Straight talk about high-fructose corn syrup: what it is and what it ain’t1–4

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ABSTRACT
High-fructose corn syrup (HFCS) is a fructose-glucose liquid sweetener alternative to sucrose (common table sugar) first introduced to the food and beverage industry in the 1970s. It is not meaningfully different in composition or metabolism from other fructose-glucose sweeteners like sucrose, honey, and fruit juice concentrates. HFCS was widely embraced by food formulators, and its use grew between the mid-1970s and mid-1990s, principally as a replacement for sucrose. This was primarily because of its sweetness comparable with that of sucrose, improved stability and functionality, and ease of use. Although HFCS use today is nearly equivalent to sucrose use in the United States, we live in a decidedly sucrose-sweetened world: >90% of the nutritive sweetener used worldwide is sucrose. Here I review the history, composition, availability, and characteristics of HFCS in a factual manner to clarify common misunderstandings that have been a source of confusion to health professionals and the general public alike. In particular, I evaluate the strength of the popular hypothesis that HFCS is uniquely responsible for obesity. Although examples of pure fructose causing metabolic upset at high concentrations abound, especially when fed as the sole carbohydrate source, there is no evidence that the common fructose-glucose sweeteners do the same. Thus, studies using extreme carbohydrate diets may be useful for probing biochemical pathways, but they have no relevance to the human diet or to current consumption. I conclude that the HFCS-obesity hypothesis is supported neither in the United States nor worldwide. Elsevier B.V.

INTRODUCTION
High-fructose corn syrup (HFCS) is a liquid sweetener alternative to sucrose (table sugar) used in many foods and beverages. Early developmental work was carried out in the 1950s and 1960s, with shipments of the first commercial HFCS product to the food industry occurring in the late 1960s. Phenomenal growth over the ensuing 35 or more years made HFCS one of the most successful food ingredients in modern history (1).

HFCS was used in relative obscurity for many years. After all, its compositional similarity to sucrose suggested that it would be metabolized in a like manner. Its safety was never seriously doubted because expert scientific panels in every decade since the 1960s drew the same conclusion: sucrose, fructose, glucose, and, latterly, HFCS did not pose a significant health risk, with the single exception of promoting dental caries (2–5).

Although there was considerable speculation in the 1980s that fructose was responsible for several metabolic anomalies (6–8), convincing proof that this was a significant health risk was never forthcoming. It came as a great surprise to many when, seemingly overnight, HFCS was transformed from a mundane ingredient into the principal focus of scientists, journalists, and consumers concerned about the growing incidence of obesity in the United States and around the world. This article will probe the basis and implications for the current hypothesis that HFCS is somehow uniquely responsible for rising obesity rates and will challenge the science purported to demonstrate a unique role for HFCS in promoting obesity.

BRIEF HISTORY OF HIGH-FRUCTOSE CORN SYRUP
Sucrose from sugar cane or sugar beets has been a part of the human diet for centuries; sucrose from fruit or honey has been a part of the human diet for millennia. Sucrose continues to be the benchmark against which other sweeteners are measured. However, sucrose has posed significant technological problems in certain applications: it hydrolyzes in acidic systems (9), changing the sweetness and flavor characteristics of the product, and it is a granular ingredient that must be dissolved in water before use in many applications. Furthermore, sugar cane was traditionally grown in equatorial regions, some known equally well for both political and climatic instability. The availability and price of sugar fluctuated wildly in response to upsets in either one.

HFCS immediately proved itself an attractive alternative to sucrose in liquid applications because it is stable in acidic foods and beverages. Because it is a syrup, HFCS can be pumped from delivery vehicles to storage and mixing tanks, requiring only simple dilution before use. As an ingredient derived from corn—a dependable, renewable, and abundant agricultural raw material of the US Midwest—HFCS has remained immune from the price and availability extremes of sucrose. It was principally for these reasons that HFCS was so readily accepted by the food industry and enjoyed such spectacular growth.

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only of glucose—either free or bonded to itself in chains of products. Corn syrup is actually a family of ingredients made up of HFCS, but as shown in Table 1, they are clearly distinct from these products are highly specialized and are manufactured in

HFCS-80 or HFCS-90) is occasionally seen in the literature, but predominately maltose (di-glucose) and maltotriose (tri-glucose). Mention of HFCS with higher fructose content (ie, HFCS-80 or HFCS-90) is occasionally seen in the literature, but these products are highly specialized and are manufactured infrequently and in insignificant amounts.

