

CARBOHYDRATE INGESTION AND MOUTH RINSING ON METABOLISM  
AND ENDURANCE EXERCISE PERFORMANCE

by

BRIAN S. SNYDER

B.S., Loras College, 2001  
M.S., Kansas State University, 2006

AN ABSTRACT OF A DISSERTATION

submitted in partial fulfillment of the requirements for the degree

DOCTOR OF PHILOSOPHY

Department of Human Nutrition  
College of Human Ecology

KANSAS STATE UNIVERSITY  
Manhattan, Kansas

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## **Abstract**

Maximizing performance and results in competitive events is something that all athletes strive to achieve. Nutritional strategies have been developed to best optimize the likelihood of success in competitive events. While dietary protein was classically believed to be the key macronutrient in exercise performance, overwhelming evidence now supports the role of maximizing carbohydrate intake and availability in endurance performance. The role of carbohydrate intake prior to, during and after endurance exercise has been heavily studied and relevant literature will be discussed herein. This paper consists of three chapters and a summary related to carbohydrate intake and performance outcomes in endurance sports. While nutritional status surrounding the endurance events is discussed, this paper focuses on the ergogenic and metabolic effects of carbohydrates during the endurance bout.

Chapter one serves as a literature review of carbohydrate administration during endurance exercise. Types of carbohydrates, their role as substrates in liver and skeletal muscle during exercise, and their effects on endurance performance are discussed. The role of carbohydrate on central factors of fatigue and motor output also are covered.

Chapter two addresses the role of multiple carbohydrate supplements on cycling performance. The role of these supplements on blood glucose, insulin, lactate, and IGFBP-1 also are discussed. Chapter three addresses the effect of nutritional status prior to exercise on the ability of a carbohydrate mouth rinse to impart a performance enhancing effect. There were no treatment effects ( $p>0.05$ ) of the type carbohydrate ingested, compared with placebo, on selected metabolic and performance outcomes. Likewise, there was no ergogenic effect of mouth rinsing, in the fasted or fed state, in moderately trained endurance cyclists.

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Approved by:

Major Professor  
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# **The Chapter 1 – Carbohydrate Administration on Exercise Performance**

## ***Introduction***

Carbohydrates are a major energy source in the human diet and the importance of dietary carbohydrate intake to improve endurance exercise performance is well established.<sup>1-3</sup> The role of carbohydrate ingestion before, during, and after exercise has been studied extensively using various nutritional strategies to maximize endogenous carbohydrate stores and carbohydrate availability during endurance exercise. To clarify carbohydrate supplementation, this review will discuss carbohydrate characteristics, carbohydrate digestion and absorption, and carbohydrate metabolism in skeletal muscle and liver during rest and exercise. This review will then focus on the role of differing carbohydrate structures and combinations of those structures on athletic performance. The mechanisms of action of carbohydrate ingestion and the role of carbohydrate mouth rise in athletic performance also will be discussed. Novel aspects of carbohydrate administration and endogenous status such as training in a glycogen reduced status and the effects of exercise in the fasted state also will be discussed.

## ***Basic Characteristics of Carbohydrates***

Carbohydrates are compounds that contain carbon, hydrogen, and oxygen, typically in a 1:2:1 ratio. This is true of most, but not all carbohydrates such as sugar alcohols and some polysaccharides. Dietary carbohydrates have typically been classified by dietitians as simple or complex, and further classified as monosaccharides (single sugars), disaccharides, oligosaccharides, and polysaccharides. The primary dietary monosaccharides include glucose, fructose, and galactose. The primary dietary disaccharides are sugars consisting of two monosaccharides linked by a glycosidic bond and include sucrose (glucose + fructose), lactose

(glucose + galactose) and maltose (glucose + glucose). Maltose and trehalose are less prevalent in the food supply but have been used as dietary supplements. Oligosaccharides are carbohydrates with three to nine sugar units and are prevalent in many differing foods in the food supply. Polysaccharides containing 10 or more units are the major source of carbohydrates in the human diet but there are less data pertaining to their specific effects on athletic performance.

Starch is one of the primary polymers of glucose containing  $\alpha$ -(1,4) or  $\alpha$ -(1,6) linkages and is the storage form of carbohydrates in plants, while glycogen is the storage form of carbohydrates in animals. Amylose is a starch that contains only  $\alpha$ -(1,4) bonds and is a straight (linear) polymer. Amylopectin contains both  $\alpha$ -(1,4) or  $\alpha$ -(1,6) linkages and makes highly branched structures. The majority of the research regarding carbohydrate ingestion for athletic performance has primarily focused on the effects of mono and disaccharides, but there are some data illustrating effects of longer chain carbohydrates.

### ***Digestion of Carbohydrates***

Digestion of carbohydrates begins in the mouth with mastication as salivary  $\alpha$ -amylase begins to hydrolyze glycosidic bonds to form units of glucose, maltose, and starch fragments. After swallowing, the bolus travels to the stomach where the salivary amylase is deactivated by the acidic environment. The rate of gastric emptying controls the release of glucose and carbohydrate fragments into the small intestine, which is partially responsible for the rate of glucose appearance in the blood.

From an athletic performance standpoint, many of the calories consumed immediately before and during exercise are typically from high carbohydrate foods, and the bulk of the data are derived from tests of these sports supplements and foods. When carbohydrate concentration

of a sports beverage or food is  $\leq 7\%$ , it follows a similar pattern of gastric emptying as water.<sup>4</sup> Greater concentrations of carbohydrates tend to slow gastric emptying, but this reduced rate of gastric emptying does not appear to reduce the rate of appearance of blood glucose.<sup>1</sup> Large amounts of fat or protein in the food source can also slow gastric emptying and rate of appearance of glucose.<sup>5</sup> Moreover, exercise intensities above 75% of maximal oxygen uptake can increase gastric emptying time by reducing gastric blood flow.<sup>6</sup> Extended periods of time at these high intensities reduce blood flow to the gastric region, but also make ingestion of foods and/or water more difficult. Both the physical action of drinking/eating are difficult at this rate of respiration and reduced blood flow to the stomach can cause nausea, which can increase upon introduction of food or beverage. Additionally, high absolute doses of carbohydrates can induce gastric distress during exercise, resulting in cramping, nausea, vomiting, or bloating.<sup>1</sup> Gastrointestinal complaints are a common occurrence among endurance athletes when they are trying to maximize performance with carbohydrate ingestion.<sup>7</sup> Some of the most common complaints include nausea, heartburn, abdominal pain, loose stool or diarrhea, and occasionally vomiting.<sup>7</sup> These symptoms appear to be more prevalent in women than men and in runners as compared to cyclists.<sup>7</sup>

Once carbohydrates enter the small intestine, they are further metabolized by pancreatic  $\alpha$ -amylase to glucose, maltose, maltotrioses, and dextrans. Carbohydrates must be broken down to individual monosaccharide units to be absorbed. Hydrolysis of the remaining disaccharides occurs via disaccharidases attached to the intestinal brush-border. The majority of carbohydrates are absorbed in the duodenum, except some dietary fibers and resistant starches, which enter the large intestine undigested. While dietary fiber and resistant starch may contain metabolizable energy, the carbohydrate sources have not been well studied in the context of athletic

performance. Their lack of small intestinal absorption and insulin response likely do not make them good candidates as potential contributors to athletic performance. However, at least one study has examined the effects of resistant starch on endurance performance.<sup>8</sup>

### ***Absorption of Carbohydrates***

Once carbohydrates enter the small intestine and are in monosaccharide form, they are absorbed by active transport or facilitated diffusion. Glucose and galactose are absorbed at the brush border of the small intestine by a sodium/glucose co-transporter (SGLT1) by active transport. Adenosine triphosphate is used during absorption to pump glucose and galactose against their concentration gradient as sodium moves down its gradient. Fructose is absorbed by GLUT5 transport, as GLUT 5 has a higher affinity for fructose than for glucose. Fructose is better absorbed when ingested with other sugars, as in sucrose, than when ingested as fructose alone. Since glucose and fructose use differing transporters for absorption, and absorption appears to be a primary limiting factor in glucose appearance in the blood,<sup>9</sup> recent data from studies using combined glucose and fructose sources have been able to increase available exogenous carbohydrate during exercise.<sup>1, 10-12</sup> Monosaccharides are transferred into the blood from the enterocyte by a passive process using GLUT2 and GLUT5. Glucose transporter-2 has a higher affinity for glucose and galactose while GLUT5 transports fructose. Glucose, fructose, and sucrose are the three main carbohydrate sources that have been studied and used in augmenting athletic performance.<sup>13</sup>

### ***Carbohydrate Transport***

Throughout the body, glucose is transported across cell membranes by specific glucose transporters which are named GLUT1 through GLUT12. These glucose transporters have differing properties and affinities for glucose and carbohydrate compounds. Glucose transporter-1 is ubiquitously expressed but is most prevalent in red blood cells and brain cells. Glucose transporter-2 is located in the liver, pancreas, kidney and small intestine. In the liver, GLUT2 is responsible for uptake of galactose and fructose. Galactose is phosphorylated and converted to glucose-1-phosphate in the liver (precursor for glycogen synthesis). Fructose is phosphorylated to form fructose-1-phosphate in the liver. Glucose transporter-3 is located mainly in the brain. Glucose transporter-4 is the insulin and exercise sensitive form of glucose transporter in cardiac, adipose, and skeletal muscle tissues. Glucose transporter-4 is the glucose transporter responsible for the majority of postprandial glucose disposal.<sup>13</sup>

### ***Energy Yield of Carbohydrates***

From a basic teaching perspective, carbohydrates provide 4 kcal/g. This value has been derived from Atwater's calculations of heat production of foods. The actual caloric values, or more specifically the energy (ATP) yield from different carbohydrates can vary from almost zero in some dietary fibers and resistant starch to 4.2 kcal/g for many of the starches. When carbohydrates are ingested as monosaccharides (glucose) they have a value of 3.75 kcal/g.<sup>14</sup> Resistant starch and dietary fibers are largely left undigested in the small intestine and pass into the large intestine. These carbohydrates are fermented in the large intestine to short chain fatty acids by the bacteria. The exact contribution of these carbohydrates to energy is not fully known.

### ***Control of Blood Glucose***

Blood glucose concentration is tightly controlled in the body of healthy individuals. Insulin and glucagon are two primary regulatory hormones of glucose metabolism and homeostasis at rest. Additional hormones that regulate glucose metabolism include amylin, glucagon-like peptide (GLP-1), glucose-dependant insulinotropic peptide (GIP), insulin-like growth factor-1 (IGF-1), and the insulin-like binding proteins (IGFBP). These hormones maintain blood glucose within a narrow range in healthy individuals. The typical fasting blood glucose values range from 4 – 5.5 mM (72 – 100 mg/dl) but can increase due to a meal and decrease due to prolonged exercise or fasting. Blood glucose concentration is determined by the rate of glucose appearance in circulation from dietary sources and hepatic glucose output (HGO), and removal of glucose from circulation by tissues including the brain, skeletal muscle, and adipose tissue. The rate of gastric emptying and intestinal absorption of carbohydrates discussed above are the main determinants of glucose rate of appearance in the fed state. In the fasted state and during exercise, glycogenolysis and gluconeogenesis contribute to glucose appearance via hepatic glucose output (HGO). The liver is the primary site of glucose output via glycogenolysis and gluconeogenesis during normal fasting conditions, but the kidneys can increase their contribution to gluconeogenesis during starvation. Skeletal muscle does not release glucose per se, but does release important gluconeogenic precursors (amino acids and lactate) which can be converted to glucose in the liver via the Cori Cycle.

Insulin is the key hormone driving glucose disappearance from circulation in the resting state. After a meal containing available carbohydrate, blood glucose concentration rises, stimulates release of insulin from  $\beta$ -cells of the pancreas, and reduces release of glucagon from  $\alpha$ -cells. The pancreas absorbs glucose via GLUT2 and releases insulin and C-peptide in

secretory vesicles to regulate blood glucose concentration. Insulin typically increases glucose uptake into skeletal muscle via an intracellular signaling cascade, which results in GLUT4 translocation to the membrane. It was originally thought that the liver was a major source of postprandial glucose disposal as ingested glucose was stored as liver glycogen. This is not the case as less than one-third of liver glycogen is formed from direct glucose to glycogen storage in the liver.<sup>15</sup> The major source of glycogen in the liver is derived from 3-carbon gluconeogenic precursor compounds such as lactate, glycerol, and alanine.<sup>15</sup> At rest, dietary fructose is more readily converted to liver glycogen than dietary glucose. Dietary fructose can also be converted to lactate, used for triacylglycerol synthesis, converted to glucose for HGO, or oxidized in the liver.<sup>16, 17</sup>

Insulin also promotes fat synthesis, triglyceride storage, and a reduction of lipolysis, reducing the availability of fat for oxidation in peripheral tissues. The primary site of blood glucose storage is glycogen in skeletal muscle at rest, assuming skeletal muscle is insulin sensitive and able to store more glycogen. The typical amount of glucose stored as glycogen is higher in skeletal muscle than in liver tissue, storing upwards of 400 g and 100 g, respectively. Normal glycogen content of skeletal muscle is 12 to 16 g/kg w.w., which equates to 65 to 90 mmol glucosyl units/kg w.w.<sup>7</sup> The total amount of glycogen that can be stored in skeletal muscle depends on total muscle mass and trained state of the individual, as well as energy balance and dietary carbohydrate intake. In individuals who participate in endurance exercise, both skeletal muscle glycogen and liver glycogen are in a constant state of flux, as endurance exercise lowers glycogen stores which are then replaced post-exercise by carbohydrate intake. The rate and amount of glucose uptake postprandially in skeletal muscle is dependent on insulin signaling pathway capacity, glycogen stores, and metabolic activity.<sup>18</sup> The typical postprandial

pattern of blood glucose and insulin in healthy individuals is a rise over the first hour and then return to near baseline within two hours of the original glucose load.

Exercise increases skeletal muscle glucose uptake both during and after an exercise bout.<sup>19,20</sup> The magnitude of this increase is controlled in part by intensity and duration of the exercise bout with greater exercise intensities resulting in greater glucose uptake.<sup>21</sup> Longer duration exercise at moderate to high intensities results in reduced skeletal muscle glycogen content, and thus greater rates of glucose uptake and glycogen synthesis upon carbohydrate ingestion post-exercise.<sup>7</sup> During exercise, insulin secretion is reduced by increased blood content of epinephrine and norepinephrine, which also increase glucagon release, thereby increasing HGO. Exercising skeletal muscle takes up blood glucose, independent of insulin, through exercise-induced GLUT4 translocation to the membrane.<sup>7</sup> This occurs in the absence of an insulin spike above basal insulin concentration.<sup>22</sup> The rate-limiting step in glucose uptake during exercise is transport across the membrane.<sup>23</sup> However, the effects of insulin and muscle contraction may be additive<sup>24</sup> and stemming from different signaling cascades to two distinct GLUT4 vesicle pools.<sup>23,25</sup> The combination of exercise, increased blood glucose concentration, and increased insulin concentration during exercise may increase the rate of glucose uptake in skeletal muscle and impact muscle glycogenolysis.

To maintain adequate glucose availability during exercise, hepatic glucose output is increased compared to rest and is intensity and duration dependent (Figure 1) to match glucose uptake in the working muscles.<sup>7</sup> The substrates for HGO during exercise are liver glycogen, glycerol, amino acids, and lactate. The use of gluconeogenic pre-cursors increases as liver glycogen is depleted. During very high intensity bouts of exercise, HGO may increase beyond glucose uptake capacity in the peripheral tissues, resulting in an increase in blood glucose.<sup>26</sup>

Ingestion of a high glycemic/high carbohydrate load resulting in an insulin spike within the two hours before exercise can lead to exercise induced rebound hypoglycemia,<sup>27</sup> as exercise induced and insulin stimulated glucose disposal (Rd) are greater than HGO and intestinal absorption (Ra). This typically does not negatively affect performance outcomes,<sup>28-30</sup> but, for some individuals, is not the most pleasant experience. Hypoglycemia induced by this rebound effect is not universal among athletes,<sup>29, 30</sup> thus the best advice is for each individual to determine the optimal performance and fueling strategies.

### ***Substrate Metabolism in Cells (Skeletal Muscle and Liver)***

Substrate metabolism (both oxidation and storage) in liver and skeletal muscle depends on numerous factors, including macronutrient composition of dietary intake, fitness/training state, glycogen content, and metabolic state (energy balance, intensity, mode, and duration of exercise). Substrate metabolism also depends on whether metabolic processes are functioning normally, as in healthy, physically active individuals, or is impaired, as in sedentary and/or those with type 2 diabetes who have difficulty processing glucose/fat and are “metabolically inflexible.”<sup>31</sup> Since substrate metabolism is related to metabolic factors of fatigue, it is therefore important for athletic performance. This ability of skeletal muscle to continuously produce adequate ATP for contraction is crucial for continued generation of work. The use of substrate in skeletal muscle and liver under the varying metabolic conditions will be discussed.

### ***Carbohydrate Metabolism at Rest***

The two main sources for energy metabolism under standard conditions are fat and glucose. Protein is not a major source of energy directly but does provide some lipid and glucose

precursors and is metabolized at a higher rate in skeletal muscle and liver late (3 – 4 hours) in endurance exercise. Lean, healthy individuals are metabolically flexible and are able to switch their primary fuel source between fat and glucose oxidation depending on the availability of free fatty acids and/or glucose.<sup>31</sup>

At rest and in the fasting state, a small percentage of muscle fuel is coming from carbohydrate in metabolically flexible individuals. Up to 80% of the oxygen uptake in resting skeletal muscle can be associated with metabolism of non-esterified fatty acids (NEFAs).<sup>32</sup> Blood glucose concentration is maintained via HGO from liver glycogen and gluconeogenesis.

Postprandial substrate metabolism at rest is dependent upon the dietary composition of the meal and the metabolic state of the target cells. Liver is more metabolically active at rest and has a higher substrate oxidation rate than skeletal muscle. When skeletal muscle glycogen content is not replete, muscle tissues use available blood glucose to replenish glycogen stores and primarily oxidize fat for its relatively low energy needs. When skeletal muscle glycogen is relatively depleted, glycogen re-synthesis is a high priority, as intramuscular triglycerides fuel oxidative metabolism.<sup>33</sup> It is of interest to note that dietary fructose alone in the post exercise period leads to a ~45% lower glycogen synthesis rate compared to glucose.<sup>34</sup>

### ***Substrate Metabolism during Exercise***

Exercise increases the reliance on carbohydrate metabolism dramatically depending on the trained state of the individual, intensity, and duration of the exercise bout. Muscle glycogen is the primary fuel source during moderate to rigorous exercise. In the fasted state, muscle glycogen depletion (~ 25 mmol/kg w.w.) is one of the major reasons that work rate must either decrease or exercise must stop completely late in exercise.<sup>35</sup> The rate of muscle glycogen

utilization in the absence of exogenous carbohydrate intake is intensity dependent, with greater intensities using glycogen at a faster rate (Figure 2).<sup>7</sup> This point emphasizes the importance of pre-exercise glycogen stores in the maintenance of exercise performance in the absence of exogenous carbohydrate intake as well as the ability to increase metabolic reliance on non-glycogen (intramuscular triacylglycerol (IMTGs) and free fatty acid (FFAs)) sources of energy in the trained state. During exercise, NEFAs and IMTGs continue to contribute to ATP production, but their relative contribution decreases with increasing exercise intensity.<sup>36, 37</sup> (Figure 3).

