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Effects of high fructose corn syrup and sucrose on the pharmacokinetics of fructose and acute metabolic and hemodynamic responses in healthy subjects

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Abstract

Objective—It is unclear whether high fructose corn syrup (HFCS), which contains a higher amount of fructose and provides an immediate source of free fructose, induces greater systemic concentrations of fructose as compared to sucrose. It is also unclear whether exposure to higher levels of fructose leads to increased fructose-induced adverse effects. The objective was to prospectively compare the effects of HFCS- versus sucrose-sweetened soft drinks on acute metabolic and hemodynamic effects.

Materials/Methods—Forty men and women consumed 24 oz of HFCS- or sucrose-sweetened beverages in a randomized crossover design study. Blood and urine samples were collected over 6 hr. Blood pressure, heart rate, fructose, and a variety of other metabolic biomarkers were measured.

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Conflict of Interest: RJJ has a patent application on inhibition of fructokinase as a mechanism to treat sugar craving. RJJ also has a lay book, The Sugar Fix: The High-Fructose fallout That Is Making You Fat and Sick (Rodale and Simon and Schuster, 2008). None of the authors declared a conflict of interest.

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Results—Fructose area under the curve and maximum concentration, dose normalized glucose area under the curve and maximum concentration, relative bioavailability of glucose, changes in postprandial concentrations of serum uric acid, and systolic blood pressure maximum levels were higher when HFCS-sweetened beverages were consumed as compared to sucrose-sweetened beverages.

Conclusions—Compared to sucrose, HFCS leads to greater fructose systemic exposure and significantly different acute metabolic effects.

Keywords

soft drinks; sweetened beverages; adverse metabolic effects; carbohydrate metabolism

INTRODUCTION

Over the past four decades, the prevalence of health disorders, including hypertension, obesity, metabolic syndrome, diabetes, and kidney disease, has drastically increased. In the United States, one-third of the population has hypertension, one-third of adults and one-sixth of children are obese, 7% have diabetes, and about 20 million have kidney disease [1–5]. In parallel to the dramatic rise in the prevalence of these cardio-renal diseases, a similar increase in the consumption of fructose has occurred. Recent studies have implicated excessive fructose intake as one of the factors driving the increases in these health disorders [3, 6–8].

Rapidly metabolized by the body, fructose has been shown to cause a variety of metabolic effects, such as lactic acidosis, lipogenesis, hypertriglyceridemia, liver injury, high blood pressure, insulin resistance, and increased weight gain [7, 9–15]. Fructose is also the only natural sugar capable of causing a rise in uric acid levels [16]. Thus, there is a growing concern that fructose may pose a great health risk and several studies have suggested that the excessive consumption of fructose-containing sweeteners, regardless of its composition, may be a contributing factor in the pathogenesis of cardio-renal diseases [6, 12, 13, 17–23].

While fructose is a simple sugar that exists naturally in fruits and vegetables, the majority of dietary fructose comes from two sweeteners, sucrose and high fructose corn syrup (HFCS), which are commonly used in manufactured foods and beverages. Specifically, the increase in fructose consumption is primarily due to the increased use of HFCS in the Western diet. Based upon disappearance data, the annual per capita intake of HFCS from 1967 to 2006 increased from 0.03 lbs to 58.2 lbs, while sucrose decreased from 98.5 lbs to 62.3 lbs [6, 24].

Sucrose is a disaccharide and consists of 50% fructose and 50% glucose. The HFCS grade used in soft drinks consists of 55% fructose, 42% glucose, and 3% oligosaccharides [25]. Because of the higher fructose dose, soft drinks sweetened with HFCS would provide more fructose into the systemic circulation than soft drinks sweetened with sucrose. Furthermore, HFCS provides an immediate source of free fructose and glucose, while sucrose must first be broken down by sucrase. The expression and function of sucrase has been shown to be negatively influenced by such factors as genetic polymorphisms and regulatory inhibition by glucose [26–29].

Due to the potential inefficiency of sucrase, we hypothesized that the amount of fructose available for absorption is reduced, resulting in a lower relative fructose bioavailability from sucrose. Therefore, we speculated that higher fructose systemic concentrations, either through the higher fructose dose or also from increased fructose bioavailability from HFCS, would lead to increased fructose-induced adverse metabolic effects. Thus, the aim of the

present study was to conduct a prospective randomized crossover study comparing the effects of HFCS- versus sucrose-sweetened beverages on the pharmacokinetics of fructose and acute metabolic and hemodynamic changes.

SUBJECTS AND METHODS

Subjects

Sixty-nine healthy subjects, aged 18 years or older, of either gender, and of any ethnicity were recruited to participate in the study through advertisements or from the study participant database. During a screening visit, a participant's eligibility was ascertained through a health information questionnaire and limited laboratory analyses. Specifically, individuals with a history of hypoglycemia, gout, hepatic or renal disease, diabetes mellitus, or who had a fasting blood glucose level ≥ 126 mg/dl or random blood glucose ≥ 200 mg/dl at the screening visit were excluded from the study. Subjects who consumed more than 7 alcoholic drinks per week, who took medication (except for oral contraceptives), who were pregnant or lactating, or who donated blood within 8 weeks prior to the screening visit were also excluded. Blood glucose levels were determined using the OneTouch Ultra Test Strips and OneTouch Ultra 2 Blood Glucose Meter (LifeScan, Inc., Milpitas, CA). The study was approved by the University of Florida IRB and all study participants signed informed, written consent.