Gross et al (16) and others have confused HFCS with common corn syrup, but as shown in Table 1, they are clearly distinct products. Corn syrup is actually a family of ingredients made up of glucose—either free or bonded to itself in chains of various lengths up to $\approx 10$, depending on the specific corn syrup product.

HFCS is also frequently confused with pure fructose, probably because of its name. “High-fructose corn syrup” is, in retrospect, an unfortunate choice of name, because it conjures up images of a product with very high fructose content. The original intent of the name was simply to distinguish it from ordinary, glucose-containing corn syrup. Pure crystalline fructose has been available to the food industry since the late 1980s, but is still used in relatively minor amounts. The obvious differences between HFCS and pure fructose are aptly demonstrated in Table 1: the latter contains no glucose and is a low-moisture crystalline material. It must be emphasized that from a composition standpoint, pure fructose is a poor model for HFCS.

The glucose-to-fructose ratio in HFCS is nearly 1:1; similar to the ratio in sucrose, invert sugar, and honey. A similar ratio is also found in many fruits and fruit juices. The only practical distinction in composition between sucrose and other fructose-containing sweeteners is the presence of a bond linking fructose and glucose (sucrose chemical name: $\beta-d$-fructofuranosyl-$\alpha-d$-glucopyranoside; 17). The glucose and fructose in HFCS, invert sugar, honey, and fruit is principally monosaccharide (free, un-bonded). Thus, when HFCS historically replaced sucrose in formulations, no increase in dietary fructose occurred.

Invert sugar is the name given to sucrose in which the bond linking fructose and glucose has been hydrolyzed. This may be accomplished either with acid or enzyme (invertase). Acid-catalyzed inversion of sucrose is accelerated by increased temperature and reduced pH and takes place within time spans as short as minutes to as long as months (9). Because carbonated beverages are low in pH (colas are near pH 3.5) and are stored in warehouses at ambient temperature—sometimes for weeks before they reach supermarket shelves—considerable inversion can take place before the product reaches the consumer. It is a sweet irony that purists who must have their sucrose-sweetened sodas end up drinking a sweetener composition more similar to HFCS and have been doing so since the first cola was formulated in the 1880s.

Availability

The HFCS-obesity hypothesis of Bray et al relies heavily on the positive association between increasing HFCS use and obesity rates in the United States (10). However, Bray et al treated this association in isolation, offering no perspective on trends in total caloric intake or added sweeteners use in comparison with
use of other dietary macronutrients. Loss-adjusted food availability data from the US Department of Agriculture Economic Research Service to provide that missing perspective are compared in Figures 1 and 2 (18). Availability data attempt to provide a more realistic estimate of the amount of food actually available for consumption by subtracting losses in manufacturing, transportation, food preparation, spoilage, and table wastage from food production figures.

Plotted in Figure 1 are per capita daily calories over the 35-y period from 1970 to 2005, the most recent data available. As has been widely reported, per capita daily calorie intake increased 24% over that time period.

Trends in caloric intake of major dietary nutrients over the same period are illustrated in Figure 2 to determine whether added sugars increased disproportionately, which is something they surely would have had to do to uniquely impact obesity. In fact, use of added sugars as a fraction of daily calorie intake actually decreased slightly, along with vegetables, dairy, and meat, eggs, and nuts. It is significant that added fat was up 5%, because evidence is growing that added fat is more strongly associated with obesity than are added sugars (19).

It is widely believed that HFCS eclipsed sucrose long ago as the primary nutritive sweetener in the US diet and that fructose concentrations have risen disproportionately as a result, but this is just not so. Per capita daily calories from cane and beet sugar, HFCS, honey, and their total are plotted over the past 35 y in Figure 3. The following points are important to note:

- There was essentially a one-for-one replacement of sucrose with HFCS from 1970 to 1998;
- Since 1998, sucrose use and HFCS use have been roughly equivalent, a significant fact that has escaped too many writers on the subject;
- Fructose contributes \( \frac{1}{2} \)–\( \frac{2}{5} \) kcal/d (sucrose and HFCS are each half fructose), \( \approx 7–8\% \) of the current 2700-kcal/d per capita total calorie intake reported in Figure 1;
- Honey use is slight in comparison with the other 2 and has remained largely unchanged; and
- Although availability of sugars was up over this period, which confirms the data shown in Figure 2, use of added sweeteners as a percent of total calories has declined in recent years.

