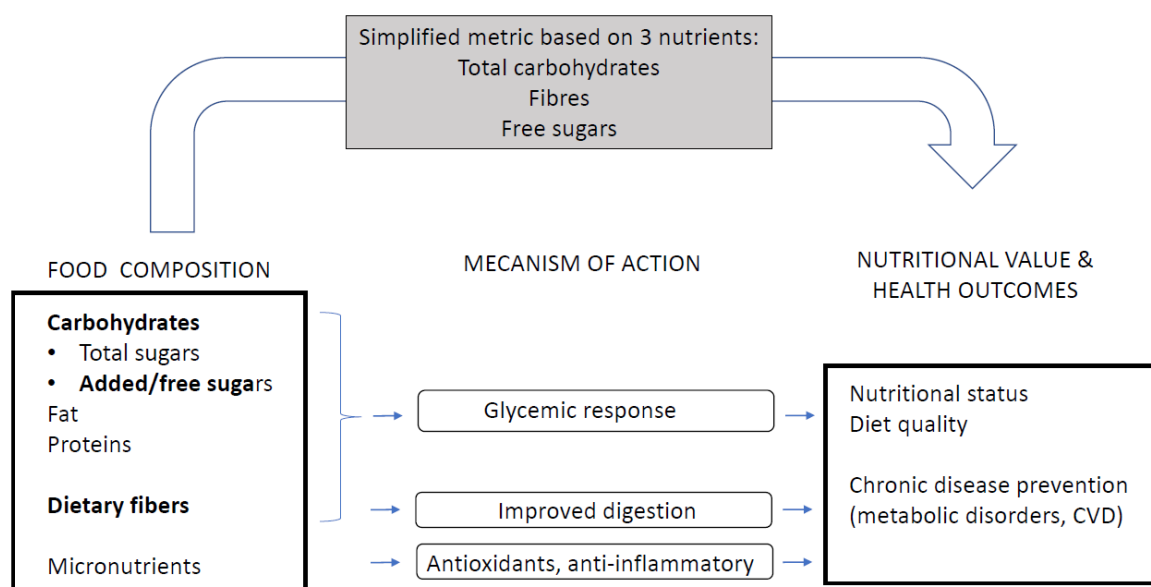
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Table 1. Carbohydrate quality ratios

Ratio	Definition
10:1 carb:fiber ratio	Original validated ratio defined as ≥ 1 g of fiber per 10 g of carbohydrate
10:1:1 carb:fiber:added sugars ratio	Ratio defined as ≥ 1 g of fiber <i>and</i> < 1 g of added sugars per 10 g of carbohydrate
10:1:2 carb:fiber:added sugars ratio	Ratio defined as ≥ 1 g of fiber <i>and</i> < 2 g of added sugars per 10 g of carbohydrate
10:1 1:2 carb:fiber and fiber:added sugars ratio	Ratio defined as ≥ 1 g of fiber per 10 g of carbohydrate <i>and</i> < 2 g of added sugars per 1 g of fiber

Note: adapted from (54).

ORIGINAL UNEDITED MANUSCRIPT



Legend to Figure 1:

Proposed new carbohydrates metrics to reflect food composition and its impact on health outcomes:

The nutritional quality of a product is reflected by the sum and interaction of its individual nutrients, including macro- and micronutrients. A simplified extract of this full nutritional composition can be represented by a metric taking into account only three nutrients: total carbohydrates, fibres and added sugars. Products compliant with such metric were showed have higher nutritional quality, which may positively impact diet quality and health outcomes.