

EFFECTS OF A HIGH FRUCTOSE CORN SYRUP BEVERAGE ON  
INDICES OF RESTING METABOLISM AS COMPARED  
TO A SUCROSE BEVERAGE

by

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## ABSTRACT

High fructose corn syrup (HFCS) has gained notoriety concerning possible negative effects on metabolism. A limited amount of research regarding possible differences between the metabolism of sucrose (Sucr) and HFCS exists. The purpose of this research was to examine whether a HFCS beverage alters indices of acute resting metabolism when compared to a sucrose beverage. Thirteen (5 male, 8 female; Mean $\pm$ SD; 23.8  $\pm$  3 yrs, 71.6  $\pm$  14.0 kg, 171.0  $\pm$  11.2 cm) adults from the local area volunteered for this study. After a baseline blood sample was acquired, each subject ingested a 300 milliliter (mL) beverage sweetened with 30 grams (g) of either HFCS or sucrose. Order of treatments was counter-balanced and subjects were blinded. Venous blood samples (approximately 5 mL) were taken at 30, 60, 90 and 120 minutes, allowed to coagulate for 20 minutes, and then centrifuged for 10 minutes to separate the serum. Samples were analyzed for glucose, lactate, insulin and triglyceride concentrations. An ANOVA with repeated measures was used for statistical analysis and Tukey's post hoc test was used to differentiate means upon a significant interaction. Significance was set at an alpha level  $<$  0.05. Data are listed as mean  $\pm$  SD. No interaction effect was observed between time and treatments for any variable. Additionally, no treatment main effect was found for glucose (Sucr 4.13 $\pm$ 1.1 mM/L, HFCS 4.33 $\pm$ 1.1 mM/L,  $p=0.154$ ), lactate (Sucr 2.2 $\pm$ 0.8, HFCS 2.2 $\pm$ 0.7,  $p=0.526$ ), insulin (Sucr 11.13 $\pm$ 13.0 pmol/L, HFCS 8.18 $\pm$ 9.6 pmol/L,  $n=11$ ,  $p=0.168$ ), or triglycerides (Sucr 80 $\pm$ 27.8 mg/dL, HFCS 81 $\pm$ 14.7 mg/dL,  $p=0.861$ ). There was a significant time effect found within the variables. The mean serum glucose and insulin concentrations at 30 minutes (Glu 5.6  $\pm$  0.98 mM/L,  $p<0.001$ , Ins 22.69 $\pm$ 17.3 pmol/L,  $p<0.001$ ) were significantly increased over baseline, 60, 90, and 120 minutes. Mean lactate concentration at 30 minutes (2.7 $\pm$ 0.9 mM/L,  $p<0.001$ ) was greater than at baseline, 90, and 120 minutes. The triglyceride concentration at 120 minutes was significantly lower than at baseline in both conditions (baseline 84 $\pm$ 22.1 mg/dL, 120 minutes 76 $\pm$ 21.6 mg/dL,  $p=0.008$ ). In the current study, there were no differences between interventions for any of the variables.

## CHAPTER 1

## INTRODUCTION

Coinciding with the increased use of high fructose corn syrup (HFCS) as a sweetener, the rates of obesity have increased (1). This has led to negative perceptions and notoriety of HFCS and fructose in general. Moreover, many popular media outlets have reported the ‘dangers’ of HFCS. For example, one author states “High-fructose doesn’t just make your body fat, it makes your heart fat too” (2). Additionally, many of these claims are without credible references or citations and authors have taken liberties on spreading a cause and effect relationship between HFCS intake and obesity. Information such as this is easily accessible to the general public and misconceptions are instantly formed.

While these claims sound outlandish, they may not be completely inaccurate. Researchers have reported an association between HFCS and/or fructose ingestion and adverse health effects such as dyslipidemia and increased energy intake (3-7). Other authors have reported that fructose and/or HFCS ingestion affects circulating levels of hormones such as insulin, lipoproteins, and triglycerides (3-8), which are risk factors for obesity and cardiovascular disease. The changes in these metabolic variables may negatively affect metabolism and caloric intake and therefore contribute to obesity by the disruption of energy balance regulation (3, 4).

The development of HFCS in the 1960’s led to its replacing sucrose (table sugar) in many food and beverage products. High fructose corn syrup contains the

monosaccharides fructose, typically making up 42 or 55% of the total solution, and glucose free in solution. The syrup is a starch that has been extracted from corn, undergone saccharification then liquefaction (hydrolysis reactions) to convert it to glucose. Saccharification is a process in which a starch is broken down into oligosaccharides while liquefaction further breaks down oligosaccharides into dextrose. The process continues with isomerization to convert glucose to fructose, and ends with fractionation to produce a specific percentage of fructose in the syrup (9). In contrast, sucrose is a disaccharide composed of one molecule each of fructose and glucose.

High fructose corn syrup has unique chemical and physical properties that allow it to be a commonly used sweetener. For example, high fructose corn syrup nearly matches the sweetness of sucrose while having longer shelf life. High fructose corn syrup also has a lower freezing point than sucrose (this is advantageous when freezing fruit while preventing damage in the form of ice crystals) and HFCS is also a reducing sugar, which enables the browning process, an important quality for baked goods (9). Additionally, the process by which HFCS is manufactured has been studied and improved upon since its inception. A result of the improvements is that it is more economically viable to use as a sweetener because it is cheaper to manufacture compared to sucrose (9).

There has been research specifically comparing the effects of HFCS consumption in comparison to sucrose consumption on energy intake, hormone response, metabolic profiles, and appetite over 24 hours of measurement. Several of these studies have observed no significant differences in the body's metabolic response to the two sugars (5, 6, 8). Despite the lack of metabolic difference between the sugars, negative health effects

may occur as a result of ingestion of either one. The sweetness of HFCS and sucrose may lead to an increased consumption of some food and beverage products. Excess ingestion of these sugars may contribute to the disruption of metabolic profiles from indirect effects of the increased energy intake. The possibility that chronic excessive intake of fructose leading to an adaptation of enzyme activity in fructose metabolism is evident (10).

An overwhelming amount of the recent literature is focused on pure fructose while research involving HFCS is limited. Fructose alone is rarely consumed in average diets with the exception of fruit. Examination of the effects of HFCS consumption on metabolism is essential due to the glucose component and its prevalence in most diets. Moreover, metabolism of the additional glucose component may affect various processes differently than fructose alone. Additionally, there is no research to date regarding acute response of variables after HFCS and sucrose ingestion. Establishment of how HFCS ingestion affects acute metabolism when consumed in typical amounts while at rest is necessary to examine if differences exist in the time period immediately following ingestion. Furthermore, HFCS should be examined in direct comparison to sucrose because HFCS has replaced sucrose in most products. Investigation of metabolism after consumption of each type of sugar may have implications on the use of HFCS in future food products and even exercising metabolism.

### Statement of Purpose

The purpose of this study was to examine whether a HFCS-sweetened beverage alters indices of resting metabolism when compared to a sucrose-sweetened beverage in healthy non-diabetic adults between 18-32 years of age.

### Hypothesis

The null hypothesis was that there will be a difference between mean concentrations of serum glucose, lactate, triglyceride, and insulin over 120 minutes after sucrose (Sucr) ingestion and mean concentrations of the same variables after high fructose corn syrup (HFCS) ingestion. The alternative hypothesis was that there will be no difference in mean concentrations of variables after consumption of each beverage.

$$H_0: \mu(\text{Sucr}) \neq \mu(\text{HFCS})$$

$$H_A: \mu(\text{Sucr}) = \mu(\text{HFCS})$$

### Delimitations

The study was delimited to “low risk”, moderately active adults between the ages of 18 and 32 years of age (11). The investigation was also delimited to subjects that have no signs or symptoms of metabolic disorders and/or cardiovascular disease as determined by a health history form.

### Limitations

Subjects were asked to keep a diet log and to replicate their diets on the day preceding data collection to minimize altered results due to diets, but was dependant on the subjects' adherence to instructions. Thirty grams of carbohydrate was a different relative percentage of each subjects energy needs. This may have elicited differences in metabolism.

### Assumptions

It was assumed that all equipment used to measure glucose, lactate, triglycerides, and insulin was reliable and valid. It was also assumed that subjects adhered to all pre-test day and test-day instructions and protocols.

## CHAPTER 2

## REVIEW OF RELATED LITERATURE

Fructose is a common monosaccharide naturally found in foods such as honey, fruits, and fruit juices. These sources provide a modest and healthy amount of fructose in the diet. Fructose is the primary sugar in HFCS as well. High fructose corn syrup is a sweetener derived from corn and composed of the monosaccharides fructose and glucose. It has been the added sweetener in many products in the food and beverage industry, such as carbonated beverages and sports drinks, in replacement of sucrose. In HFCS, glucose and fructose molecules are both free in solution, which give it unique properties such as a longer shelf life and depression of freezing points. Sucrose (table sugar), however, is a disaccharide and is comprised of one molecule of glucose and fructose each, linked by an  $\alpha$ 1,4 glycosidic bond. Sucrose is typically derived from sugar cane or sugar beets. The simple difference in structure accounts for distinguishing properties associated primarily with enzymatic digestion and absorption, while mechanical digestion and metabolism of these two sugars are similar.