Two additional facts are worthy of note here: 1) although commercially available, pure crystalline fructose remains a specialty sweetener used in very limited quantities, and 2) the ratio of fructose-to-glucose from added sugars is \( \approx 0.7 \), and this value has likely remained unchanged since sucrose use became widespread a century ago (20).

Sweetness

A common misconception about HFCS is that it is sweeter than sucrose and that this increased sweetness contributed to the obesity crisis by encouraging excessive caloric food and beverage consumption (10). HFCS is not sweeter than sucrose. The sweetness of several common nutritive sugars in crystalline and liquid or syrup form is compared in Table 2.
Sucrose, with a value of the same experimental conditions, HFCS-42 is less sweet than HFCS-55 and sucrose yield the same relative sweetness. Under industry taste panels. In syrup form at 10% solids (the approximate to the sucrose standard as established by trained, expert food tarotation to give a mixture of several tautomers with lower and inappropriately attributed to HFCS, a blend of equal amounts of glucose and fructose in liquid or syrup form.

Sweetness intensities of crystalline compounds were reported in pioneering work by Schallenberger and Acree in 1971 (21). They determined that fructose in the crystalline, β-d-fructopyranose anomeric form has ~1.8 times the sweetness of crystalline sucrose; the relative sweetness of crystalline glucose is lower at 0.7–0.8. Note that the sweetness of HFCS cannot be determined in crystalline form because HFCS does not crystallize. It is this marked difference in sweetness between fructose and sucrose in crystalline samples that is often confused and inappropriately attributed to HFCS, a blend of equal amounts of glucose and fructose in liquid or syrup form.

Once in solution, β-d-fructopyranose undergoes rapid mutarotation to give a mixture of several tautomers with lower and differing sweetness intensities (23, 22). White and Parke (13) reported the sweetness values of liquid and syrup samples relative to the sucrose standard as established by trained, expert food industry taste panels. In syrup form at 10% solids (the approximate sweetener concentration in most carbonated beverages), HFCS-55 and sucrose yield the same relative sweetness. Under the same experimental conditions, HFCS-42 is less sweet than sucrose, with a value of ∼0.9.

In 2000 Schiffman et al (22) reported the absolute sweetness of syrups at various concentrations and temperatures. The HFCS absolute sweetness value reported in Table 2 was calculated by regressing Schiffman’s data for fructose and glucose to 10% solids and then substituting the resulting values into the known compositions of HFCS-55 and sucrose. Using sucrose once again as the standard by setting its sweetness equal to 100, a sweetness value of 97 was calculated for HFCS-55, providing independent validation for the value reported by White and Parke. Schiffman’s work also confirmed the earlier work of Hyvonen et al (24) and White (25) that temperature has little effect on sweetness intensity.

These data confirm what the food industry has claimed for more than 20 y: the sweetness intensities of HFCS-55 and sucrose are equivalent. The replacement of sucrose by HFCS-55 did not change the sweetness intensity of foods and beverages, nor did it lead to a “sweetening of America” (26).

Caloric value

HFCS and sucrose are both carbohydrate ingredients that contribute ~4 kcal/g on a dry solids basis. There can be no argument that long-term overconsumption of foods and beverages containing either one without compensation for energy expenditure may lead to weight gain.

Absorption and metabolism

All fructose-containing nutritive sweeteners appear to share the same intestinal sites for absorption. Honey, fruit sugars, and HFCS reach the small intestines predominantly as monosaccharides. The minor amount of polysaccharide glucose in HFCS is quickly broken down to free glucose by salivary and intestinal amylases. Glucose is absorbed into the portal blood through an active, energy-requiring mechanism mediated by sodium and a specific glucose transport protein. Fructose is absorbed via the sodium independent GLUT-5 transporter (27). Disaccharide sucrose requires hydrolysis before absorption, which is rapidly accomplished by a plentiful sucrase in the brush border.

