Metabolic danger of high-fructose corn syrup

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Article Type: Clinical report
Geographic Code: 1USA
Date: Dec 1, 2008
Words: 6251
Publication: Life Extension
ISSN: 1524-198X

Americans are being poisoned by a common additive present in a wide array of processed foods like soft drinks and salad dressings, commercially made cakes and cookies, and breakfast cereals and brand-name breads.

This commonplace additive silently increases our risk of obesity, diabetes, hypertension, and atherosclerosis.

The name of this toxic additive is high-fructose corn syrup. It is so ubiquitous in processed foods and so over-consumed by the average American that many experts believe our nation faces the prospect of an epidemic of metabolic disease in the future, related in significant degree to excessive consumption of high-fructose corn syrup.

The food industry has long known that "a spoonful of sugar helps the medicine go down in the most delightful way." And cane sugar had been America's most delightful sweetener of choice, that is, until the 1970s, when the much less expensive corn-derived sweeteners like maltodextrin and high-fructose corn syrup were developed. While regular table sugar (sucrose) is 50% fructose and 50% glucose, high-fructose corn syrup can contain up to 80% fructose and 20% glucose, almost twice the fructose of common table sugar. Both table sugar and high-fructose sweetener contain four calories per gram, so calories alone are not the key problem with high-fructose corn syrup. Rather, metabolism of excess amounts of fructose is the major concern.

The alarming rise in diseases (1,2) related to poor lifestyle habits has been mirrored by an equally dramatic increase in fructose consumption, particularly in the form of the corn-derived sweetener, high-fructose corn syrup. (3-12) In this article, we'll examine the evidence for these associations, and we'll attempt to determine if high-fructose corn syrup is a benign food additive, as the sweetener industry has lobbied us (and the FDA) to believe, or a dangerously overlooked threat to public health.

RISING CONCERN

While cardiovascular disease remains the number one killer in America, (1) scientists have noted that "we are experiencing an epidemic of [heart and kidney] disease characterized by increasing rates of obesity, hypertension, the metabolic syndrome, type 2 diabetes, and kidney disease." (2) Add to this list a disturbing rise in new cases of non-alcoholic fatty liver disease, and you have a public health crisis of enormous proportions.

With a growing sense of urgency, scientists are examining the relationship between consumption of high-fructose corn syrup (HFCS) and numerous adverse medical conditions. And they're coming away with a sour taste in the mouth. Emerging research shows that excessive dietary fructose,
largely from consumption of HFCS, represents "an important, but not well-appreciated dietary change," which has "...rapidly become an important causative factor in the development of the metabolic syndrome," (9) a conglomeration of risk factors that greatly elevates the risk of cardiovascular disease and diabetes. Other research suggests that high dietary fructose consumption contributes to obesity and insulin resistance, (5,7) encourages kidney stone formation, (13) promotes gout, (14-17) and is contributing to an upsurge in cases of non-alcoholic fatty liver disease. (4,18,19) Furthermore, high dietary fructose consumption is associated with increased production of advanced glycation end products (AGEs), which are linked with the complications of diabetes and with the aging process itself. (2,5,7)

STEALTHY INSERTION INTO THE FOOD CHAIN

With little fanfare, and even less scrutiny, HFCS was introduced into the food supply decades ago. It is now commonly found in an astounding array of popular food and beverage products. Sweetened, carbonated soft drinks are considered by many to be the worst offenders. (4,7) Food manufacturers embraced HFCS wholeheartedly because it is substantially cheaper than sucrose (table sugar) and mixes well with a variety of products, including beverages, baked goods, jams and jellies, candies, and dairy products. In fact, between 1970 and 1990, the annual intake of HFCS increased by more than 1,000%, greatly exceeding the change in intake of any other food or food group. High-fructose corn syrup is now the primary caloric sweetener added to soft drinks in the United States, and comprises more than 40% of caloric sweeteners added to foods and beverages. (20,21) change in intake of any other food or food group. High-fructose corn syrup is now the primary caloric sweetener added to soft drinks in the United States, and comprises more than 40% of caloric sweeteners added to foods and beverages. (20,21)

While it is derived from a natural source, HFCS is essentially an unnatural product, in the sense that for most of human history we consumed no more than about 15 grams of fructose per day (approximately one-half ounce), mostly from fruits and vegetables.