During exercise, skeletal muscle takes up blood glucose using insulin and exercise stimulated GLUT4 transporters. The activity and amount of GLUT4 transporters at the cell surface are increased during exercise and remain elevated after exercise training.<sup>22</sup> Myocellular hexokinase activity also increases during exercise.<sup>32</sup> However, the primary source of carbohydrate for myocellular energy metabolism is endogenous muscle glycogen.<sup>37</sup> The contribution of blood glucose during exercise depends on intensity, training state, and duration.<sup>1, 37</sup> The timing of exogenous carbohydrates, the subsequent insulin response, and the type of carbohydrates in accordance with the exercise bout can also influence glucose uptake, and ultimately oxidation of that carbohydrate in the muscle.

### ***Glucose Metabolism Overview***

This section will review the metabolic pathways to process glucose into ATP within liver and skeletal muscle cells. Once glucose is inside cells, it is phosphorylated by glucokinase in the liver or hexokinase in skeletal muscle. This phosphorylation step essentially “traps” glucose in the cell. Skeletal muscle does not have glucose-6-phosphatase and does not release glucose once it has been transported into the cell. Liver cells contain glucose-6-phosphatase, which allows

glucose release into circulation for HGO. Inside skeletal muscle and liver cells, glucose is a substrate used to produce ATP (oxidized) or stored as glycogen depending on the energy demand and/or glycogen level of the cell.

When ATP demand is increased, glucose enters glycolysis, which takes place in the cytoplasm of skeletal muscle cells. Glycolysis is a set of ten reactions which breakdown primarily glucose to produce two molecules of pyruvate, 2 NADH and 2 ATP. Other organic compounds can enter/leave the pathway at some intermediate steps. The first control step in glycolysis is the phosphorylation of glucose to glucose-6-phosphate by hexokinase/glucokinase. This is not a committed step in glycolysis, as glucose-6-phosphate can be converted to glycogen during rest, but during exercise as the tissue is working, glucose entering skeletal muscle is primarily used for ATP production. The first committed step in glycolysis occurs as fructose-6-phosphate is converted to fructose 1,6-bisphosphate by phosphofructokinase-1 (PFK-1) using an ATP. High levels of ATP allosterically inhibit PFK-1 activity, as the energy state of the cell is high. Exercise consumes ATP and thus lowers the ATP:AMP ratio as ATP is reduced in contracting skeletal muscle, removing the inhibition of PFK-1 so that glycolysis can proceed. The decreased ATP/AMP ratio also stimulates phosphofructokinase-2 (PFK-2) activity, which produces fructose 2,6-bisphosphate from fructose-6-phosphate and ATP. Fructose 2,6-bisphosphate activates PFK-1 to enhance the breakdown of glucose. The higher the energy demand of the skeletal muscle (intensity or work load) the lower the ATP/AMP ratio, and thus the more active glycolysis can become. However, lower pH in skeletal muscle can inhibit PFK-1 and PFK-2 as a feed back to potentially protect against muscle damage. Pyruvate and an ATP are produced by pyruvate kinase from phosphoenolpyruvate and ADP. Pyruvate is the end

product of glycolysis and can be further processed anaerobically to lactate or enter the Krebs cycle.<sup>13</sup>

High workloads are associated with increased production of intracellular lactate; however, there is always a low level of lactate produced in skeletal muscle. It was originally thought that the increased appearance of lactate at work rates at or above the “lactate threshold” was due to muscle hypoxia. Even though the conversion of pyruvate to lactate via lactate dehydrogenase occurs without the use of oxygen, oxygen delivery to the exercising skeletal muscle has not decreased.<sup>38</sup> The demand for ATP at these high intensities (above “lactate threshold”) is greater than oxidative phosphorylation can provide. The conversion of pyruvate to lactate regenerates NAD<sup>+</sup> so that glycolysis can continue to provide ATP. Improvements in the cell’s ability to complete oxidative phosphorylation increase the lactate threshold. Additionally, the lactate ion is not the cause of fatigue per se; however, the dissociated H<sup>+</sup> ions are related to fatigue, as the drop in pH inhibits glycolysis via PFK. Chronic exercise training can also increase buffering capacity. Lactate, along with alanine and glycerol, are important for maintaining blood glucose levels during exercise. These substrates are transported from peripheral tissues via the blood to the liver where they are used as precursors for GNG and HGO.

Pyruvate also can enter the Krebs cycle after being converted to Acetyl-CoA by the pyruvate dehydrogenase complex (PDH). Pyruvate dehydrogenase activity is regulated by the ratio of ATP/ADP, NADH/NAD<sup>+</sup>, and acetyl-CoA/CoA as well as pyruvate dehydrogenase kinase (PDK). Adenosine diphosphate, NAD<sup>+</sup>, and CoA all have a positive influence on PDH. Adenosine triphosphate, NADH, and acetyl-CoA all inhibit PDH activity. The “back up” of NADH and acetyl-CoA during high-energy demands are thought to activate PDK, which inhibits PDH and leads to greater production of lactate. Oxidation of substrate via the Krebs cycle yields

much more ATP than glycolysis can alone. Both carbohydrate and fat derivatives are oxidized in the Krebs cycle where acetyl-CoA is combined with oxaloacetate by citrate synthase to produce citrate. There are eight steps in the Krebs cycle. The amount of ATP equivalents produced by the complete oxidation of substrates depends partly on where they enter the pathway. Adenosine triphosphate equivalents from the Krebs cycle come in the form of GTP, as well as NADH, and QH<sub>2</sub>, which are used to produce ATP in the electron transport chain.

Carbons from IMTG and other lipids also are oxidized through the Krebs cycle. Their importance to endurance exercise is not the topic of this review, but their contribution as a substrate for ATP production in exercising skeletal muscle will be discussed later.

Additionally, the metabolism of energy yielding nutrients in the “anaerobic” and “aerobic” metabolic pathways discussed previously provide ATP needed to facilitate the actin-myosin cross-bridge formation and breaking during muscle contractions. One pathway not discussed above is the creatine kinase reaction, which catalyzes the reaction to re-phosphorylate ADP to ATP during the initial phase of high intensity exercise. It serves as a buffer to regenerate ATP quickly during the early phase (0 to 10 seconds) of high intensity exercise.

### ***Skeletal Muscle Substrate Metabolism during Exercise***

Skeletal muscle is a primary consumer of substrate during exercise, as it provides locomotion and relies on fuel from both intramuscular and extra-muscular sources to meet ATP demands. Skeletal muscle glycogen stores and IMTG are the primary intramuscular sources of energy yielding nutrients during exercise, while intramuscular amino acids contribute a small percent. Extra-muscular energy sources, from both dietary intake and liver, include glucose and non-esterified fatty acids (NEFA) with circulating triacylglycerols (TAGs) contributing as well.

Adipose tissue also contributes to plasma fatty acid availability during exercise, as catecholamines increase lypolysis.

The contribution of carbohydrate and fat to substrate oxidation depends on the hormone status, exercise intensity, duration, substrate storage state (glycogen and lipids), and fitness of the individual as well as exogenous macronutrient intake. The typical dietary pattern (low vs. high carbohydrate) influences the contribution of macronutrients to substrate oxidation. This section will focus on skeletal muscle substrate oxidation in the absence of exogenous fuel sources and will discuss the complicated effects of intensity, duration, and a brief note regarding fiber type. The effect of training on substrate oxidation also will be discussed, followed by sections examining the use of exogenous carbohydrates on skeletal muscle substrate oxidation and performance.

At rest, skeletal muscle relies more on fat for ATP production. In general, the reliance on carbohydrates as an energy source increases with increasing exercise intensity as well as increasing carbohydrate intake. While there are methodological concerns regarding some of the early tracer studies, the basic premises of increased reliance on carbohydrate metabolism with increasing exercise intensity and/or ingestion holds true. A study by Romijn<sup>21</sup> illustrates the use of plasma NEFAs during low intensity exercise between 25% and 65% of  $VO_{2max}$ . Fat metabolism from both NEFAs as well as IMTGs and lipoprotein derived TAGs provide the majority of substrate during low intensity endurance exercise and continue to provide up to 50% of the relative contribution to ATP formation at moderate intensities. At higher intensities (50 – 65%), carbohydrates contribute a greater relative and absolute amount to ATP production. Figure 3 from van Loon<sup>37</sup> illustrates the contribution of fat and glucose at 40, 55 and 75% of  $Watt_{max}$ . It is thought that at very high exercise intensities, the oxidation rate of both plasma

NEFAs and IMTGs decreases. It is suggested that CPT1 is down regulated by either a decrease in free carnitine or more likely the influence of the decrease in skeletal muscle pH at higher intensities.<sup>37</sup> This reduced ability to transport fat into the mitochondria is partially responsible for the decreased fat oxidation at higher intensities. Additional discussion regarding fat metabolism as it relates to intensity duration can be found in an article by Frayn.<sup>39</sup>

The ability to store energy, as fat in adipose tissue, is much greater than the ability to store energy as glycogen in muscle and liver and of skeletal muscle to store IMTGs. Since higher intensity exercise has a greater reliance on glucose as a fuel source, the role of exogenous glucose becomes apparent if exercise is going to continue at a high intensity.

As exercise duration increases from 1 hour to two hours and up to five or more hours, the contribution of fat to substrate oxidation increases, especially in the absence of exogenous energy/carbohydrate intake. This increase in reliance on fat oxidation is due to an increase in catecholamines and glucagon leading to increased adipose lipolysis, skeletal muscle uptake, and ultimately oxidation of NEFAs while glycogen and blood glucose levels decrease.<sup>40</sup> Exogenous carbohydrate intake during extended endurance exercise decreases NEFA delivery and fat oxidation.<sup>40</sup>

One of the primary causes of fatigue and/or less than optimal performance in the later stages of prolonged endurance exercise are the result of failure to maintain blood glucose (hypoglycemia) and/or reduced skeletal muscle glycogen content to maintain exercise at a given intensity. Hypoglycemia can be related to lack of adequate liver glycogen stores in combination with lack of adequate exogenous carbohydrate ingestion. Late in exercise, whole body glucose demands may over tax HGO via glycogenolysis and GNG via substrate from the exercising muscle. Hypoglycemia may affect both the skeletal muscle directly via reduced substrate to

maintain the level of oxidation or the central nervous system (CNS). The CNS relies on blood glucose and CNS fatigue has been suggested to play a role in exercise fatigue. High intensity ( $\geq 65\%$  of  $VO_{2max}$ ) relies on a higher contribution of skeletal muscle glycogen, and since there is a limited supply of this substrate, when it is reaching the debranching stage, supply cannot meet demand. Exercise must either decrease in intensity (work rate) or stop.

### ***Training on Metabolism of Substrate in Skeletal Muscle***

With training, athletes are able to produce more work, exercise at higher intensities, and exercise for longer periods of time. Chronic endurance exercise training has numerous benefits on skeletal muscle substrate metabolism. Factors contributing to increased skeletal muscle substrate metabolism are related to substrate and oxygen delivery to exercising skeletal muscle as well as increases in the ability of the skeletal muscle to use oxygen and oxidize substrate during exercise. Substrate storage (glycogen and IMTGs) also increases with endurance training. Briefly, oxygen delivery to exercising skeletal muscle is increased through endurance training via increases in oxygen carrying capacity and delivery. Increasing capillary density in the capillary bed near the exercising skeletal muscle allows for greater delivery of oxygen and removal of metabolic “waste” ( $CO_2$ , lactate) during exercise. Endurance training also increases hemoglobin and blood volume, which allows for greater oxygen carrying capacity. The increased blood volume also leads to an increase in stroke volume increasing cardiac output. Within the skeletal muscle, mitochondrial density increases, with a concomitant increase in key enzymes in the Krebs cycle. The increased oxidative capacity via increases in mitochondrial density, Krebs cycle enzymes, and oxygen delivery, allow skeletal muscle to oxidize a greater amount of fat during exercise up to a given intensity ( $\sim 65\%$ ). This increased ability to

metabolize fat results in reduced glycogen utilization and increases lactate threshold. The increased ability to oxidize fat at the same absolute workload as before training is well established.<sup>41-43</sup> Whether this adaptation translates to the same relative work rate (i.e. higher absolute work rate after training) is not fully established. There are data supporting both points of view. If the trained athlete is able to oxidize more fat at a higher absolute work rate, then they would be able to spare skeletal muscle, liver, and exogenous carbohydrate (glycogen/glucose). Muscle glycogenolysis has been shown to decrease after training at the same relative workload.<sup>44</sup> This decreased reliance on glycogenolysis might occur due to increased glycolysis of blood glucose as training increases glucose transport into skeletal muscle via an increase in GLUT4 transporters and transporter activity.<sup>22</sup>

### ***Questions Pertaining to Exogenous Carbohydrate Intake on Athletic Performance***

Improving athletic performance has been an interest of competitors for as long as there have been sporting competitions. It has long been known that carbohydrate feeding during exercise improves endurance performance.<sup>2</sup> The advent of methods and strategies to scientifically test nutritional supplements has allowed for the testing of many different feeding strategies, nutrient combinations, and timing of nutrient ingestion. Some of the primary questions are related to the type and amount (concentration) of carbohydrate to ingest to maximize performance while minimizing gastric disturbance. Those questions lend themselves to timing of ingestion and combinations of carbohydrates, fats, and proteins. The ability of supplement to increase carbohydrate oxidation while also increasing performance has also been addressed. Relatively novel areas of research are related to carbohydrate mouth rinses which are

thought to work centrally and the concept of “Train low – Compete high” with regard to skeletal muscle glycogen and enhancing skeletal muscle adaptation.

The primary outcome is to improve athletic performance by reducing metabolic and central factors that lead to fatigue. The role of endurance training and an overview of substrate use during exercise have been reviewed previously herein. This review will now focus on the literature regarding ingestion of carbohydrates during endurance exercise with regard to increasing oxidation of exogenous carbohydrates and improving performance. The primary mechanistic outcomes including maintenance of blood glucose and/or sparing of endogenous glycogen will be addressed where appropriate. This review will then focus on the role of oral sensors and central fatigue in endurance exercise performance.

### ***Methodology to Test Supplements for Endurance Athletic Performance***

The laboratory setting can be highly controlled when testing the effects of dietary interventions on athletic performance and has been used as the testing ground much more frequently than real life tests in the field. However, even in highly controlled and well designed experimental trials, small but meaningful performance outcomes may be hard to quantify.<sup>2</sup> While the metabolic response to exercise tends to be maintained, the mental aspect of exercise testing and day to day variations may override the ability of the testing procedure to find meaningful differences. Additionally, the method to measure athletic performance can vary from laboratory to laboratory. There are three primary methods to assess performance including: 1) Total time to exhaustion at a given work rate; 2) time to complete a set amount of work (kJ) or distance (km) at self-selected rate (sometimes completed after a set amount of work, time, or distance has been completed); 3) a self-selected pace simulating a race over a given distance

(km) or amount of work (kJ). Time to exhaustion studies tend to artificially expand differences between interventions and are not very applicable to actual sporting events. Time to complete a set amount of work or a time trial over a set distance is more applicable to actual endurance sports events. However, a small benefit of 10 – 20 seconds in an endurance test in a laboratory may not be statistically significant, but is often relevant in sport, where that time gap may separate the athletes finishing 1<sup>st</sup> and 10<sup>th</sup>. While there are multiple endurance sports wherein athletes can benefit from optimal nutritional strategies, the vast majority of data have come from the use of the cycle ergometer or treadmill running as the primary modes of exercise used to test relevant hypotheses.

The metabolism of ingested carbohydrates during an endurance exercise bout can be measured directly through the use of labeled tracers or indirectly via indirect calorimetry using RER or performance outcomes. The oxidation rate of ingested carbohydrates can be measured using either radioactive tracers such as [U-<sup>14</sup>C] glucose or stable isotopes such as <sup>13</sup>C enriched substrates.

The original method to trace the oxidation of ingested glucose used a known amount of added [U-<sup>14</sup>C] glucose tracer to a carbohydrate and measured the <sup>14</sup>C in expired gases using a scintillation counter. This method is rarely used due to the exposure of the participant to radioactive substances. A potential methodological problem inherent to tracing carbohydrate oxidation is the “trapping” of the labeled carbon in CO<sub>2</sub> within the bicarbonate pool. This has led to a potential underestimation of exogenous carbohydrate oxidation in exercise trials conducted below 60% of maximal oxygen uptake.

The use <sup>13</sup>C enriched substrates is the more commonly used method to assess exogenous carbohydrate oxidation. Some studies have taken advantage of the natural heavy carbon content

derived from C4 plants such as corn and cane sugar. One main problem with this method is that the measured expired  $^{13}\text{C}$  may actually originate from glycogen breakdown during exercise, which originated from the same “heavy” source. Some methods to account for background  $^{13}\text{C}$  content are: adding a greater amount of  $^{13}\text{C}$  to the carbohydrate drink; having participants abstain from foods containing  $^{13}\text{C}$  in the week or weeks prior to the test; or, to perform control trials where the participant ingests carbohydrates with low  $^{13}\text{C}$  compared to high  $^{13}\text{C}$ . These confounding factors were unknown in some of the early studies in this area, thus some of the early data should be examined carefully as exogenous carbohydrate rates tended to be overestimated.<sup>9</sup>

Many of the studies that are available have examined the effect of carbohydrate supplementation during exercise on the oxidation of exogenous carbohydrates without direct performance outcome measures. The increased availability and oxidation of exogenous carbohydrates are a driving factor in improving athletic performance especially in exercise lasting  $\geq 2$ -hr.

### ***Carbohydrate Ingestion Schedule or Pattern***

The goal of ingesting carbohydrates during endurance exercise is to maximize performance with minimal potential to cause negative outcomes. The ingestion of carbohydrates in the hours before exercise can potentially be detrimental to performance in some individuals. This is due to the insulin response to the ingested carbohydrates in combination with the catecholamine and exercise induced glucose disposal leading to decreased blood glucose concentration.<sup>45</sup> However, ingestion of very low glycemic index carbohydrates such as complex carbohydrate or fructose does not elicit this effect to the same degree. Additionally, some

individuals are less sensitive to the reduced blood glucose concentration that occurs early in exercise. A study by Jentjens et al.<sup>30</sup> has shown that cyclists consuming varying concentrations of glucose solution 45 minutes before exercise did not have a decrease in performance even though their blood glucose concentration was reduced significantly. Sensitivity to exercise/insulin induced hypoglycemia appears to be subjective and dependent on the individual, and potentially the mode of exercise. Additionally, the continued ingestion of carbohydrates during the pre-exercise and exercise period may counteract or reduce the hypoglycemic effect. The ideal situation is to ensure that glycogen stores are replete the day before exercise by consuming a high carbohydrate diet.<sup>46</sup> In the 2 hours leading up to competition, foods eliciting an insulin response should be limited or avoided if an individual has experienced negative outcomes due to reduced blood glucose during the initial stages of exercise.