Study Design

The study was a prospective, randomized, single-blinded, crossover trial. Acute changes in metabolic and hemodynamic parameters, such as fructose, glucose, and uric acid concentration, were measured in participants over a 6-hr period on 2 separate study visits. Qualified participants were randomized in blocks of four, using Proc Plan in SAS 9.1.3. Subjects were randomized to two different sequences. Subjects randomized to the first sequence received HFCS-sweetened soft drinks at study visit 1 and sucrose-sweetened soft drinks at study visit 2. Subjects randomized to the second sequence received sucrose-sweetened soft drinks at study visit 1 and HFCS-sweetened soft drinks at study visit 2. The two 6-hr study visits were separated by a minimum of 2 days and were conducted at the Clinical Translational Science Institute (CTSI) at the University of Florida, Gainesville, FL. Both the subjects and CTSI nurses were blinded to the sweetener contained in the soft drinks.

Sugar Load from Soft Drinks

As mentioned, the majority of dietary fructose is currently ingested as HFCS and sucrose. Since soft drinks are a major source of added sugar, we elected to treat our participants with a beverage that was manufactured with either HFCS or sucrose [30, 31]. Dr Pepper sweetened with HFCS was purchased locally (Lot# NOV 24 08 12:33 to 12:58RS02218X). Dr Pepper sweetened with cane sugar (sucrose) was purchased from the Dr Pepper Bottling Company (Lot# 800807:11 TBC, http://www.dublindrpepper.com/, Dublin, TX). Except for the sweetener, the compositions of the two Dr Pepper products were similar. Sugar profiles of the two types of Dr Pepper were analyzed before and after the end of the study by Silliker, Inc. (Illinois Laboratory, Chicago Heights, IL). From 24 oz of the soft drinks, the total sugar load from the HFCS-sweetened beverage was 68.0 g and from the sucrose-sweetened beverage was 69.4 g (Table 1). The HFCS-sweetened beverage contained 39.2 g of fructose and 28.8 g of glucose. Meanwhile, the sucrose-sweetened beverage contained 34.6 g of fructose and 34.8 g of glucose. Thus, there were about 5 more grams of fructose in the 24 oz of HFCS-sweetened soft drink, resulting in about a 13% higher dose.

Study Protocol

Subjects were instructed to abstain from consuming alcohol for three days prior to each study visit. Following a minimum of an 8-hr overnight fast and no exercising, the participants reported to the CTSI in the morning. They were then assigned to a hospital room and allowed to rest for 15 min before measurement of blood pressure (BP) and heart rate (HR). Afterwards, an intravenous catheter was inserted by a CTSI nurse. The participants were then randomly challenged with 24 oz of cold, carbonated soft drinks sweetened with either HFCS or sucrose. The soft drinks were poured into 4 cups (~6 oz/cup) and participants were given approximately 5 minutes to consume the sugar load (~75 sec/cup). Subjects were not given any additional caloric intake during the 6-hr study period.

Study Measurements

Body weight and height were measured at each study visit. Body mass index (BMI) was calculated and averaged. BP, HR, and blood samples were obtained at the following time points: 0 min (fasting), 15 min, 30 min, 60 min, 90 min, 2 hr, 3 hr, 4.5 hr, and 6 hr. BP and HR were measured using a Microlife Model #3AC1-AP blood pressure monitor (Microlife USA, Inc., Clearwater, FL), which has been approved by the British Society of Hypertension [32]. Plasma from blood collected in BD Vacutainer® tubes (BD, Franklin Lakes, NJ) containing sodium heparin were used to quantify fructose. Plasma from blood collected in tubes containing sodium fluoride and potassium oxalate were used to measure glucose and lactate. Serum triglycerides, uric acid, creatinine, and insulin were assayed from blood collected in serum separation tubes. Since the study is similar to a 75-g oral glucose tolerance test, which usually lasts for 2 hr, we measured insulin only at 0, 30 60, and 120 min [33]. Samples were immediately centrifuged and separated by CTSI technicians. Urine fructose, uric acid, and creatinine were measured from samples collected prior to treatment and a 6 hr pooled urine collection after the consumption of the soft drinks. All samples were stored at −80°C until analyses.

Laboratory Analysis

Plasma fructose concentrations were measured by an assay developed on liquid chromatography-tandem mass spectrometry (Le MT, Galloway CD, Frye RF. “Simplified method for quantifying fructose in human plasma using liquid chromatography-tandem mass spectrometry.” Unpublished data, 2009.) The fractional excretion of fructose (FE_fructose) was calculated from the following equation:

$$FE\_fructose = \frac{UFr \times SCreat}{SFr \times UCreat},$$

where SCreat was serum creatinine, SFr was serum fructose, UCreat was urine creatinine, and UFr was urine fructose.

Plasma glucose and lactate concentrations were measured by CTSI with the YSI 2300 STAT Plus analyzer (YSI Inc, Yellow Springs, OH). Triglcyerides (Tg), uric acid, and creatinine concentrations were analyzed with the VetACE system (Alfa Wassermann Inc., West Caldwell, NJ). Insulin concentrations were measured with an ELISA immunoassay (ALPCO Diagnostics, Salem, NH). Fractional excretion of uric acid (FEUA) was calculated from the following equation:

$$FEUA = \frac{UUA \times SCreat}{SUA \times UCreat},$$

where SUA was serum uric acid and UUA was urine uric acid [34].