Manufacturing HFCS

Treating standard corn syrup with an enzyme to convert some of the glucose to fructose is how HFCS is made. Starch that has been removed from corn is first hydrolyzed to produce glucose, which is then isomerized to convert a portion of it to fructose (9). The most common form of HFCS is high fructose corn syrup-55 (HFCS-55) which is used to sweeten food and beverages, but it was not the first. Before the process

was improved upon, HFCS-42 was produced, and it was decided that a sweeter taste was needed to match the sweetness of sucrose. HFCS-42 is corn syrup that is comprised of 42% fructose and the rest is comprised of glucose. As the process was refined and superior techniques were formed, HFCS-90 (90% of the total is fructose) was produced, blended with HFCS-42, and HFCS-55 emerged, in which 55% of the total product is fructose (9).

The chemical structure of HFCS is attained by the isomerization of glucose to fructose. This process gives it physical properties that sucrose does not have, and makes it advantageous to use. High fructose corn syrup is primarily used due to its sweetness, which relative to sucrose is nearly indistinguishable. According to trained sensory panelists, HFCS has a relative sweetness rating of 99 compared to sucrose at a rating of 100 (9). Additionally, the free glucose and fructose in HFCS create a higher osmotic pressure than sucrose, which allows for absorption of water at lower relative humidity and a lower freezing point (9).

The absorption of water at a lower relative humidity, also called a humectant property, is advantageous because it will give the product a better eating quality due to better textures, and a longer shelf life due to the prevention of crystallization (9). Moreover, a lower freezing point enables the freezing of fruits while also preventing damaging crystallization. Fructose and dextrose free in solution in HFCS are also reducing sugars, which makes for superior browning during baking. The structure of HFCS is also beneficial to the carbonated beverage industry, as it is resistant to the low pH of the product (9).

### Absorption of HFCS

The mechanical digestion of HFCS and sucrose throughout the mouth, esophagus and stomach are similar. The intestinal absorption of HFCS and sucrose are different, however. Although the two sugars are comprised of the monosaccharides glucose and fructose, sucrose involves a covalent bond ( $\alpha$ 1,4 glycosidic) linking the molecules. It is necessary for the enzyme sucrase to split this bond at the brush border of the small intestine to allow for absorption of the two molecules. Enzymatic digestion of HFCS is not necessary, as the molecules of glucose and fructose are free in solution. From this point, fructose and glucose from either source (HFCS and sucrose) follow divergent metabolic pathways that eventually convene again.

Fructose, whether it is part of a disaccharide, or free in solution, has a specific transporter, glucose transporter 5 (GLUT5), which works by facilitated diffusion and is independent of glucose concentration (12-14). Facilitated diffusion functions via a concentration gradient and a carrier binding site (15). The transporter GLUT5 is located on the membrane of the enterocyte in the small intestine, can be saturated due to the limited number of binding sites, and is significantly slower to absorb fructose relative to the glucose transporter.

The slow and saturable GLUT5 transporter can therefore lead to incomplete fructose absorption if excess is consumed. This consequently results in gas production from the fermentation process in the colon (16). It also can cause gastrointestinal distress, diarrhea and abdominal cramping (17, 18). It has been demonstrated however, that fructose ingestion along with glucose facilitates absorption (17, 19).

The sodium dependent glucose transporter-1 (SGLT-1), like GLUT5, is saturable and located on the membrane of the enterocyte of the small intestine. This is the mechanism of absorption for glucose. The transport of glucose is an active transport system, dependant on sodium, and requires energy (ATP). The transporter GLUT5 is also expressed at lower levels in the kidney, skeletal muscle and adipose tissue (19), which may have implications concerning metabolism in these tissues.

### Metabolism of HFCS

After absorption, the molecules of fructose and glucose travel out the basolateral membrane of the enterocyte and into capillaries, primarily through glucose transporter 2 (GLUT2), another transporter using facilitated diffusion (12). The sugars are transported to the liver in the blood by the portal vein, where fructose is promptly taken up into hepatocytes and phosphorylated to fructose-1-phosphate (F-1-P) by the enzyme fructokinase. Glucose is also phosphorylated immediately to glucose-6-phosphate (G-6-P), by the enzyme glucokinase (Figure 2.2)

The conversion to from fructose to F-1-P by fructokinase is the main reaction in which fructose is converted into metabolites that enter glycolysis. Fructose can also be phosphorylated by the enzyme hexokinase to fructose-6-phosphate (F-6-P) in the liver, but it is a minor pathway (10). This reaction increases when there is excess fructose consumed, however.

The liver is the main site of fructose metabolism, so it is also the site in which it can possibly affect other substrate metabolism. Glucose metabolism can occur in the liver or other tissues, such as cells of the central nervous system or in muscle cells (Figure 2.1).

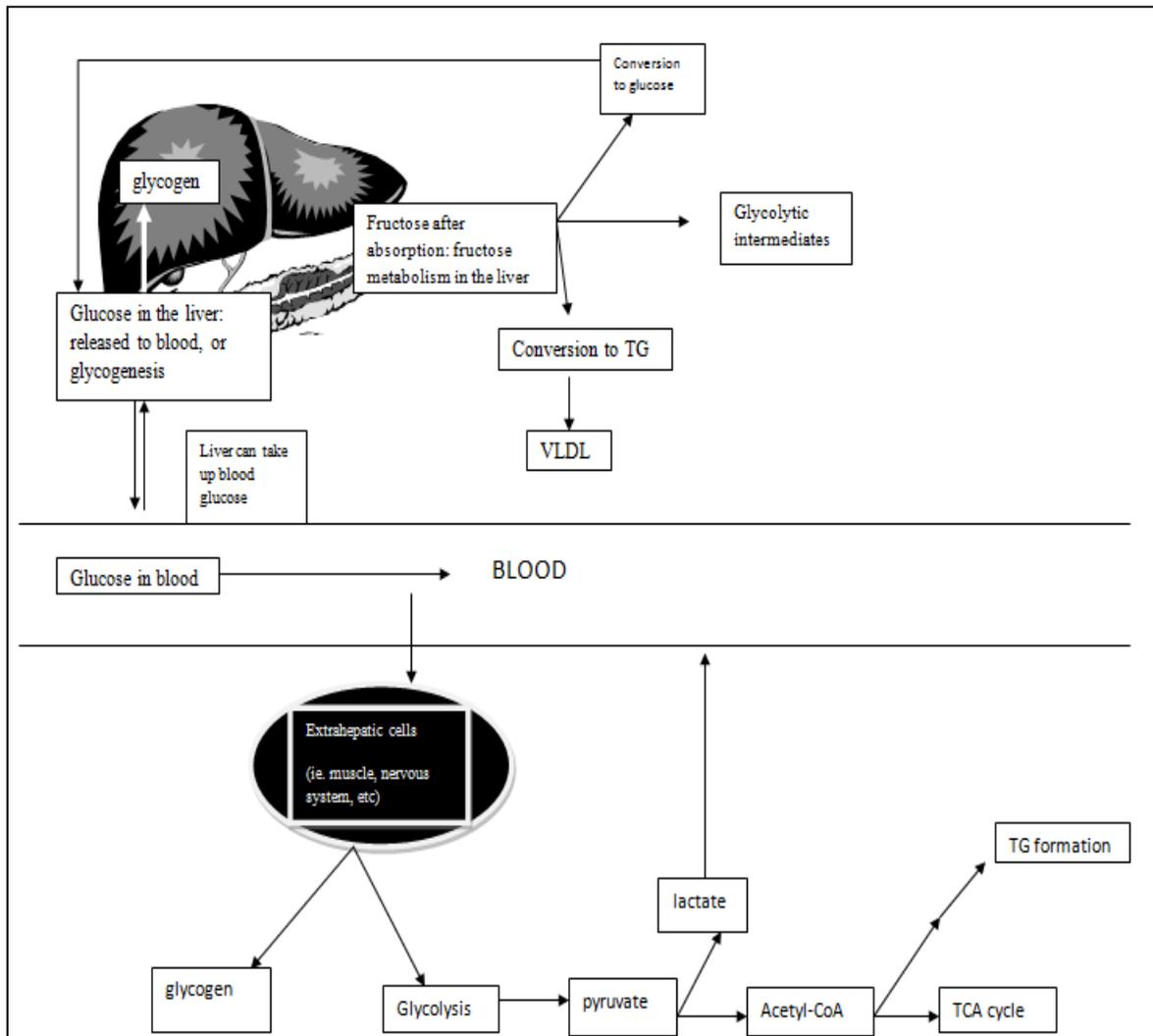


Figure 2.1 (10, 20) The general pathways of glucose and fructose metabolism.

In fructose metabolism, F-1-P is split by hepatic aldolase to form dihydroxyacetone phosphate (DHAP), and glyceraldehyde. Aldolase also has a role in glycolysis, splitting fructose-1,6-biphosphate (F-1,6 bis P) into glyceraldehyde-3-phosphate (G-3-P) and DHAP (Figure 2.2). In fructose metabolism, DHAP can be converted into glycerol-3-P, then form triglycerides when fatty acids are available, and eventually incorporated into very low density lipoproteins (VLDL) with cholesterol and other constituents (10, 20). The process by which DHAP is converted to triglycerides and VLDL is thought to be one mechanism of how fructose metabolism can affect the appearance of lipids in the blood. The intermediate DHAP can also be turned into G-3-P by triose-phosphate isomerase, and enter the distal steps of glycolysis. Triokinase is another enzyme in the fructose pathway, and by way of ATP, phosphorylates glyceraldehyde (from F-1-P) to form G-3-P, which then enters the glycolytic pathway as well (10, 20).