In contrast, daily consumption in 1997 was estimated to have increased to 81 grams (nearly three ounces) per day. (7) For the first time in history, humans are consuming fructose at extraordinarily high levels.

THE DANGERS OF FRUCTOSE

High dietary intake of fructose is problematic because fructose is metabolized differently from glucose. Like fructose, glucose is a simple sugar. Derived from the breakdown of carbohydrates, glucose is a primary source of ready energy. Sucrose (table sugar) comprises one molecule of glucose and one molecule of fructose. Thus, excessive sucrose intake also contributes to the rise in overall daily fructose consumption. Glucose can be metabolized and converted to ATP, which is readily "burned" for energy by the cells' mitochondria. Alternatively, glucose can be stored in the liver as a carbohydrate for later conversion to energy. Fructose, on the other hand, is more rapidly metabolized in the liver, flooding metabolic pathways and leading to increased triglyceride synthesis and fat storage in the liver. This can cause a rise in serum triglycerides, promoting an atherogenic lipid profile and elevating cardiovascular risk. Increased fat storage in the liver may lead to an increased incidence in non-alcoholic fatty liver disease, and this is one of several links between HFCS consumption and obesity as well as the metabolic syndrome. (7)

Fructose may have less impact on appetite than glucose, so processed foods rich in fructose can contribute to weight gain, obesity, and its related consequences by failing to manage appetite. (20) Additionally, loading of the liver with large amounts of fructose leads to increased uric acid formation, which may contribute to gout in susceptible individuals. (7)

WHAT YOU NEED TO KNOW: HEALTH-DAMAGING EFFECTS OF EXCESS DIETARY FRUCTOSE
* Dietary intake of fructose, particularly in the form of high-fructose corn syrup (HFCS), has dramatically increased in the US in recent decades. Increased HFCS consumption has paralleled increasing rates of obesity, metabolic syndrome, and other conditions associated with poor lifestyle habits.

* High-fructose corn syrup is found in sweetened carbonated soft drinks as well as in many packaged foods such as cakes, cookies, jams, jellies, and crackers.

* Excess fructose intake has been associated with adverse health effects such as metabolic syndrome, elevated triglyceride levels, hypertension, non-alcoholic fatty liver disease, excess uric acid levels (associated with gout), and elevated levels of advanced glycation end products (AGEs; linked with aging and complications of diabetes).

* Minimizing intake of dietary fructose is essential to mitigating its potentially dangerous effects. Sources of dietary fructose include HFCS, fruit juices, honey, and table sugar (sucrose; comprising fructose and glucose).

* Targeted nutritional strategies can help avert some of the damaging effects of excess fructose intake. Beneficial nutrients include benfotiamine, alpha-lipoic acid, carnosine, pyridoxamine, acetyl-L-carnitine, vitamin C, and fish oil.

FRUCTOSE LINKED WITH INSULIN RESISTANCE AND DIABETES

The high flux of fructose to the liver, the main organ capable of metabolizing this simple carbohydrate, disturbs glucose metabolism and uptake pathways and leads to metabolic disturbances that underlie the induction of insulin resistance, (9) a hallmark of type 2 diabetes. In fact, the effect of HFCS on insulin resistance has been shown to have an impact on the prevalence of diabetes. In 2004, investigators conducted an ecological correlation study, in which they compared the relationship between food consumption of refined carbohydrates and the prevalence of type 2 diabetes in the US from 1909 to 1997. They found that during this period, the use of corn syrup sweeteners, which were almost non-existent at the turn of the century, increased by more than 2,100%. During the same period, the prevalence of diabetes skyrocketed. After controlling for total energy intake from other foods such as fats and proteins, only the increase in corn syrup and a decrease in fiber intake correlated positively with the prevalence of type 2 diabetes (22).

