

COMMENTARY

Lack of evidence for high fructose corn syrup as the cause of the obesity epidemic

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High fructose corn syrup (HFCS) is one of the most misunderstood food ingredients. HFCS was developed in the mid-1960s as an alternative to sucrose and because of its physical and functional properties, was widely embraced by the food industry. The use of HFCS grew rapidly from 1970–1999, principally as a replacement for sucrose. HFCS usage in the United States peaked in 1999 and it has been in decline since that time. At its peak, HFCS was still less consumed in the United States than was sucrose, although sucrose did have a significant decline in usage during the time that HFCS usage increased. Worldwide, sucrose is still the dominant sweetener with over nine times as much consumption as HFCS.

HFCS existed as a benign and essentially non-controversial product for over 35 years until 2004 when Bray, Nielsen and Popkin published a commentary suggesting a potential link between HFCS consumption and obesity.¹ These authors buttressed their argument by charting the consumption of high fructose corn syrup along with the prevalence of obesity in the United States between 1970–2000, as illustrated in Figure 1.

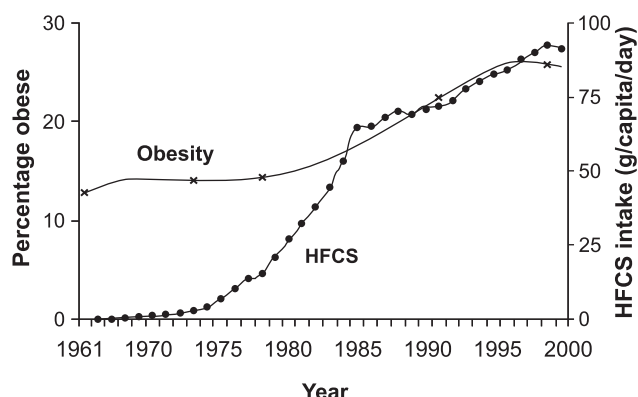


Figure 1. Adapted from: Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *Am J Clin Nutr* 2004; **79**: 537–543.

Bray *et al.*¹ based their hypothesis of a potential unique role for HFCS in beverages as a contributor to the epidemic of obesity in the United States on the following arguments:

- Obesity rates rose dramatically in the United States between 1970 and 2000.
- During the time period between 1970 and 1990, consumption of HFCS rose 1000%, far exceeding the percentage increase of any other food product.
- The digestion absorption and metabolism of fructose is different than glucose.
- Hepatic metabolism of fructose favors *de novo* lipogenesis.
- Fructose consumption results in less rise in blood glucose than does glucose, thus stimulating less of an increase in insulin, which, in turn, stimulates less of a rise in leptin and less suppression of ghrelin—all of which could contribute to lower satiety from fructose and spur increased caloric consumption, weight gain, and obesity.
- There was a temporal association of the increase of HFCS particularly in beverages and the dramatic increase in prevalence of obesity in the United States.

Bray *et al.*¹ used the temporal association as their primary evidence even though this is an example of an ecologic fallacy in which group data are extrapolated to individuals. Controversy and debate about high fructose corn syrup skyrocketed after their initial article often without the initial caution displayed by Bray *et al.* and often based on misperceptions about the metabolism and health effects of HFCS. This concern was also fueled by experiments performed with large doses of pure fructose compared to pure glucose (neither of which is commonly consumed in the human diet in isolation).^{2,3} Furthermore, this article was published at a time of increased media concern and public alarm about the growing problem of both childhood and adult obesity in the United States. Additional confusion undoubtedly arose from the name 'high fructose' corn syrup which suggested that it contained higher levels of fructose than does sucrose, which is not true.

To many researchers, the argument that there was some aspect of HFCS, which uniquely contributed to obesity, did not appear to make sense. Furthermore, since fructose and glucose are almost never consumed in isolation in the human diet, research studies or arguments related to the metabolism of fructose vs glucose were not persuasive with regard to their relevance to human nutrition.

Sucrose and HFCS are very similar in their composition. Sucrose contains 50% fructose and 50% glucose. There are two major forms of HFCS in common usage within the food industry. HFCS-55 contains 55% fructose, 42% glucose and 3% other

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carbohydrates which are readily hydrolysable polymers of glucose. HFCS-55 is the form of HFCS commonly used in soft drinks and other sugar sweetened beverages in the United States. HFCS-42 contains 42% fructose and 53% glucose as well as 5% polymers which are hydrolysable to glucose.⁴ This is the common form of fructose used in solid foods and other applications.