The amount, concentration, and dosing pattern of carbohydrate ingested during exercise can have both positive and negative effects on exercise performance due to maximal carbohydrate delivery to working tissue and gastric distress, respectively. Ingestion of a single dose of glucose consumed at the onset of exercise leads to some oxidation of the ingested glucose within five minutes<sup>9</sup> indicating that the glucose has been absorbed and is available for use as an energy substrate. During the first 75 to 90 minutes of exercise after a single dose of glucose, glucose oxidation rate continues to rise until it plateaus at about 0.9 to 1.1 g/min.<sup>9</sup> This rate of glucose oxidation is also experienced after a large dose of carbohydrates (over 60 g/h ingestion rate). However, these large single doses of glucose can be associated with a feeling of fullness and other gastric symptoms, which may actually hinder performance.

Repetitive feeding schedules are often used for various reasons. It has been shown that repeated feedings of a large total dose split into multiple smaller doses can increase the rate of

gastric emptying.<sup>47, 48</sup> Also, small frequent feedings during exercise may alleviate potential nausea and other gastric distress at high intensities and has been shown not to limit carbohydrate oxidation rate as long as the overall delivery rate is maximized.<sup>9, 49, 50</sup>

A study conducted by McConell et al.<sup>51</sup> examined calorie matched carbohydrate supplementation ingested either throughout the exercise bout or only late in exercise. Performance in a 15-minute performance ride after 2 hours of steady state cycling was improved only when carbohydrates were ingested throughout the exercise bout. This study and others discussed below support the notion that carbohydrate supplementation must begin near the beginning of exercise to maximize performance benefit. If ingestion of carbohydrates is started late (over 2 hours) into continuous exercise, it appears that the maximum performance benefits are lost potentially due to already decreased liver and muscle glycogen levels. The length of acceptable delay in ingestion of carbohydrates to still maintain a performance benefit is unknown. However, late ingestion of carbohydrates remains beneficial compared with no ingestion of carbohydrates during long duration exercise.<sup>52</sup> Coggan and Coyle<sup>52</sup> fed cyclists either carbohydrate solution or placebo after 135 minutes of exercise at 70% of  $VO_{2max}$  (fatigue) and found that the carbohydrates restored blood glucose concentrations and allowed cyclists to continue for 21% longer than placebo.

### ***Types of Carbohydrate Supplements for Exercise***

There are numerous carbohydrate sources and supplements available for athletes to consume before, during, and after endurance exercise. These include sport drinks (Gatorade®), sport beans (Jelly Belly®), gels (GU, Nestlé Powerbar®), gummies (Clif Bloks®) and the original carbohydrate source, real food (fruit, bagels, sandwiches, etc). Ideal products are

palatable, easy to use during exercise, taste good, and actually improve performance. This review will focus on carbohydrates as they relate to performance during an endurance exercise bout. However, the state of glycogen repletion and carbohydrate intake before exercise will be discussed, but not fully reviewed. A brief discussion of post-exercise recovery strategy will be included. The carbohydrate source that has been clinically tested the most is glucose. However, there are many sources of carbohydrate that have been tested including fructose, high fructose corn syrup (HFCS), corn syrup, maltodextrins, honey, and galactose. There are less data regarding the use of food sources on athletic performance directly in a laboratory setting.

### ***Glucose and Glucose Polymers on Carbohydrate Oxidation***

Glucose is a carbohydrate that, when ingested, needs no additional digestion and is absorbed and available for oxidation in skeletal muscle very readily. The absorption of glucose in the small intestine appears to be the limiting factor in its availability as an exogenous source of energy (Figure 4). Even large doses given at the initiation of an exercise bout tend to peak at 0.9 to 1.1 g/min of oxidation.<sup>9</sup> Maltose, a glucose polymer composed of two glucose molecules, essentially behaves the same as glucose during exercise.<sup>53</sup> Longer glucose polymers such as maltodextrins<sup>9,54</sup>, amylopectin<sup>55</sup>, and even high molecular weight glucose polymers<sup>56</sup> appear to be oxidized at a similar rate to glucose during exercise. The digestion and absorption of these glucose polymers does not appear to limit their availability for oxidation during exercise compared to glucose. Overall, glucose and glucose polymers ingested at a rate of up to 60 to 70 g/hr will maximize availability and oxidation of these carbohydrate sources during exercise. Higher ingestion rates (or absolute amounts) do not appear to provide additional benefits and may cause gastrointestinal distress.<sup>1</sup>

Amylopectin and amylose are two starches that make up the carbohydrate content of some foods that have been tested in an exercise setting. Amylopectin is highly branched, and this branching allows for much quicker digestion compared to the straight glucose chains in amylose. Foods such as corn, potatoes, rice, and wheat contain a mixture of amylose and amylopectin. In a study that compared the oxidation rate of 23:77 amylose:amylopectin ratio to 100% amylopectin found that peak oxidation rates after 316 g were ingested over 2.5-hr of cycling to be 0.8 and 1.1 g/min respectively.<sup>55</sup> This mixture was reported to cause some gastrointestinal distress among participants in the study.

### ***Galactose on Carbohydrate Oxidation***

Galactose is a sugar that is found primarily in milk products. Due to galactose being part of milk products, and milks inherent propensity to spoil, galactose has been largely ignored in the athletic performance literature. One study<sup>57</sup> did compare galactose oxidation to glucose oxidation during exercise at 70% of maximal oxygen uptake and reported that galactose oxidation was one-half that of glucose. Galactose appears to be an inappropriate carbohydrate for use during athletic performance if performance and carbohydrate availability are the goal.

### ***Fructose on Carbohydrate Oxidation***

Dietary fructose is not a direct source of fuel for skeletal muscle as it is primarily taken up by the liver and phosphorylated into fructose-1-phosphate via fructokinase or phosphorylated into fructose-6-phosphate by glucokinase. Fructokinase is not regulated by energy status in the liver which leads to the vast majority of ingested fructose being taken up by the liver.<sup>58</sup> Fructose can be used by the muscle directly if it is infused, thus bypassing the liver first pass. Fructose

ingestion does increase systemic plasma fructose levels to  $\leq 0.5\text{mM}$ .<sup>58</sup> Additionally, a small amount (10 – 30%) of ingested fructose is converted to glucose, lactate, or alanine by the intestinal epithelium.<sup>18</sup>

While not a direct supplier to myocellular ATP production, fructose has been a carbohydrate of interest for athletic performance for a variety of other reasons. Fructose is sweeter than glucose, and can add palatability to a drink or supplement. Performance outcomes aside, positive sensory characteristics may increase fluid intake and make a product more marketable. Fructose has been shown to produce a 20 – 30% smaller increase in plasma insulin levels compared with glucose,<sup>59</sup> resulting in less inhibition of lipolysis.<sup>9</sup> Fructose consumed during the pre-exercise period, with its lower insulin response, can reduce the rebound hypoglycemia that some individuals experience when they ingest carbohydrates that can elicit an untoward insulin response prior to the commencement of exercise. One negative aspect of fructose ingestion is malabsorption in some individuals with as many as 40 to 80% of individuals showing some ill effects of fructose ingestion with doses as low as 15 g.<sup>60</sup> However, these negative outcomes often do not occur when fructose is ingested with glucose, starch, or as part of another sugar such as sucrose.<sup>9, 11</sup> The combination of fructose and glucose facilitates fructose absorption<sup>61</sup>, and a 2:1 ratio of glucose to fructose appears to minimize malabsorption and maximize oxidation of exogenous carbohydrate.<sup>1, 11</sup>

Large doses of fructose ingestion alone are not advised as it can lead to malabsorption and negative gastrointestinal effects. The oxidation of fructose alone is approximately 25% less than a similar dose of glucose.<sup>9</sup> Since fructose is taken up more readily by the liver, high doses of fructose ( $\geq 0.6\text{ g/min}$ ) tend to increase blood lactate concentrations during exercise.<sup>12, 35, 62, 63</sup> Fructose ingestion during exercise may also lead to greater liver glycogen sparing as more of this

substrate is taken up by the liver. However, this hypothesis is largely untested in humans due to the invasiveness of a liver biopsy.

### ***High Fructose Corn Syrup (HFCS) and Sucrose on Carbohydrate Oxidation***

High fructose corn syrup (HFCS) is a product that has been increasingly added to the American diet.<sup>16</sup> High fructose corn syrup is produced by hydrolyzing corn syrup (glucose only) into individual glucose units and then enzymatically converting glucose to fructose. Thus, the end product is individual units of glucose and fructose typically consisting of 42% or 55% fructose. Thus, HFCS is primarily glucose with the remaining portion fructose and is typically available in two ratios (58:42 or 45:55). Both of the sugars exist as monosaccharides and have favorable flavor and food chemistry properties that sucrose does not. However, the disaccharide sucrose is made up equally of glucose and fructose sugars. The hydrolysis of sucrose into glucose and fructose is very fast, thus it behaves very similarly to HFCS in the small intestine and upon absorption.

There are not many studies that have investigated sucrose or HFCS alone as far as oxidation or endurance athletic performance. Studies have tested the effects of multiple combined carbohydrate sources, which will be discussed below. In a study by Wagenmakers et al.<sup>64</sup> participants consumed 8% sucrose while cycling at 65%  $\text{VO}_{2\text{max}}$ . They ingested 145 g of sucrose over the 2-hr cycling bout and oxidized approximately 81 g at a peak rate of 0.87 g/min. It appears that even high doses of sucrose are oxidized at a similar rate to glucose. This may be due to the 1:1 ratio of glucose:fructose in sucrose. There are no studies this author could find indexed in Web of Science or Pubmed that used HFCS alone to study oxidation or performance during endurance exercise. A recent study conducted in the Metabolism and Sports Science

laboratory at Kansas State University compared HFCS to three other carbohydrate supplements, a caffeine supplement, and an artificially sweetened placebo on performance, but did not measure oxidation directly. Participants completed a 45-minute cycling bout at 56% of  $Watt_{max}$  followed by a simulated 10-km time trial at a self selected pace. There were no performance differences in time to complete the 10-km time trial between HFCS, processed honey, glucose, nor raw Honey (unpublished data).

### *Honey*

While honey has been consumed for centuries, it has only recently been tested as a supplement for endurance exercise performance. Recent interest in honey as a sports supplement may originate from the fact that it is a “natural” carbohydrate source and has a lower glycemic index rating compared to glucose and sucrose. Other health benefits outside of athletic performance have been attributed to honey with varying degrees of scientific support. There is some evidence that honey ingestion can reduce makers of inflammation<sup>65</sup> and act as an antioxidant,<sup>66</sup> which may improve recovery from athletic activity. Nonetheless, honey is a carbohydrate composed mainly of glucose and fructose. The exact carbohydrate concentration depends on the botanical origin and processing.<sup>66</sup> Natural honey also contains organic acids, proteins, amino acids, minerals, polyphenols, and vitamins. Processed honey commonly found in supermarkets is processed and diluted with HFCS such that 51% of the honey has been filtered and heated and the remaining 49% is HFCS. There appear to be no published studies that have examined the effects of honey ingestion on carbohydrate oxidation to this author’s knowledge. However, with the composition of honey being similar to sucrose, it would be safe to assume that oxidation is similar to these known supplements. However, differences in glucose: fructose ratio

would likely influence absorption, and thus oxidation rate of ingested honey especially when higher doses are consumed.

There are limited data that illustrate the effects of honey on athletic performance. A recent study by Earnest et al.<sup>67</sup> examined the effects of ingestion of 15 g of honey, dextrose, or placebo gel and 250 mL of water consumed every 16-km of a 64-km time trial. Participants completed the exercise trial 4 hours after a standard higher carbohydrate meal. There was no significant difference in performance times between treatments, but both carbohydrate sources had a trend ( $P = 0.08$ ) toward decreasing time/increasing average wattage during the time trial. While not statistically significant, the time difference of 2 minutes over this distance could be the difference of 10 or more places in an actual race. A recent study by Snyder et al. (unpublished data) examined the effects of processed honey, unprocessed raw honey, glucose, HFCS, and placebo on 10-km time trial performance after 45 minutes of cycling at 56% of  $\text{Watt}_{\text{max}}$ . There was no statistical difference in performance between supplements.

### ***Multiple Transportable Carbohydrates on Oxidation during Endurance Exercise***

The idea to investigate combinations of glucose and fructose during endurance exercise trials stems from their use of differing transporters during absorption.<sup>68</sup> The rate of absorption of exogenous carbohydrates from the gut partially determines their availability in systemic circulation, and thus increased absorption using multiple transportable carbohydrates to potentially increase exogenous carbohydrate oxidation was investigated. When one carbohydrate is ingested, oxidation appears to peak at approximately 1.0 g/min even when higher doses are ingested. When multiple transportable carbohydrates are ingested, the rate of carbohydrate oxidation can reach 1.75 g/min<sup>1</sup>. The combination of two or more carbohydrate

sources which rely on different transporters increased carbohydrate oxidation.<sup>1</sup> The greatest oxidation efficiency<sup>9</sup> was seen when glucose and fructose were ingested at a rate of 144 g/hr to result in a peak oxidation of 105 g/hr. Thus, it appears that carbohydrate combinations of glucose and fructose increase oxidation of carbohydrate during prolonged endurance exercise. Many studies in this area do not report gastric effects of carbohydrate supplements during endurance exercise. With the limited data, it is difficult to suggest the best combination regarding negative gastric effects of supplements. However, the combinations of carbohydrates with the greatest efficiency for absorbance and oxidation should have the least negative gastric effects as the time in the gut is lowest for these supplements. In fact, participants tend to experience less negative gastric effects when consuming a combination of glucose and fructose drinks compared to glucose alone.<sup>1</sup>

### ***Carbohydrate Ingestion on Performance during Exercise Lasting More Than 1 Hour***

There are many nutritional factors that can influence endurance athletic performance. Overall, increasing exogenous carbohydrate delivery without inducing gastric problems should increase performance during long endurance events. This is the accepted conclusion and has been shown in numerous studies.<sup>35, 52, 69-73</sup> However, the measured performance outcome (time to exhaustion vs. time trial), carbohydrate dose, schedule of ingestion, and source, as well as gastric problems can contribute to results which do not support this conclusion.<sup>74-76</sup>

From the available data, the lowest doses of carbohydrate that elicit a positive performance outcome are 16 to 22 g/h.<sup>2, 73, 77</sup> These doses are likely sufficient to increase endurance performance under certain circumstances, but have not always shown to be sufficient.<sup>78</sup> Higher doses are more likely to increase performance, but a balance between

performance benefits and potential negative gastric effects needs to be examined. The dose responsible for a negative gastric effect tends to be highly specific to the individual and depends on the concentration of carbohydrates, the type of carbohydrate, and the intensity of the exercise bout. Many of the studies available have not recorded or reported negative gastric effects in their reports. A recent study by Snyder et al. reported that some participants expressed gastric complaints with glucose gels at a dose as low as 30 g total provided as four, 7.5 g doses accompanied by 180 mL of water. The intake of doses of single types of carbohydrates up to 60 to 70 g/min appears to be the maximum that can be ingested without negative gastric outcomes in some individuals.<sup>1</sup> A balance between intake and gastric effects appears to be a major concern and warrants further investigation and personalization as individuals react differently to carbohydrate intake during endurance exercise. The performance dose response of carbohydrate ingestion is likely dependent on both carbohydrate availability and gastric response.

In a study by Mitchell et al.<sup>78</sup> participants cycled for 105 minutes at 70% of  $VO_{2max}$  followed by a 15 min time trial. Performance was improved only in the group who consumed a 12% solution (74 g CHO total), consisting of 8.5% glucose and 3.5% fructose. When the participants consumed 6% (37 g CHO total 4% glu:2% sucrose) or 18% (111 g CHO total 14.5 glu:3.5fructose) there was no performance benefit. While they did not measure gastric emptying or distress they conclude that these gastric effects may be impairing the effects of the supplement on performance. A recent study by Smith et al.<sup>79</sup> examined the effects of 15, 30, or 60 g/hr ingestion of glucose in 1.5, 3.0, or 6.0% solution split into 250 ml doses consumed every 15 minutes during a 2-hr ride at 77% of  $VO_{2max}$  followed by a 20-km time trial. They concluded that there was a dose response with all supplements increasing performance compared to

placebo. The higher the dose, the more likely the participant was to improve power output during the time trial.

A study by Currell and Jeukendrup<sup>70</sup> examined the effects of ingesting either water, glucose (1.8 g/min), or a glucose:fructose (2:1 1.8 g/min) beverage on performance in a time trial following 2 hours of cycling at 55%  $Watt_{max}$ . The combined ingestion of the glucose:fructose beverage lead to an 8% increase in performance compared to glucose alone and a 19% increase compared to water placebo. Additionally, participants in the glucose plus fructose group expressed fewer symptoms of gastric distress.

Overall, the use of combined carbohydrates at the highest dose acceptable to the individual should have the best likelihood of increasing performance. The likelihood of a positive effect appears also to be dependent on duration of the event with a greater performance benefit resulting during long events. More data are needed to determine the best dose for a given event to elicit the best improvement in performance. However, the consensus is that carbohydrate ingestion greater than 16 g/hr is likely to benefit endurance performance compared to no carbohydrate ingestion during exercise. Individual athletes and coaches will have to determine the optimal strategy to maximize performance and minimize potential gastric effects.

### ***Carbohydrate Ingestion on Performance during Exercise Lasting 1 Hour or Less***

The overall benefit of ingesting carbohydrates during endurance exercise lasting more than 1.5 to 2 hours is well accepted. The benefits of carbohydrate ingestion during short (15 minute) to moderate (1-hr, 15 min) exercise bouts is equivocal. Some studies illustrate a clear performance benefit compared to placebo<sup>80-84</sup> and others have shown no improvement.<sup>85-89</sup> While the primary benefit of ingesting carbohydrates during long endurance exercise bouts is

attributed to the continued availability of exogenous glucose and maintenance of blood glucose, glucose levels do not decrease during the first hour of endurance exercise even in the absence of an exogenous carbohydrate intake.<sup>21</sup> The amount and type of carbohydrate ingested during the first hour of endurance exercise determines the rate of glucose rate of appearance in systemic circulation but the rate of appearance is relatively low during the first hour of exercise, and may be as low as 5 to 15 g.<sup>2</sup> Additionally, short athletic events tend to be completed at very high absolute work rates in excess of 85% of  $\text{VO}_{2\text{max}}$ , which can further reduce absorption, and thus availability of ingested carbohydrates. However, carbohydrates have been shown to have ergogenic effects during exercise bouts lasting less than 60 minutes and at intensities greater than 75% of  $\text{VO}_{2\text{max}}$ .<sup>80-84</sup> The contribution of endogenous stores of muscle and liver glycogen to total carbohydrate oxidation far outweigh the contribution for exogenous sources during these exercise bouts. Therefore, the ergogenic effects of carbohydrate administration cannot be wholly explained by carbohydrate oxidation and maintenance of plasma glucose concentration as observed in longer endurance exercise bouts since carbohydrate oxidation and plasma availability are not limiting factors during shorter duration exercise in well-trained athletes.<sup>90</sup> These observations lead to the speculation that carbohydrate ingestion during exercise may have central effects modulating motivation or motor output via an oral or gastric mechanism.