The glucose in HFCS or sucrose follows the glycolysis pathway in the liver (not a major pathway), is stored as glycogen, or enters circulation and can be taken up by other cells such as a muscle cell. If it is taken up by extra-hepatic cells, it can be metabolized through glycolysis there, or be stored as glycogen depending on the circumstances and hormone levels. Upon entrance to either the hepatocyte or alternative cell, it is immediately phosphorylated to G-6-P by glucokinase in the liver, and by hexokinase in muscle cells. The activity of glucokinase is regulated positively by insulin and hexokinase is regulated by the concentration of G-6-P. At this point, in an extra-hepatic cell, G-6-P can enter glycogenesis and glycogen will be synthesized if glucose and

insulin levels are elevated (21). Insulin stimulates glucose uptake by the translocation of the GLUT4 transporter. G-6-P can also enter the hexomonophosphate shunt or it can proceed through glycolysis.

Glycolysis will progress by the conversion of G-6-P to F-6-P by glucose phosphate isomerase, which is one of ways that fructose can also enter glycolysis (after being converted to F-6-P by hexokinase). F-6-P is then converted to F-1,6-bis-P by phosphofructokinase (PFK), a major rate limiting step in glycolysis. This enzyme is regulated by ATP (negatively) and AMP/ADP (positively). F-1,6-bis-P is then split by the enzyme aldolase into DHAP and G-3-P (20, 21). These two intermediates can be interconverted, depending on the concentrations of both. Glucose can be turned to G-3-P, then be converted to DHAP and then proceed into the lipid formation pathway and vice versa with fructose. This is the point where the paths of fructose and glucose metabolism converge.

At the point of conversion to G-3-P, glucose and fructose can proceed in an identical pathway to be eventually converted to pyruvate (Figure 2.2). Pyruvate can then be converted to acetyl-CoA and proceed to the tricarboxylic acid (TCA) cycle to be aerobically metabolized. Acetyl-CoA can also follow a pathway leading to TG and VLDL formation via malonyl-CoA (10). Pyruvate can also continue through the latter stages of glycolysis to produce lactate (20, 21).

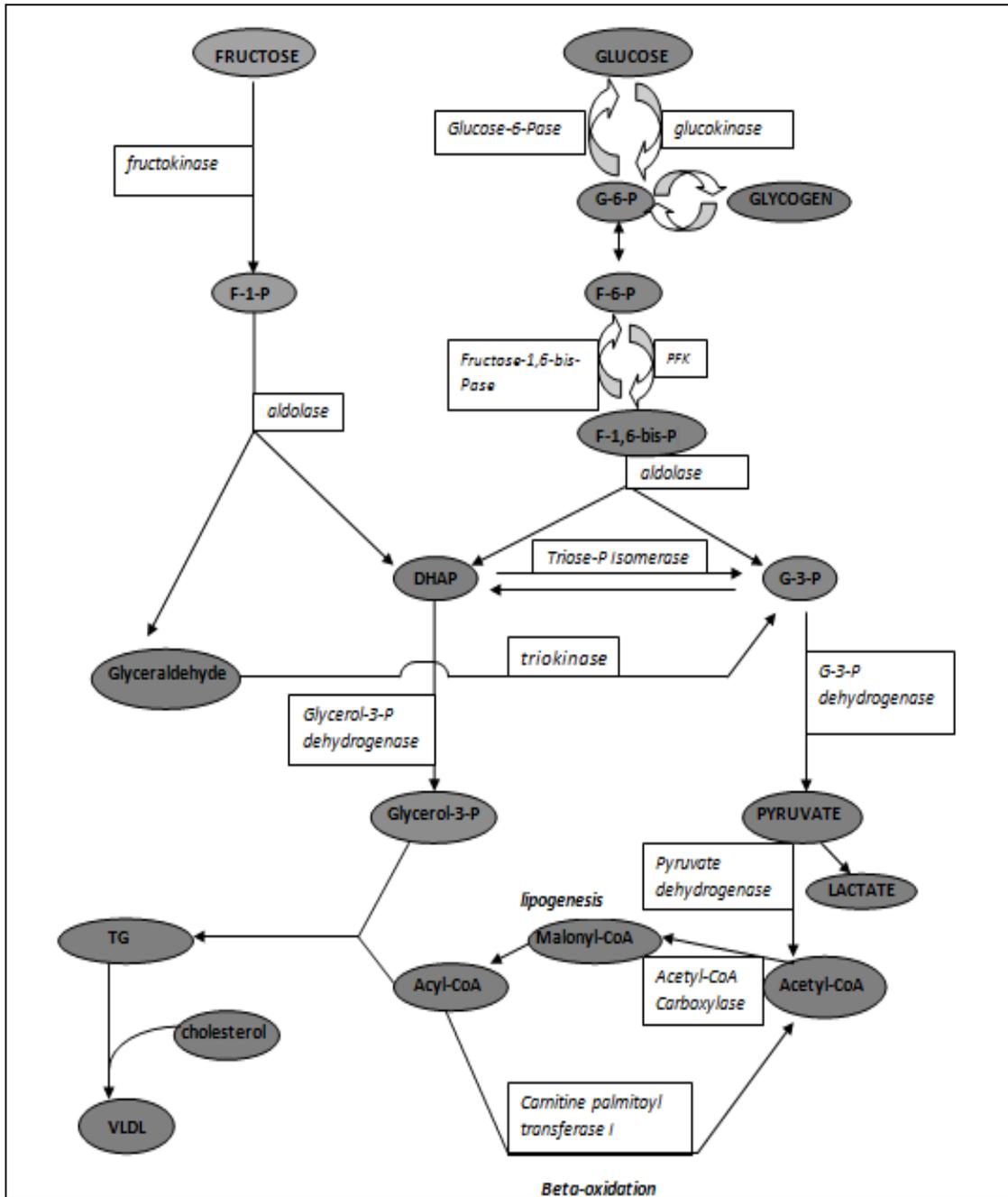


Figure 2.2 Intermediate metabolism of fructose and glucose (10, 20).

Fructose can also travel through glycolysis in reverse, essentially (with subtle differences), from the point of DHAP or G-3-P, and be converted to glucose and/or glycogen through gluconeogenesis and glycogenesis, respectively (10). A key point in fructose metabolism is that it is largely unregulated because the enzymes in the pathway are not rate limiting. Additionally the glycolytic intermediates of fructose metabolism enter distal to the rate limiting step, PFK. The fact that both fructose and glucose have multiple pathways in which they can be converted to lipids is important to note. Ingestion of either sugar can result in different metabolites changing in concentration, due to the activation of these pathways (22). The complexity of fructose metabolism allows for several opportunities for alterations in variables such as hormone fluctuation, diet and energy intake, blood glucose and lactate concentrations, and lipid metabolism (Figure 2.2).

### Effects of Fructose Metabolism

The obesity epidemic has played a role in the curiosity surrounding the possible adverse health effects to which fructose may contribute. The effects of fructose on metabolic variables such as insulin, ghrelin, leptin, glucose, lactate, cholesterol, and triglycerides have been a major focus of recent research. These variables are of interest because they could be negatively affected by fructose metabolism and thus promote unhealthy metabolism.

Authors have reported that increased amounts of F-1-P due to fructose ingestion increased the activity of pyruvate kinase and resulted in additional pyruvate and lactate production in rats (23). Pyruvate kinase is an enzyme that catalyzes the final step of

glycolysis. The reaction is the conversion of phosphoenolpyruvate (PEP) to pyruvate through the donation of a phosphate to adenosine diphosphate (ADP) to make adenosine triphosphate (ATP). Other researchers have observed consistent results to Eggelston and Woods. The researchers measured serum glucose, insulin, fructose, triglyceride, glycerol, uric acid, lactate and pyruvate after ingestion of 0.25, 0.5, 0.75, or 1.0 g of glucose, fructose, sucrose or sorbitol per kilogram (kg) of body weight. The doses of sugars were dissolved in 4.0 milliliters (mL) of water per kg of body mass. The sucrose solution resulted in a significant rise over baseline after 90 minutes in pyruvate and lactate concentration at the 3 highest dose levels, and the fructose solution resulted in a significant rise in lactate at 2 doses (0.5 g/kg and 1.0 g/kg) and pyruvate at the 3 highest dose levels. The rise in pyruvate concentration was greater in response to sucrose, however (24).

The implications of increased pyruvate and specifically, lactate production in response to fructose consumption at rest are unclear. It is possible the effects of fructose intake, and thus increased pyruvate, are that the enzymes associated with the lipogenic pathway are increased. Pyruvate dehydrogenase activity is thought to increase when fructose is present, increasing the conversion of pyruvate to acetyl-CoA, a major source for lipogenesis (10).

Moreover, glycerol-3-P dehydrogenase activity may increase due to the increase in glycerol-3-P, promoting the formation of acyl glycerols and thus TG and VLDL formation. The results of a previous study were consistent with this theory (25). The authors reported that the presence of fructose decreased fatty acid oxidation, and

increased esterification in rat livers. The livers were perfused with 300 milligrams (mg) of fructose per 100 mL of blood and measurement occurred every 30 minutes for 2 hours (25). This research is focused on pure fructose, however, and HFCS metabolism may affect various processes differently due to the glucose content. Fructose alone is rarely consumed in average diets with the exception of fruit. It is therefore imperative to study the effects of HFCS. Additionally, comparisons with glucose provide interesting and valuable information, but research focusing on HFCS in comparison to sucrose is necessary.

Insulin, an important hormone in metabolism, has been a focus of research as well. After fructose ingestion, it has been observed that a lower amount of insulin has been released by the beta cells of the pancreas compared to other sugars. It has been reported that after ingesting complex food items sweetened with fructose (cake; 63 g, ice cream: 52 g), lower levels of serum glucose and insulin resulted as compared to responses after ingesting sucrose-sweetened foods (same amount as fructose) in 10 healthy subjects during 180 minutes of data collection. This is consistent with the relative amount of glucose in the sugars. Ingestion of both sucrose and fructose elicited lower blood glucose and insulin responses than glucose- (40 g/m<sup>2</sup> of body surface area) sweetened foods (26). When comparing the ice cream to the cake, however, the ice cream elicited lower glucose and insulin response, which is underscored by the lower amount of sugar (fructose/sucrose) amount and thus a lower glucose amount.

