Sugars and Health
the Current Science

How does the human body process sugars consumed in the diet? What are the relationships between sugars intake and obesity, blood glucose response, appetite regulation, addiction, dental caries, and micronutrient adequacy? These are among the most discussed topics in current media but unfortunately are often less understood by the public and sometimes health professionals. Single scientific studies reporting associations with obesity or other chronic diseases have been popularized to imply causation where robust scientific evidence is lacking. Inconsistent terminology, such as sugar, added sugar, free sugars, total sugars, sugary foods, etc., has further confused scientific analysis and reporting. This article presents an overview of sugars metabolism in humans, followed by a FAQ session with renowned experts in the field on these most discussed topics related to sugars and health.

SUGARS METABOLISM

What are sugars?

The term "sugars" is the general term used for all monosaccharides and disaccharides. Sugars occur naturally in foods such as milk (lactose) and fruits and vegetables (sucrose, fructose, glucose). Other sources of sugars such as table sugar (sucrose), honey and high fructose corn syrups can be added to a variety of foods not only for sweetness but also a number of important functional properties such as assisting food preservation, supporting yeast fermentation, acting as a bread tenderizer and so on[1,2].

How are sugars digested and absorbed?

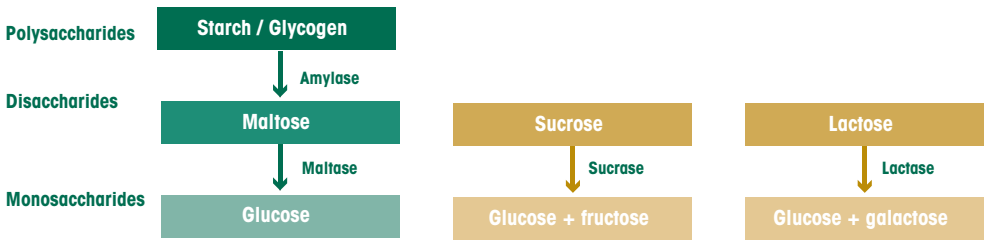
All dietary sugars are digested in the small intestine; the body does not distinguish between added or naturally occurring sugars and metabolizes them the same way based on their chemical structure. All disaccharides are digested by enzymes secreted from the pancreas into the intestinal lumen or enzymes at the brush-border membrane, resulting in a mixture of monosaccharides (glucose, fructose and galactose) (Figure 1)[3]. These digestive products are then absorbed across the membrane of the small intestine and transported to the liver via the portal vein. Another significant contributor of glucose is starch, which is exclusively made of glucose molecules (Figure 1).

Various factors affect sugars digestion and absorption, including the food matrix or other foods eaten together with sugars-containing foods. For example, the presence of fibre can interfere with gastric emptying, interfere with sugars digestion and slow down the diffusion of monosaccharides to the absorptive surface of the small intestine, all of which slow down the appearance of monosaccharides in the blood stream.

What happens to monosaccharides once they are absorbed?

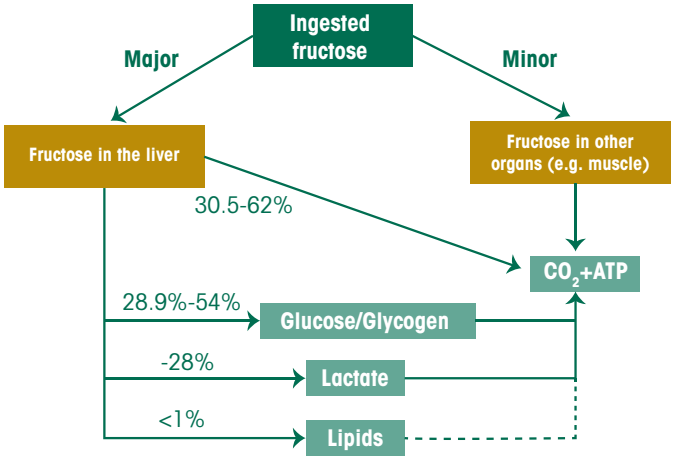
The liver plays a central role in receiving dietary monosaccharides and directing them into respective downstream metabolic pathways[4]. As the primary fuel, glucose can be used by all tissues in the body for energy production, and some specialized cells such as red blood cells are completely dependent on glucose for their energy needs. Glucose is derived from dietary carbohydrates (e.g. starches, sugars), body glycogen stores, or formed in the body from fructose, amino acids, lactate and other precursors. These sources provide constant availability of glucose, whose homeostasis is strictly regulated. The balance among glucose oxidation, glucose biosynthesis and glucose storage is dependent upon the hormonal and nutritional status of the whole body.