Statistical Analysis

Pharmacokinetic parameters—WinNonlin™ Professional Edition Version 2.1 (Pharsight Corporation, Mountain View, CA) was used to calculate the following pharmacokinetic parameters: area under the curve (AUC) of plasma concentration versus time, maximum observed concentration (Cmax), elimination half-life (HL), mean residence time (MRT), and time of Cmax (Tmax). Due to differences in doses, fructose and glucose AUC/D and Cmax/D were calculated by normalizing by the average doses of the respective sugars from each treatment. Noncompartmental analysis was conducted using linear/log trapezoidal as the calculation method.

Relative fructose bioavailability between sucrose and HFCS was calculated using the following equation (AUC_H = AUC from HFCS, AUC_S = AUC from sucrose, Cl_H= clearance from HFCS, Cl_S = clearance from sucrose, D_H = dose from HFCS, D_S = dose from sucrose, F_H = bioavailability from HFCS, and F_S = bioavailability from sucrose):

$$Relative\ bioavailability = \frac{F_H}{F_S} = \frac{D_S \times AUC_H}{D_H \times AUC_S}$$

Relative glucose bioavailability was also calculated. Paired t-test was used to compare relative bioavailability.

Statistical methods

For 40 completed subjects, the study had at least 80% power at $\alpha = 0.05$ two-sided to detect a paired difference in means of 0.455σ ($\sigma = 1.00$ μmol/L for fructose and $\sigma = 66$ μmol/L for serum uric acid) [35]. Data for non-fasting participants were excluded from analyses for each study visit. Non-fasting state was determined by elevated glucose, insulin, or fructose levels measured at time 0.

Linear mixed effect models for a crossover design were used to compare the effects of HFCS versus sucrose treatments on AUC, Cmax, HL, MRT, and Tmax of the various response parameters [36]. The treatment, sequence, and visit effects were assessed in the models as fixed effects with subjects within sequence as random effect. In addition, fasting values of the metabolic and hemodynamic parameters during study visits 1 and 2 were included in the model as covariates.

Linear mixed effect models were also used to compare the effects of HFCS versus sucrose treatments on the repeated measures data collected over the 6 hr study period of each of the response parameters. Treatment, time, interaction of treatment and time, and sequence were included in the models as fixed effects with fasting values as a covariate and subjects within sequence as random effect. Autoregessive (1) covariance structure was used for the repeated measures over time within each treatment and unstructured covariance structure was used for the repeated measures over two treatments within same subjects. Pre-planned contrasts were utilized to compare between the treatments at each time point. Based on the Shapiro-Wilk test, fructose, glucose, insulin, lactate, triglyceride, FE_fructose, and FEUA were not normally distributed. Analyses for these variables were based on $\log_{10}$ transformed data. Results were reported by back transforming the least square means and 95% confidence interval (CI). Fructose and glucose concentrations were also normalized by their respective doses from each treatment. Dose adjusted concentrations from 15 min to 6 hr time period

were analyzed. All analyses were conducted using SAS 9.2. To adjust for multiple comparisons, statistical significance was defined as $p < 0.005$.

RESULTS

Baseline Characteristics

Fifty-one subjects, from ages 18 to 52, met the inclusion criteria and were randomized to participate in the study (Figure 1). Four subjects were withdrawn for reasons unrelated to the study. An additional seven subjects (3 after consuming HFCS-sweetened soft drinks and 4 from sucrose-sweetened soft drinks) were withdrawn after developing asymptomatic reactive hypoglycemia (mean blood glucose 52.3 ± 4.0 mg/dl) from the sugar load. Hypoglycemia was defined as blood glucose ≤ 60 mg/dl that was confirmed by two separate measurements. Overall, 40 individuals completed both study visits and their baseline characteristics are shown in Table 2.

Effects of HFCS versus Sucrose on Acute Metabolic and Hemodynamic Parameters

Table 3 lists the fasting levels of the various response parameters measured at the two study visits for both of the treatment sequences. The sequence and visit effects were insignificant for all of the response parameters.

Fructose, FE_fructose, and Relative Bioavailabilty of Fructose

Fructose AUC was about 20% greater and Cmax was about 15% greater from the HFCS-sweetened beverages than from the sucrose-sweetened beverages (Table 4). From the repeated measures data, there was also a significant treatment effect of HFCS ($p = 0.0032$) versus sucrose on changes in postprandial fructose concentrations over the 6 hr study period (Figure 2A). Fructose levels were higher from the HFCS treatment at 30 and 90 min.

Although the values were higher from HFCS, treatment effects were no longer significant when normalized for the differences in dose of fructose between HFCS and sucrose (Table 4, Figure 2B). Thus, a gram of fructose from either HFCS or sucrose is absorbed in a similar manner, which is indicated by a lack of difference in relative fructose bioavailability between the two sweeteners (1.07 ± 0.24, $p = 0.1219$). Although there was a greater fractional excretion of fructose from HFCS-sweetened soft drinks, the effect was not significant (Figure 2C).

Glucose

Glucose AUC, Cmax, and changes in postprandial glucose concentrations were very similar between HFCS and sucrose (Table 4, Figure 2D). However, dose normalized glucose AUC and Cmax were significantly higher from the HFCS treatment compared to sucrose. In addition, dose normalized glucose concentrations were higher at all time points (Figure 2E). The relative bioavailability of glucose indicates that a gram of glucose from HFCS reaches the systemic circulation more efficiently than from sucrose (1.20 ± 0.07, $p < 0.0001$).