Other research has also compared fructose and glucose metabolism. Fructose ingestion also elicited lower blood glucose and insulin response in 19 healthy subjects

after ingestion of 50 g of fructose in 12% solution (22). Measurements were taken periodically throughout a 120 minute trial. Again, the effect of HFCS on appearance of glucose, and thus insulin stimulation may differ from that of fructose alone due to its glucose content.

There has been additional research that is consistent with previous results (22) when comparing the effects of various loads of glucose, sucrose and fructose on metabolites in the blood. The insulin response after fructose ingestion was found to be minimal compared to all the other sugars at all doses (0.25, 0.5, 0.75 and 1.0 g/kg body mass) during a 90 minute trial (24). Insulin may acutely stimulate leptin, a hormone that inhibits appetite (7). A lesser insulin response would inhibit appetite less than other sugars and thus result in an increased appetite and perhaps increased energy intake. Furthermore, Macdonald and colleagues reported that pure fructose and sucrose resulted in decreased serum triglycerides and glycerol at most loads, and both decreases were similar to each other (24). This response was not insulin dependent, however, because there was not a significant increase of insulin from fructose and sucrose feedings compared to glucose feedings. Part of the decrease in TG levels may have been due to uptake and storage from muscle or adipose tissue, however.

In addition to the research of Macdonald and colleagues, there has been research regarding fructose and its effect on lipogenesis and the appearance of lipids in the blood, insinuating that it may have an atherogenic effect. In contrast to Macdonald et al, other researchers have specifically examined the effects of HFCS in comparison to sucrose on resting metabolism (6). After consumption of 3 meals which included either a sucrose or

HFCS sweetened beverage (25% of total energy, 11% solutions), there were significant increases in lipid variables over baseline, but in similar amounts. The researchers observed no significant differences between sucrose and HFCS regarding levels of plasma triglycerides, cholesterol, low density lipoprotein (LDL), and high density lipoprotein (HDL) during 24 hours of measurement in a total of 34 healthy men and women, 20-50 years of age (6). Eight of the male subjects also participated in trials in which they consumed solutions sweetened with glucose or fructose. Triglyceride levels from the previous sucrose and HFCS trials were not intermediate of responses to the glucose and fructose beverages, as hypothesized, but closer to the responses to pure fructose beverage.

Other research examined the effects of fructose- and glucose-sweetened beverages (30% of total daily calories, 15% solutions) with 3 meals on metabolites over 24 hours in 12 healthy women aged 19-33 years old (3). The authors measured circulating glucose, insulin, leptin, ghrelin, glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide (GIP), plasma TG and free fatty acids (FFA) during separate fructose- and glucose-sweetened beverage trials. Plasma glucose, leptin, and insulin levels were found to be lower in the fructose trial. GLP-1 and TG changes were greater in the fructose trial, and no differences were observed between glucose and fructose trials in GIP or FFA measurements. Additionally, the suppression of ghrelin was more pronounced in the glucose trial than in the fructose trial (3).

HFCS may affect specific appetite regulating hormones such as leptin and ghrelin. Leptin is an adipocyte-derived hormone that inhibits appetite and under normal

conditions, circulates in levels proportional to the amount of body fat. Ghrelin is a hormone released by the stomach and stimulates hunger (27). The effect of HFCS and sucrose (30% of energy intake in a beverage) on leptin, ghrelin, blood glucose and insulin was previously examined in 30 women between 20 and 60 years of age (8). The researchers observed no significant differences in appetite, total caloric intake, levels of ghrelin and leptin, or in glycemic or insulinemic response between the sugars during 24 hours of measurement (8).

Additional research has compared the effects HFCS- and sucrose- sweetened solutions (800 mL with 1.5 MJ of energy, or about 60 g of sugar and 7.5% solution) on satiety, energy intake, and hormone levels (5). The authors found no differences in energy intake between the HFCS and sucrose drink in addition to no difference in satiety ratings (5). Additionally, the changes in plasma GLP-1, ghrelin, leptin, and insulin after consumption of HFCS and sucrose solutions were not different from each other. However, when compared to the control (beverage containing no energy), some variables were significantly different. Satiety ratings between energy containing (sucrose and HFCS) drinks were not different from each other, but collectively were increased compared to the control. This was probably due to the increase that was noted in GLP-1 and insulin over the control, which is consistent with the findings of previous research (3). The hormone GLP-1 may have stimulated insulin, which could have contributed to satiety (5).

Previous researchers have also found no differences in circulating levels of leptin, ghrelin, and glucose in addition to levels of lipids, as stated previously, when comparing

HFCS- and sucrose-sweetened beverages (6). There was a small, but significant difference found in the insulin response between the two, however. Interestingly, the sucrose containing beverage elicited increased insulin levels but only had 10% more glucose (6). These results are consistent with previous research (24).

It is necessary for more research to be carried out pertaining to the effects of HFCS metabolism on lipogenesis due to the discrepancy of results in the literature. The discrepancy may be due to the glucose component in HFCS and perhaps to differences in measurement time. Fructose metabolism results in glycolytic intermediates that are distal to the rate limiting enzyme of glycolysis, PFK. As a result, fructose metabolism is largely uninhibited. This could contribute to increases in several different metabolites if fructose and/or HFCS are consumed.

In contrast to the previous work (5, 6, 8), most research in this area has been carried out on the effect of pure fructose compared to glucose on measures of variables (3, 16, 18, 22, 24, 25, 26). Few studies in the literature have focused on comparing HFCS to sucrose, the sugar that it has replaced in food and beverage products. The ratio of glucose to fructose is similar in the two sweeteners. Since glucose comprises 45% of HFCS and half of sucrose, it is important to investigate if that component affects metabolism. The structure of both sugars is also very similar, meriting investigation of whether they behave similarly in the body.

Differences between the effects of HFCS and sucrose metabolism appear to be minimal. Research that focuses on HFCS exists, but it is an area in the literature that is deficient. High fructose corn syrup and sucrose both contain fructose and glucose and it

is necessary to examine the metabolism both to establish if differences exist. Research concerning this topic may aid in changing misconceptions about HFCS.

Examining the effects of HFCS and sucrose in a dose and a volume of beverage that physically active individuals would normally consume is also pertinent.

### Dose and Volume of the Carbohydrate Beverage

Researchers that have examined pure fructose have used doses as high as 50-60 g (3, 6, 24, 26). This should be avoided due to the slow transport of fructose into the enterocyte of the intestine. Malabsorption will most likely occur with a high dose of fructose and gastrointestinal distress may be a result (17). Absorption capacity is not within the scope of the present research. Much of the literature includes doses of HFCS and sucrose ingestion of 25% of total calories across three meals, which is likely according to recommended daily intakes of sugar.

Fluid replacement varies among individuals, even within the recreationally active population. Average fluid intake among male and female athletes competing in running, triathlon and cycling events ranged from 50 mL per hour to 1.1 L per hour, with an average of about 400 mL per hour (28). A volume of 1.1 L of a carbohydrate beverage in one sitting may not be appropriate for a resting, moderately active individual.

Researchers have examined glycemic response to ingestion of 25 g of glucose, sucrose and fructose dissolved in 200 mL or 600 mL of water. The investigators found that decreasing the solution from 600 to 200 mL of total volume, a smaller glycemic response occurred (29). Although that study was aimed at reducing variability in oral

glucose tolerance testing, it is helpful for determining an appropriate amount of sugar and an appropriate volume to produce an effective and realistic concentration for a solution.

A large enough volume (300mL) to produce a realistic concentration (10%) with 30 g of carbohydrate was used in the present study. The volume of solution was a reasonable amount for a subject to consume in about 10 minutes. As most sports drinks are 6% solutions and most soft drinks are 11% solutions, a 300 mL, 10% solution (30 g of sugar total) was a realistic and reasonable to elicit responses in a 120 minute trial for a resting subject who is moderately active.

CHAPTER 3

EFFECTS OF A HIGH FRUCTOSE CORN SYRUP BEVERAGE ON INDICES OF  
RESTING METABOLISM AS COMPARED TO A SUCROSE BEVERAGE

Contribution of Authors and Co-Authors

Chapter 3

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Abstract

High fructose corn syrup (HFCS) has gained notoriety concerning possible negative effects on metabolism. A limited amount of research regarding possible differences between the metabolism of sucrose (Sucr) and HFCS exists. The purpose of this research was to examine whether a HFCS beverage alters indices of acute resting metabolism when compared to a sucrose beverage. Thirteen (5 male, 8 female: Mean±SD; 23.8 ± 3 yrs, 71.6 ± 14.0 kg, 171.0 ± 11.2 cm) adults from the local area volunteered for this study. After a baseline blood sample was acquired, each subject ingested a 300 milliliter (mL) beverage sweetened with 30 grams (g) of either HFCS or sucrose. Order of treatments was counter-balanced and subjects were blinded. Venous blood samples (approximately 5 mL) were taken at 30, 60, 90 and 120 minutes, allowed to coagulate for 20 minutes, and then centrifuged for 10 minutes to separate the serum. Samples were analyzed for glucose, lactate, insulin and triglyceride concentrations. An ANOVA with repeated measures was used for statistical analysis and Tukey's post hoc test was used to differentiate means upon a significant interaction. Significance was set at an alpha level < 0.05. Data are listed as mean ± SD. No interaction effect was observed between time and treatments for any variable. Additionally, no treatment main effect was found for glucose (Sucr 4.13±1.1 mM/L, HFCS 4.33±1.1 mM/L, p=0.154), lactate (Sucr 2.2±0.8, HFCS 2.2±0.7, p=0.526), insulin (Sucr 11.13±13.0 pmol/L, HFCS 8.18±9.6 pmol/L, n=11, p=0.168), or triglycerides (Sucr 80±27.8 mg/dL, HFCS 81±14.7 mg/dL, p=0.861). There was a significant time effect found within the variables. The mean serum glucose and insulin concentrations at 30 minutes (Glu 5.6 ± 0.98 mM/L, p<0.001, Ins 22.69±17.3 pmol/L, p<0.001) were significantly increased over baseline, 60, 90, and 120 minutes. Mean lactate concentration at 30 minutes (2.7±0.9 mM/L, p<0.001) was greater than at baseline, 90, and 120 minutes. The triglyceride concentration at 120 minutes was significantly lower than at baseline in both conditions (baseline 84±22.1 mg/dL, 120 minutes 76±21.6 mg/dL, p=0.008). In the current study, there were no differences between interventions for any of the variables.

