

## Fructose: Pure, White, and Deadly? Fructose, by Any Other Name, Is a Health Hazard

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### Abstract

The worldwide consumption of sucrose, and thus fructose, has risen logarithmically since 1800. Many concerns about the health hazards of calorie-sweetened beverages, including soft drinks and fruit drinks and the fructose they provide, have been voiced over the past 10 years. These concerns are related to higher energy intake, risk of obesity, risk of diabetes, risk of cardiovascular disease, risk of gout in men, and risk of metabolic syndrome. Fructose appears to be responsible for most of the metabolic risks, including high production of lipids, increased thermogenesis, and higher blood pressure associated with sugar or high fructose corn syrup. Some claim that sugar is natural, but natural does not assure safety.

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### Introduction

**P**ure, White and Deadly is the title of a book by Professor Yudkin that describes his view of the dangers of sugar consumption, which has risen exponentially in industrialized countries for the past 200 years (Figure 1).<sup>1</sup> This figure shows the per capita production of sugar (lb/year) using population figures for world population growth since 1800 and for industrialized countries for this same time interval. In Germany, the consumption of sugar rose from 2 kg/person in 1825 to 36 kg/person in 1980.<sup>1</sup> The exposure to fructose, which is half of the sucrose (sugar) molecule, has also risen exponentially in industrialized countries and is now more than 50-fold higher than in 1800! Exposure to fructose was accelerated by the introduction of high fructose corn syrup (HFCS).<sup>2</sup> High fructose corn syrup is made by converting glucose into fructose using enzymes grown in bacteria and then diluting the fructose to provide the commercially

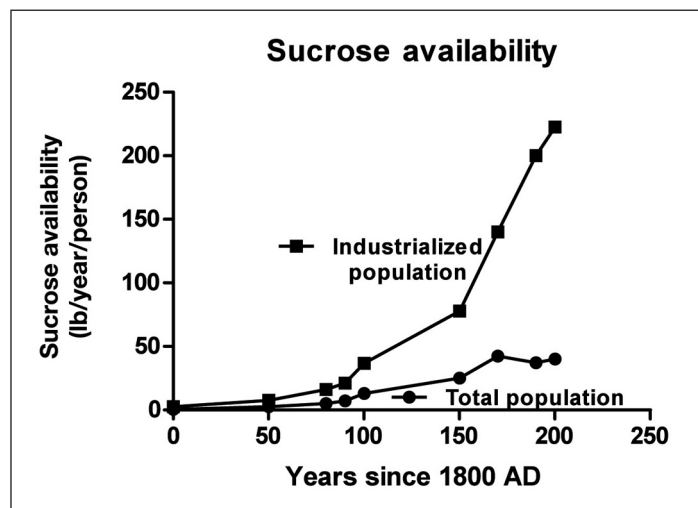


Figure 1. Growth in per capita sugar production since 1800.

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**Abbreviations:** (CI) confidence interval, (HFCS) high fructose corn syrup, (LDL) low density lipoprotein, (RR) relative risk

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available HFCS solutions that have 55% or 42% fructose. Some would argue that sucrose (sugar), as opposed to HFCS, is natural. But natural is no assurance of safety. Morphine, strychnine, and arsenic are all “natural” but not safe.

In this article, I explore the proposition that the large amounts of fructose now consumed from sugar or HFCS are hazardous to our health. Sugar production is big business.<sup>3</sup> Prior to the cultivation of the sugar plant more than 2000 years ago or so, fructose in the diet came largely from whole fruits and vegetables. Now, our major sources of dietary fructose are from sugar (sucrose) or HFCS. Fructose is estimated to provide, on average, 54.7 g/day or 10.2% of our daily energy intake.<sup>3</sup> For many adolescents, fructose intake is 15% or more of their daily energy intake. Beverages provide 29–45% of the average dietary intake of fructose.<sup>4</sup> Fruits and vegetables provide 20–26%, with the remainder coming from sugar or HFCS used in baked goods or other refined products, such as ready-to-eat cereals. To make a distinction between the fructose that comes from fruits and vegetables and the fructose that comes from most other sources, I use the terms “good fructose” and “bad fructose.” The fructose that comes from whole fruits and vegetables, dairy products, and 100% fruit juices is referred to as “good fructose” because it is associated with the vitamins, minerals, and fiber that come with these “natural” products. Biologically, the sweetness of fructose and sucrose found in fruits was a clue that these foods contained other healthful nutrients. Numerous epidemiological studies have provided convincing evidence that higher intakes of fruits and vegetables reduce blood pressure<sup>5,6</sup> and reduce risk of cancer<sup>7</sup> and heart disease.<sup>8</sup> “Bad fructose” refers to the fructose that comes in refined foods and beverages that usually have few nutrients.<sup>9</sup>

Beverages are a major source of our dietary fructose. The amount of calorically sweetened beverages we drink is related to our energy intake, risk of obesity, and risk of cardiometabolic disease. The higher the consumption, the greater the risk. Thus, if fructose poses a health problem, then beverages are a target for change.<sup>9</sup>