Figure 1. Carbohydrate digestion in humans



Fructose and galactose are converted to intermediates in glycolysis. There are two major pathways for the metabolism of fructose [5,6]: the more prominent pathway is in the liver and the other occurs in skeletal muscle. The breakdown of fructose in skeletal muscle is similar to glucose. In the liver and depending on exercise condition, gender, health status and the availability of other energy sources (e.g. glucose), the majority of fructose is degraded for energy production, or enters the gluconeogenic pathway to produce glucose and potentially glycogen, or is converted to lactic acid (Figure 2). The notion that fructose is an unregulated energy substrate and directly fuels fat synthesis in the liver is not supported by the scientific literature; within the normal consumption range very minimal amounts (<1%) of fructose are converted to fat [5,6]. It is important to note that the metabolism of fructose involves many regulated reactions and its fate may vary depending on nutrients consumed simultaneously with fructose (e.g. glucose) as well as the energy status of the body. It is chronic positive energy balance (i.e., "energy in" greater than "energy out" over an extended period of time), regardless of the macronutrient source of calories (i.e., sugars, starches, proteins or fat), that will eventually prompt the body to store excess energy as fat.

Figure 2. Acute metabolic fate of fructose in the body within 6 hours of ingesting 50-150 grams (about 12-36 teaspoons) of fructose (adapted from Sun et al. 2012 [6]).



FREQUENTLY ASKED QUESTIONS ON SUGARS AND HEALTH

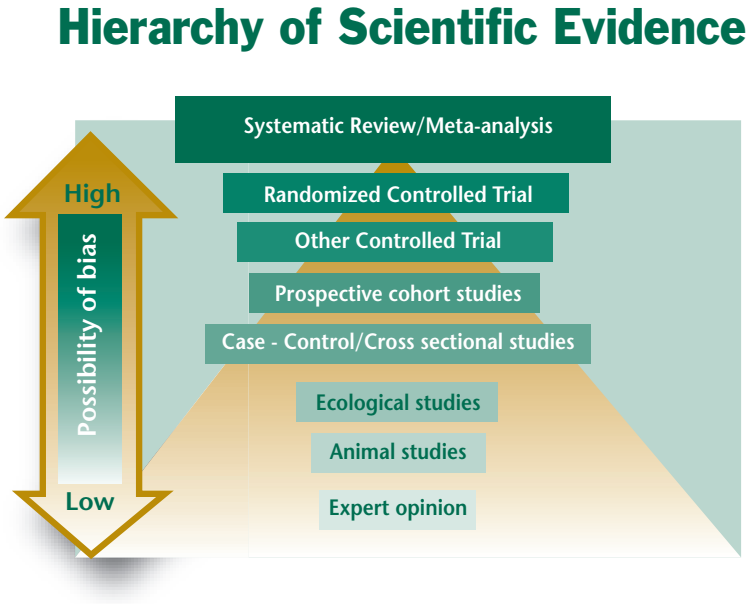
Some have argued that fructose has an effect on health beyond its caloric contribution to the diet. What is your opinion?

***John Sievenpiper, MD, PhD, FRCPC**, Associate Professor, Dept. of Nutritional Sciences, University of Toronto Scientist, Li Ka Shing Knowledge Institute, St. Michael's Hospital Consultant Physician, Division of Endocrinology & Metabolism, St. Michael's Hospital*

The quality of scientific research is usually scrutinized against the hierarchy of scientific evidence (Figure 3), with systematic reviews/meta-analyses being those of the highest level of evidence. The best evidence from systematic reviews and meta-analyses of controlled feeding trials has consistently shown that in relation to cardio-metabolic risk (i.e. risk factors for obesity, diabetes and cardiovascular disease), fructose-containing sugars do not result in any more harm than other sources of calories which would replace sugars, particularly calories from other carbohydrates (namely starch)[7-10]. Researchers that have done dose modelling also have not found a threshold of additional health impact that goes beyond the calories in fructose-containing sugars.

We've looked at liver health in relation to fructose and have published systematic reviews and meta-analyses of controlled

Figure 3. Schematics of the hierarchy of scientific evidence



feeding trials[11]. The results suggest that fructose does not behave differently than glucose on markers of non-alcoholic fatty liver disease.