Scientists have therefore come to realize that all sugars are not created equal, which has been borne out in a number of studies. In one study, investigators looked at whether reduction in insulin sensitivity was caused by glucose or fructose components of the diet. They took two groups of young healthy men and fed one group a high-glucose diet, while the other received a diet high in fructose. At the end of one week, high-fructose feeding was accompanied by a significant reduction in insulin sensitivity and insulin binding, whereas no significant changes were seen in the high-glucose group. (23)

Another study found that diets containing a moderate amount of fructose produced undesirable changes in glucose metabolism in both normal and hyper-insulinemic men. (24)

STRATEGIES TO PREVENT OR MINIMIZE DANGERS OF EXCESS DIETARY FRUCTOSE
Today, high-fructose corn syrup (HFCS) has become nearly ubiquitous in the food supply. The sticky stuff features prominently in everything from packaged cereals and convenience drinks to ketchup and baked goods. Sugary soft drinks are thought to be the single largest source of this fructose-rich sweetener. The best way to avoid the dangers of excess dietary fructose is to avoid foods with added sugars as well as processed or prepackaged foods and undiluted fruit juices. Instead, focus on a heart-healthy diet—such as the Mediterranean diet, which emphasizes whole grains, fresh vegetables, low-fat dairy, fresh fish, and limited meat.

Other tips to protect yourself against the danger of excess fructose include:

* Avoid all sweetened soft drinks. Consider switching to an alternative, such as sparkling water, herbal tea, or green tea (stick to home-brewed teas, since most commercially available bottled tea is brimming with HFCS).

* Read product labels carefully. Avoid any products containing "high-fructose corn syrup" or fructose. Fruit juices—even unsweetened juices—contain fructose and should not be consumed in excess. Fruit juice diluted with sparkling water is delicious and contains less fructose than undiluted juice.

* Find ways to cut your overall intake of table sugar. Sucrose consists of one molecule of glucose and one of fructose. Thus, sucrose consumption can contribute to unnaturally high fructose levels. (7) Furthermore, research suggests that sucrose may have similar adverse metabolic effects as fructose, thus contributing to obesity and metabolic syndrome. (49)

* Try using the natural non-caloric sweetener stevia extract in your coffee, tea, or homemade desserts.

* Consider writing a letter to the manufacturers of your favorite products; ask them to market alternatives to HFCS-sweetened products. If enough people vote with their pocketbooks, manufacturers may eventually respond with more healthful products.

* Consider taking supplements that may prevent or ameliorate the damage associated with elevated blood sugar.

FRUCTOSE-INDUCED HYPERTENSION

Very few people realize that excess fructose intake may contribute to hypertension. (25) High blood pressure is a well-known comorbidity associated with obesity, hyperinsulinemia, and hyperlipidemia. (12) Hypertension is part of a cluster of dangerous disorders called the metabolic syndrome, which is characterized by insulin resistance and is a key factor in the development of many vascular diseases.

Excess fructose contributes to hypertension by inhibiting a key enzyme called endothelial nitric oxide synthase, (26) which is located in blood vessels walls and is essential for the production of the vasodilator, nitric oxide. By allowing healthy blood vessels to relax and ensuring smooth blood flow in vessels, nitric oxide is absolutely necessary for preventing hypertension, coronary artery disease, and erectile dysfunction. (26) which is located in blood vessels walls and is essential for the production of the vasodilator, nitric oxide. By allowing healthy blood vessels to relax and ensuring smooth blood flow in vessels, nitric oxide is absolutely necessary for preventing hypertension, coronary artery disease, and erectile dysfunction.