Many of the following studies focus on consumption of soft drinks that are sweetened with either sucrose or HFCS, because these are the major commercial caloric sweeteners and also the major sources of fructose in our diet; these studies do not allow us to separate the effects of fructose from glucose. Studies examining sucrose, fructose, and glucose independently and together, however, argue strongly that it is fructose, NOT glucose,

that accounts for the major detrimental effects of soft drinks. Cohen and Schall<sup>10</sup> compared the effect on plasma triglycerides of adding 100 g of sucrose, 50 g of fructose, or 50 g of glucose to a standard meal. They found that the lipemic response to the glucose was not significantly different from the ingestion of fat alone. In contrast, the lipemic response increased after adding either fructose or sucrose, suggesting that it was fructose and not glucose that increased triglyceride levels. In the remaining sections, I will review three groups of studies:

1. The impact of calorically sweetened beverage consumption on energy intake and the risk of developing obesity;
2. The detrimental health consequences of soft drinks;
3. Mechanisms for the effects of fructose.

## The Impact of Calorically Sweetened Beverage Consumption on Energy Intake and the Risk of Developing Obesity

Concerns about the detrimental effects of soft drinks sweetened with sugar or high fructose corn syrup have been on the rise for more than a decade.<sup>2,11,12</sup> In one review of this problem, Malik and colleagues<sup>13</sup> found 30 publications (15 cross-sectional, 10 prospective, and 5 experimental) that met their selection criteria. Findings from large cross-sectional studies, in conjunction with those from well-powered prospective cohort studies with long periods of follow-up, showed a positive association between greater intake of sugar-sweetened soft drinks and weight gain and obesity in both children and adults. Findings from short-term feeding trials in adults also support induction of positive energy balance and weight gain from consuming sugar-sweetened sodas, but these trials are few.

Another meta-analysis by Olsen and Heitmann<sup>14</sup> concluded that consumption of soft drinks was a determinant of obesity. Their analysis included 14 prospective and 5 experimental studies. The majority of the 14 prospective studies found positive associations between intake of calorically sweetened beverages and obesity, and none found that these beverages were beneficial. Three experimental studies found positive effects of calorically sweetened beverages and subsequent changes in body fat, but two experimental studies did not. Eight prospective studies adjusted statistically for energy intake. Seven of these eight studies reported associations that were essentially similar before and after energy adjustment, suggesting that

the caloric sweeteners might offer “additional” effects. The authors concluded that a high intake of calorically sweetened beverages was a determinant of obesity.

## Detrimental Health Consequences of Soft Drinks

Consumption of soft drinks predicts the risk of developing cardiometabolic disease.<sup>15</sup> Malik and associates<sup>15</sup> identified 8 prospective cohort studies evaluating sweetened soft drink consumption and weight gain, and 10 prospective cohort studies evaluating soft drink consumption and the risk of cardiometabolic disease. Six of them related soft drink consumption to the risk of diabetes mellitus,<sup>16–21</sup> 3 to the risk of metabolic syndrome,<sup>21–23</sup> and 1 to the risk of coronary heart disease.<sup>23</sup> The meta-analysis included 294,617 participants, with 10,010 cases of type 2 diabetes, 6,236 cases of metabolic syndrome, and 3,105 cases of coronary heart disease. There was a clear and consistent positive association between consumption of sweetened soft drinks and weight gain, particularly in larger studies with longer durations of follow-up. Individuals in the highest quantile of soft drink intake had a 24% greater risk of cardiometabolic disease than those in the lowest quantile [RR:1.24 (95% CI: 1.12, 1.34)]. This increased to 30% when studies that adjusted for mediating effects of energy intake and BMI were excluded from analysis [RR: 1.31 (95% CI: 1.16, 1.48)]. The authors concluded that higher consumption of calorie-sweetened soft drinks was associated with weight gain and increased risk of cardiometabolic diseases.<sup>15</sup> Fructose intake is also related to the risk of developing gout in men.<sup>24</sup> Fructose intake has also been related to the increased level of small dense LDL-cholesterol (bad cholesterol) in children.<sup>25</sup> Clearly, fructose can be hazardous to the health of some people.