### Introduction

Coinciding with the increased use of high fructose corn syrup (HFCS) as a sweetener, the rates of obesity have also increased (1). This has led to negative perceptions and notoriety of HFCS and fructose in general. Moreover, many popular media outlets have reported the ‘dangers’ of HFCS. For example, one author states “High-fructose doesn’t just make your body fat, it makes your heart fat too” (2). Additionally, many of these claims are without credible references or citations and authors have taken liberties on spreading a cause and effect relationship between HFCS intake and obesity. Information such as this is easily accessible to the general public and misconceptions are instantly formed.

While these claims sound outlandish, they may not be completely inaccurate. Researchers have reported an association between HFCS and/or fructose ingestion and adverse health effects such as dyslipidemia and increased energy intake (3-7). Other authors have reported that fructose and/or HFCS ingestion affects circulating levels of hormones such as insulin, lipoproteins, and triglycerides (3-8), which are risk factors for obesity and cardiovascular disease. The changes in these metabolic variables may negatively affect metabolism and caloric intake and therefore contribute to obesity by disruption of energy balance regulation (3, 4).

The development of HFCS in the 1960’s led to its replacing sucrose (table sugar) in many food and beverage products. High fructose corn syrup contains the monosaccharides fructose, typically making up 42 or 55% of the total solution, and glucose free in solution. The syrup is a starch that has been extracted from corn,

undergone saccharification then liquefaction (hydrolysis reactions) to convert it to glucose. Saccharification is a process in which a starch is broken down into oligosaccharides while liquefaction further breaks down oligosaccharides into glucose. The process continues with isomerization to convert glucose to fructose, and ends with fractionation to produce a specific percentage of fructose in the syrup (9). In contrast, sucrose is a disaccharide composed of one molecule each of fructose and glucose. It is typically derived from cane or beets.

High fructose corn syrup has unique chemical and physical properties that allow it to be a common sweetener. For example, high fructose corn syrup nearly matches the sweetness of sucrose while having longer shelf life. High fructose corn syrup also has a lower freezing point than sucrose (this is advantageous when freezing fruit while preventing damage in the form of ice crystals) and HFCS is also a reducing sugar, which enables the browning process, an important quality for baked goods (9). Additionally, the process by which HFCS is manufactured has been studied and improved upon since its inception. A result of the improvements is that it is more economically viable to use as a sweetener because it is cheaper to manufacture compared to sucrose (9).

There has been research comparing the effects of HFCS consumption in comparison to sucrose consumption on energy intake, hormone response, metabolic profiles, and appetite over 24 hours of measurement. Several of these studies have observed no significant differences in the body's metabolic response to the two sugars (5, 6, 8). The sweetness of HFCS and sucrose may lead to an increased consumption of some food and beverage products. Excess ingestion of these sugars may contribute to the

disruption of metabolic profiles from indirect effects of the increased energy intake. The possibility that chronic excessive intake of fructose leads to an adaptation of enzyme activity in fructose metabolism is evident (10).

An overwhelming amount of the recent literature is focused on pure fructose while research involving HFCS is limited. Examination of the effects of HFCS on metabolism is essential due to the glucose component and its prevalence in most diets. Fructose alone is rarely consumed in average diets with the exception of fruit. Moreover, metabolism of the additional glucose component may affect various processes differently. Additionally, no research has been done regarding acute response of variables after HFCS and sucrose ingestion. Establishment of how HFCS ingestion affects acute metabolism when consumed in typical amounts while at rest is necessary to examine if differences exist in the time period immediately following ingestion. Additionally, HFCS should be examined in direct comparison to sucrose because of its replacement in most products. Investigation of metabolism after consumption of each type of sugar may have implications on the use of HFCS in future food products and even exercising metabolism.

Therefore the purpose of this study was to examine whether a HFCS-sweetened beverage alters indices of acute resting metabolism when compared to a sucrose-sweetened beverage in healthy non-diabetic adults between 18-32 years of age. It was hypothesized that no differences in concentrations of glucose, lactate, insulin and triglycerides after consumption of each carbohydrate beverage.

## Methodology

### Subjects

Subjects were “low risk”, non-diabetic, recreationally active adults who volunteered (11). All subjects were between 18 and 32 years of age and had no signs or symptoms of metabolic or cardiovascular disease according to the health history form.

### Experimental Design

This study was approved by the Montana State University Institutional Review Board. Subjects read an informed consent document, and signed and dated the document if they chose to volunteer for the study. A health history form was filled out to ensure that the subject was “low risk” and free from metabolic/cardiovascular disease (11). The study was a repeated measures crossover design so that each subject would serve as their own control. Each subject participated in two experimental trials that consisted of 120 minute- data collection periods, each after a 12 hour overnight fast. Order of treatments was counter balanced, and subjects were blinded to the treatment received. Subjects were instructed to refrain from exercise and ingestion of alcohol one day prior to data collection, and reminded to avoid caffeine during fasting periods. Subjects were asked to follow their normal dietary habits, record a diet log, and to ingest the same diet on each day preceding their lab visit.

### Procedures

Subjects entered the Movement Science Laboratory (MSL) in the morning and anthropometric information (height [cm] and body mass [kg]) was obtained. Baseline

blood sampling via an indwelling catheter occurred, followed by ingestion of one of the carbohydrate solutions. Subjects were allowed 10 minutes to ingest the entire solution after which the 120-minute trial began. The subjects then sat quietly for the remainder of the trial. Blood samples were also acquired at 30, 60, 90, and 120 minutes after beverage ingestion. The volume of each blood sample was approximately 5 mL. The samples were allowed to coagulate for 20 minutes, centrifuged for 10 minutes, and serum was separated and frozen (-20° Celcius) for later analysis. Triglyceride concentration was measured at baseline and 120 minutes only (pre-post). The subject returned to the MSL no sooner than one week later to repeat the procedure with ingestion of the other carbohydrate beverage.

#### Carbohydrate Beverage

A 300 mL solution (10% carbohydrate, 30 total grams) sweetened with either sucrose or HFCS was prepared using water, cane sugar (sucrose) or HFCS, and a common flavoring (Kool-Aid) to mask any identifying tastes. The volume of solution was a reasonable amount for a subject to consume in about 10 minutes. As most sports drinks are 6-8% carbohydrate solutions and most soft drinks are around 11% carbohydrate solutions, this dose and volume was appropriate. Additionally, it is typical for individuals to select drinks that are a fixed dose and volume in normal conditions. On average, athletes will consume a volume of about 400 mL after activity (28). The solutions were prepared on the same day as each experimental trial.

### Biochemical Analyses

Serum samples were analyzed for glucose and lactate using a Contour blood glucose meter (Bayer HealthCare LLC, Mishawaka, IN, USA) and a LactatePro portable blood lactate analyzer (Arkray Factory, Inc., Shiga, Japan), respectively. Triglyceride concentration was analyzed in an external medical laboratory using a photometric assay (Siemens Healthcare Technology, Tarrytown, NY). Insulin was analyzed using a microplate enzyme-linked immunosorbent assay (ELISA) according to manufacturer instructions (MP, Diagnostic Division, Solon, OH).

### Statistical Analysis

Data were analyzed using a 2 x 4 (Triglyceride 2x2) analysis of variance with repeated measures ( $\alpha$  level of 0.05). A Tukey-Kramer post hoc analysis was conducted to differentiate means upon a significant interaction. All data listed as mean  $\pm$  standard deviation (SD).

## Results

### Subject Characteristics

Descriptive data of the participating subjects are presented in Table 3.1.

Table 3.1 Summary of descriptive data for study subjects (Mean  $\pm$  SD)

	<b>n</b>	<b>Age (yrs)</b>	<b>Body Mass (kg)</b>	<b>Body Height (cm)</b>
<b>Total</b>	13	23.8 $\pm$ 3	71.6 $\pm$ 14.0	171.0 $\pm$ 11.2
<b>Male</b>	5	25.2 $\pm$ 4	83.2 $\pm$ 10.3	180.7 $\pm$ 5.8
<b>Female</b>	8	23.0 $\pm$ 3	64.4 $\pm$ 10.9	164.9 $\pm$ 9.2

### Serum Glucose

There was no time by treatment interaction effect ( $p=0.630$ ) in addition to no main treatment effect in glucose responses observed after consumption of HFCS and sucrose (Sucr  $4.13\pm 1.1$  mM/L, HFCS  $4.33\pm 1.1$  mM/L,  $p=0.154$ ). There was a time effect observed for the 30 minute time interval for both conditions (Figure 3.1). This interval was significantly increased over baseline, 60, 90 and 120 minutes ( $5.52\pm 1.2$  mM/L,  $p<0.001$ ).