### ***Carbohydrate Mouth Rinse and Oral Carbohydrate Sensing***

Two recent exercise studies by Carter et al.<sup>90, 91</sup> were carried out to rule out the role of increased exogenous carbohydrate available for oxidation on performance and uncover the location of potential central effect receptors. The effect of increased glucose availability during 1-hr of cycling was examined by infusing a 20% glucose-saline solution or a glucose-

free saline solution to 6 endurance athletes cycling at 75%  $W_{max}$ .<sup>90</sup> There was no performance benefit associated with the increased blood glucose level despite increased glucose uptake into the skeletal muscle and carbohydrate oxidation. These data led to the hypothesis that the role of carbohydrates on short endurance performance is centrally modulated and is signaling through the mouth or gastric region. To test the role of carbohydrates in the mouth, Carter et al.<sup>91</sup> used a similar exercise protocol while participants swished a 6.4% maltodextrin solution or an indistinguishable placebo in their mouth for 5 seconds before expectorating into a bucket approximately every 7.5 minutes of the 1-hr time trial. This method allows only minimal if any carbohydrate to enter the stomach. The participants in this study showed a 2.8% increase in performance (less time to complete set amount of work) when they rinsed their mouth with the carbohydrate solution. This was one of the first studies to show a performance benefit using a carbohydrate mouth rinse, likely indicating an oropharyngeal mechanism that is “sensing” carbohydrate availability.

The role of carbohydrate solution on activating areas of the brain to improve performance is becoming clearer. A study by Chambers et al.<sup>92</sup> reported that both sweet (glucose) and non-sweet (maltodextrin) carbohydrate solutions improved performance when compared to indistinguishable placebos. It has been proposed that the anterior cingulate cortex (ACC), the insula/frontal operculum, and the striatum, in part, are responsible for the effect. The activities of these areas of the brain are related to ratings of perceived exertion (RPE). The study by Chambers et al.<sup>92</sup> illustrated that glucose and maltodextrin activate the ACC. Activation of ACC, via carbohydrate intake or mouth rinse, may reduce perceived effort, allowing the athlete to produce more work at the same RPE during short duration, high intensity exercise. The role of carbohydrate compounds rinsed in the mouth on improving exercise performance is thought to

be expressed via a positive afferent signal, which modifies motor output. Moreover, that positive afferent signal may be assisting the body to increase work (watt output) at a given rate of perceived exertion (RPE) so that cyclists are able to produce more work for the same perceived work rate. However, the concentration of the solution used in the fMRI studies was more concentrated (18%) as compared to many of the performance studies (6 – 6.4%).

The study by Chambers et al. also reported that the neural responses did not occur with sweet-tasting, non-caloric saccharin.<sup>92</sup> Since the artificial sweeteners were recognized as sweet by the participants but failed to activate the same areas of the brain as glucose and maltodextrin, these authors suggest that there may be a class of yet to be identified oral receptors that respond to caloric content of carbohydrates independent of sweetness. Rodents given free choice of either low concentrations of maltodextrin, sucrose, maltose, glucose, or fructose preferred maltodextrin.<sup>93</sup> Whether these same receptors are present in humans is unknown.

Two recent studies examined the discrepancy in the literature regarding the results from ingestion and mouth rinse studies. A study by Pottier et al.<sup>94</sup> tested the effects of ingestion or mouth rinse of a carbohydrate/electrolyte drink (CES) or artificially sweetened electrolyte drink. The four conditions were CES rinse, placebo rinse, CES ingestion, and placebo ingestion. The supplement was either rinsed for 5s or ingested at the beginning and after each 12.5% of the 1-hr time trial. Supplement was ingested at a rate of 1.5 mL/kg and each 100 mL contained 5.4 g sucrose, 0.46 glucose and electrolytes. The CES mouth rinse significantly improved time trial performance compared to placebo rinse. There was no effect of ingestion compared to placebo ingestion. These authors speculate that time in the mouth, i.e. 5 seconds vs. < 1 second, may play a role in the performance outcome via oral sensors. More data are needed to determine the effect of time in the mouth on performance. A recent study by Rollo et al.<sup>95</sup> examined the effects

of ingesting or mouth rinsing a 6.4% maltodextrin solution during a 1-hr performance run after an overnight fast (14 – 15-hr). The transit time in the mouth was standardized in both the mouth rinse and the two ingestion trials by having participants swish the final sip of the beverage for 5 seconds. Participants covered more distance when they rinsed followed by ingesting the maltodextrin solution compared to when they ingested and rinsed the placebo solution. There was no difference between the maltodextrin mouth rinse trial and the rinsing followed by ingestion of the placebo solution trial. This is an interesting finding, but appears to add support to the thought fluid replacement and carbohydrate administration may be additive in enhancing performance.<sup>82</sup> It is possible that ingestion of the placebo solution provided a performance benefit in the Rollo study,<sup>95</sup> which caused the observed performance difference in the mouth rinse trial to be insignificant. However, the study of Pottier et al.<sup>94</sup> does not support these findings as the participants in their study improved performance with mouth rinsing only and showed no performance benefit upon ingestion. Clearly more data are needed to better understand these variables including the frequency of administration, the total amount of fluid, the temperature during which the exercise bout took place, and the amount of time the solution spends in the mouth.

While supplementation during exercise is important, the nutritional status of the participants prior to the exercise performance trials appears to influence the ability of carbohydrate administration to improve performance. It seems that carbohydrate mouth rinsing<sup>96</sup> or ingestion<sup>85, 87, 89, 97, 98</sup> generally do not improve performance when the exercise trial is completed within 3-hr of a higher carbohydrate meal. The pre-exercise fast and nutritional status has been reported to impact cortical activation. A study by Haase et al.<sup>99</sup> reported greater activation of numerous brain regions after an overnight fast in response to carbohydrates

compared to after a 700 kcal liquid meal. Variations of gut hormones including ghrelin, peptide YY, and leptin are reported to modulate areas of the brain related to satiety and pleasure.<sup>100, 101</sup>

A recent study by Beelen et al.<sup>96</sup> found no effect of carbohydrate (maltodextrin) mouth rinse using the same methods as Carter et al.<sup>91</sup> but in the postprandial state (2-hr after a standard meal) as opposed to fasted state. A lack of performance benefit has also been shown in a running trial by Rollo et al.<sup>98</sup> conducted 3-hr after a standard meal. A recent study by Snyder et al. (unpublished data) compared the effects of carbohydrate mouth rinsing in the fasted and fed state. Participants completed a 1-hr time-trial while rinsing their mouth every 7.5 minutes with a 6.4% maltodextrin-lemon juice solution or indistinguishable placebo after an overnight fast (10-hr) or 2-hr after a standardized high carbohydrate meal. There was no significant performance benefit of carbohydrate mouth rinsing observed. A study by Whitham and McKinney<sup>102</sup> also failed to show a performance benefit of mouth rinsing with a maltodextrin-lemon juice solution during an approximate 1-hr running time-trial conducted 4-hr after a standard meal. The use of lemon juice (citric acid) is a potential unforeseen factor complicating the interpretation of the results from these two studies. A study by Haase et al.<sup>99</sup> reported that sucrose and citric acid activate similar areas of the brain but citric acid showed a reduced activation of the orbitofrontal cortex compared to sucrose. It is also of interest to note that citric acid imparts a sour taste in the mouth and was reported as moderately unpleasant by participants in the Haase study. It is possible that divergent brain activities and unpleasant taste stimuli related to citric acid can influence the results from these performance studies.<sup>99</sup>

### ***Potential Mechanisms for Improved Performance***

Several mechanisms by which carbohydrates may improve exercise and sport performance have been mentioned and include maintenance of blood glucose, increased levels of carbohydrate available for oxidation, potential sparing of endogenous glycogen stores (liver or muscle), and central affects manipulating RPE. It seems apparent that continued ingestion of higher rates ( $\geq 60$  g/hr) of carbohydrate would allow for continued exercise during long exercise bouts. This is most apparent in a study by Jeukendrup et al.<sup>35</sup> in which participants cycled for 5 hours at 58% of  $VO_{2max}$  while consuming water, 1.5 g/min glucose, or a 2:1 ratio of glucose:fructose at 1.5 g/min. Both carbohydrate supplemented groups were able to maintain blood glucose levels throughout the 5 hours, while blood glucose steadily dropped after 1-hr in the water only trial. Three subjects were unable to complete the water-only trial as they were unable to maintain the work rate and essentially were unable to continue exercising due to reduced blood and skeletal muscle carbohydrate content. It would be interesting if the muscle glycogen levels of these participants, who were unable to continue, were reported as the critical muscle glycogen concentration at failure is 25 mmol/kg w.w.

For short, intense workouts, endogenous glucose content is sufficient to meet oxidation needs if glycogen content is replete before the start of exercise. The role of oral receptors, and more specifically the ACC, in the brain may be partially responsible for the athletic performance benefits seen in shorter, high intensity trials. Thus, the nutrition, and subsequently the gut hormonal status, may be influencing the results of studies examining the central response during these short exercise bouts. An unpublished question, to our knowledge, is whether the oral receptors are re-activated late (2+ hr) in exercise in the absence of carbohydrate intake. This may be important because liver glycogen is reduced late in exercise in the absence of

carbohydrate intake and may influence the ability of carbohydrate to activate oral sensors. While the long duration exercise studies may provide mechanistic insight into some metabolic situations, many athletes exercise for an hour or less. Thus, more data are needed on performance and metabolic parameters that occur in shorter, intense bouts of exercise especially when these exercise bouts are completed with suboptimal glycogen stores.

Carbohydrate feedings tend to spare liver glycogen while simultaneously maintaining blood glucose levels. Hepatic glucose output is regulated mostly by insulin and glucagon in the fasting state. During exercise, the regulation of HGO is more complicated as insulin is suppressed and glucagon and catecholamines are increased. When carbohydrates are ingested during exercise, there is a progressive decrease from liver glycogenolysis and gluconeogenesis with increasing rates of carbohydrate intake<sup>103</sup> limiting or stopping HGO.<sup>104</sup> This liver glycogen sparing effect can benefit athletes late in exercise if the athlete has more distance to cover but does not ingest a source of exogenous fuel. Hepatic glucose output can temporarily maintain blood glucose until a carbohydrate source is ingested or exercise ceases.

Understanding the role of carbohydrate ingestion on skeletal muscle glycogen breakdown and or sparing has been a complicated issue with data illustrating either a sparing effect or no effect. The first study to show that carbohydrates spare muscle glycogen was a classic study by Bergstrom and Hultman<sup>105</sup> which showed a 25% reduction in skeletal muscle glycogen breakdown during one-legged cycling. However, glucose was infused at a rate of 21 mM/L which is a supraphysiological dose, yielding both hyperglycemia and hyperinsulinemia, which likely contributed to the results.

Factors complicating the understanding of the role carbohydrate metabolism plays during exercise include: the intensity and duration of the exercise bout; the dose of carbohydrate and

subsequent insulin response; the measurement technique; and ability to separate out the effect of fiber type. These issues appear to be at the root of the differing results between studies. For example, greater exercise intensities utilize more skeletal muscle glycogen (Figure 2), and longer duration exercise tends to deplete muscle glycogen (Figure 3).

That said, there are several studies that have used the biopsy method<sup>75, 78, 106, 107</sup> or stable isotope method<sup>103, 104</sup> to measure skeletal muscle glycogen and have reported no effect of carbohydrate intake on sparing of skeletal muscle glycogen. Conversely, there are studies which have shown reduced muscle glycogen breakdown with carbohydrate administration during cycling<sup>108, 109</sup> and running.<sup>110</sup> Fiber type of the muscle tissue is another factor that may contribute to conflicting data. A study by Tsintzas et al.<sup>110</sup> found that skeletal muscle glycogen breakdown was reduced in type I muscle fibers after 60 minutes of treadmill running at 70% of VO<sub>2</sub>max with carbohydrate intake with no effect on glycogen content in type II fibers. In a follow up study, the depletion of carbohydrate content in type I fibers coincided with fatigue.<sup>111</sup> Additionally, the amount of skeletal muscle glycogen spared was also shown to be related to the magnitude of the insulin concentration in the first 20 minutes of exercise.<sup>111</sup> Typically, type I fibers are responsible for the majority of energy consumption (work) during long, sub-maximal exercise bouts. Type II fibers are recruited to less of an extent during long, lower intensity exercise, but their recruitment may increase late in exercise as type I fibers have reduced glycogen stores and begin to fatigue.<sup>112</sup>

Additionally, increased insulin response to carbohydrate feedings at the onset or prior to exercise as well as intermittent exercise has been shown to play a role in glycogen sparing. The changes in glucose uptake due to increased insulin may allow for metabolic changes that reduce skeletal muscle glycogen use during exercise. Intermittent exercise has periods of reduced ATP

demand during rest or decreased exercise intensity that may allow glucose transport to “catch-up” with glucose demand, resulting in spared muscle glycogen.<sup>113</sup>

A study by Stellingwerff et al.<sup>40</sup> supports the notion of fiber type, timing, and insulin response on muscle glycogen sparing. During 3 hours of cycling at 63% of  $VO_{2max}$ , muscle glycogen use was reduced during the first hour of cycling, coinciding with increased insulin and blood glucose concentrations. Additionally, they found that carbohydrate ingestion reduced glycogen use in both type I and type II fibers. Overall, carbohydrate intake has been shown to benefit athletic performance so long as the dose is large enough and does not cause gastric distress, which reduces the ability of the athlete to produce work. The debate as to whether or not carbohydrate intake spares muscle glycogen appears to be more academic than practical as the continued availability of exogenous carbohydrates is sufficient to maintain exercise performance. Nonetheless, more data are needed to better understand these metabolic issues.

### ***Fructose and IGFBP-1***

As discussed previously, dietary fructose is taken up more readily by the liver than glucose during the first pass. Fructose in the liver is more readily converted to liver glycogen than dietary glucose.<sup>16</sup> Whether dietary fructose can further decrease liver glycogen depletion is not fully understood, but the preference for fructose in the liver as a metabolic substrate makes this a plausible hypothesis. Additionally, during exercise fructose can be converted to lactate, converted to glucose for HGO, or oxidized in the liver.<sup>17</sup>

IGFBP-1 is a binding protein that is responsive to nutritional, metabolic, and exercise factors. It is inversely related to insulin at rest<sup>114</sup> and has been shown to be inversely related to liver glycogen content during exercise in rats.<sup>115</sup> It has been reported that IGFBP-1 demonstrate

a dose-response relationship to aerobic exercise of moderate intensity in humans<sup>116</sup> which likely indicates its relation to liver glycogen status. IGFBP-1 is typically bound to IGF-1 and prolongs its half-life. Both IGF-1 and IGFBP-1 play a role in the regulation of blood glucose via binding to receptors that increase glucose uptake directly or by modulating insulin signaling through the PI3-K pathway.<sup>114</sup> IGFBP-1 is also regulated by glucocorticoids, and has been suggested to direct IGF-1 to skeletal muscle during prolonged exercise.<sup>117</sup>

### ***Train Low Compete High***

“Train low, compete high” has nothing to do with altitude, but it pertains to nutritional and metabolic strategies aimed at improving endurance performance. It is a novel method of training during which an athlete trains in a low or glycogen depleted state and then competes in a glycogen replete state. This review has not discussed the effect of glycogen state on exercise performance thus far as the vast majority of research pertaining to athletic performance employs athletes in the glycogen replete state. The belief that athletes have to train with optimal, or increased, glycogen levels to be able to train for long durations and at high intensities is well known. The idea to train in a glycogen lowered or depleted state stems from the observation that training “low” increases the translation, transcription, and mRNA expression for various metabolic and stress related genes.<sup>118-120</sup>

A study by Hansen et al.<sup>121</sup> illustrated that in untrained individuals, performance as time to exhaustion at 90% of maximal power was almost doubled in the low glycogen trained leg compared to the glycogen replete trained leg when both were tested in a glycogen replete state. Another study by Yeo et al.<sup>122</sup> compared the effects of training for three weeks in the glycogen loaded state or when half the training was completed in the high state and half in the “low” state.

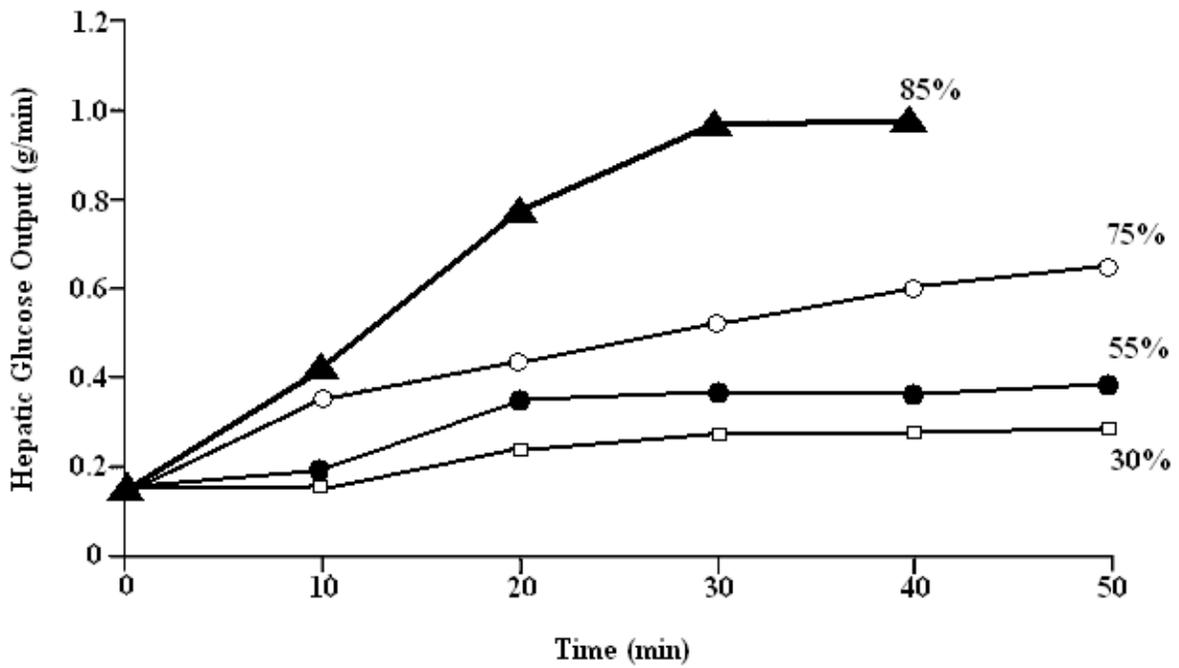
Exercise performance was equally improved after three weeks in both groups, regardless of the glycogen content during training. However, the group that did half high, half low training actually trained at a greatly reduced exercise intensity during the low glycogen state. Thus, the benefit of this training regimen needs further investigation to better understand nutritional and metabolic factors that are important for exercise training to ultimately improve exercise performance.