BP and HR

The observed maximum SBP was significantly different between the two treatments (Table 5). In contrast, DBP did not differ between the treatment groups and neither did heart rate (Table 5).

SUA and FEUA

There were no treatment differences in AUC and Cmax of serum uric acid or fractional excretion of uric acid (Table 6). However, there was a significantly higher effect from HFCS

than from sucrose on postprandial changes in levels of SUA (p = 0.0042, Figure 3A). Although, FEUA was higher at the end of the 6 hr study visit from HFCS, the treatment effect did not meet our definition of statistical significance (p = 0.0254, Figure 3B).

Tg, Insulin, and Lactate

There were no treatment differences in AUC and Cmax of Tg, insulin and lactate (Table 6). There were also no contrast differences in postprandial concentrations at any time points between HFCS versus sucrose for Tg (Figure 3C), insulin (Figure 3D), and lactate (Figure 3E).

DISCUSSION

In this study, we compared the acute metabolic and hemodynamic effects of HFCS and sucrose in 40 healthy subjects. We found treatment differences in fructose, glucose, SUA, and SBP. The following metabolic parameters were higher from the HFCS-sweetened beverages than from the sucrose-sweetened beverages: fructose AUC and Cmax, dose normalized glucose AUC and Cmax, relative bioavailability of glucose, changes in postprandial concentrations of SUA, and observed maximum of SBP. There were no differences in relative fructose bioavailability, FE_fructose, FEUA, DBP, HR, Tg, insulin, and lactate. To our knowledge this is the first study to show HFCS is more likely to cause acute adverse effects than sucrose.

We hypothesized that the formulation of HFCS would result in greater systemic fructose exposure than from sucrose. First, HFCS contains more fructose than sucrose. Second, HFCS consists of free fructose and glucose, thus, allowing for the immediate transport of these simple sugars in the intestine. Meanwhile, sucrose must first be metabolized by sucrase before fructose and glucose are available for uptake. Studies have shown that the expression of sucrase can be negatively affected by genetic polymorphisms [26, 27]. Its activity has also been shown to be inhibited by glucose [28, 29]. Thus, we hypothesize that sucrase may potentially be a bottleneck, preventing complete metabolism of sucrose in the gut. Therefore, less fructose would be available for transport. In our study, we found that fructose AUC was about 20% greater and Cmax was about 15% greater from the HFCS-sweetened beverages than from sucrose-sweetened beverages. However, the relative bioavailability was not different. Thus, the difference in fructose plasma concentrations between the sweeteners is most likely due to the higher fructose dose from HFCS, which was about 13% greater than from sucrose. Interestingly, we also detected a significant difference in dose normalized glucose AUC and Cmax. This was surprising since the glucose dose from sucrose was 6 g or about 21% higher than from HFCS. This finding suggests that glucose is more efficiently absorbed into the body from HFCS than from sucrose. The mechanism for this enhanced bioavailability of glucose needs to be further elucidated.

Our study found a significant increase in SBP, about 3 mmHg, from HFCS compared to sucrose. However, the increase was very acute. The impact of chronic exposure of higher fructose bioavailability on affecting sustained elevated blood pressure needs to be investigated. Nevertheless, our finding potentially supports the postulated link between high fructose intake and increased SBP. Jalal et al recently reported an association between high fructose intake from added sugars and increased risk of elevated SBP in the National Health and Nutrition Examination Survey [8]. In a randomized study consisting of 74 men, Perez-Pozo showed that the ingestion of fructose was associated with an increase in BP [37]. Others have also found a relationship of sugar-sweetened soft drink intake with BP [38, 39], although this was not observed in a study in which much of the fructose intake originated from fruits [40].

Several mechanisms have been proposed for fructose-induced high blood pressure, including fructose-induced hyperuricemia [38]. This is an appealing mechanism since previous studies have shown that fructose can increase uric acid levels [16, 41]. Fructose increases uric acid both by acute effects related to ATP consumption and purine degradation, but also via chronic effects to stimulate uric acid synthesis [16, 41, 42]. Importantly, Feig et al showed that by lowering uric acid levels there was a decrease in BP in hypertensive adolescents with newly diagnosed hypertension [43]. Futhermore, Perez-Pozo et al showed that by lowering uric acid with allopurinol, the effect of fructose (200 g/d for two weeks) on elevated BP was prevented in healthy adults [37]. Finally, an epidemiological study has linked uric acid with soft drink ingestion and hypertension in adolescents [44]. In our study, we detected a treatment difference in SUA levels, which was higher from HFCS than sucrose. Although the difference was small, about 0.2 mg/dL, our findings highlight that SUA levels can increase when fructose levels increase in the body. Thus, our data potentially support the link between higher fructose levels, elevated uric acid levels, and higher SBP levels, although other mechanisms by which fructose could raise blood pressure remains possible [45].