### Serum Lactate

There was no time by treatment interaction effect ( $p=0.525$ ) and no main treatment effect observed in lactate concentrations after consumption of HFCS and sucrose beverages (Sucr  $2.2\pm 0.8$ , HFCS  $2.2\pm 0.7$ ,  $p=0.526$ ). There was a time effect observed at the 30 minute time interval (Figure 3.2). The lactate concentration at 30 minutes was significantly increased over baseline, 90, and 120 minutes time periods ( $2.7\pm 0.9$  mM/L,  $p<0.001$ ), but not over 60 minutes.

### Serum Insulin

Insulin data for only 11 of the 13 subjects was available due to catheter and coagulation problems. No main treatment effect was observed for insulin response to each beverage (Sucr  $11.13\pm 13.0$  pmol/L, HFCS  $8.18\pm 9.6$  pmol/L,  $p=0.168$ ). There was a time effect observed in insulin concentration in both conditions (Figure 3.3). At 30 minutes, the serum insulin concentration was significantly increased over baseline, 60, 90 and 120 minute concentrations ( $22.69\pm 17.3$  pmol/L,  $p<0.001$ ).

### Serum Triglycerides

No main treatment effect was found in triglyceride concentrations after consumption of each beverage (Sucr  $80 \pm 27.8$  mg/dL, HFCS  $81 \pm 14.7$  mg/dL,  $p=0.861$ ). Additionally, no treatment by time interaction effect was observed (Figure 3.4). The triglyceride concentration at 120 minutes was significantly lower than at baseline in both conditions (baseline  $84 \pm 22.1$  mg/dL, 120minutes  $76 \pm 21.6$  mg/dL,  $p=0.008$ ).

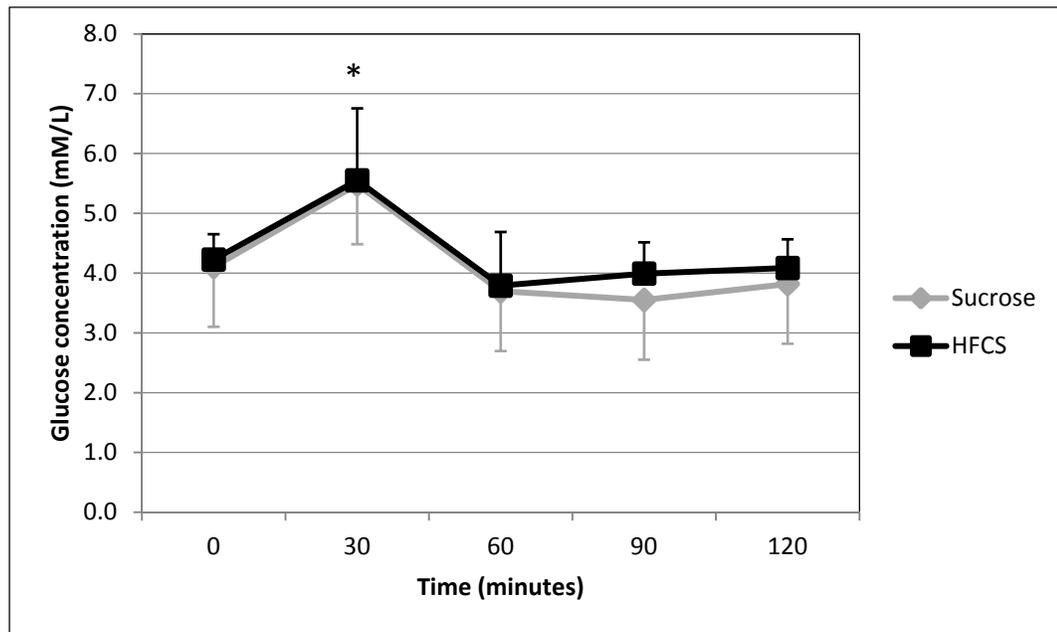


Figure 3.1 Mean ( $\pm$ SD) glucose concentration after ingestion of HFCS and sucrose (n=13).  
\*Significantly different from baseline

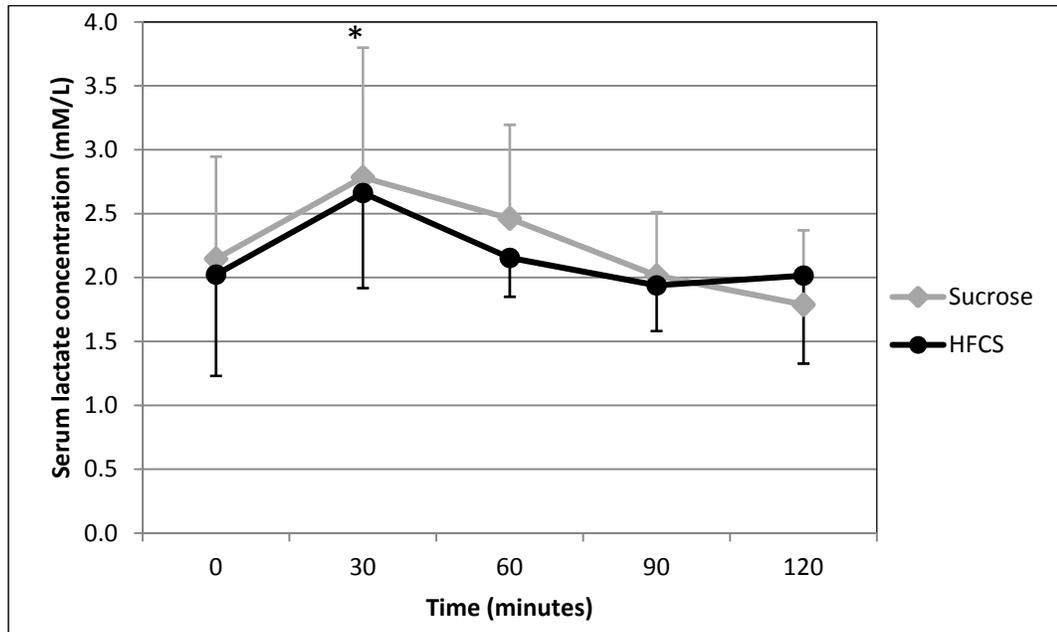


Figure 3.2 Mean ( $\pm$ SD) lactate concentration after ingestion of HFCS and sucrose (n=11)  
\*Significantly different from baseline

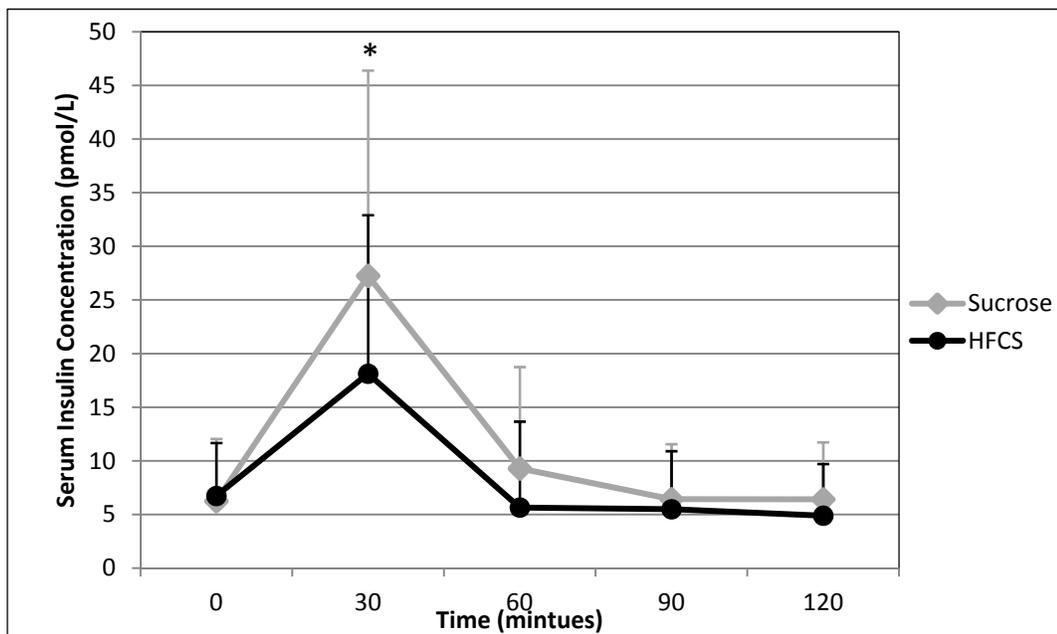


Figure 3.3 Mean ( $\pm$ SD) insulin concentration after ingestion of HFCS and sucrose (n=13).  
\*Significantly different from baseline