However, when you match carbohydrates for calories in a different food matrix, a different metabolic effect may be observed. Examples include a diet with "low glycemic index" compared to "high glycemic index" carbohydrates, or the addition of a viscous sticky fibre to starch compared to energy-matched starch alone. In these cases, we do observe improvements in risk factors such as blood pressure, blood cholesterol, blood lipids or blood sugar levels. But when it comes to body weight, a calorie is still a calorie, as shown in the best available data when we look at sugars in comparison to other energy sources.

Suggested readings:

1. Chiu S et al. Eur J Clin Nutr. 2014; 68:416–423;
2. Sievenpiper JL et al. Ann Int Med. 2012;156(4):291-304.

Satiation and Satiety are important components of appetite control. Can you tell us what the difference is between the two concepts, and how dietary sugars are involved in these regulated pathways?

Nick Bellissimo, PhD

Associate Professor and Director, Nutrition Discovery Labs, School of Nutrition, Ryerson University

Satiety and satiation are two important principles in the study of food intake regulation[12,13]. Satiety is defined as the state of eating cessation, and it delays the initiation of subsequent meals. Satiation, on the other hand, is the process of feeling full during the course of eating, a form of intra-meal satiety that affects meal size and is assessed by measuring energy content of the consumed meal.

Food consumption triggers a multitude of neural and hormonal signals, originating from the periphery and interacting with the central nervous system, that regulate food intake according to energy requirements. In response to the macronutrient composition in one's diet, the body releases hormones–gastrointestinal, pancreatic, and adipose derived–that ultimately signal the hypothalamus to contribute to the cessation of eating (i.e. satiation). This powerful feedback system is sensitive to the overall macronutrient composition of the diet and not specific to its sugars content per se.

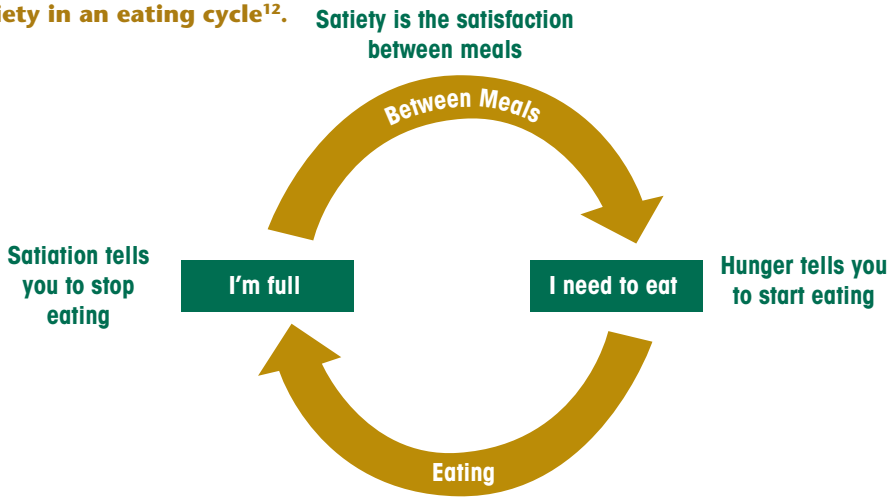
While there is a positive association between the meal size and the length of the satiety response, the effect of macronutrient composition on satiety is mixed. The satiety index of common foods (developed by Holt et al.) showed that satiety scores varied both within and in comparison to other food groupings[14]. Therefore, many sources within the fruit, carbohydrate and protein-rich breakfast cereal, snack, confectionery, and bakery product groups are satiating. The overlap between levels of protein, carbohydrate and fat makes it difficult to suggest that one particular type of macronutrient (e.g. sugars) produces weaker satiety signals than others. However, this fact is often overlooked in comparative food trials, an omission that contributes to further confusion about the effect of macronutrient composition on food intake regulation, especially in relation to sugars.

Generally speaking, there is a positive association between glycemic response and satiety. In the short term, carbohydrates that tend to elicit a higher glycemic response are associated with lower food intake at the next meal. The initial release of glucose and insulin signal satiety centres in the central nervous system to suppress appetite and food intake. In my own studies in children, glucose in solution consumed as a pre-meal snack has consistently suppressed caloric intake at a subsequent meal by an amount greater than the caloric contribution of the pre-meal snack[15,16].