Because of the similarity in composition between HFCS and sucrose, it has been speculated that the metabolic effects of these sweeteners are also similar. Studies directly comparing the effects of HFCS versus sucrose are limited. Nevertheless, Melanson et al, Akhaven et al, Soenen et al, and Stanhope et al conducted short-term studies comparing the two sweeteners. These studies found no significant differences on glucose, ghrelin, leptin, insulin, Tg, uric acid, glucagon-like peptide 1, appetite, and food intake [14, 46–48]. While their findings seemingly conflict with our results, these studies did not assess fructose bioavailability and did not account for fructose levels. If fructose is an important factor driving the development of various adverse metabolic effects, we hypothesizes that higher fructose exposure would lead to greater effects. If in these studies, there were no differences in exposure to fructose between their study groups, it would not be surprising that HFCS and sucrose resulted in similar effects. Importantly, fructose bioavailability can vary greatly due to various factors, such as individual differences in fructose absorption and metabolism, the effects of glucose on impacting fructose uptake, and liquid versus solid versus mixed sources of fructose-containing sweeteners [49–54]. In our study, we were able to detect a higher exposure to fructose from HFCS than from sucrose. Thus, this may explain why we were able to detect a difference in metabolic and hemodynamic effects between the two sweeteners whereas other studies have not.

Our study has several limitations. First, it was determined from the sugar profile analyses that the sucrose in the soft drinks was being hydrolyzed. At the start of the study, about 60% of the sucrose had already been hydrolyzed and by the end of the study, all of the sucrose had been broken down. As a result, the potential important role of sucrase was marginalized and may have reduced our ability to detect a difference in fructose relative bioavailability between HFCS and sucrose, which may have resulted in greater differences in fructose AUC and Cmax. However, the external validity of the study is high since soft drinks are a major source of sucrose and HFCS. For future studies, a more controlled environment can be obtained by having the sugar mixtures made immediately prior to the study visits. Second, the study population consisted of young and healthy individuals. Their responses may have been less dramatic than older individuals who are metabolically at risk, such as those with abdominal obesity or those with metabolic syndrome.

In conclusion, our findings suggest there are differences on various acute metabolic and hemodynamic responses between HFCS and sucrose. A major strength of our study was the fructose measurements. This allowed us to determine that the consumption of HFCS resulted in higher systemic fructose exposure, which may have driven the significant treatment

differences detected on glucose, SUA, and, SBP. Although the treatment effects on acute metabolic responses were small, the effects may increase with continued chronic exposure to these sweeteners. Furthermore, it still needs to be determined if there are differences in fructose exposure and metabolic effects from HFCS and sucrose if the sweeteners were consumed over a longer period of time versus the acute bolus that was given in our study. Importantly, further studies are needed to evaluate the impact of variable fructose absorption and/or metabolism on higher fructose exposure and how that may affect long-term metabolic responses and disease risks. Although we did find differences between HFCS and sucrose, both sweeteners are currently consumed in excessive amounts, which may play an important role in driving the prevalence of cardio-renal diseases.

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List of Abbreviations

AUC	area under the curve
AUC_H	AUC from HFCS
AUC_S	AUC from sucrose
AUC/D	dose normalized area under the curve
BMI	body mass index
BP	blood pressure
Cl_H	clearance from HFCS
Cl_S	– clearance from sucrose
Cmax	maximum observed concentration
CTSI	Clinical Translational Science Institute
D_H	dose from HFCS
D_S	dose from sucrose
F_H	bioavailability from HFCS
F_S	bioavailability from sucrose
FE_fructose	fractional excretion of fructose
FEUA	fractional excretion of uric acid
HFCS	high fructose corn syrup
HL	elimination half-life
HR	heart rate
MRT	mean residence time
SCreat	serum creatinine
SFr	serum fructose
SUA	serum uric acid

Tg	triglycerides
Tmax	time of maximum observed concentration
UCreat	urine creatinine
UFr	urine fructose
UUA	urine uric acid

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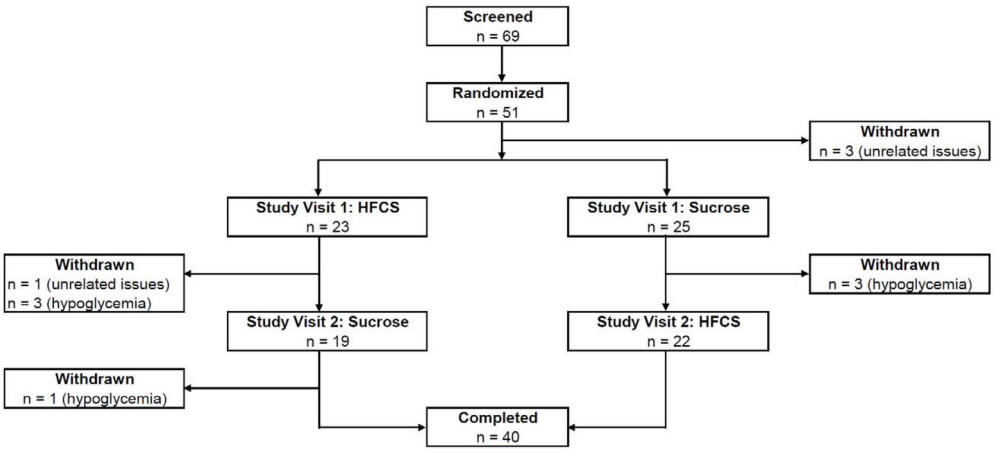

Figure 1.
Study population. Sixty-nine subjects were recruited. Forty participants completed both treatment arms.