ATHEROGENIC LIPID PROFILES AND CORONARY ARTERY DISEASE

Unlike glucose, fructose is readily converted to fat by the liver, leading to an excessive concentration of fats and lipoproteins in the body. (9) High and prolonged fructose ingestion increases unfavorable lipid profiles in the body. By increasing triglyceride levels (12,27)—an independent risk factor for coronary heart disease—fructose promotes potentially dangerous lipoprotein changes that increase atherogenic risk. For example, fructose increases apoB100—
primary lipoprotein responsible for carrying cholesterol to the tissues—which leads to the formation of fatty deposits. Conversely, high-density lipoprotein (HDL), which is responsible for carrying cholesterol particles back to the liver to be eliminated, is decreased by fructose. (28) Fructose ingestion therefore contributes to fat deposits in the liver (fatty liver) (7) and increases the amount of dangerous lipoproteins that enhance cholesterol deposits in blood vessels walls. (29) This can lead to plaque buildup and narrowing of the blood vessels—a ticking time bomb for the development of both stroke and heart attack.

POTENTIAL CONSEQUENCES OF EXCESS DIETARY FRUCTOSE CONSUMPTION

* Accelerated aging
* Insulin resistance
* Type 2 diabetes
* Diabetic complications
  --Retinopathy (may lead to blindness)
  --Nephropathy (may lead to severe kidney disease, requiring chronic dialysis)
  --Neuropathy (may involve numbness, pain, impotence, speech impairment, loss of bladder control, etc.)
* Non-alcoholic fatty liver disease
* Abnormally high blood uric acid levels (hyperuricemia; may result in the development of gout; implicated in the development of diabetes and the metabolic syndrome)
* Abnormally high triglyceride levels (hypertriglyceridemia; implicated in the development of atherosclerosis and cardiovascular disease).5,7,15

NON-ALCOHOLIC FATTY LIVER DISEASE

Once a relatively rare clinical oddity, non-alcoholic fatty liver disease is now estimated to affect 20-30% of adult populations in developed countries. (19) Like obesity and diabetes, the rise in non-alcoholic fatty liver disease cases has paralleled the rise in consumption of dietary fructose. (4) For example, a recent study by scientists at the University of Florida, Gainesville, determined that fructose consumption in patients with established non-alcoholic fatty liver disease was about two to three-fold higher than among normal control subjects. (4)

As its name suggests, non-alcoholic fatty liver disease is a constellation of conditions affecting the liver, characterized by excessive accumulation of fat in the organ, and unrelated to alcoholism. It is associated with higher rates of death from liver diseases, such as cirrhosis and liver cancer, and with cardiovascular disease. (30-32) It is intimately linked to insulin resistance and the metabolic syndrome, and often progresses to an inflammatory condition known as non-alcoholic steatohepatitis. (33) 30-32 It is intimately linked to insulin resistance and the metabolic syndrome, and often progresses to an inflammatory condition known as non-alcoholic steatohepatitis. (33)

THE AGE CONNECTION

The adverse effects of excess dietary fructose are not limited to detrimental effects on blood sugar metabolism, lipid profiles, or liver health. Excess fructose also encourages the formation of toxic advanced glycation end products (AGEs). These are aberrant hybrid proteins, formed when sugars and lipids react with these molecules, altering their structures and damaging their functionality. As AGEs accumulate they encourage inflammation and oxidative stress. They have also been linked to accelerated aging. Advanced glycation end products are believed to play a key role in the development of hypertension as well as complications associated with type 2 diabetes like neuropathy and retinopathy. (5,7,34-37) Neuropathy afflicts the nerves and can cause tingling,
prickling sensations, numbness, and pain, while retinopathy damages the eye's retina and may lead to blindness.

In terms of the reactions that lead to the development of AGEs, fructose is far more reactive than glucose, so even a small amount of fructose circulating in the bloodstream is potentially damaging. In the laboratory, it has been shown that the rate of fructose/protein cross-linking is 10 times greater than the linkage rate associated with glucose. (38) This suggests that excess dietary fructose is intimately linked to accelerated aging, as this type of protein cross-linking is a common manifestation of aging. (7,39-41)

These aging-accelerating effects of dietary sugars were investigated in lab rats fed diets featuring sucrose, glucose, or fructose. Three measures of aging, including the cross-linking of collagen (a protein that provides structure and support for the skin and other tissues), were each significantly greater in rats that were fed fructose than rats that consumed glucose or sucrose. "The data suggest that long-term fructose consumption induces adverse effects on aging," concluded researchers. (42)