Much has been made of the metabolic differences between fructose and glucose in the human body: fructose is rapidly taken up by the liver and bypasses a key regulatory step in glycolysis. There are, however, several points of intersection where the metabolism of fructose and glucose interchange. This metabolic flexibility works to man’s evolutionary advantage by allowing a variety of food and energy sources to be processed efficiently. It is only when any single nutrient is consumed to excess and overwhelms the body’s metabolic capacity that untoward consequences occur.

Fructose malabsorption appears only to be a problem when too little accompanying glucose is present. This was quickly recognized in early sports drinks formulated solely with fructose to enhance performance by exploiting fructose’s low glycemic index. Riby et al (28) subsequently showed that the addition of even small amounts of free or polymeric sucrose can ameliorate fructose malabsorption and accompanying gastric distress.

The inability of the body to distinguish fructose-containing nutritive sweeteners from one another once they reach the bloodstream is critical to the HFCS discussion, but often overlooked. Sucrose, HFCS, invert sugar, honey, and many fruits and juices deliver the same sugars in the same ratios to the same tissues within the same time frame to the same metabolic pathways. Thus, if one accepts the proposition that a given product will be sweetened with one of the fructose-containing nutritive sweeteners, it makes essentially no metabolic difference which one is used.

**TABLE 2**
Sweetness comparison for selected nutritive sweeteners*

<table>
<thead>
<tr>
<th>Sugars</th>
<th>Sweetness intensity (crystalline)**</th>
<th>Relative sweetness (10% syrup)**</th>
<th>Absolute sweetness (syrups)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fructose</td>
<td>180</td>
<td>117</td>
<td>—</td>
</tr>
<tr>
<td>Sucrose</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>HFCS-55</td>
<td>—</td>
<td>99</td>
<td>97</td>
</tr>
<tr>
<td>Glucose</td>
<td>74–82</td>
<td>65</td>
<td>—</td>
</tr>
</tbody>
</table>

*HFCS, high-fructose corn syrup.
**Adapted from Schallenberger and Acree (21).
***Adapted from White and Parke (13).
****Calculated from Schiffman et al (22).

High-fructose corn syrup is not uniquely obesity-promoting

If the HFCS-obesity hypothesis is correct, there should be something quantifiably unique about HFCS that is absent from sucrose. The data presented thus far in support of the hypothesis rely heavily on the metabolic comparison of glucose and fructose. It has been known for many years that fructose fed to experimental animals or human subjects in high concentration (up to 35% of calories) and in the absence of any dietary glucose will produce metabolic anomalies (7, 8). The 1994 Fructose Nutrition Review commissioned by the International Life Sciences Institute was highly critical of this line of experimentation (29).

A pure fructose diet is surely a poor model for HFCS, because HFCS has equivalent amounts of glucose. Because no one in the world eats a pure fructose diet, such experimentation must be recognized as highly artificial and highly prejudicial and not at all appropriate to HFCS.

Sucrose is a far more satisfactory model for HFCS. Experiments that test the HFCS-obesity hypothesis in a reasonable way,
by comparing it with sucrose, are only now beginning to be published. In a notable current study from 2007, Melanson et al (30) compared the effects of HFCS and sucrose at 30% of calories in 2 randomized 2-d visits in normal-weight women. Concluding that there is nothing uniquely quantifiable about HFCS, they reported no significant difference between the 2 sweeteners in fasting plasma glucose, insulin, leptin, or ghrelin or in energy or micronutrient intake.

HIGH-FRUCTOSE CORN SYRUP IS NOT PREDICTIVE OF US OBESITY

Central to the HFCS-obesity hypothesis is its value in predicting US obesity: Bray et al (10) associated its increased use with increasing obesity rates between 1960 and 2000. But does the association continue beyond 2000?

The Centers for Disease Control and Prevention recently reported that overall, age-adjusted obesity rates obtained from the Behavioral Risk Factor Surveillance System were 15.6%, 19.8%, and 23.7% for 1995, 2000, and 2005, respectively (31). The US obesity crisis continues to worsen. From Figure 2, however, it can be seen that per capita calories from HFCS have been stagnant since 1998 and in decline since 2002. Clearly, the association between HFCS and obesity is no longer valid, and HFCS is not predictive of US obesity.