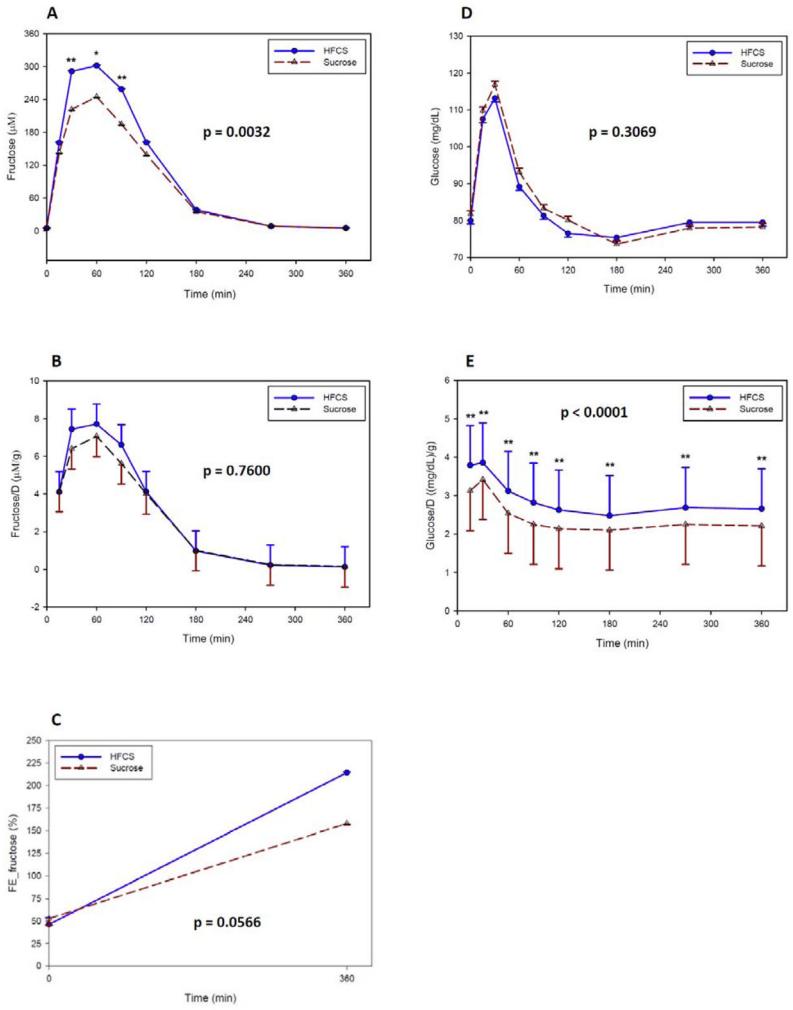

Figure 2.

Effect of consuming HFCS- versus sucrose-sweetened beverages during a 6 hr period on (A) fructose, (B) normalized fructose by dose of each treatment, (C) FE_fructose, (D) glucose, and (E) normalized glucose by dose of each treatment. Values are least square means ± standard errors. P-value shown represents overall treatment effect. P-value: * = < 0.05; ** = < 0.005. FE_fructose fractional excretion of fructose; HFCS high fructose corn syrup.

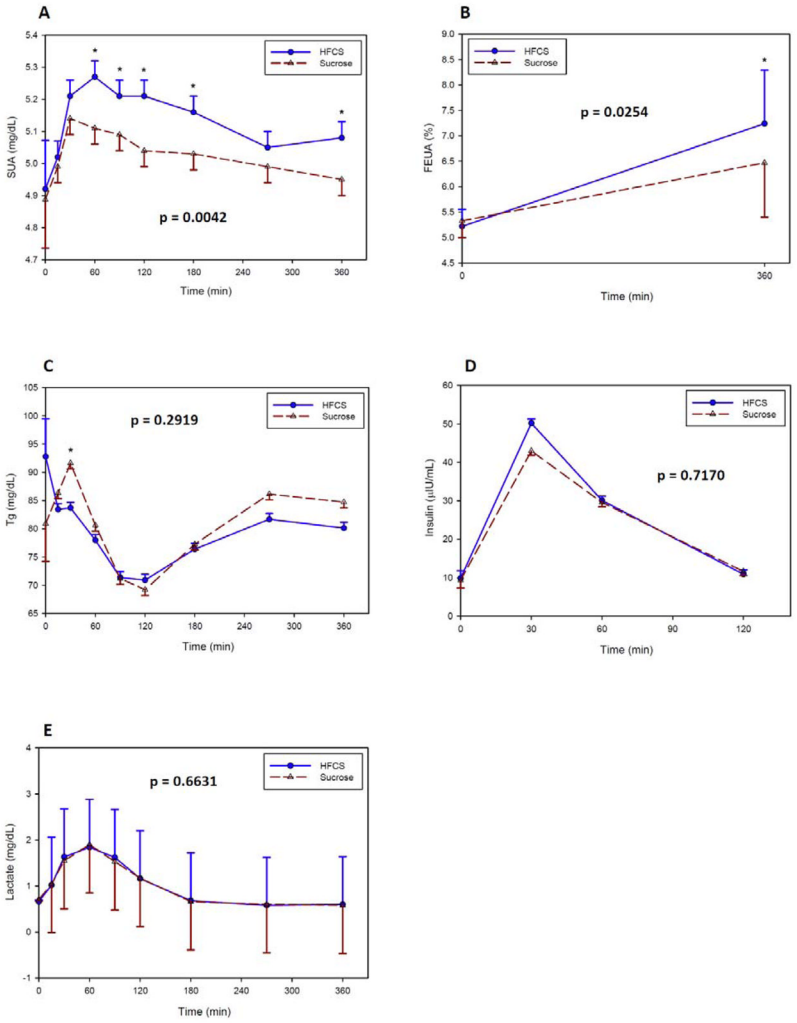

Figure 3.