Moreover, sucrose and HFCS are absorbed identically in the human GI tract. HFCS consists of free fructose and free glucose when consumed. Sucrose contains a covalent bond between fructose and glucose which is hydrolyzed by enzymes in the brush border of the GI tract. Thus it is also absorbed as free fructose and free glucose.⁵ It is worth pointing out that slightly acidic environments (such as found in carbonated soft drinks) enhance the hydrolysis of sucrose into free fructose and free glucose as does any degree of warmth such as the storage of such carbonated soft drinks at room temperature. Thus, in a major source of sucrose consumption in the human diet, most of the sucrose may have already been hydrolyzed to free fructose and free glucose. Finally, HFCS and sucrose have the same sweetness and the same calories.

In the past decade, a number of research trials have demonstrated no short-term differences between HFCS and sucrose in any metabolic parameter or health related effect measured in human beings including blood glucose, insulin, leptin, ghrelin and appetite.^{6–8} This includes work in both lean and obese individuals and both men and women. Both the American Medical Association⁹ and the Academy of Nutrition and Dietetics¹⁰ have concluded that HFCS is not a unique cause of obesity.

In addition to the data from randomized controlled trials cited above, there are a number of other factors which further diminish the likelihood that HFCS is a unique cause of the obesity epidemic. For example, the consumption of HFCS has declined for the past ten years despite obesity levels staying constant or rising in most groups in many countries.¹¹ Furthermore, as already indicated, sucrose is the leading source of fructose in the American diet, not HFCS. Finally, there are epidemics of obesity and diabetes in areas where there is little or no HFCS available such as Mexico, Australia, and Europe.

Perhaps G Harvey Anderson summarized the prevailing scientific consensus related to the postulated link between HFCS and obesity best when he wrote:

'The hypothesis that the replacement of sucrose with HFCS in beverages plays a causative role in obesity is not supported on the basis of its composition, biological actions or short-term effects on food intake. Had the hypothesis been phrased in the converse, namely that replacing HFCS with sucrose in beverages would be a solution to the obesity epidemic, its merit would have been seen more clearly. Put simply, a proposal that a return to sucrose containing beverages would be a credible solution to the obesity epidemic, would have been met with out right dismissal.'¹²

While the scientific debate is largely over, the public debate related to HFCS and obesity has, by no means, concluded. There are literally thousands of postings on the internet related to putative links between HFCS and obesity as well as a variety of other metabolic abnormalities. Moreover, a number of manufacturers have yielded to adverse publicity and removed HFCS from their products and replaced it with sucrose despite overwhelming scientific evidence that the two sugars are metabolically equivalent. These sequelae of the initial scientific debate, which persist long after the scientific debate is over, remind us that issues that are important to the public may persist and be misinterpreted long after scientific debate has been concluded.

While the scientific debate related to the initially proposed link between HFCS and the obesity epidemic has been largely settled, a new theory has emerged which argues that while HFCS and sucrose are metabolically equivalent, both are significantly related

to the obesity epidemic and associated metabolic abnormalities.¹³ This argument is based on the belief that the fructose moiety of both HFCS and sucrose causes metabolic derangement.

Once again, this argument is based largely on theoretical constructs, epidemiologic studies, and animal research, often where fructose, glucose, HFCS, or sucrose is fed in very large doses as the sole carbohydrate. It has been further argued that since the largest source of either sucrose or HFCS in the human diet is sugar sweetened beverages (SSBs) and that since consumption of these beverages may result in less satiety than solid foods, a potential linkage between HFCS or sucrose overconsumption and obesity could exist.

While it is beyond the scope of the current commentary to discuss whether or not SSBs are a significant cause of obesity, it is worth noting that the epidemiologic literature in this area is mixed. Meta-analyses of normal consumption levels of fructose have yielded mixed results related to obesity. Randomized controlled trials at levels even exceeding normal human consumption have also been inconclusive related to SSBs and obesity. Nonetheless, there have even been calls to restrict or heavily tax SSBs as a means of reducing their consumption. These debates rage on, even though it is clear that public policy in such an important area should not be made in the absence of higher levels of proof than are currently available.

This debate is by no means settled. More and longer randomized controlled trials are clearly needed to establish an appropriate knowledge base related to sugar sweetened beverage consumption and its alleged link to obesity. Yet the debate has already begun to resemble the now disproven HFCS/obesity hypothesis. Even at this early stage in this emerging debate related to SSBs and obesity, it is worth remembering the words of the American philosopher George Santayana which were frequently quoted by former President John Kennedy when he said 'Those who cannot remember the past, are condemned to repeat it.'¹⁴

CONFLICT OF INTEREST

Dr Rippe and Rippe Lifestyle Institute received research grants and consulting fees from a variety of companies and organizations. Including ConAgra, Kraft Foods, PepsiCo, Weight Watchers and the Corn Refiners Association. Dr Foreyt is a member of the scientific advisory panel of the corn refiners association.

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