HIGH-FRUCTOSE CORN SYRUP IS NOT PREDICTIVE OF GLOBAL OBESITY

There is a misconception that HFCS is not only the dominant US sweetener, but the dominant world sweetener as well. Neither is true. HFCS accounts for about one-half of the nutritive sweetener used in the United States, but for only 8% of the nutritive sweetener used worldwide; sucrose accounts for the rest (32). The sugar economy is firmly established in many countries and receives heavy government economic and trade protection from competing sweeteners and technologies. Until recently, Mexico imposed a high use tax on HFCS to protect its domestic sugar industry. In addition, HFCS production requires not only an abundant and consistent starch source, but also the use of sophisticated technology. These conditions are satisfactorily met in only a few geographic locations.

This point is illustrated in Figure 4, in which 2005 obesity rates derived from World Health Organization data (33) for 5 non-US countries are plotted against HFCS as a percentage of national nutritive sweetener use (32); US data are provided for comparison. The non-US countries with the highest percentage use of HFCS were South Korea, Japan, and Canada. However, the highest obesity rates were in Mexico and Argentina, the 2 countries with the lowest percentage use of HFCS. Thus, HFCS is not predictive of global obesity either, providing further evidence that the HFCS-obesity hypothesis is not valid.

ELIMINATING HIGH-FRUCTOSE CORN SYRUP WOULD NOT HAVE A SIGNIFICANT EFFECT ON OBESITY

Nutritive sweeteners are used in foods and beverages for many reasons, including sweetness, mouthfeel, colligative properties (eg, freezing point manipulation), moisture control, crystal structure, bulk, browning, caramelization, color, and fermentable solids. They are not easily replaced in products without risking customer notice and displeasure. One could reasonably assume, then, that if the use of HFCS were to be restricted or entirely eliminated in the United States—as some advocate—an alternative nutritive sweetener with similar physical and functional properties would be sought. Because honey and fruit juice concentrates are produced in such limited quantities, it is likely that companies would revert back to formulas circa 1970 and replace HFCS with sucrose.

What would be the impact on obesity in the United States of a change back to sucrose from HFCS? On the basis of the similarities between sucrose and HFCS noted above, it can be predicted with some certainty that there would be no change in caloric intake, no change in basic metabolism, and no change in rates of obesity. The substitution of sucrose for HFCS would be a nutritional wash. The one change consumers would notice is higher prices as sucrose is substituted for the less-expensive HFCS.

CONCLUSIONS

The hypothesis that HFCS is a unique cause of obesity is not supportable in the United States or elsewhere, and the reasons are clear:

- HFCS has the same sugars composition as other “benign” fructose-glucose sweeteners such as sucrose, honey, and fruit juice concentrates and dietary sources such as fruits and juices;
- Increased caloric intake since 1970 was not due to added sugars (including HFCS) but rather was due to increased consumption of all caloric nutrients, especially fats and flour and cereals;
- HFCS is consumed in equal amounts with sucrose in the United States, but at <10% of the amount of sucrose worldwide;
Fructose-glucose sweeteners are metabolized through the same pathways regardless of dietary source; although pure fructose can cause metabolic upsets at high concentrations and in the absence of glucose, such experiments are irrelevant for HFCS, which is not consumed at extreme high levels and contains both fructose and glucose; there is no longer an association between HFCS and obesity in the United States: per capita consumption of HFCS has declined in recent years, whereas obesity rates continue to rise; and there is absolutely no association between HFCS use and worldwide obesity: HFCS is really a minor sweetener in the global perspective.

No one would disagree that HFCS as a caloric ingredient can lead to weight gain if products sweetened with it are consumed to excess. After all, the same may be said for all caloric ingredients, such as fats, protein, alcohol, and other carbohydrates. But there is absolutely no proof that HFCS acts in any exclusive manner to promote obesity. It is time to retire the hypothesis that HFCS is uniquely responsible for obesity. (Other articles in this supplement to the Journal include references 34–37.)

The author is a consultant to the food and beverage industry in nutritive sweeteners, including HFCS and sucrose. His professional associations, past and present, include individual food industry companies as well as such organizations as the American Chemical Society, American Council on Science and Health, Calorie Control Council, Corn Refiners Association, Institute of Food Technologists, and International Life Sciences Institute.

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