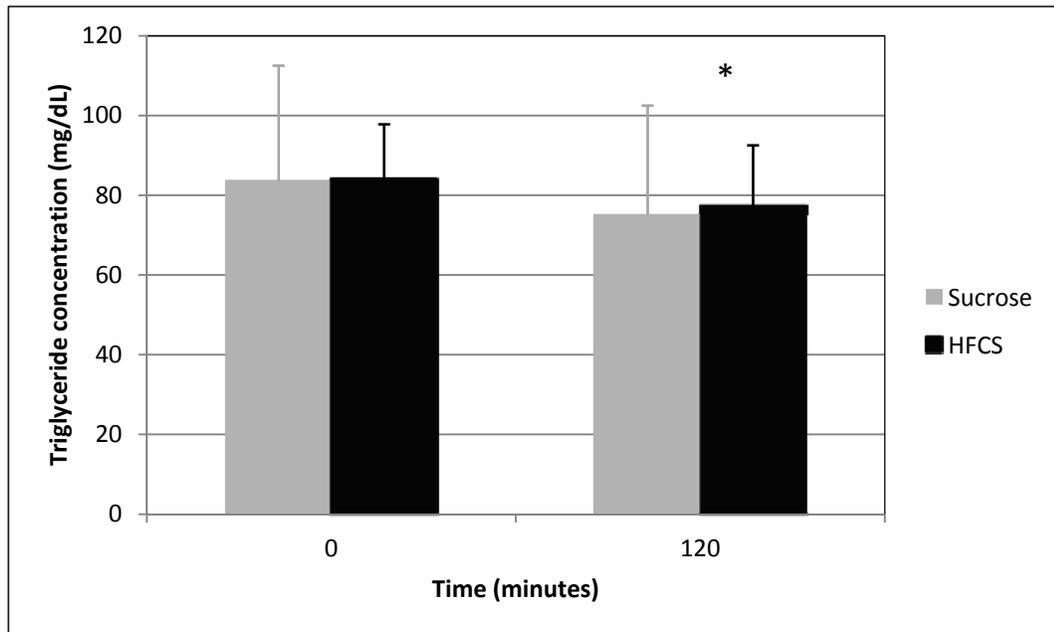


Figure 3.4 Mean ( $\pm$ SD) triglyceride concentrations at baseline and 120 minutes after ingestion of HFCS and sucrose (n=13).

\*Significantly different from baseline

### Discussion

Previous research concerning the metabolism of HFCS and sucrose has primarily summarized responses after ingestion of three meals over at least 24 hours (5, 6, 8), whereas the current study focuses on acute responses after ingestion of a single beverage over 120 minutes. Currently, there is no research regarding acute responses to HFCS versus sucrose ingestion. Therefore, the primary purpose of this study was to determine if differences exist between indices of acute resting metabolism after ingestion of HFCS- and sucrose-sweetened beverages. No differences were observed in variables indicative of resting metabolism after ingestion of the given beverages.

As expected, serum glucose concentration in both conditions was elevated significantly at 30 minutes after beverage ingestion, then dropped slightly (but not significantly) below baseline, at 60 minutes and returned to baseline by the end of the trial. The previous research that compared HFCS and sucrose also reported no differences in glucose concentration after 24 hours (5, 6, 8). Although studying the effects of pure fructose and sucrose ingestion, there have been similar increased levels of blood glucose at 30 minutes ( $\approx 132$  mg/dL; 7.33 mM/L) with 63 g of sucrose, which returned to baseline by 180 minutes in previous research (26).

Ingestion of HFCS and sucrose elicited insulin responses that were consistent with changes in serum glucose. Mean insulin concentrations elevated with serum glucose, and returned to near baseline at 60 minutes and leveled to baseline within 90 minutes. Insulin concentrations in the two conditions were not different from each other, however, at any of the time intervals. Many researchers have reported a lesser insulin response to pure fructose (3, 24, 26) compared to sucrose. As HFCS-55 contains 55% and 45% fructose to glucose respectively, and sucrose contains 50% of each, the response of insulin to each sugar in the present study are as stated the alternative hypothesis and inconsistent with previous research on pure fructose. Conversely, previous research observed significantly increased insulin concentrations in response to sucrose after ingestion of 3 meals over 24 hours, which contained 10% more glucose than the HFCS (25% of estimated total energy intake was ingested as HFCS or sucrose)(6). The results from the current study could be explained by the shorter amount of time that metabolites were measured (2 hours versus 24 hours), and by the absolute amounts of sugar used (one

beverage feeding versus 3 meals). Although not significant, the mean insulin response was slightly higher in the sucrose condition (Figure 3.3), and could potentially become significantly increased over the HFCS condition after larger amount of time and with ingestion of additional carbohydrate. Subsequent carbohydrate ingestion at increased doses could result in a compounding effect of insulin response. Larger and subsequent glucose entering the blood would potentially increase the insulin response (18, 21).

Serum lactate concentration was also significantly elevated in both conditions after 30 minutes, and neither returned to baseline until nearly the end of the trial. These particular results were interesting, as lactate production is generally associated with exercise. It is possible, however, for blood lactate to increase to accommodate significant increases in blood glucose as a means of efficient removal (10). As previously mentioned, the implications of increased lactate concentrations at rest are unclear, if existent, but it is nonetheless important to note. Increased utilization of glycolysis, which can result in increased lactate, has potential to increase production of acetyl-coA with large increases in blood glucose, which could then proceed to the TCA cycle (although not likely at rest) or to lipogenic pathway (10). Future research could also focus on the implications of lactate concentration increases with differing doses of HFCS and sucrose.

Serum triglyceride concentration was measured due to the previous reports that HFCS/fructose and sucrose ingestion may increase the activity of the lipogenic pathway (6, 24). The TG concentration at 0 and 120 minutes between conditions was not significantly different, indicating that the metabolism and lipogenic pathways of each sugar are similar under the current ingestion amount, regarding acute response. The

concentration at 120 minutes, however, was significantly lower than baseline in both conditions, which may signify an increase in uptake and storage of blood lipids. This is consistent with previous work (24), although the response was not insulin dependent. The findings in the present study could be explained by the increase in insulin concentration at 30 minutes in both conditions due to the stimulation of lipoprotein lipase by insulin. Stimulation of insulin by an increase in blood glucose concentration will stimulate the enzyme in adipose cells to actively take up fatty acids from the blood (20). Additionally, the amount of sugar used in the current study is modest compared to most research currently in the literature (3, 6, 24, 26).

The smaller amount of sugar ingested may not have been enough to elicit increases in serum TG, as some researchers have observed in response to 50-60 g of HFCS/fructose (3, 6). The current results are also inconsistent with research that specifically looks at triglyceride concentration after ingestion of HFCS and sucrose after 24 hours. It was reported that TG concentration significantly increased in both conditions after 24 hours of measurement. That research involved ingestion of three meals which included either HFCS or sucrose beverages, containing 25% of total energy intake (6). This, with the present results, suggests that chronic rather than acute intake of HFCS or sucrose may negatively affect TG concentrations, which in turn may affect the risk of cardiovascular disease.

### Conclusion

No differences between concentrations of serum glucose, lactate, insulin and triglycerides after ingestion of HFCS and sucrose were observed, and it is therefore

concluded that the effects on indices of resting metabolism by the low dose of each sugar are similar over a period of 120 minutes. It can be speculated that the chronic overconsumption of carbohydrate such as HFCS may contribute more to obesity than simply consuming it in moderate amounts. The sweetness of these sugars may lead to an increase in consumption of a particular food. Although it appears that acute metabolism of HFCS and sucrose are similar, chronic differences may exist, and it is suggested that future research focus on this. Additionally, it is suggested that future research regarding HFCS and sucrose comparisons introduce exercise as a variable and observe the possible effects. It is also recommended that future research examine possible differences between HFCS and sucrose regarding larger amounts and over longer periods of time.

In summary, no differences in glucose and insulin response, or lactate and triglyceride concentration were observed during 120 minutes of measurement at rest after 30 g of HFCS and sucrose were ingested as a 300 mL beverage. This indicates that minimal differences exist in the acute metabolism of HFCS and sucrose. Contrary to popular press reports, the ingestion of 30 g of HFCS or sucrose did not lead to a negative change in variables.

## CHAPTER FOUR

## CONCLUSIONS

In the current study, serum glucose, lactate, insulin and triglycerides were measured over 120 minutes after consumption of either a HFCS or sucrose beverage at rest. The results were that no significant differences were observed in any variables between the two conditions. It was found, however, that serum glucose, lactate and insulin were significantly increased at 30 minutes over other time intervals in both conditions. Moreover, serum triglyceride concentration at 120 minutes was decreased compared to baseline in both conditions. The concentrations of variables after ingestion of HFCS and sucrose indicate similar acute metabolism of both sugars.

Additionally, the contribution of moderate HFCS consumption to adverse health effects is most likely not different from moderate sucrose consumption. It is concluded that the acute effects of modest HFCS consumption appear to be similar to the effects of modest sucrose consumption. Negative perceptions about HFCS may not be completely accurate according to the results of the current research.

Although it appears that acute metabolism of HFCS and sucrose are similar, chronic differences may exist, and it is suggested that future research focus on this. Furthermore, research focusing on the effects of overconsumption of these sugars to narrow what contributions HFCS ingestion may have regarding negative health effects. Additionally, it is suggested that future research regarding HFCS and sucrose comparisons introduce exercise as a variable and observe the possible effects. It can be speculated that it may be the overconsumption of carbohydrate such as HFCS or sucrose

that contributes more to the increased risk of obesity and cardiovascular disease than consuming it in moderate amounts. Since no differences between responses of serum glucose, lactate, insulin and triglycerides to HFCS and sucrose were observed, it is concluded that the effects on indices of resting metabolism by each sugar are similar over a period of 120 minutes.

In summary, the concentrations of glucose, lactate, insulin and triglycerides in serum after ingestion of 30 g of HFCS and sucrose as a 300 mL beverage were not different during 120 minutes of measurement at rest. This is an indication that minimal differences exist in the acute metabolism of HFCS and sucrose, despite the negative associations popular press have established.