### ***Conclusion and Practical Application***

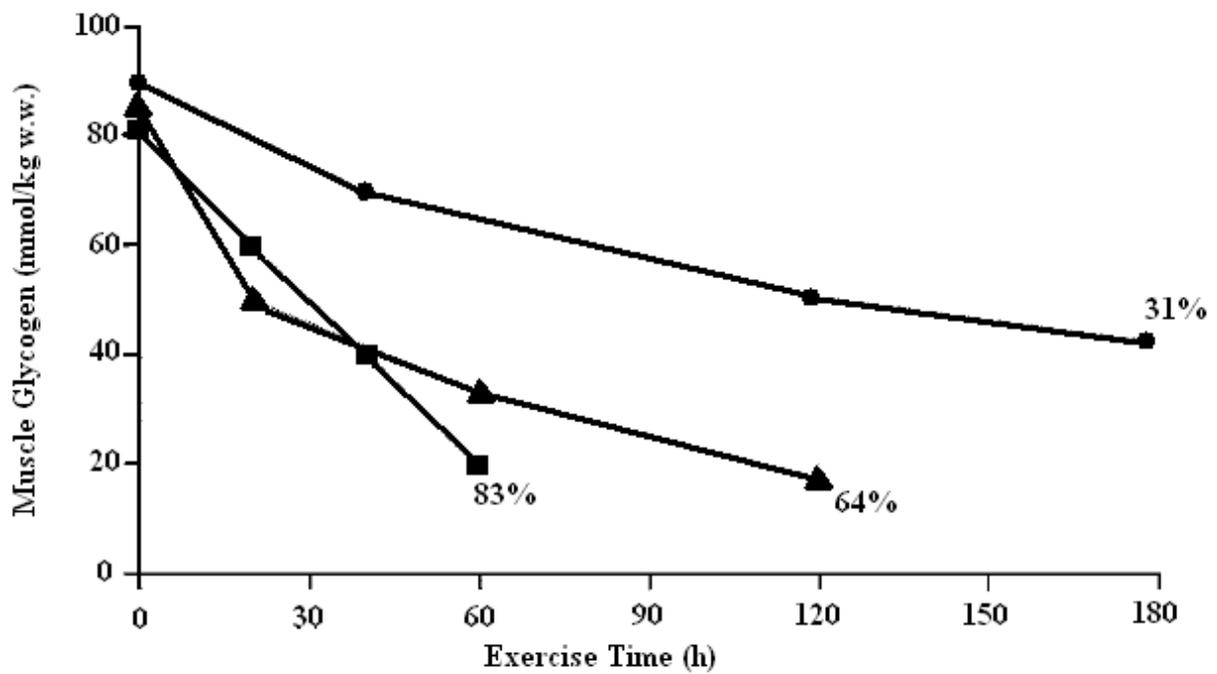
The benefit of carbohydrate ingestion during endurance exercise lasting longer than 2 hours is undisputed, as a continued supply of exogenous carbohydrate prevents hypoglycemia. However, the exact dose, type, and feeding schedule to optimize performance warrants further investigation. It appears that the use of carbohydrates which rely on differing intestinal transporters, such as a glucose/fructose solution mixed at a 2:1 ration and doses which deliver  $\geq 60$  g/min of carbohydrate, ingested early and throughout exercise, are the most beneficial. This feeding strategy appears to have the greatest likelihood of success and least likelihood of gastric problems, which may ultimately lead to decreased performance if severe enough to impede work output. It also appears that the use of multiple transportable carbohydrates increases the availability of exogenous carbohydrate for oxidation during exercise when doses delivering carbohydrate at approximately 1.75 g/min are administered. The potential for a dose to performance relationship effect needs further clarification as well. These data will be useful to athletes who are concerned about maximizing performance while maintaining or altering energy balance to change to the amount of stored energy and body mass.

Contrary to the beneficial effects of carbohydrate intake during exercise bouts lasting more than 2 hours, the benefit of carbohydrate ingestion on exercise performance during events lasting less than 1.5 hours is equivocal. This may be due, in part, to the role of carbohydrates on central factors and mouth sensors and, thus, warrants further investigation to clarify this issue. It has been suggested that there may be a threshold of time that the carbohydrate must spend in the mouth to fully activate these sensors. Additionally, it appears that the nutritional status prior to exercise can impact the ability of mouth rinses to improve performance. However, from a practical point of view, athletes would most likely benefit from a swish and ingest strategy, as the effects of carbohydrate mouth rinsing and fluid ingestion appear to be additive. Additionally, many endurance athletes will include a warm up period prior to their competitive event, such that the total bout of exercise may push into the time when substrate becomes a limiting factor in performance especially when exercising in the fasted state. The only clear benefit in practice to mouth rinse only during an exercise bout would be in cases where the athlete has severe sensitivity to ingestion of fluid or carbohydrate during said exercise bout, or the athlete is exercising in the fasted state while trying to limit caloric consumption.

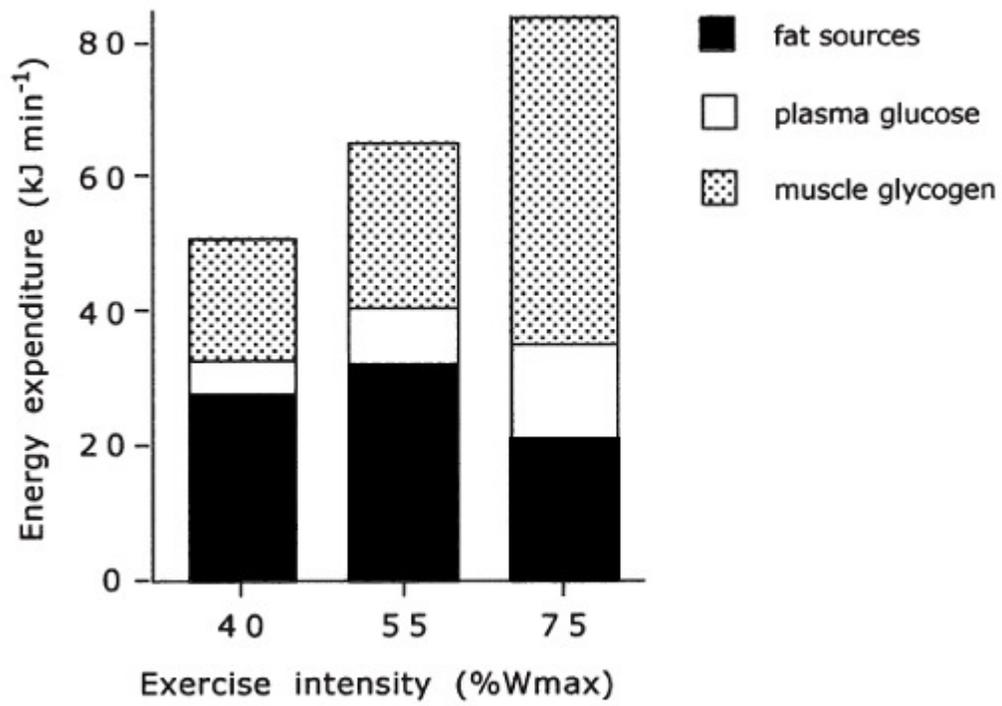
The role of carbohydrate ingestion at maintaining blood glucose is established, but its role in sparing liver glycogen as well as skeletal muscle glycogen is more controversial. Regardless of these controversies, exercise intensities  $\geq 60\%$  of  $VO_{2max}$  typically require an exogenous carbohydrate source in order to be maintained for longer than 1.5 to 2 hours, and it becomes more difficult to continue exercise as the duration increases beyond 2.5 hours. The novel aspect of train low, compete high also warrants further investigation to determine if the long-term metabolic benefits outweigh the reduced ability to train at high intensity when preparing for competitions.



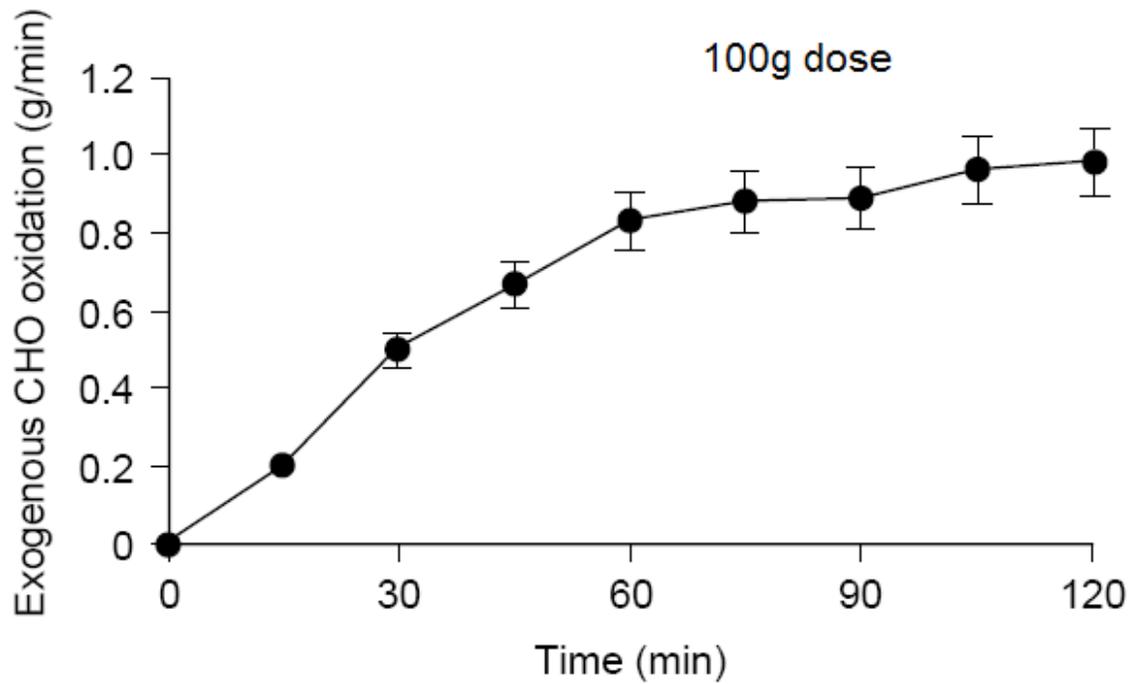
**Figure 1** Hepatic glucose output (g/min) per exercise intensity (percent  $VO_{2max}$  ). As exercise intensity increases, HGO increases. Adapted from Sports Nutrition, Second edition.<sup>7</sup>



**Figure 2** Skeletal muscle glycogen usage (mmol/kg w.w) per exercise intensity (percent  $VO_{2max}$ ). Greater exercise intensities utilize muscle glycogen at a faster rate. In the absence of exogenous carbohydrate intake, exercise tends to stop or require reduced intensity when muscle glycogen content reaches approximately 25 mmol/kg w.w. Adapted from Sports Nutrition, Second edition.<sup>7</sup>



**Figure 3** Contribution of substrate at a given exercise intensity. Adapted from van Loon et al.<sup>37</sup>



**Figure 4** Modified from Jeukendrup and Jentjens.<sup>9</sup> Oxidation of a 100 g dose of carbohydrates given prior to exercise in the fasted state.

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## Chapter 2 - Comparison of Carbohydrate or Caffeine Supplements on 10-km Cycling Time Trial Performance Following 1 Hour of Cycling

### *Abstract*

The primary aim of this study was to investigate the effects of novel carbohydrate supplement gels compared to more standard ingredient gels, a caffeine supplement, and a placebo on simulated 10-km cycling time trial performance after ~1 hour of cycling. A secondary aim was to investigate the glucose, insulin, and IGFBP-1 responses to these treatments during exercise. Ten (male:8, female:2) endurance trained cyclists (age  $27.6 \pm 2.4$  years; body fat  $13.2 \pm 1.2\%$ ;  $VO_{2max}$   $4.45 \pm 0.3$  L/min) completed a simulated 10-km time trial up a 2% grade while consuming one of six supplements throughout each ride. Supplement treatments included a commercially available caffeine product (Caf), glucose gel (Glu), processed honey (ProH), high fructose corn syrup (HFCS), raw unprocessed honey (RawH), or placebo drink (P). Supplements were ingested with 180 mL of water 5 minutes prior to exercise and at 15, 30, and 45 minutes during the constant load exercise bout at  $56 \pm 0.79\%$  of  $W_{peak}$ . This was followed by the 10-km performance time trial. No differences were observed for completion time ( $P = 0.77$ ), Watt output ( $P = 0.87$ ), plasma glucose ( $P = 0.93$ ), plasma lactate ( $P = 0.61$ ), or oxygen consumption ( $P = 0.94$ ) between treatments. No difference was observed between treatments for insulin ( $P = 0.15$ ) or IGFBP-1 ( $P = 0.71$ ). Times to complete the 10-km time trial were  $22:29 \pm 0:58$  (Caf),  $23:30 \pm 1:00$  (Glu),  $23:17 \pm 0:56$  (ProH),  $22:59 \pm 1:00$  (HFCS),  $22:55 \pm 0:57$  (RawH),  $23:19 \pm 1:19$  (P). Average power outputs were  $220 \pm 16$  W (Caf),  $204 \pm 14$  W (Glu),  $207 \pm 14$  W (ProH),  $213 \pm 15$  W (HFCS),  $213 \pm 14$  W (RawH), and  $211 \pm 17$  W (P). There were no performance benefits or reductions of IGFBP-1 production in moderately trained endurance athletes during exercise bouts lasting approximately 1 hour.

## **Introduction**

The benefit of ingesting carbohydrates during endurance exercise events lasting more than 2 hours is well established,<sup>1-4</sup> as exogenous carbohydrate availability late in exercise is likely contributing to performance benefits by maintaining blood glucose levels and providing additional substrate for oxidation. However, the benefit associated with ingestion of carbohydrates during exercise bouts lasting approximately one hour is less certain in the literature.<sup>5-21</sup> Some studies have shown a clear performance benefit compared to placebo<sup>5, 6, 9, 12, 13</sup> and others have shown no improvement.<sup>10, 11, 14, 22, 23</sup> During the first hour of exercise, blood glucose levels do not decrease even in the absence of exogenous carbohydrate intake as hepatic glucose output is capable of maintaining glucose levels.<sup>24</sup> Additionally, muscle glycogen does not seem to be a limiting factor for exercise performance lasting up to 1.5 hours when pre-exercise glycogen levels are replete.

There are recent data to support the existence of receptors in the mouth which may be contributing to the performance benefits of carbohydrates during exercise bouts lasting less than 1 hour.<sup>25-28</sup> Carter et al.<sup>25</sup> found that mouth rinsing with carbohydrate solution for 5 seconds by cyclists reduced the time to complete a set amount of work compared with placebo.

Interestingly, a recent study by Pottier et al.<sup>19</sup> supports the performance benefit of carbohydrate mouth rinse but failed to show a performance benefit when carbohydrates were ingested.

There are numerous products currently in use by cyclists during training and racing events, most of which are designed to be swallowed and digested. However, there are numerous products that are more mouth coating compared to drinks when the carbohydrate source is administered as gels. Typical ingestion patterns of these supplements tend to spend more time in the mouth and may be better able to activate these oral receptors than sips of sports beverage.

Activation of these oral receptors has been shown to independently improve exercise performance<sup>29</sup> and facilitate motor output.<sup>27</sup>

The combination of multiple transportable carbohydrates has been shown to increase carbohydrate availability and oxidation during long endurance exercise<sup>30</sup> and many sport supplement products available combine fructose and glucose in some manner (sucrose, HFCS, maltose + fructose). High fructose corn syrup (HFCS) is a product that is composed of glucose and fructose sugars and is one of the main ingredients in popular sports beverages. However, to our knowledge, the effects of HFCS ingestion alone as a gel on exercise performance have not been examined. Honey is another relatively novel ingredient for use as a supplement to benefit endurance performance and commercially available honey typically contains a mixture of HFCS and processed honey. Raw and unprocessed honey also contains a natural mixture of glucose and fructose as well as other disaccharides and its use during exercise has not been tested to our knowledge. The thicker consistency of these products may allow them to spend more time in the mouth upon ingestion, which may be important because activation of the oral receptors appears to be a primary factor in improving endurance performance during shorter (~1-hr) exercise bouts.

Both HFCS and honey contain fructose, which is absorbed and metabolized differently than glucose. The liver takes up dietary fructose more readily during the first pass via the portal vein with very little reaching systemic circulation directly following absorption. Fructose taken up by the liver is more readily converted to glucose and liver glycogen than ingested glucose.<sup>31</sup> It has been suggested that IGFBP-1 concentration is inversely related to liver glycogen content during exercise.<sup>32</sup> If dietary fructose can spare liver glycogen usage during exercise, the typical rise in IGFBP-1 concentration with exercise would be expected to be attenuated.

The primary aim of this study was to investigate the effects of relatively novel carbohydrate supplement gels compared to more standard ingredient gels and a placebo on a simulated 10-km cycling time trial performance after ~1 hour of cycling. A secondary aim was to explore the glucose, lactate, and IGFBP-1 response to these supplements during exercise. A caffeine supplement was also included, as caffeine has been shown to impart performance benefits by reducing central fatigue even in the absence of calories.

## **Methods**

### *Subjects*

Ten endurance trained cyclists (8 male, 2 female; Table 1) volunteered to participate in this study. All cyclists were competitive in either road or cyclocross racing and ranged from USAC categories 5 to 2. Participants were training a minimum of 3 days per week with most (n = 6) training 5 to 6 days per week. Road race competitors were ending their season and cyclocross participants were nearing the end of their base preparations for the season. All participants volunteered and signed an informed consent form approved by the Institutional Review Board at Kansas State University.

### *Experimental Design*

Participants completed six experimental trials, consuming one of five different supplements or placebo during each trial. Participants were randomly assigned to supplement order and the supplements provided during each trial were double-blinded, with each supplement provided in an opaque tube. Supplement order was assigned such that there was equal representation of each supplement at each trial point (incomplete Latin square). Testing for each

participant was separated by seven days in 90% of cases. Variations in testing repetition were due to participant scheduling conflicts ( $n = 3$ ) or illness ( $n = 3$ ). Of the remaining 10% of trials, no trial was performed in closer proximity than four days or longer than fourteen days. All trials were performed at the same time of day for each subject to minimize circadian variation.