Scientific evidence does not support the notion that sugars bypass the regulatory mechanisms that control food intake[17]. The magnitude of effect of sugars may vary by the source, the food matrix, the dose, the inter-meal interval, and the time-point of measure. Sugars suppress food intake and, like other macronutrient sources, activate the normal hormonal cascade of signals that contribute to the suppression of food intake. Sugars, similar to other carbohydrates, do not bypass regulatory mechanisms of food intake [e.g. fructose, glucose, and sucrose all suppress ghrelin (a "hunger hormone" produced by ghrelin cells in the gastrointestinal tract) to a similar extent].

Furthermore, published literature does not support the common view that energy from solid food suppresses satiety more than that from liquids[18]. Timing of consumption on appetite control may therefore be more important than the vehicle in which the energy is delivered.

Figure 4. Satiation and satiety in an eating cycle[12].



Suggested readings:

1. Bellisle F et al. J Nutr. 2012 Jun;142(6):1149S-54S.
2. Anderson GH et al. Am J Clin Nutr. 2003 Oct;78(4):843S-849S.

Are sugars naturally-occurring in fruits and vegetables structured or metabolized differently from those added to foods? What are the factors that may affect the digestion, absorption and glucose response in the body?

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When we think about the digestion and absorption of sugars, we need to consider the complexity of the food matrix and meals. Components of the food matrix (e.g. cell walls) would delay the availability of sugars for digestion and absorption. In addition, the action of chewing may stimulate saliva secretion resulting in different degrees of gastric emptying. Sugars also stimulate taste receptors on the tongue, possibly enhancing the so-called cephalic phase of insulin secretion which has been shown to reduce postprandial glucose responses[19]. In addition, there are studies suggesting that polyphenols inhibit the activity of sucrase (the enzyme that breaks down sucrose), which delays the release of glucose and fructose molecules from sucrose and their subsequent absorption[20]. Many people may not be aware that pure sucrose actually elicits a lower glycemic response than many refined starches, because its fructose component is associated with reduced postprandial glycemic response and improved glycemic control in diabetes.

However sucrose is seldom consumed in isolation. All components of the meal can influence the rate of the absorption of sugars. For example, there are many components in tea and coffee (e.g. polyphenols) that may alter the body's response to sugars added to these drinks [21,22]. Similarly, breakfast cereals, legumes or condiments have many components that impact the absorption of the sugars added to them.

Consuming sugars with healthy foods so that they are tastier is not necessarily a bad thing. We want to have flavour in foods and if we don't use sugars, we may end up using fat, which will contribute more calories. A moderate amount of sugars is fine. We recently reported (Experimental Biology 2015) that the glycemic response of oatmeal made with 30 g oats plus 9 g of sugar was no different from what would be expected from 45 g of oats (containing the same amount of available carbohydrate as 30 g oats and 9 g sugar). From this perspective, sugar seems to be neutral and may encourage the consumption of healthy foods such as oatmeal.

Suggested readings:

1. Wolever TM. Nutr Rev. 2003;61:S40-8.
2. Southgate D et al. Am J Clin Nutr. 1995;62 (Suppl): 203S-11S.

What is "food addiction" and what is the available scientific evidence related to food addiction and sugars?

David Benton, PhD
Professor, Swansea University, UK

A preference for a sweet taste or palatable foods should not be confused with addiction[23]. Evolution has resulted in a genetically based liking for a sweet taste that is present at birth; breast milk is sweet. The term "addiction" is used in many ways, and some have suggested that similar to drugs of abuse, consumption of sweetened foods may lead to physical addiction and withdrawal symptoms due to changes to dopamine mechanisms associated with the brain's reward system.

Any palatable food results in the release of dopamine. In fact, any pleasant event, even a joke or a smile, will cause dopamine release. Neurophysiological techniques have been used to study the impact of consuming sugar on the release of dopamine and the pattern differs from that observed with drugs of abuse. With sucrose, less dopamine is released prior to consumption and for a shorter time. With drugs of abuse dopamine is released for longer and in larger amounts both before and after consumption, hijacking the brain's normal reward pathways.

A review that looked for the symptoms of addiction such as withdrawal, craving and tolerance could find no evidence of an association with sugar consumption[23].

The NeuroFAST consortium, a multidisciplinary project involving twelve teams from seven countries funded by the European Union, concluded that a single food substance acting via a single specific biological mechanism cannot account for overeating and obesity[24]. No strong evidence was found that people become addicted to chemical substances in foods or that the brain's response to nutrients behaves the same way as to addictive drugs. Humans do not restrict their diets to specific nutrients, rather it is the wide range of palatable foods that may contribute to overeating among susceptible individuals. The term "eating addiction" rather than "food addiction" was proposed; that is, some people develop a psychological compulsion to eat, driven by the positive feelings they associate with eating. The consortium suggested that the focus should be moved from food itself towards the individual's relationship with eating.