Advanced glycation end products are also known to induce acute endothelial dysfunction. (43) Endothelial dysfunction is implicated in the development of atherosclerosis, and thus cardiovascular disease. (44) Scientists also believe that AGEs may contribute to the development and progression of chronic heart failure by inducing vascular and myocardial stiffening. (45)

SUPPLEMENTS THAT MAY PROTECT AGAINST FRUCTOSE-INDUCED DAMAGE

Excessive intake of dietary fructose from sources such as high-fructose corn syrup (HFCS) may contribute to myriad adverse health effects ranging from metabolic syndrome to kidney stones to the complications of diabetes. In addition to limiting exposure to dietary fructose, nutritional supplements may offer important protection against these harmful effects.

PROTECT AGAINST ADVANCED GLYICATION END PRODUCTS.

Fructose promotes the formation of advanced glycation end products (AGEs), which are clearly linked to some of the worst side effects of diabetes. (5,50) Advanced glycation end products are also linked to accelerated aging, even among the healthy. (7,39,40)

* Benfotiamine: This highly bioavailable vitamin B1 analog has been shown to prevent some of the damage associated with diabetes-related high blood sugar levels. Benfotiamine blocks three of the "major molecular pathways" by which hyperglycemia damages cells. (51) A recent study of patients with type 1 diabetes confirmed that benfotiamine, in combination with supplemental alpha-lipoic acid, "... completely normalized increased AGE formation ..." associated with diabetic complications. Benfotiamine also corrected endothelial cell deficits associated with high blood glucose levels. (52) Benfotiamine similarly shows promise against the adverse effects of type 2 diabetes. (5)

* Benfotiamine also acts as an antioxidant. According to new research published by German scientists, "benfotiamine shows a direct antioxidant action. This effect of benfotiamine may be involved in the improvement of diabetic late complications, including peripheral neuropathy." (54)

* Alpha-lipoic acid: Recommended to prevent glycation and reduce the accumulation of AGEs as well as enhance glucose utilization. (55) Alpha-lipoic acid may decrease the development or improve the symptoms of neuropathy in diabetic patients. (56) Alpha-lipoic acid offers powerful antioxidant effects in both aqueous and lipid environments. Only lipid-soluble antioxidants readily enter cells' organelles to prevent damage from free radicals. Alpha-lipoic acid is a mitochondrial metabolite; it is particularly effective at protecting these vulnerable cellular "powerhouses" from oxidative damage. (57-61)

* Carnosine: This dipeptide acts as an anti-glycating agent that inhibits AGE formation as well as protein glycation, oxidation, and cross-linking associated with aging and its associated pathologies.
Animal studies suggest that carnosine suppresses the complications of diabetes. (62-65) Late research suggests that carnosine may prevent diabetes associated atherosclerosis. (66)

* Pyridoxamine: Harvard-based researchers recently showed that pyridoxamine, an advanced formulation of vitamin B6, acts as a "broad inhibitor" of advanced glycation to benefit patients with diabetic nephropathy (kidney disease). (67,68) Fight the Metabolic Syndrome. Excessive fructose intake is intimately linked with metabolic syndrome and its components such as elevated triglycerides, high blood pressure, and increased cardiovascular risk.

* Supplement regularly with omega-3 fatty acids (fish oil). Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are omega-3 fatty acids, found primarily in fish oil, which have been shown to decrease inflammation, improve the lipid profile, reduce insulin resistance, and improve cardiovascular health. (69-73)

* Alpha-lipoic acid: Ameliorates several components of the metabolic syndrome in animal studies, including insulin resistance, atherogenic lipid profiles, and high blood pressure. (74)

* Acetyl-L-carnitine: In combination with alpha-lipoic acid (also a mitochondrial antioxidant), acetyl-L-carnitine has been shown to improve blood pressure in patients with coronary artery disease. (75)

REDUCE THE RISK OF ELEVATED URIC ACID BLOOD LEVEL.