### *Baseline $VO_{2peak}$ Test*

One to three weeks before experiment one, participants completed a  $VO_{2peak}$  test to volitional exhaustion to determine individual peak oxygen consumption and power output. This baseline and all experimental trials were performed in the Metabolism and Sports Science Lab (MASS) at Kansas State University on a Cardigirus ergometer with Server 2002vb4.08 software (Madrid, Spain), medical edition. The ergometer had fully adjustable seat and handle bar positions so that each subject could mimic the fitting of his or her own bike. Bike fit measurements were recorded so that bike settings were maintained throughout the study. Participants were instructed to come into the MASS lab ready to provide their best effort for baseline testing (pre-race preparation). Participants were allowed to perform a self-selected warm up (10 to 35 minutes), and when ready, the incremental exercise test began. Participants started cycling at 0 Watts and continued until pedaling rate dropped below 60 rpm for  $> 5$  seconds or volitional exhaustion was reached. Work rate increased 1 Watt every 2 seconds (30 watts/minute). A polar heart rate monitor continuously monitored heart rate. During the exercise test, gas exchange was measured using a TrueOne 2400 Parvo Medics Metabolic cart (Sandy, Utah). All participants achieved a peak on their first attempt as respiratory exchange ratio (RER) values were  $> 1.05$  and HR values were within 10 beats of age predicted maximum. Watts peak ( $W_{peak}$ ) was determined as the maximum watts achieved at the end of the exercise

test. This value was then used to determine 60% of  $W_{\text{peak}}$  workload for the experimental trials. Some subjects felt that 60% of  $W_{\text{peak}}$  was too difficult to maintain for the 45 minute exercise bout and thus work rate for constant load exercise was reduced and averaged  $56 \pm 0.79\%$  of  $W_{\text{peak}}$ .

### *Diet and Training Schedule*

Participants were asked to keep a detailed dietary record for the 24 hours prior to experimental test 1. They were instructed to try to maintain their habitual diet, but were requested to eat foods that would be easily accessible as they needed to eat these same foods 24 hours prior to all trials. They were also instructed on proper portion size recording for accurate repeatability. Participants were instructed to eat until comfortably full but not to consume caffeine or stimulants for 12 hours before their exercise trial. Participants were also instructed to choose an exercise activity that was not strenuous ( $\leq 60\%$  of  $VO_{2\text{peak}}$ ) and that could be repeated the day before each trial. All but one participant chose to rest (no structured exercise) the day before the exercise trials. Participants were given a copy of their diet record and were asked to repeat the 24 hour diet each week so that habitual nutrition before each trial was similar. Participants were instructed to maintain current training intensity and duration for the six to seven weeks of the study.

### *Protocol*

On the morning of each experimental trial (Figure 1), participants reported to the MASS lab after a 10-hr fast. Upon arrival, participants were asked to void their bladder before testing began and were weighed in cycling attire. On the first testing day, participants were assessed for body composition using a G.E. Lunar Prodigy DEXA (total body scans, Lunar, Madison, WI).

Participants then laid supine for insertion of an indwelling catheter into the antecubital vein, which was kept patent by 0.9% Na saline drip. A baseline fasting blood sample was collected at this time. Figure 1 illustrates the experimental protocol. Participants were then provided one of six supplements with 180 mL of water to consume. Five minutes after consumption of the first supplement, participants began the standardized warm-up consisting of 5 minutes of cycling equivalent to half of their  $56\% W_{\text{peak}}$  followed by 5 minutes of cycling equivalent to  $80\%$  of their  $56 \pm 0.8\% W_{\text{peak}}$ . After the warm-up, participants cycled for 45 minutes at  $56 \pm 0.8\% W_{\text{peak}}$ . Participants were given a 45 second break at 15 minutes and 30 minutes to consume the supplement and water, and to have blood collected. During this break, participants remained on the bike while the Watts were reduced to zero. Some participants stretched or stood briefly during this 45-second break. Participants were given 3 minutes of rest at the end of 45 minute constant load phase to consume the supplement and water, have blood drawn, and prepare for the time trial. The Cardgirus software also was switched from continuous load mode to time trial mode at this time. The 10-km time trial was set to simulate an outdoor condition up a  $2\%$  grade to minimize “coasting” if the participant stopped pedaling briefly. Gas exchange was measured during the final 7 minutes of each 15-minute segment (8-15, 23-30, and 38-45) and throughout the entire time trial. The first minute of each segment and the time trial was not included in the analysis as gas exchange equilibrates immediately after beginning a new measurement. The gas analyzer on the metabolic cart was calibrated using reference gas before each segment and prior to the time trial.

During the warm up and constant load exercise segments, Watts were clamped at a given work rate such that participants exercised at a constant load. The software continuously adjusts resistance to meet set Watts based on cadence (RPM). Most participants chose to maintain a

high cadence throughout the exercise trials. During the time trial, however, the bike is able to shift “gears” to simulate outdoor riding. Participants were able to self-select their gear ratio and cadence, and thus Watts by matching cadence to gear selection. Participants were not blinded to gear selection, Watt output, nor heart rate, and were able to see elapsed time and distance covered as occurs during typical time trial competitions. The same investigator provided similar encouragement at each 2-km checkpoint.

Blood samples were collected at baseline and at 15, 30, and 45 minutes of the constant load exercise segment and end of the time trial. Blood samples were not collected during the time trial to minimize distraction during the performance test. Blood samples were analyzed for plasma glucose and lactate using a YSI 2300 STAT Plus analyzer (Yellow Springs, Ohio). Rating of perceived exertion (RPE) was measured at 8, 15, 30, and 45 minutes of the constant load segment as well as every 2-km and the completion of the 10-km time trial. Heart rate and Watts were also recorded every 2-km of the 10-km time trial.

#### *Fluid and Supplement Intake*

Supplements were provided semi-double-blind in plain white tubes accompanied by 180 mL of water. While the supplements were not matched for taste or texture, participants were not informed as to which supplement they were receiving. Supplements provided included a commercially caffeinated drink (Caf), glucose gel (Glu), processed honey (ProH), high fructose corn syrup (HFCS), raw unprocessed honey (RawH), and an artificially sweetened non-caloric placebo drink (P). The caffeine supplement contained approximately 140 mg of caffeine per 60 mL bottle, a proprietary vitamin and amino acid mixture and 4 kcal. The dose for the Caf trial was one 60 mL bottle split into two doses at -15 and 15 minutes and water only was consumed at

30 and 45 minutes. All other supplements were consumed at -15, 15, 30, and 45 (Figure 1) with 180 ml of water. Additional water was provided *ad libitum* to the participants during the warm up and 45 minute pre-load exercise bout. Each dose of carbohydrate supplement contained approximately 7.5 g of carbohydrate and total ingestion for each trial (Glu, ProH, HFCS, and RawH) was 30 g of carbohydrate. Tubes were provided so that approximately half of the contents of the tube 1 were ingested at -15, and then the other half at 15 minutes. Tube 2 was ingested at in this same way at 30 and 45 minutes so that approximately 7.5 g of carbohydrates were ingested at each time point.

### *Statistics*

One way blocked analysis of variance (ANOVA) using repeated-measures was used in the analysis of performance time and power output. Trials were used as blocks. Data evaluation was completed using SAS version 9.2. Post-hoc paired t-tests were used to compare data points of time point or segment averaged data. Significance level was accepted at  $P \leq 0.05$ .

## **Results**

### *Performance*

There were no observed differences in time to complete the time trial for any of the supplement treatments (Table 2). Times to complete the simulated 2% grade 10-km time trial were 22:29  $\pm$  0:58 (Caf) 23:30  $\pm$  1:00 (Glu), 23:17  $\pm$  0:56 (ProH), 22:59  $\pm$  1:00 (HFCS), 22:55  $\pm$  0:57 (RawH), 23:19  $\pm$  1:19 (P) minutes ( $P = 0.77$ ). Power output (watts) was also not significantly different between supplements 220  $\pm$  16 W (Caf), 204  $\pm$  14 W (Glu), 207  $\pm$  14 W (PH), 213  $\pm$  15 W (HFCS), 213  $\pm$  14 W (RevH), and 211  $\pm$  17 W (P) ( $p = 0.87$ ). Heart rate and

oxygen consumption were not significantly different between supplements during the time trial ( $p \geq 0.05$ ).

### *Glucose and Lactate*

There were no differences between supplements or placebo for plasma glucose ( $P = 0.93$ ) or lactate ( $P = 0.61$ ) concentrations. Plasma glucose and lactate values are displayed in Figure 2 as the average value  $\pm$  standard deviation for each time point. Fasting plasma glucose was approximately 4.7 mM and increased over the first 30 minutes of exercise to plateau at approximately 5.4 mM ( $p \leq 0.05$ ). Resting lactate was  $0.99 \pm 0.45$  mM and rose to  $3.8 \pm 1.22$  mM at 15 minutes of exercise, until it stabilized at  $4.16 \pm 1.48$  mM at 30 minutes and  $4.30 \pm 1.62$  mM at 45 minutes of constant load exercise. Plasma lactate increased significantly during the time trial and averaged  $7.5 \pm 2.22$  mM ( $p \leq 0.05$ ).

### *Insulin and IGFBP-1*

There were no differences between supplements for insulin ( $P = 0.15$ ) or IGFBP-1 ( $P = 0.71$ ) concentrations. Plasma insulin and IGFBP-1 values are displayed in Figure 3 and Figure 4  $\pm$  standard deviation respectively for each time point. Average insulin concentration was reduced significantly ( $P = 0.01$ ) after completion of the time trial. Average IGFBP-1 concentration increased ( $P < 0.001$ ) after completion of the time trial.

### *Oxygen Consumption, Perceived Exertion, and Heart Rate*

There were no differences in oxygen uptake between supplements or placebo neither during constant load exercise nor the time trial ( $P = 0.94$ ). Segment values reflect the average  $\text{VO}_2$  for the final six minutes of each segment and all but the first minute of the time trial. Participants did not reach steady state oxygen consumption until the second segment (24 to 30 min) as  $\text{VO}_2$  values increased from  $3.07 \pm 0.57$  to  $3.14 \pm 0.62$  L/min.  $\text{VO}_2$  values during the time trial averaged  $3.33 \pm 0.76$  L/min. Participants were exercising at 71% of  $\text{VO}_{2\text{peak}}$  during the 45-minute constant work portion and 75% of  $\text{VO}_{2\text{peak}}$  during the time trial. Ratings of perceived exertion (RPE) and heart rate were not different ( $P > 0.05$ ) between supplements during constant load exercise or the time trial.

### **Discussion**

The primary finding of this study was that the ingestion of different carbohydrate supplements and a caffeine supplement did not improve cycling performance in moderately trained cyclists while completing a simulated 10-km time trial after 45 minutes of constant load moderate exercise. This finding is in agreement with some<sup>10, 11, 14, 18, 22, 23</sup> but not all<sup>6, 12, 13, 25</sup> of the studies examining carbohydrate intake on performance during exercise bouts lasting less than 1.5 hours. The performance times and power outputs in this study were similar between supplements. However, while statistical differences were not observed, relatively small differences in athletic performance may be meaningful during actual race situations. Day-to-day variability in performance in moderately trained athletes is much higher than highly trained and much greater than in elite athletes.<sup>33</sup> The participants in this study were moderately trained and were also in different stages of their training year. The coefficient of variation was 4.1% in these

athletes which is higher than the 3.35% previously reported.<sup>34</sup> The average coefficient of variation of the 4 most fit (highest  $\text{VO}_{2\text{max}}$ ) individuals in this study was 2.6%. A larger sample size and /or better control of the participants training outside of the experimental protocol could lead to increased likelihood of finding meaningful differences and was a limitation of this study. Additionally, the inclusion of a familiarization trial has been shown to reduce the coefficient of variation between performance tests.<sup>34</sup> Data obtained using elite and highly trained athletes may also decrease intra-subject variability, but are typically less applicable to the average, recreationally trained athlete.

The fasted or fed state prior to exercise testing may play a role in the observed performance benefit.<sup>28, 35-37</sup> Studies using a 1-hr time trial in the fasted state tend to show a performance benefit of carbohydrate ingestion.<sup>12, 13, 21, 25</sup> Studies in the fed state have tended to show no performance benefit of carbohydrate ingestion during exercise bouts ranging from 25 to 70 minutes.<sup>10, 11, 14, 18, 20</sup> Participants in the present study were tested in the fasted state and the performance portion was 10 kilometers (~22 minutes) after 45 minutes of constant load exercise as opposed to the commonly used 60 minute time trial. Fasted versus fed state comparisons and standardized performance testing protocols are needed to reveal these potential differences. Participants in this study were also able to see their performance data (speed, Watts, and HR) during the performance time trial as they would during actual racing situations. It has been suggested<sup>2, 33</sup> that blinding participants to their performance data may increase the likelihood of finding small differences between interventions. However, this study was designed to simulate performance near the end of a race during which participants would be able to view their performance data.

A recent study by Campbell et al.<sup>7</sup> reported improved performance from carbohydrate ingestion in the form of carbohydrate jelly beans, gel, and drink during a 10-km time trial after 80 minutes of exercise at 75% of  $\text{VO}_{2\text{peak}}$  compared to water. The total duration of exercise in that study was approximately 110 minutes, was conducted in the fed state, and participants were not able to see performance data other than distance completed. The differing gels in the current study did not impart a performance benefit during exercise bouts lasting approximately 77 minutes. The additional 30 plus minutes of exercise, and the accompanying reduction of blood glucose that tends to occur after 1.5 hours of endurance exercise may be the primary difference between the present study and that of Campbell et al.<sup>7</sup> The present study is among the first to examine honey (both raw and processed) as well as HFCS. The results of the present study are also in agreement with those of Earnest et al.,<sup>38</sup> who investigated the effects of honey, dextrose, or placebo on 64-km time-trial performance and reported no performance benefit even though total exercise time was 128+ minutes.

Some participants in the current study reported negative gastrointestinal effects as a result of supplement ingestion. These negative outcomes may not always negatively affect performance, but generally do not elicit ergogenic properties (Table 3). High intensity exercise while consuming sports supplements can produce negative gastrointestinal symptoms that should be reported in all studies on the topic. The ideal endurance sports supplements are those that do not elicit negative side effects and have the greatest likelihood of improving performance.<sup>2</sup> It appears that at least for long endurance exercise, the use of multiple transportable carbohydrates yields the least gastrointestinal negative outcomes and the greatest likelihood of increased performance outcomes.<sup>2</sup> Evidence suggests that early and continuous delivery of carbohydrates is an important aspect of performance late in an event. However, as shown by Pottier et al.,<sup>19</sup>

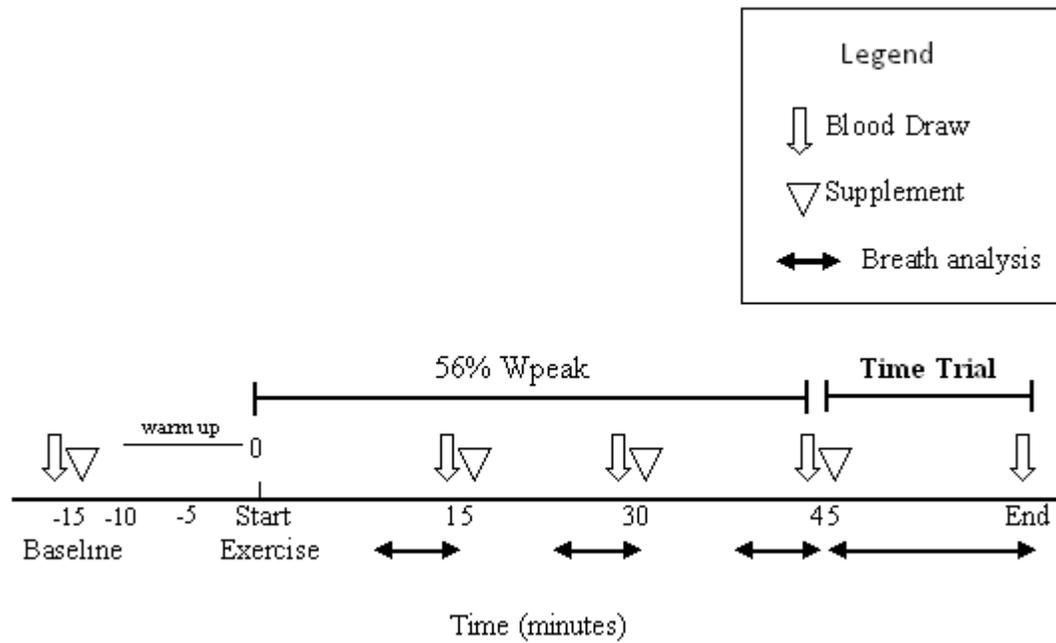
carbohydrate mouth rinsing improved performance in short, high intensity cycling, where as ingestion of the carbohydrate did not. Contrary to the study of Pottier et al., Rollo et al.<sup>21</sup> reported that runners completing a 1-hr running time trial showed a non-significant increase in distance covered while rinsing their mouths with carbohydrate, while the rinse and ingest group showed a significantly greater distance covered. The time that carbohydrate spends in the mouth potentially affects its ability to activate oral sensors signaling to the brain. Additionally, fluid ingestion alone has been suggested to be ergogenic and additive to the effects of carbohydrates.<sup>6</sup> Clearly more research is needed to determine the root of the reported discrepancies.

Insulin and IGFBP-1 did not differ between supplements. However, insulin significantly decreased after the time trial while IGFBP-1 significantly increased. Based upon previous studies,<sup>39</sup> the difference in IGFBP-1 and insulin values between caloric and non-caloric treatments begins to diverge shortly after 1 hour of exercise, becoming highly significant at two hours. While the present study was designed to examine the effects of these supplements in moderately trained individuals who will tend to be exercising for approximately 1.5 hr, the true differences may be exerted approaching the two hour mark and beyond. Future studies are needed using athletes who are more fit, completing longer exercise bouts to determine the effects of carbohydrate ingestion of insulin, IGFBP-1, and liver glycogen status. Additionally, the dose of carbohydrates was rather low compared to the amount expected to be oxidized during exercise at this intensity and of this duration.<sup>4</sup> A larger dose of carbohydrate may further influence the difference in IGFBP-1 between placebo and carbohydrate containing supplements during endurance exercise.

The caffeine supplement in this investigation numerically produced faster times and higher watt outputs during the time trial compared to placebo, however they were not significant.

Typically, doses of caffeine at or above 3 mg/kg have been shown to impart a performance benefit.<sup>40</sup> The dose of caffeine in this study was a more modest 1.9 mg/kg. Most studies which show a performance benefit use longer duration exercise bouts<sup>41, 42</sup> or higher doses of caffeine.<sup>42-44</sup> Additionally, the benefit of caffeine is most prominent when habitual caffeine intake is reduced in the days and weeks prior to the exercise test. Habitual caffeine intake was not controlled in this trial other than the 22 hours prior to the exercise tests. However, this project was designed to test the effects of these supplements as used by moderately trained individuals in simulated race situations.

Overall, the data from this study show that carbohydrate or caffeine supplement ingestion during moderate intensity exercise followed by a high intensity time trial did not improve performance compared with an artificially sweetened placebo drink in moderately trained individuals. These supplements did not differ in their effects on insulin, glucose, lactate, or IGFBP-1 concentrations during the constant load and time trial exercise bouts.