Suggested readings:

1. Benton D. Clin Nutr. 2010 Jun;29(3):288-303.
2. Hebebrand J et al. Neurosci Biobehav Rev. 2014 Nov;47:295-306.

The World Health Organization (WHO) has suggested a 10% free sugars guideline and a conditional 5% guideline (based on very low quality evidence) as targets to reduce dental caries. Based on your research and expertise in preventative dentistry, do you think this guideline could achieve a decrease in the incidence of dental caries?

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Academic Centre for Dentistry Amsterdam (ACTA), The Netherlands

There is no doubt that dental caries are caused by acids produced by bacteria through the fermentation of sugars and other fermentable carbohydrates. The evidence indicates it is not the amount of sugars or fermentable carbohydrates that determines the caries rate, but the frequency of consumption[25, 26]. The first and most important dietary advice is to reduce the frequency of intake. With a sensible diet the frequency can be reduced without necessarily reducing the amount.

Another weakness of this guideline is the term "free sugars". It suggests that whole fruits are different from fruit juices. However there is evidence that eating whole fruits and drinking fruit juices have comparable effects on caries development. All sugars equally affect the risk of dental caries with the exception of lactose[25]. Focusing specifically on "free sugars" for dental caries prevention is therefore not justified.

Most of the studies, on which these guidelines are based, were performed when fluoride use was not yet widespread (1945-1954) and oral hygiene was poor. Under those circumstances the focus on diet as a preventive tool is understandable. The focus since then has been to reduce the frequency of intake and the stickiness of foods as an important co-risk factor.

In modern times the use of fluoride in drinking water and toothpaste provides strong protection against dental caries. This knowledge, ignored in the WHO guideline, should be integrated in our dietary advice for the prevention of caries. Not doing so is like forbidding people to cross the street instead of helping them with traffic lights. Our oral health education should exchange the explanation model for a dialogue model which allows for individual support based on the experiences, values and resources of our patients.

Suggested readings:

1. Riva Touger-Decker et al. Am J Clin Nutr. 2003;78 (suppl): 881S-92S.
2. Nutrition and Oral Medicine. 2005. Edited by Riva Touger-Decker, et al. Humana Press.

Dietary guidelines that recommend a reduction in added sugars intake to less than 10% energy or less than 5% energy imply that there are no adverse effects of low sugars intakes. How would you comment on such recommendations from the perspective of nutrient adequacy?

Sigrid Gibson, MSc, MA, RNutr
Director, Sig-Nurture Ltd, UK

We simply don't know what the consequences to micronutrient intake would be if people were to reduce free sugars to less than 5% of energy because no modern Western population has intakes at this level. In terms of calories, substituting sugars with starch is not going to make any difference. Meeting recommended fibre intakes (e.g. DRI: 38 grams for males and 25 grams for females aged between 19-50 years) will be more difficult without the use of sugars to enhance palatability.

From cross-sectional studies, there is some evidence that at high sugar intakes (>25% of energy), micronutrient intakes decline; but there is also some evidence that very low sugar intakes (<5% of energy) are also associated with unbalanced diets including low intakes of some micronutrients[27]. It may be an 'n-shape' association where the highest micronutrient intakes are associated with added sugars consumption levels of between 5-12% of energy. However, we can't put a figure to it because it differs between micronutrients, populations and age groups[27,28].

The desire of the WHO recommendation was to reduce energy intake. The implication is that nutrient density will have to rise to satisfy recommended micronutrient intakes. That means choosing foods more carefully. There are only a few ways to do that; cutting some sugars out of the diet may work, if you reduce soft drinks for example. But it won't work if you try to reduce all sugars in the diet as this would also include nutrient-rich sources such as fruit yogurt or fibre-rich breakfast cereals.

The concept of "free sugars" or "added sugars" is artifact. It is a convenient measure adopted to try to encourage people to eat fewer energy dense processed foods without cutting down on fruits, vegetables or milk. However, the body metabolizes sugars based on their chemical structure, not the source. Overall, focusing mainly on sugars distracts the public from more sustaining messages on energy balance, portion size, and physical activity.

Suggested readings:

1. Gibson S et al. Br J Nutr. 2009;101:100-7.
2. Rennie KL et al. Br J Nutr. 2007; 97:832-41.
3. van Buul VJ et al. Nutr Res Rev. 2014;27: 119-30[29].

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