Effect of consuming HFCS- versus sucrose-sweetened beverages during a 6 hr period on (A) SUA, (B) FEUA, (C) Tg, (D) insulin, and (E) lactate. Values are least square means ± standard errors. P-value shown represents overall treatment effect. * p-value < 0.05. FEUA fractional excretion of uric acid; HFCS high fructose corn syrup; SUA serum uric acid; Tg triglycerides.

Table 1

Carbohydrate amounts in HFCS- and sucrose-sweetened soft drinks.

Sweetener	Carbohydrate	Amount (g in 24 oz)	
		Before Study	After Study
HFCS	Fructose	41.6 ± 0.1	36.8 ± 0.3
	Glucose	30.2 ± 0.2	27.4 ± 0.1
	Sucrose	BLD	BLD
Sucrose	Fructose	27.1 ± 0.4	32.2 ± 0.1
	Glucose	27.4 ± 0.4	32.2 ± 1.9
	Sucrose	20.0 ± 0.3	BLD

BLD below level of detection; HFCS high fructose corn syrup. For each sugar analysis, three 12 oz cans were used. For each Data given as mean ± standard deviation.

Table 2

Baseline characteristics of study participants.

Variable	Completed Subjects (n = 40)
Age	27.1 ± 8.6
Female	24 (60.0)
Race	
White, European American	23 (57.5)
Black, African American	4 (10.0)
Asian	7 (17.5)
Other/Multiracial	6 (15.0)
BMI	25.9 ± 4.9
Glucose (mg/dL)	81.0 ± 4.8
Insulin (μIU/mL)	9.8 ± 12.7
Tg (mg/dL)	86.5 ± 39.1
SBP (mmHg)	118.4 ± 9.7
DBP (mmHg)	75.0 ± 6.4
HR (bpm)	66.2 ± 8.3
Fructose (μM)	5.4 ± 4.5
FE_fructose (%)	55.0 ± 57.7
SUA (mg/dL)	4.9 ± 1.0
FEUA (%)	5.5 ± 2.0
Lactate (mg/dL)	0.7 ± 0.2

BMI body mass index; DBP diastolic blood pressure; FE_fructose fractional excretion of fructose; FEUA fractional excretion of uric acid; HR heart rate; SBP systolic blood pressure; SUA serum uric acid; Tg triglycerides. Data given as either mean ± standard deviation or n (%). For completed subjects, data for response parameters represent fasting levels at study visit 1.

Table 3

Fasting levels of response parameters at each study visit of completed subjects.

Parameter	Treatment Sequence			
	ALL			
	HFCS → Sucrose		Sucrose → HFCS	
	Visit 1	Visit 2	Visit 1	Visit 2
Fructose (μM)	5.4 ± 3.9	4.4 ± 1.4	5.4 ± 5.0	4.6 ± 2.0
FE_fructose (%)	45.9 ± 28.3	42.0 ± 23.2	62.5 ± 73.5	48.0 ± 35.9
SUA (mg/dL)	4.9 ± 0.9	4.8 ± 0.8	4.9 ± 1.0	5.0 ± 1.0
FEUA (%)	5.5 ± 1.5	5.1 ± 2.2	5.5 ± 2.3	5.0 ± 2.1
Glucose (mg/dL)	79.7 ± 5.3	81.4 ± 6.5	82.1 ± 4.1	80.3 ± 6.7
Insulin (μIU/mL)	10.4 ± 15.7	9.0 ± 13.1	9.2 ± 9.8	9.6 ± 10.7
Lactate (mg/dL)	0.6 ± 0.2	0.7 ± 0.2	0.8 ± 0.3	0.7 ± 0.3
Tg (mg/dL)	92.2 ± 46.5	79.9 ± 45.7	81.9 ± 32.2	94.6 ± 44.0
SBP (mmHg)	118.1 ± 9.5	119.8 ± 9.5	118.7 ± 10.1	119.1 ± 10.2
DBP (mmHg)	74.7 ± 6.2	74.4 ± 8.5	75.3 ± 6.8	74.9 ± 6.8
HR (bpm)	66.5 ± 7.3	66.4 ± 7.4	65.9 ± 9.2	66.5 ± 9.3

DBP diastolic blood pressure; FE_fructose fractional excretion of fructose; FEUA fractional excretion of uric acid; HR heart rate; SBP systolic blood pressure; SUA serum uric acid; Tg triglycerides. Data given as mean ± standard deviation.

Table 4

Effects of consuming HFCS- versus sucrose-sweetened beverages on fructose, FE_fructose, and glucose.