**Figure 1** Experimental protocol. Exercise includes the 10-minute warm up starting at -10 minutes continuing through the 45 minutes clamped exercise as well as the time trial. Time to complete time trial was variable as indicated by “End” instead of a time distinction.

**Table 1** Participant Characteristics

Age	27.6 ± 2.4 years
% Body Fat	13.2 ± 1.2%
Watt <sub>peak</sub>	353.8 ± 17.8 Watts
VO <sub>2max</sub> (L/min)	4.45 ± 0.3 L/min

Data shown as average ± standard deviation.

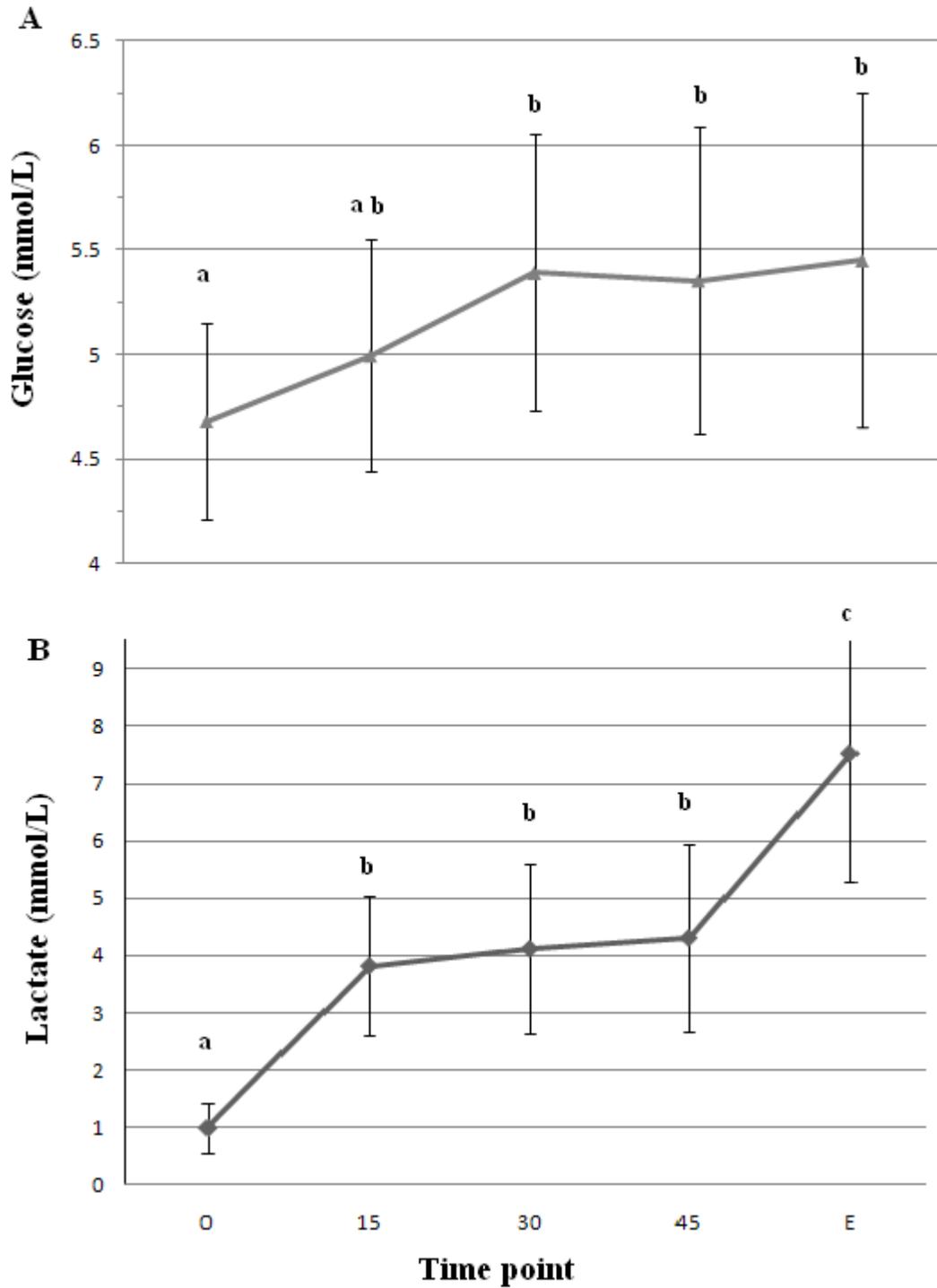
**Table 2** Results of 10-km time trial

	Caf	Glu	ProH	HFCS	RawH	P
Time to completion (min:s)	22:29±3:01	23:30±3:08	23:17±2:56	22:59±3:08	22:55±3:01	23:19±3:48
Average power output (watts)	220±49	204±45	207±44	213±47	213±44	211±51
Average heart rate (bpm)	175±9	167±7	170±9	171±9	169±10	170±9
Average VO <sub>2</sub> (L/min)	3.44±0.8	3.18±0.7	3.26±0.8	3.48±0.7	3.33±0.8	3.30±0.8

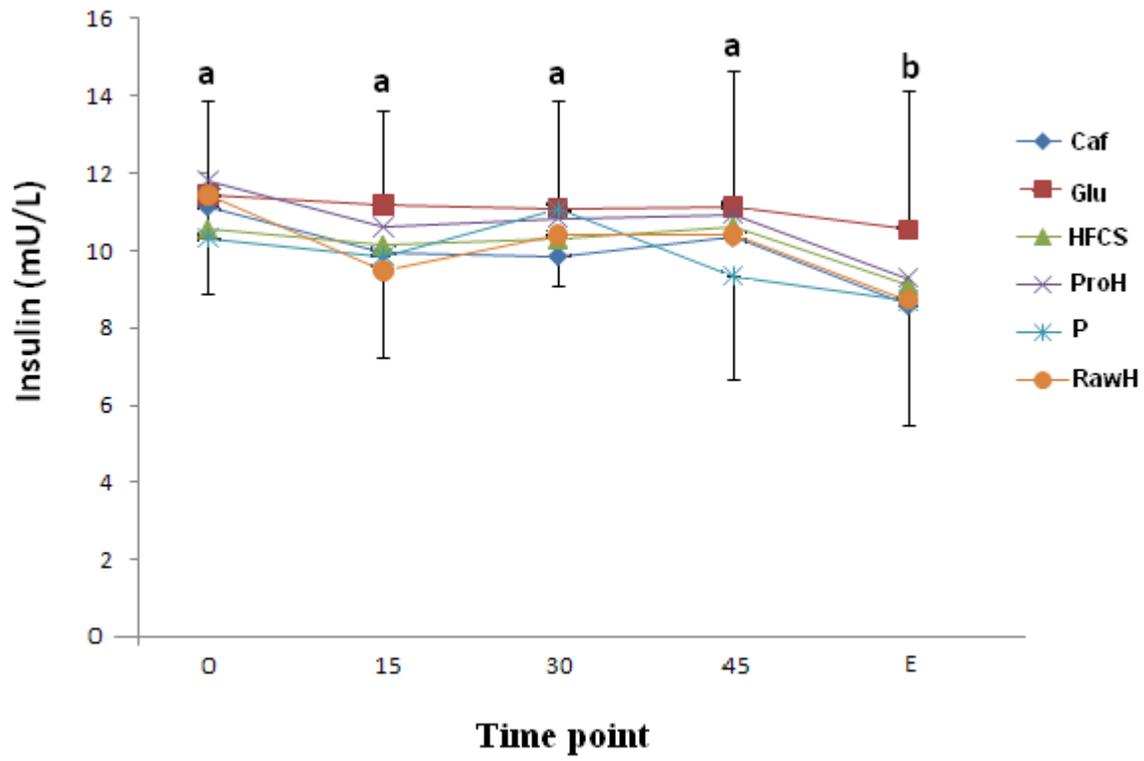
Exercise performance during the 10-km time trail. There is no difference between supplement treatments. Data are expressed as mean ± SD. n = 10.

**Table 3** Number of gastrointestinal side effects and complaints

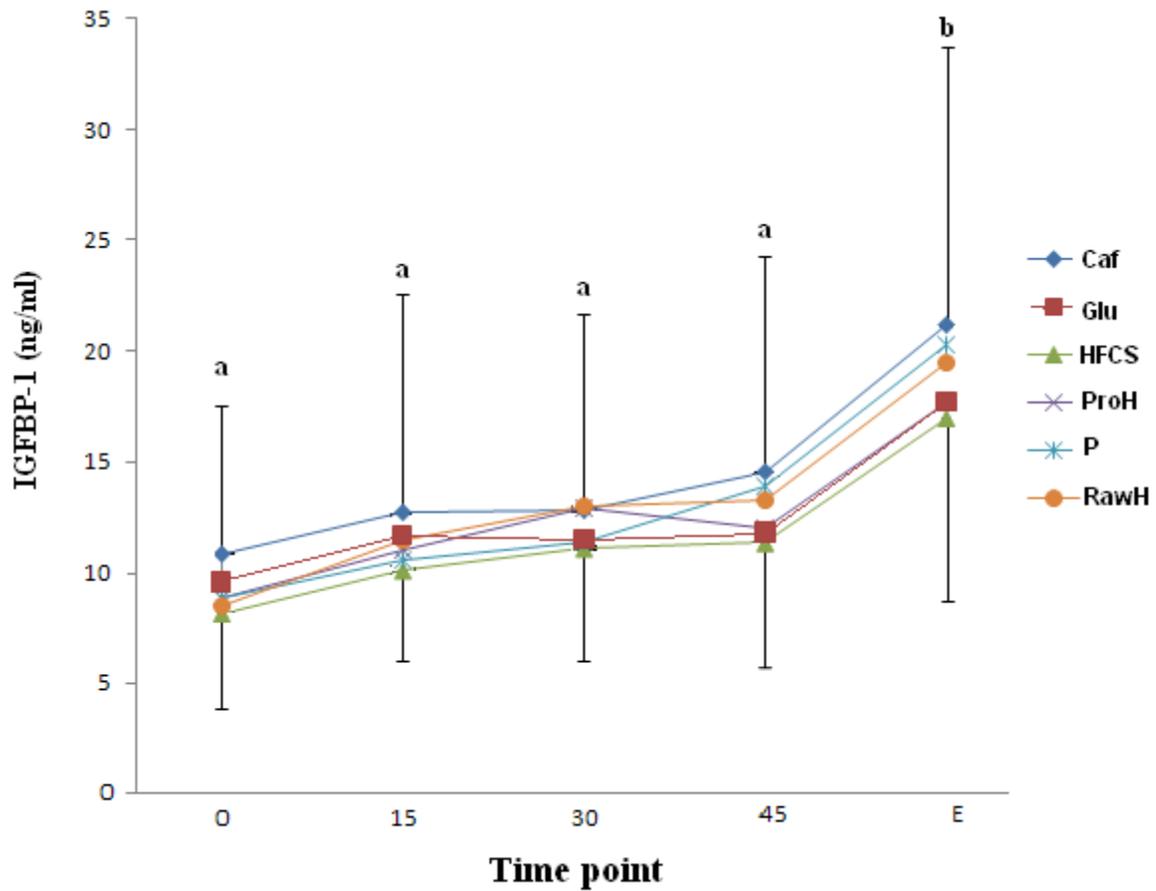
Supplement	Nausea	Vomit	Cramp	Bad taste
Caf	1			
Glu	2	2	1	
ProH	1			
HFCS			1	4
RawH	3			1
P	1			



**Figure 2** There are no effects of supplements on glucose or lactate values by treatments or placebo. Plasma glucose (A) and lactate (B) are displayed as the average of all trials per time point. Data are the average of all supplement trials as mean  $\pm$  SD. Letters indicate difference between time points ( $P \leq 0.01$ ).



**Figure 3** There was no difference between supplements in insulin response to exercise. Letters indicate difference between time points ( $P = 0.01$ ). Mean  $\pm$  SD.



**Figure 4** There was no difference between supplements in IGFBP-1 response to exercise. Error bars are presented as standard deviation. Letters indicate difference between time points ( $P \leq 0.001$ ).

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## **Chapter 3 - No Effect of Carbohydrate Mouth Rinsing in the Fed or Fasted State**

### **Abstract**

It has been reported that rinsing a carbohydrate solution in the mouth during short (~1-hr) high intensity cycling events can have an ergogenic effect. However, the nutritional status of the participants prior to engaging in the exercise test appears to influence the ability of carbohydrate mouth rinsing to produce an ergogenic effect. The purpose of this study was to investigate the effects of carbohydrate mouth rinsing on exercise performance during a 1-hr cycling time trial in the fasted and fed state. Twelve endurance-trained athletes (n=12; male n=10, female n=2) participated in 4 performance trials consisting of 1-hr of cycling while rinsing their mouth before and every 7.5 minutes of the time trial with either a 6.4% maltodextrin-lemon juice solution (C) or 0% maltodextrin-lemon juice solution (P). After a familiarization trial, in a double-blind, randomized crossover design, participants completed the trial in one of four conditions: Fasted placebo (FastP), fasted carbohydrate (FastC), fed placebo (FedP), or fed carbohydrate (FedC). Participants fasted for 10 hours prior to all trials but were fed a standard breakfast two hours before exercise for the two fed trials. There was no significant difference ( $P > 0.05$ ) between treatments in distance covered ( $27.5 \pm 3.1$  (FastC),  $27.8 \pm 3.0$  (FedC),  $28.1 \pm 2.5$  (FedP), and  $27.4 \pm 3.2$  (FastP)), average watts, heart rate, or rating of perceived exertion. These data demonstrate that carbohydrate mouth rinsing did not elicit an ergogenic effect in either the fasted nor fed states in trained cyclists.

### **Introduction**

Carbohydrate ingestion is known to increase performance during endurance exercise bouts lasting more than 90 minutes<sup>1-3</sup> The performance benefits of carbohydrate ingestion

were attributed to maintenance of plasma glucose concentration and high glucose oxidation rates in the later stages of exercise. However, the role of carbohydrate ingestion as an ergogenic aid during shorter ( $\leq 1$ -hr) bouts of intense endurance exercise is not clear as plasma glucose concentration does not decrease and increases in some cases due to increased hepatic glucose output.<sup>4</sup> Additionally, it is estimated that only 5 – 15 g of exogenous carbohydrates are oxidized during the first hour of exercise,<sup>5</sup> with the majority of oxidized carbohydrates being provided by endogenous stores.

While several studies have reported ergogenic effects of acute carbohydrate administration (mouth rinsing and ingestion) during exercise bouts lasting  $\leq 1$ -hr,<sup>6-16</sup> several others have reported no effect of acute carbohydrate administration on similar performance tests<sup>17-26</sup> (Table 1). Explanations for the ergogenic effects of carbohydrate administration cannot be wholly explained by carbohydrate oxidation and maintenance of plasma glucose concentration as observed in longer endurance exercise bouts since carbohydrate oxidation and plasma availability are not limiting factors during shorter duration exercise in well-trained athletes.<sup>27</sup> Two recent studies by Carter et al. elucidate a potential non-metabolic mechanism by which carbohydrates can elicit an ergogenic effect during shorter bouts of endurance exercise. To rule out the effect of increased exogenous carbohydrate available for oxidation, Carter et al.<sup>27</sup> infused a 20% glucose-saline solution or glucose free saline solution to 6 endurance athletes exercising at 75%  $W_{\max}$  for approximately 1-hr. They reported no performance benefits even though the infused glucose significantly increased carbohydrate oxidation. These data led to the hypothesis that there is an oral carbohydrate sensing mechanism which signals the presence of carbohydrate in the mouth. To test this concept, Carter et al.<sup>10</sup> conducted a study of carbohydrate mouth rinsing using a 6.4% maltodextrin

solution and an indistinguishable placebo while completing an exercise protocol similar to their previous study. Participants rinsed a carbohydrate or placebo solution in the mouth for 5 seconds and then expectorated into a bowl to ensure that minimal exogenous carbohydrate entered the stomach. Participants increased ( $p < 0.05$ ) performance (less time to complete work) when they rinsed their mouths with carbohydrate than with the placebo (MD =  $59.6 \pm 1.5$  min; and Placebo =  $61.4 \pm 1.6$  min).

The role of oral carbohydrate solution on the brain activity and the 'Central Governor'<sup>28</sup> is becoming clearer. A recent study<sup>11</sup> reported that sweet (glucose) and non-sweet (maltodextrin) carbohydrate solutions activated areas of the brain including the anterior cingulate cortex and ventral striatum. However, these neural responses did not occur with sweet-tasting, non-caloric saccharin. The affected areas of the brain are thought to be involved in reward and motor control.<sup>11, 29</sup> Since artificial sweeteners fail to activate the same areas of the brain, the authors suggest that there may be a class of yet to be identified oral receptors that respond to caloric carbohydrates independently of those for sweetness.<sup>11</sup> The role of carbohydrate compounds rinsed in the mouth on improving exercise performance is thought to be expressed via a positive afferent signal which modifies motor output. Moreover, that positive afferent signal may be assisting the body to increase work (watt output) at a given rate of perceived exertion (RPE) so that cyclists are able to produce more work for the same perceived work rate.

Upon inspection of the available studies regarding carbohydrate ingestion or mouth rinse on exercise performance bouts lasting < 1-hr (Table 1), it appears that differing nutritional states (fasted vs. fed) prior to an exercise bout might explain the discrepancy in the ergogenic potential of carbohydrate mouth rinsing. A study by Beelen et al.<sup>17</sup> reported that

there is no ergogenic effects of rinsing the mouth with a 6.4% maltodextrin solution during a simulated ~ 1-hr time trial when participants completed the exercise trials two hours after a standard breakfast meal. Most of the studies which have failed to report an ergogenic effect from carbohydrate mouth rinsing have fed or encouraged a high carbohydrate meal 2 – 3-hr prior to the exercise test.<sup>17, 19-21, 23, 26</sup> It is conceivable that the pre-exercise fasting period is influencing the ability of carbohydrate mouth rinsing to elicit an ergogenic effect during short exercise bouts.

The purpose of the current study was to determine whether mouth rinsing a 6.4% maltodextrin solution or indistinguishable placebo affects performance during a simulated 1-hr time trial with each treatment conducted in the fed and fasted states. Based on previous studies, it was hypothesized that the carbohydrate mouth rinse would increase performance measured as the total distance covered when participants exercised in the fasted condition.

## **Methods**

### *Participants*

Twelve endurance trained cyclists (10 male, 2 female; age range = 18-38 yr; body mass = 70.6±9 kg; VO<sub>2</sub>peak = 61.3±8.8 ml/kg/min; and a W<sub>max</sub> = 301.6 ± 42.9 W) participated in this study. All participants were competitive cyclists who exercised at least three times per week. Signed informed consent forms were obtained from all participants after the procedures and nature of the trials were fully explained. The Institutional Review Board at Kansas State University approved the study.

