The State of the Science on Dietary Sweeteners Containing Fructose: Summary and Issues to BeResolved¹,²

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Abstract

This article highlights the discussion of the issues that had been raised during the International Life Sciences Institute North America- and USDA Agricultural Research Service-sponsored workshop surrounding the consumption of fructose. One conclusion of the discussion was that the metabolic effects of high-fructose corn syrup (HFCS) and sucrose appear to be similar in humans. However, there have been few studies directly comparing the effects of fructose to other caloric sweeteners, such as glucose, HFCS, and sucrose. Differential effects may include those related to insulin sensitivity, triglyceride and lipoprotein levels, and glycated protein levels. Further exploration of the differences between nutritive sweeteners should be the basis of a research agenda. Studies should also further investigate factors that might affect the results; such as the amount and form of the sweetener consumed, the macronutrient composition of the basal diet, the length of the study, and the characteristics of the subjects. Meanwhile, health professionals could help consumers by providing simple messages, such as the importance of consuming lower levels of energy, including those from all caloric sweeteners. J. Nutr. 139: 1269S–1270S, 2009.

Introduction

At the International Life Sciences Institute North America- and USDA Agricultural Research Service-sponsored workshop on dietary sweeteners containing fructose, several papers were presented on this topic (1–9). A summary of the workshop is given in the overview paper at the beginning of this series (10). Following the scientific presentations, the speakers and workshop attendees held a discussion of the issues that had been raised during the workshop and a possible research agenda to further address relevant concerns. The following is a summary of that discussion.

Where is there agreement on the effects of dietary sweeteners containing fructose?

High-fructose corn syrup (HFCS) is a mixture of monosaccharides, fructose, and glucose, typically with a fructose:glucose ratio of either 55:45 or 42:58. In this regard, it is similar to the disaccharide sucrose, with a molar ratio of fructose:glucose of 1:1. The metabolic effects of HFCS and sucrose appear to be similar in humans. At this time, there is little evidence directly comparing the metabolic effects of fructose to glucose, HFCS, and sucrose. What evidence is available suggests that whether or not differences are observed depends on the parameter measured and the control carbohydrates against which fructose is tested. New studies comparing the endocrine and metabolic effects of glucose, fructose, sucrose, and HFCS at graded levels of consumption in different populations are needed.

Possible differential effects of dietary fructose and glucose on energy metabolism

Given the concern expressed about HFCS as a possible contributing factor to obesity, one focus of the workshop was the metabolic effects of these sweeteners. There is little evidence that fructose and glucose have differing effects on satiety or overall energy balance. Energy provided by sweeteners may play a role in promoting positive energy balance; it is not clear whether the differential metabolic effects between fructose and glucose can result in differences in energy storage. More research is needed on the metabolic effects of common caloric sweeteners on both weight gain and on regional fat distribution.

Possible differential effects of dietary fructose and glucose on risk factors for chronic diseases

Controlled feeding studies utilizing high doses of various sugars have highlighted several important differences in the biochemical effects of glucose and fructose that might affect the risk for...
chronic disease if also observed at intake levels commonly consumed. These include measurable differences in: plasma glucose concentration and effects on insulin sensitivity; postprandial and fasting triglyceride and lipoprotein levels (such as apolipoprotein-B); and levels of glycated proteins.

Other associations under investigation that require additional research include: levels of insulin, leptin, ghrelin, and related compounds; plasma or intracellular uric acid levels; and reactive carbonyls and advance glycation products.

Understanding the potential relationships among these variables and chronic disease(s) is also appropriate for future research.

What are appropriate research designs to address these issues?

Further exploration of the differences between nutritive sweeteners should be the basis of a research agenda. More research is needed to answer many questions about the effects of different types of sweeteners on both energy metabolism and risk factors for chronic diseases. Several types of studies can contribute. Animal studies are important for generating hypotheses, but the results are difficult to extrapolate to humans. Observational studies may also be used to generate hypotheses, but associations with chronic diseases must be interpreted carefully due to the presence of many confounding variables. Human metabolic studies are needed to test hypotheses in a controlled environment and clinical trials are needed to test hypotheses in a free-living environment.

A major difficulty in understanding differential effects among sweeteners is the varying conditions under which the research investigations take place. Speakers identified many factors that might affect the conclusions of a research study: amount of the sweetener consumed (total and percentage of energy in the diet); form of the sweetener (e.g. monosaccharides vs. di- or polysaccharides) and the type of food in which it is present (e.g. liquid vs. solid); presence of other saccharides and macronutrient composition in the basal diet; length of the study (short-term vs. long-term); characteristics of the subjects in the study, such as sex, age, body size, physical activity level, energy balance status (weight gain or loss vs. weight stable); and health status (such as the presence of diabetes or metabolic syndrome). There is an increasing realization that genetic differences among subjects might also have important effects on the metabolism of sweeteners.

It might be useful to consider a systematic review of the literature for the purpose of identifying any consistently different metabolic effects among sweeteners after considering variations in research designs and subject characteristics. Such a review would also provide a means for placing research outcomes into perspective by identifying whether experimental data constitute normal or aberrant human metabolism.

One suggestion, which is in agreement with general toxicological theory, was that there may be a threshold for the differing effects of fructose; that is, that intake would need to exceed some level before such effects are seen. However, all of the factors outlined above could affect the level of the threshold as well as the nature and quantitative significance of any response. Dose-response studies, particularly including the range of typical intakes, are needed to better understand this possibility.

There are many challenges in designing studies that can investigate the role of these potential confounding variables. Several attendees noted the importance of determining whether effects in laboratory feeding studies can be extrapolated to free-living subjects consuming typical diets.

What are appropriate professional messages regarding sweeteners containing fructose?

Because health professionals, such as dietitians, are often the providers of advice to the public regarding dietary sweeteners containing fructose, there were several suggestions for messages that could help them summarize the current state of the research. For example, health professionals could help consumers understand that metabolically, HFCS and sucrose are similar and one is not “better” or “worse” than the other. Another message relates to the use of sugars by people with diabetes: small amounts of sugars containing fructose may be appropriate for use by diabetics, due to the blunted glycemic response, but they should be avoided in large amounts due to demonstrated negative effects on triglyceride levels; research is ongoing to identify thresholds for these effects.

What are appropriate consumer messages regarding fructose?

It is difficult for consumers to identify the sweetener–fructose, glucose, sucrose, HFCS, or their mixtures—in a particular food, either naturally occurring or added. Therefore, it does not appear to be practical to base dietary guidance on selecting or avoiding these specific types of sweeteners. Furthermore, typical foods and diets seldom contain pure fructose or pure glucose but contain mixtures of different sweeteners. All of the naturally occurring sweeteners are caloric and consumers, on average, consume more energy than they expend. A simple message regarding the importance of consuming lower amounts of energy, including those from caloric sweeteners, seems to be the appropriate approach. The Dietary Guidelines 2005 consumer brochure suggests, “A healthy eating plan is one that ... is low in saturated fats, trans fats, cholesterol, salt (sodium), and added sugars.” (11). At this time, there does not appear to be a need for a more complex message for consumers.

Literature Cited