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APPENDICES

APPENDIX A

SUBJECT CONSENT FORM

SUBJECT CONSENT FORM  
FOR  
PARTICIPATION IN HUMAN RESEARCH AT  
MONTANA STATE UNIVERSITY

**Project Title: Does ingestion of a high fructose corn syrup-sweetened beverage alter resting metabolism compared to a sucrose-sweetened beverage?**

You are being asked to participate in a study that will investigate any alterations in metabolism after consumption of a 300 mL beverage sweetened with 30 grams of either high fructose corn syrup (HFCS) or sucrose.

The results from this study can perhaps identify if HFCS alters metabolism compared to sucrose as indicated by measurement of blood glucose and lactate, triglyceride (a fat), and insulin. High fructose corn syrup has been associated with adverse health effects such as obesity, but it may not contribute any more than what it often replaces: sucrose. The current research may help increase the understanding of HFCS metabolism. Data collection and analysis at rest will perhaps have implications on exercising metabolism and if HFCS may affect it.

You have been identified as a possible subject as you are between the ages 18-32 and do not have any signs or symptoms of metabolic/cardiovascular disease or disorder and are non-diabetic as reported on the health history form.

**Procedures:** If you choose to participate, you are asked to report to the Movement Science Laboratory in Romney Gymnasium on the date and at the time of your scheduled sessions.

1. You will be asked to come into the lab in the morning on two separate occasions, at least one week apart. Each of these sessions will last approximately two hours.
2. You will be asked, prior to each of these visits, to refrain from exercise and alcohol the day before and fast for 12 hours (overnight). You are asked to eat your last meal by 8pm. You may drink water after this period. You are also asked to refrain from caffeine after noon the previous day.
3. You will also be asked to keep a diet log and to replicate your diet the day before your next session.

4. After obtaining your body weight and height, you will be asked to sit quietly for the remainder of the visit.
5. Blood samples at baseline, 30, 60 and 90 and 120 minutes will be obtained and analyzed for glucose, lactate, triglyceride, and insulin. Approximately 5 milliliters (1 teaspoon) of blood will be removed through a venous catheter. The catheter will be inserted into a forearm vein prior to ingestion of the solution and remain there for the remainder of the trial. This is a standard method used to obtain multiple blood samples.
6. Data collection will end at 120 minutes after beverage consumption.

**Risks:** You will be asked to complete a health history form prior to participating. This form will help screen potential health problems before participation in the study. Possible risks from this study include: gastrointestinal discomfort from the fast or ingested carbohydrate beverage. You may experience slight pain when the catheter is inserted. Other than this momentary pain, the discomfort of blood sampling should be minimal. However, in about some cases a small amount of bleeding under the skin will produce a bruise (hematoma). A small scar may persist for several weeks. Researchers will use standard, universal safety precautions to minimize risk associated with blood sampling. The individual performing the blood sampling has over two decades of experience. If any complications arise, you will be referred to the appropriate medical attention and if needed, medical personnel will be summoned, however, there are no funds available from MSU for this medical treatment.

**Time Commitment:** The total time of your participation in this study is about two and a half hours for each of the two lab visits. You may discontinue your participation at any time.

**Benefits:** Results of analyzed data will be forwarded to you. The investigator is available to discuss and/or answer any questions that you may have. Results from this study can increase your knowledge regarding HFCS.

**Compensation:** You will receive a \$30 gift certificate for completion of the project.

**Confidentiality:** All personal information and data from your lab visits will be kept in a locked office and will only be shown to you.

**Questions:** Your participation in this study is greatly appreciated, and you are free to withdraw at any point in time without any penalty or risk of jeopardizing your relationship with the researcher or the Movement Science Laboratory. Please direct any questions to the primary researcher, Amy Bloemendal via phone 320-429-0427 or email [amy.bloemendal@msu.montana.edu](mailto:amy.bloemendal@msu.montana.edu). Additional questions regarding the rights of human subjects can be directed to the Chairman of the Institutional Review Board, Mark Quinn 406-994-4707.

You do not need to sign this form. If you choose not to sign this form, you cannot be in the research study. You need to sign this form and the attached consent form if you want to be in the research study. We cannot do the research if we cannot collect, use and share your health information

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**Does ingestion of a high fructose corn syrup-sweetened beverage alter resting metabolism compared to a sucrose-sweetened beverage?**

Freedom of Consent

I have been given ample opportunity to read this document in its entirety and to ask questions which have been answered to my satisfaction. I hereby consent to become a participant in this study knowing the health risks involved and that I may withdraw my consent at any time, for any reason. I also understand that project personnel may screen me from this study for any reason deemed appropriate.

AUTHORIZATION: I have read the above and understand the discomforts, inconvenience and risk of this study. I, \_\_\_\_\_ (*name of subject*), agree to participate in this research. I also agree that my health information can be collected and used by the researchers and staff for the research study described in this consent form. I understand that I may later refuse to participate, and that I may withdraw from the study at any time. I have received a copy of this consent form for my own records.

Signed: \_\_\_\_\_

Date \_\_\_\_\_

Witness: \_\_\_\_\_

Investigator: \_\_\_\_\_

APPENDIX B

HEALTH HISTORY FORM

## Health History Form

### Personal Information

Name: \_\_\_\_\_ Sex: [ ] Male [ ] Female Date of Birth: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ Age: \_\_\_\_\_

Address: \_\_\_\_\_ City: \_\_\_\_\_ State: \_\_\_\_\_  
 Zip: \_\_\_\_\_

Day Phone: ( \_\_\_\_ ) \_\_\_\_ - \_\_\_\_ Night Phone: ( \_\_\_\_ ) \_\_\_\_ - \_\_\_\_ Email: \_\_\_\_\_

Height: \_\_\_\_\_ Weight: \_\_\_\_\_

### Emergency Contact

Name: \_\_\_\_\_ Relationship: \_\_\_\_\_

Day Phone: ( \_\_\_\_ ) \_\_\_\_ - \_\_\_\_ Night Phone: ( \_\_\_\_ ) \_\_\_\_ - \_\_\_\_

Insurance: \_\_\_\_\_

### Medications

List any prescribed medications you are currently taking: Reason


List any self-prescribed medications you are currently taking (including herbal and NSAIDS such as Advil, Motrin, Tylenol, etc.):


### ACSM Coronary Artery Disease Risk Factors

To the best of your ability, please check the appropriate yes/no box for each of the following questions:

Risk Factor Defining Criteria Yes No

Family history:

Has your father or brother had a heart attack, stroke, or died suddenly of heartdisease before the age of 55?

Has your mother or sister had a heart attack, stroke, or died suddenly of heart disease before the age of 65?

Cigarette Smoking Are you currently a cigarette smoker or have you quit within the past 6 months? \_\_\_\_\_

Hypertension (high blood pressure)

- Is your blood pressure over 140/90 mm Hg?
- Are you on medication to control your blood pressure?

Hypercholesterolemia (high cholesterol)

- Is your total serum cholesterol > 200 mg/dl, low-density lipoproteins (LDL) > 130 mg/dl, or high-density lipoproteins (HDL) < 35 mg/dl?
- Are you on medication to control your cholesterol?

Please list your cholesterol numbers if you know them:

Total: \_\_\_\_\_ LDL: \_\_\_\_\_ HDL: \_\_\_\_\_

Impaired fasting glucose  Do you have diabetes mellitus?

Have you had fasting blood glucose measurements of  $\geq 110$  mg/dL confirmed on at least 2 separate occasions?

Sedentary lifestyle  Are you physically inactive and/or sedentary (little physical exercise on the job or after work)?

Do you have any of the following known diseases? Please elaborate on any yes answers below.

Category Diseases Yes No

Cardiovascular  Cardiac, peripheral vascular, or cerebrovascular disease \_\_\_\_\_

Pulmonary  Chronic obstructive pulmonary disease, asthma, interstitial lung disease, cystic fibrosis

Metabolic  Diabetes mellitus (type I or II), thyroid disorders, renal or liver disease \_\_\_\_\_

Comments:

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Signs and Symptoms. Please elaborate on any yes answers below. Yes/No answers

Have you experienced unusual pain or discomfort in your chest (pain due to blockage in coronary arteries of the heart)?

Have you experienced unusual shortness of breath during moderate exercise (such as climbing stairs)? \_\_\_\_\_

Have you had any problems with dizziness or fainting? \_\_\_\_\_

When you stand up, or sometimes during the night, do you have difficulty breathing? \_\_\_\_\_

Do you suffer from swelling of the ankles (ankle edema)? \_\_\_\_\_

Have you experienced a rapid throbbing or fluttering of the heart? \_\_\_\_\_

Have you experienced severe pain in your leg muscles during walking? \_\_\_\_\_

Has your doctor told you that you have a heart murmur? \_\_\_\_\_

Have you felt unusual fatigue or shortness of breath with usual activities? \_\_\_\_\_

Comments:

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**Musculoskeletal**

Do you have any current musculoskeletal limitations that would impair your ability to perform maximal exercise (back pain; swollen, stiff, or painful joints; arthritis; etc.)? If yes, please explain below.

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Comments:

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**Other**

Please list and explain any other significant medical problems that you consider important for us to know:

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**EXERCISE**

Are you currently involved in a regular training program?  Yes  No

Frequency (x / wk) Duration (minutes, miles, etc / session) Type of exercise

Cardiovascular \_\_\_\_\_

Strength training \_\_\_\_\_

Flexibility \_\_\_\_\_

Assess your overall fitness in each of the categories:

Cardiovascular  Excellent  Good  Fair  Poor  Don't know

Strength  Excellent  Good  Fair  Poor  Don't know

Flexibility  Excellent  Good  Fair  Poor  Don't know