High dietary intake of fructose--particularly in the form of HFCS--is associated with elevated blood levels of uric acid, which are linked with gout.

* Supplemental vitamin C: A recent study of more than 1,300 men showed that a greater intake of vitamin C decreases the risk of abnormally high blood levels of uric acid (hyperuricemia). (76) Hyperuricemia is strongly linked to the risk of developing gout. Intakes of 500 mg vitamin C per day or more were associated with correspondingly low levels of uric acid in the bloodstream. (76)

URIC ACID ELEVATION, GOUT, AND KIDNEY STONES

A recent study by Canadian researchers clearly shows that drinking high-fructose sugar-sweetened beverages is associated with elevated blood levels of uric acid. Known as hyperuricemia, this condition is incontrovertibly linked to elevated risk of suffering from the painful joint disease, gout. Researchers drew their conclusions based on data gathered from nearly 15,000 adult Americans who participated in the Third National Health and Nutrition Examination Survey (1988-1994). "Serum uric acid levels increased with increasing sugar-sweetened soft drink intake," wrote the scientists. Tellingly, drinking diet soft drinks, which do not contain HFCS, was not associated with elevated uric acid levels. (15)

"Fructose-induced hyperuricemia might have a causal role in metabolic syndrome, hypertension, and other chronic disease," noted Harvard-based scientists in 2007. (46) In 2008, Canadian researchers narrowed the focus of their previous inquiries, examining the relationship between soft drinks, fructose consumption, and the risk of gout in men. In this study, more than 46,000 men with no history of gout were followed for a dozen years. Writing in the influential British Medical Journal, they concluded: "Prospective data suggest that consumption of sugar-sweetened soft drinks and fructose is strongly associated with an increased risk of gout in men." (17)

In a recent study, researchers at Harvard Medical School analyzed data gathered from literally hundreds of thousands of subjects, comparing fructose intake with risk of developing kidney stones. While "non-fructose carbohydrates" were not associated with increased risk, the relative risks of kidney stones "significantly increased" for subjects with the highest intake of dietary fructose, compared with subjects who had the lowest intake. It should be noted that sucrose (table sugar) acts as a source of dietary fructose, as it comprises fructose and glucose. "Our study suggests that fructose intake is independently associated with an increased risk of incident kidney stones,"
researchers concluded. (13) This information is so new few scientists have had time to even attempt to replicate it. But the enormous sample size of the study, and the prestige of its authors, lends credence to the results.

Abnormally elevated levels of blood uric acid have been cited as one potential mechanism by which HFCS precipitates the undesirable metabolic changes leading to conditions such as the metabolic syndrome. (47,48) It is likely that this fructose-driven increase in serum uric acid also plays a role in the increased risk of kidney stones. The ability of fructose to induce an increase in uric acid may be a major mechanism by which fructose can cause cardiorenal (heart and kidney) disease.

CONCLUSION

High-fructose corn syrup (HFCS) quietly and grimly entered the food supply decades ago. Today HFCS is ubiquitous in a wide variety of foods, including pasta sauces and salad dressings. High-fructose corn syrup has been linked to an increased risk of a broad range of metabolic diseases and conditions. Fructose is preferentially stored in the liver as fat, and is associated with abnormal spikes in blood levels of uric acid.

High levels of fructose consumption are also associated with the development of AGEs, which, in turn, are linked to accelerated aging and some of the worst side effects associated with type 2 diabetes. Despite assurances of safety by the corn sweetener industry, prudent health-conscious consumers would do well to decrease their intake of sweeteners containing HFCS. The nutritional content of HFCS offers "empty calories"—calorie-dense, with no micronutrient (e.g. vitamins, minerals, phytonutrients) value. Because sucrose (table sugar) is half fructose, intake of this sweetener should also be limited whenever possible. The best way to reduce your intake of high-fructose corn syrup (HFCS) is to read the label of food products before you purchase them. One can slash their dietary intake of HFCS by avoiding foods that contain it and other added sugars such as sucrose. Dana Flavin, MS, MD, PhD is former science assistant to the associate bureau director for toxicology at the FDA. If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370

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