## Potential Mechanisms for the Detrimental Effects of Fructose

At least two main mechanisms<sup>2,12,15</sup> can account for most of the detrimental effects of calorically sweetened beverages and the fructose they provide: (1) failure to suppress intake of other foods to compensate for the calories in soft drinks;<sup>26–28</sup> and (2) differences in the metabolic pathways for fructose and glucose that facilitate conversion of carbon from fructose into the backbone of triglycerides<sup>2,12</sup> and the formation of uric acid during metabolism of fructose.<sup>29,30</sup>

Failure to suppress caloric intake to offset the calories from calorie-sweetened beverages is part of the

mechanism for increased energy intake and the risk for obesity.<sup>26–28</sup> Drinking sugar-sweetened beverages at lunch did not suppress intake of solid food; rather, the calories from beverages added on to total calorie intake.<sup>28</sup> For example, drinking apple juice reduced energy intake less than when the same amount of apple was eaten as applesauce or as pieces of apple.<sup>27</sup>

## Short-term Effects of Fructose on Human Metabolism

Fructose alone is poorly absorbed from the gastrointestinal tract, but when ingested with glucose, its absorption is enhanced.<sup>11,12</sup> Both fructose and glucose enter the portal blood supply and are then transported to the liver. Since the transport system for fructose is absent in most cells, the liver and kidney are the main site for fructose metabolism. Upon entering the liver, glucose is phosphorylated at the 6-position to form glucose-6-phosphate, whereas fructose is phosphorylated at the 1-position by ketohexokinase to form fructose-1-phosphate.<sup>30</sup> The fructose-1-phosphate is readily converted to the backbone of triglyceride, whereas glucose-6-phosphate is not so readily converted to triglyceride because its metabolism is regulated by phosphofructokinase. This probably explains why fructose—but not glucose—stimulates the formation of lipids in the liver and increases circulating levels of triglycerides, particularly at night.<sup>31</sup>

To compare the acute effects of fructose and glucose on plasma lipids, Teff and colleagues<sup>32</sup> gave 17 individuals with obesity meals with beverages containing either fructose or glucose that provided 30% of the total calories. Following fructose, the rise in plasma glucose was significantly smaller than after glucose. Following fructose, triglycerides rose almost 200% higher than after glucose, and lactate production was five times greater. Insulin and leptin both rose less in response to fructose than to glucose. These responses in lipids are seen primarily in men, with smaller or limited responses seen in women.<sup>33,34</sup>

Fructose increases thermogenesis and blood pressure more than glucose,<sup>35,36</sup> but both have this effect. When a 75 g oral load of glucose or fructose was given to 17 volunteers, fructose stimulated oxygen consumption more than glucose but produced a much smaller stimulation of insulin.<sup>35</sup> Fructose increased the respiratory quotient more than glucose, which is consistent with *de novo* lipogenesis. Both patients with obesity and patients with diabetes had a similar stimulation of oxygen uptake after infusion of glucose that was smaller than the response to fructose.<sup>35</sup>

## Effects of Ingesting Fructose Over Several Weeks in Human Subjects

Two carefully conducted 10-week studies compared beverages. In one study, 21 adults received a minimum amount of sugar-containing beverages or sugar-sweetened foods each day for 10 weeks that contributed about 23% to their energy intake (about 2 g sucrose per kg body weight per day).<sup>37</sup> The other 20 received comparable amounts of beverages (80%) or foods (20%) sweetened with aspartame. For their other foods, subjects could select freely from items available at a kiosk run by the study group. After 10 weeks, energy intake had increased by 380 kcal/day (1.6 MJ/day) and sucrose to 28% of calorie intake in the group receiving the sugar-containing beverages. Protein and fat intakes declined.<sup>37</sup> Body weight and fat mass increased by 1.6 and 1.3 kg respectively in the sugared-beverage group and decreased by 1.0 and 0.3 kg in the aspartame-sweetened group. Blood pressure increased by 3.8/4.1 mm Hg in the sugared-beverage consuming group but did not change in the other group, mimicking the acute response of blood pressure to fructose.<sup>36</sup> Concentrations of several inflammatory markers were also changed. In the group consuming sucrose, haptoglobin increased by 13%, transferrin by 5%, and C-reactive protein by 6%, whereas in the group receiving the aspartame-sweetened beverages, haptoglobin decreased by 16%, C-reactive protein decreased by 26% and transferrin was basically unchanged with a small 2% fall.<sup>38</sup>

In a second 10-week study, fructose or glucose were provided as 25% solutions as part of the total diet. Stanhope and co-workers<sup>31</sup> found that visceral fat was significantly increased in the group drinking fructose-containing beverages. When 32 men and women ate a diet with 15% protein, 30% fat, and 55% carbohydrate, with either 25% of calories as glucose-sweetened beverages or as fructose-sweetened beverages, visceral fat increased by 14% in the fructose-consuming group compared to about 5% in the control group, with no significant change in body weight or subcutaneous fat. De novo lipogenesis increased and post-prandial triglycerides increased, particularly at night.<sup>31</sup>

## Conclusion

The rising consumption of calorie-sweetened beverages, both soft drinks and fruit drinks, provides a readily identifiable pathway for an increasing amount of energy intake and dietary fructose. Based on this review of the literature, I conclude that in the amounts currently

ingested, fructose is hazardous to the health of some people. The term “good fructose” is used to identify the fructose that comes from fruits and vegetables, and “bad fructose” the fructose that comes from calorie-sweetened beverages and refined products. Is fructose the “pure, white and deadly” that Yudkin had in mind?

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