		Treatment				
		HFCS		Sucrose		
Variable	Parameter	Mean	95% CI	Mean	95% CI	P-value
AUC (min*μM)*	Fructose	38791 ± 1624	35533 – 42049	32327 ± 1614	29087 – 35567	<.0001
AUC/D ((min*μM)/g)	Fructose	989.5 ± 43.3	902.6 – 1076.3	934.4 ± 43.0	848.0 – 1020.8	0.1076
Cmax (μM)*	Fructose	363.4 ± 17.6	328.1 – 398.8	317.0 ± 17.5	281.9 – 352.2	0.0043
Cmax/D (μM/g)	Fructose	9.3 ± 0.5	8.3 – 10.2	9.2 ± 0.5	8.2 – 10.1	0.8039
Tmax (min)	Fructose	57.4 ± 4.2	49.1 – 65.8	59.7 ± 4.1	51.4 – 68.0	0.6172
MRT (min)	Fructose	87.8 ± 2.0	83.8 – 91.8	89.6 ± 2.0	85.6 – 93.5	0.3063
Half-life (min)	Fructose	35.4 ± 2.2	31.0 – 39.8	39.3 ± 2.2	34.9 – 43.7	0.2079
Relative bioavailability*R*	Fructose	1.07 ± 0.24				0.1219
ΔFE_fructose (%)	FE_fructose	311.8 ± 66.7	178.8 – 444.8	302.9 ± 66.0	171.4 – 434.4	0.9249
AUC (min*mg/dL)	Glucose	29911 ± 323	29266 – 30557	30053 ± 320	29413 – 30694	0.6492
AUC/D ((min*mg/dL)/g)*	Glucose	1038.2 ± 9.9	1018.4 – 1058.0	863.1 ± 9.8	843.5 – 882.7	<.0001
Cmax (mg/dL)	Glucose	120.3 ± 2.6	115.2 – 125.4	123.5 ± 2.5	118.4 – 128.6	0.1778
Cmax/D ((mg/dL)/g)*	Glucose	4.2 ± 0.1	4.0 – 4.3	3.5 ± 0.1	3.4 – 3.7	<.0001
MRT (min)	Glucose	172.5 ± 0.9	170.8 – 174.3	170.4 ± 0.9	168.6 – 172.1	0.0292
Tmax (min)	Glucose	30.1 ± 2.7	24.8 – 35.4	30.2 ± 2.6	24.9 – 35.4	0.9842
Relative bioavailability *R*	Glucose	1.20 ± 0.07				<.0001

AUC area under the curve; AUC/D AUC divided by the respective sugar dose of the treatment; Cmax maximum observed concentration; Cmax/D Cmax divided by the respective sugar dose of the treatment; MRT mean residence time; Tmax = time of Cmax. FE_fructose fractional excretion of fructose. CI confidence interval. Data given as least square mean ± standard error. Linear mixed effect models were used to analyze the parameters.

R Paired t-test was used.

* p-value < 0.005.

Table 5

Effects of consuming HFCS- versus sucrose-sweetened beverages on SBP, DBP, and HR.

		Treatment				
		HFCS		Sucrose		
Variable	Parameter	Mean	95% CI	Mean	95% CI	P-value
AUC (min * mmHg)	SBP	43832 ± 309	43214 – 44449	43588 ± 306	42977 – 44200	0.4802
Observed max (mmHg) *	SBP	133.5 ± 1.0	131.4 – 135.5	130.2 ± 1.0	128.1 – 132.2	0.0047
AUC (min * mmHg)	DBP	27460 ± 263	26935 – 27985	27363 ± 260	26842 – 27883	0.7425
Observed max (mmHg)	DBP	84.1 ± 0.8	82.4 – 85.7	84.0 ± 0.8	82.4 – 85.6	0.9470
AUC (min * bpm)	HR	23856 ± 263	23328 – 24384	23791 ± 262	23266 – 24316	0.7745
Observed max (bpm)	HR	75.3 ± 0.9	73.5 – 77.1	75.0 ± 0.9	73.2 – 76.8	0.7488

AUC area under the curve; DBP diastolic blood pressure; HR heart rate; SBP systolic blood pressure. CI confidence interval. Data given as least square mean ± standard error. Linear mixed effect models were used to analyze the parameters.

R Paired t-test was used.

* p-value < 0.005.

Table 6

Effects of consuming HFCS- versus sucrose-sweetened beverages on SUA, FEUA, Tg, Insulin, and Lactate.

		Treatment				
		HFCS		Sucrose		
Variable	Parameter	Mean	95% CI	Mean	95% CI	P-value
AUC (min * mg/dL)	SUA	1848.6 ± 15.1	1818.5 – 1878.7	1811.3 ± 14.9	1781.5 – 1841.0	0.0827
Cmax (mg/dL)	SUA	5.4 ± 0.1	5.3 – 5.5	5.4 ± 0.1	5.2 – 5.5	0.4947
ΔFEUA (%)	FEUA	7.6 ± 0.4	6.8 – 8.3	7.0 ± 0.4	6.2 – 7.7	0.2671
AUC (min * mg/dL)	Tg	30661 ± 798	29069 – 32253	31964 ± 790	30387 – 33540	0.1949
Cmax (mg/dL)	Tg	101.7 ± 2.4	97.0 – 106.5	108.4 ± 2.4	103.7 – 113.1	0.0108
AUC (min * μUI/mL)	Insulin	3717.2 ± 304.4	3106.7 – 4327.8	3824.3 ± 302.2	3217.8 – 4430.7	0.6846
Cmax (μUI/mL)	Insulin	58.1 ± 5.8	46.4 – 69.8	61.2 ± 5.8	49.6 – 72.8	0.5905
AUC (min * mg/dL)	Lactate	355.4 ± 11.1	333.1 – 377.8	354.2 ± 11.0	332.1 – 376.4	0.8907
Cmax (mg/dL)	Lactate	2.0 ± 0.1	1.9 – 2.2	2.1 ± 0.1	1.9 – 2.2	0.4401

AUC area under the curve; Cmax maximum observed concentration. FEUA fractional excretion of uric acid; SUA serum uric acid; Tg triglycerides. CI confidence interval. Data given as least square mean ± standard error. Linear mixed effect models were used to analyze the parameters.

R Paired t-test was used.

* p-value < 0.005.