### *Experimental Design*

The study protocol consisted of six visits to the Metabolism and Sports Science Lab. All exercise tests were carried out on a magnetically braked cycle ergometer (Cardgirus, Spain) in a room which was maintained at 19 – 22° C and 15 – 40% relative humidity. The first visit (visit 1) to the laboratory involved an incremental exercise test to volitional exhaustion to determine participants' maximal workload ( $W_{\max}$ ) and maximal oxygen consumption ( $VO_{2\text{ peak}}$ ). Visit 1 also included baseline measurements including height (stadiometer), weight, and body composition (GE Lunar Prodigy version 11.40.004 DXA, Madison, WI). The second visit (Visit 2) was a familiarization to the time trial protocol during which participants were asked to complete as much work/distance as possible in 1 hour. The 24-hr period prior to Visit 2 also served as a familiarization to the controlled diet period and dietary recording for experimental trials. The next four visits (Visits 3 – 6) were experimental trials, which were randomly assigned to participants using a Latin rectangle. The participants completed the exercise trial in the following conditions: fasted placebo (FastP), fed placebo (FedP), fasted carbohydrate (FastC), fed carbohydrate (FedC). In the morning prior to each exercise condition, participants consumed a standard high carbohydrate meal consisting of pancakes, syrup, and 1% milk for the FedP and FedC or continued to fast while seated in the MASS lab during the fasted trials (FastP and FastC). All experimental treatments were carried out at approximately the same time of day ( $\pm 45$  minutes) for each participant. The experimental trials were carried out in a double blind (for carbohydrate vs. placebo), randomized order. Treatments were separated by at least seven days and no more than 14 days.

### *Pre-Treatment Diet and Exercise Control*

Prior to Visit 1, participants were asked to prepare for an aerobic capacity test by eating and exercising as they would the day before a typical racing event. Prior to Visit 2, participants were asked to keep a detailed record of their food and liquid intake as well as time of waking and sleeping for the 24 hr prior to the exercise test. Participants were also asked to keep a daily journal of their exercise training for the duration of the study. They were instructed not to exercise for the 24 hr period before an exercise trial and not to exercise at a heart rate above 145 beats per minute and not longer than 2 hr in the 48 hr period prior to the exercise test. Participants were instructed to refrain from alcohol and caffeine other than their habitual caffeine upon waking prior to exercise trial if that caffeine intake was less than 100 mg and at least 22 hr before the exercise trial. Participants were instructed to consume their typical diet but to include foods that they could easily repeat prior to each exercise test. They were also instructed to ensure that they consume adequate carbohydrates and were given a sports beverage containing 946 ml and 56 g carbohydrates to increase the likelihood that carbohydrate stores were adequate and similar for each performance test. They were to drink the beverage in the afternoon or early evening prior to exercise trials.

Diet records were individually reviewed using a 24-hr recall method upon participant arrival to the laboratory prior to each exercise trial. During Visit 2, some modifications were made to participants' standard diet log so that repeatability and accuracy might be better achieved for the experimental trials. The diet that was agreed upon by both the investigator and participant after this visit was repeated prior to visits 3 – 6. The 24-hr recall method was used in concert with the 24-hr diet record to better attempt dietary compliance and accurate reporting. Diet records were analyzed with Nutritionist Pro version 4.6.0 (Axxya Systems, Stafford, TX).

### *VO<sub>2peak</sub> and Watt<sub>max</sub> test*

Visit 1 consisted of an incremental exercise test to volitional fatigue. This test was conducted to determine the participants' maximal work rate ( $W_{\max}$ ) and  $VO_{2\text{peak}}$ . After fitting the participant on the cycle ergometer to match the fit of their racing bicycle, participants began cycling at 100 watts for 5 minutes. Following the 5 minute warm up, wattage was increased 50 watts every 2.5 minutes until their heart rate exceeded 160 beats per minute. The workload then only increased by 25 watts every 2.5 minutes until the participant could no longer maintain the workload at a cadence of at least 60 rpm or the succumbed to volitional fatigue.<sup>30</sup> Maximum Watts attained ( $W_{\max}$ ) was calculated as the last completed wattage value plus the fraction of time spent at that work rate times 25 watts.<sup>31</sup>

$$W_{\max} = W_{\text{complete}} + (t/150) * 25$$

$W_{\max}$  was used to determine an estimate for each participants work rate for the experimental trials corresponding to 75% of  $W_{\max}$ . Verbal encouragement was only given during this initial test during Visit 1.

Breath-by-breath gas measurements were performed after the 5-minute warm-up using a ParvoMedics TrueOne 2400 metabolic cart (Salt Lake City, UT). All participants achieved a maximal effort as indicated by a respiratory exchange ratio > 1.05 and maximal heart rate within 10 beats of age predicted max.<sup>21</sup>

### *Exercise Trials*

For Visits 2 – 6 participants reported to the MASS lab after a 10-hr fast and having followed the dietary and exercise guidelines as described previously. Participants were weighed

on a digital scale in their cycling clothing. Twenty four-hour recall of diet and compliance was completed and a variance of < 300 kilo-calories was deemed to be acceptable. Participants then either consumed a standard breakfast consisting of ready-to-eat pancakes, syrup, and 354 mL of 1% milk or remained fasting for 2-hr while seated in the MASS lab. Syrup and pancake allotment for each participant was based on 25% of Harris-Benedict estimates for heavy exercisers (1.75 activity factor) and averaged  $728 \pm 89$  calories. The standard meals contained an average of 22 g protein, 15 g fat, and 124 g carbohydrate. Participants were instructed to consume the standard meal within 15 minutes. Participants then rested for 1 hour and 45 minutes until the exercise trial. One participant felt that the pancakes amount was too much to consume during the familiarization trial so that individual's intake for trials 3 – 6 was reduced by one pancake. Also, two participants opted for more pancakes and less syrup for exercise trials 3 – 6. All participants consumed their same standard meal prior to fed experimental trials (FedC and FedP). Participants were allowed water *ad libitum* during this time in both fasted and fed exercise trials.

Prior to all the exercise tests, participants were asked to void their bladder and put on a heart rate monitor. Participants then mounted the cycle ergometer, which was set to mimic the fit of their racing bicycle. They were given 25 ml of the appropriate treatment solution to rinse in their mouth for 5 seconds and spit into a bucket held by the investigator prior to the 5 minute warm-up. Participants then cycled at 100 watts for males and 75 watts for females for 5 minutes. Immediately following the warm-up, participants were again provided the appropriate mouth-rinse solution and given these instructions by the same investigator each trial: "Treat this time trial like a race. Cover as much distance as possible and give your best effort. Any questions?" The time between the warm-up and beginning the time trial was 1m 30s. Participants then

cycled as fast as possible trying to cover as much distance/work as possible. Participants were provided 25 ml of the appropriate treatment solution to rinse in their mouth for 5 seconds and spit into a bucket held by the investigator every 7.5 minutes (12.5%) of the 1-hr exercise test. This mouth rinse dosing strategy has been used previously.<sup>10, 17</sup>

The cycle ergometer was set up to mimic a single speed bicycle with the gear selection set so that the cyclists' preferred cadence would result in them working at 75% of their previously determined  $W_{max}$ . Faster cadence results in greater work/distance and slower cadence results in less work/distance. Preferred cadence ranged from 85 to 101 rpms. Cadence averaged  $91 \pm 7$  during exercise trials. Work (watts), heart rate, distance covered, and cadence were recorded every 5 minutes. Participants received no information during the time trial other than elapsed time which was displayed on a count up clock in front of them. Participants were not given encouragement during the time trial and were only interrupted every 7.5 minutes to record rating of perceived exertion (Borg-scale) and administer/collect a mouth-rinse dose. A standard air fan was set to the same speed setting and placed in the same location in front of the participant for cooling during all trials. Participants were also partially enclosed in a "U" shape by large partitions so that any movement by the investigator was not visually distracting. Participants were not provided any data from the exercise trials until all data was collected from all participants.

### *Mouth-Rinse*

The mouth rinse solution contained either maltodextrin (NOW FOODS, Bloomingdale, IL) and lemon juice in distilled water (FedC and FastC), or lemon juice in distilled water (FedP and FastP) that were designed to be indistinguishable in taste and mouth feel. Both the

investigator and the participant were blinded to the carbohydrate content of the rinse solutions. After completing the final exercise trial, participants were asked if they were able to distinguish between the rinse solutions. The maltodextrin was a partially hydrolyzed cornstarch. Beverages were mixed and coded by a non-affiliated researcher to ensure double blinding.

### *Statistical Analyses*

Data are expressed as means  $\pm$  SD. Data were analyzed using a repeated measures analysis of variance (ANOVA) with two within-participant factors, solution and nutritional status. Significance was set at  $P < 0.05$ . Data evaluation was completed using SAS version 9.2. Scheffe's method was used post-hoc for comparing means.

## **Results**

### *Distance and Power Output*

Participants performed the four different exercise trials after a familiarization trial in randomized order (Latin rectangle) to minimize any order effect. The average distance covered during the experimental exercise trials (Visits 3 – 6) were  $28.0 \pm 3.0$  km,  $27.7 \pm 3.1$  km,  $27.5 \pm 2.8$  km, and  $27.6 \pm 3.0$  km, respectively. There was no significant order effect ( $P = 0.16$ )

No significant differences were observed for distance covered during the time trials with any of the treatments (Table 2). Average distance covered during the 1-hr time trial was  $27.5 \pm 3.1$  km (FastC),  $27.8 \pm 3.0$  km (FedC),  $28.1 \pm 2.5$  km (FedP), and  $27.4 \pm 3.2$  km (FastP) ( $P = 0.24$ ). The average coefficient of variation for all experimental testing conditions was 2.8 %. The individual and mean power outputs for treatments are shown in figure 1. There was no difference in average power output ( $P = 0.94$ ) between treatments. There was no effect of

nutritional status when data was pooled into fasted and fed groups ( $P = 0.59$ ) or when data was combined into carbohydrate and placebo groups ( $P = 0.89$ ).

#### *Heart Rate and Rating of Perceived Exertion*

Heart rate was not different between treatments ( $P > 0.05$ ) but increased during exercise (figure 2). There was no difference between treatments for RPE ( $P = 0.52$ ). RPE did increase with duration of the exercise trial ( $P < 0.0001$ ) (Figure 3).

#### *Mouth Rinse*

One of the 12 participants reported that they could distinguish between the treatments, but was not able to correctly identify which treatment they received at each of the 4 exercise trials. All other participants reported that they were not able to distinguish between the carbohydrate and placebo treatments.

#### *Dietary analysis*

Participants consumed an average of  $3157 \pm 928$  kcal,  $126 \pm 49$  g protein,  $417 \pm 104$  g carbohydrate, and  $113 \pm 50$  g fat. The average composition of the diets as a percent was 16% protein, 53% carbohydrate, and 31% fat. The range for carbohydrate intake for men was 345 to 605 g/d and 256 to 285 g/d for women. The average carbohydrate intake for men was 6.3 g/kg and the average intake for women was 4.7 g/kg. Seven of the twelve participants were able to correctly repeat the diet prior to each of the four experimental trials. The other 5 participants had dietary variations displayed in Table 3.

## Discussion

The main finding of this study is that rinsing of the mouth with a 6.4% maltodextrin solution did not improve cycling performance during a 1-hr time trial in the fasted or the fed state when compared to a placebo solution. The coefficient of variation for all experimental testing conditions was 2.8 % which is in accordance with the expected range of values in cycling exercise trials.<sup>32</sup> The results of this study are contrary to the hypothesis that carbohydrate mouth rinsing would have an ergogenic effect when used in a fasted state. While contrary to the expected outcome, other studies have, also, failed to report ergogenic effects when testing was conducted in the fasted state.<sup>22, 24, 25, 33</sup> (Table 1).

Rollo et al.<sup>33</sup> recently showed a non-significant change in running performance when participants rinsed their mouth with a carbohydrate-electrolyte solution (1.8%), but did show a significant improvement when participants ingested and swished the same solution (2.3%). Those results were contrary to the cycling study of Pottier et al.<sup>31</sup> who reported a significant benefit only when the carbohydrate-electrolyte solution was rinsed (3.7%) and not when ingested. A critical issue is that Rollo<sup>33</sup> standardized the time in the mouth for both the ingestion and rinse conditions and did not include a placebo mouth rinse group. Additionally, the role of fluid ingestion may be additive to the effect of carbohydrate mouth rinsing in improving endurance performance.<sup>7</sup> It is possible that the placebo group in the Rollo et al. study experienced a performance benefit from the fluid ingestion which minimized the difference between treatments. Clearly more research is needed in this area.

The general line of thinking is that carbohydrates in the mouth during exercise impart a positive afferent signal that modifies motor output. The receptors in the oral cavity responsible for this are yet to be discovered<sup>34</sup> but are thought to activate the anterior cingulate cortex and

ventral striatum among other brain regions.<sup>35</sup> The positive afferent signal as a result of activation of these areas of the brain is thought to be involved in reward and motor control. In the study by Pottier et al.,<sup>31</sup> participants who rinsed their mouth with the carbohydrate solution reported that participants were able to produce more power for the same degree of discomfort or RPE. This finding is also reported in the study by other mouth rinsing studies.<sup>10, 11, 33</sup> The RPE of participants in the present study was not significantly different between treatments.

The pre-exercise fasting period has been shown to impact the ability of carbohydrate mouth rinsing to impact performance and cortical activation.<sup>35</sup> The fMRI study of Haase et al.<sup>35</sup> reported greater activity of numerous brain regions in the fasted state (overnight) as compared to the postprandial state after a 700 kcal liquid mixed meal. The variations of gut hormones including ghrelin, peptide YY, and leptin have been reported to modulate areas of the brain related to satiety and pleasure.<sup>34, 36</sup> It is possible that the state of these hormones, based upon the nutritional and homeostatic status of the athlete, is modulating the effectiveness of carbohydrate mouth rinsing on exercise performance.

Participant expectations are also important and not always controlled and/or described, which can affect performance in exercise trials.<sup>19</sup> This effect is described by Clark et al.<sup>19</sup> who reported that the placebo effect of carbohydrate was greater than the real effect of carbohydrate in their study. In the present study, it was interesting to note that all of the participants expressed some degree of trepidation about their ability to perform an all out 1-hr time trial in the fasted state. This lack of self-confidence may have negatively affected their ability or motivation to perform to the best of their ability during each fasted exercise trial. This manner of thinking is common among athletes, but appears not to have been discussed in prior mouth rinse literature, especially when using longer fasting periods and using dietary strategies that might differ from

the athletes' normal pre-race preparation. However, if the carbohydrate mouth rinsing had a true effect in this study, we would expect that it would still improve performance compared to the fasted placebo trial, which it did not. One out of the twelve participants felt they were able to differentiate between the supplements but was not able to correctly identify which treatment was which. It would appear that the nutritional status prior to the exercise trials could influence participants' performance, but their expectations regarding the treatment versus placebo did not.

Another potential factor contributing to the lack of an ergogenic effect in this study was the use of lemon juice as the masking agent for the carbohydrate mouth rinse solutions. Both the present study and the study by Whitham and McKinney<sup>25</sup> used a lemon juice with maltodextrin mouth rinse solution and failed to show an ergogenic effect of carbohydrate mouth rinsing. Lemon juice was chosen as a masking agent in this study so that the placebo and maltodextrin mouth rinses would be indistinguishable and non-sweet. The fMRI study of Haase et al.<sup>35</sup> did show similar area of brain activation when comparing sucrose and citric acid. However, citric acid alone showed a reduced activation of the orbitofrontal cortex compared to sucrose alone and was perceived as moderately unpleasant by participants in that study. In the current study, a few of the participants either displayed an unpleasant facial expression (sour face) or verbally expressed discontent for the mouth rinse solutions even with the low lemon juice concentration. Additionally, it is possible that the taste stimuli (citric acid from lemon juice) used to further mask the carbohydrate content of the mouth rinse in this study impacted the brain activation via hedonic and prior experiences with the stimuli.<sup>35</sup> These factors need to be addressed in future studies and may be applied to sports beverages in general. Future studies should list all of the ingredients of the beverages to address potential receptor interactions.

In conclusion, mouth rinsing a non-sweet carbohydrate solution in the fasted or fed state did not improve performance in a 1-hr cycling time trial when compared to an indistinguishable placebo.

Table 1. Summary of studies investigating carbohydrate administration on exercise bouts lasting  $\leq$  1-hr.

Author (Mode)	n	Supplement	Performance Measurement	Meal Standardization	Fed State	Effect %	Indistinguishable Supplement
Jeukendrup et al. <sup>13</sup> (Ingest)	19	7.6% CES vs. PLA	~ 1-hr cycling Time (min)	24-hr Repeated	1-hr	2.3 (58.74, 60.15)	Stated Indistinguishable
Clark et al. <sup>19</sup> (Ingest)	7	7.6% MD vs. PLA Saccharin in both	40 km cycling TT ~ 1-hr	48-hr Repeated	Unknown Likely 1-hr	NS Not reported	Stated Indistinguishable
Beelen et al. <sup>17</sup> (Mouth rinse)	14	6.4% MD vs. Water	~ 1-hr cycling Time (min)	Standard dinner 48-hr repeated	2-hr Standard meal	NS (68.14, 67.52)	4 of 14 Correctly identified
Desbrow et al. <sup>20</sup> (Ingest)	9	6% CHO vs. PLA Aspartame PLA	~ 1-hr cycling Time (min)	24-hr controlled	2-hr Standard meal	NS (62:34, 62:40)	3 of 9 Correctly identified
Jeukendrup et al. <sup>21</sup> (Ingest)	8	6% CES vs. PLA Artificial sweetener (both)	16 km cycling TT ~ 25 min	24-hr Repeated	3-hr Postprandial	NS (25:51, 25:45)	Stated Indistinguishable
El-Sayed et al. <sup>12</sup> (Ingest)	8	8% CHO vs. PLA Artificial sweetener (both)	1-hr cycling Watts	Habitual diet	3-hr Postprandial	1.2 (277, 269) W	0 of 8 Could identify
Palmer et al. <sup>23</sup> (Ingest)	14	6.8% CES vs. PLA Sugar free PLA additive	20 km cycling TT ~ 1-hr	24-hr Repeated	3-hr Postprandial	NS (57.41, 57.41)	Stated Indistinguishable
Pottier et al. <sup>31</sup> (Mouth rinse)	12	6% CES vs. PLA Aspartame	~ 1-hr cycling Time (min)	24-hr Repeated	3-hr Postprandial	3.7 (61.7, 64.1)	Yes Triangle tested
Pottier et al. <sup>31</sup> (Ingest)	12	6% CES vs. PLA Aspartame	~ 1-hr cycling Time (min)	24-hr Repeated	3-hr Postprandial	NS (63.2, 62.5)	Yes Triangle tested
Rollo et al. <sup>26</sup> (Ingest)	10	6.4% CES vs. PLA Matched (PLA no CHO)	1-hr Run Distance (km)	48 -hr Repeated	3-hr Standard meal	NS (13.59, 13.68)	Not stated

Author (Mode)	n	Supplement	Performance Measurement	Meal Standardization	Fed State	Effect %	Indistinguishable Supplement
Neufer et al. <sup>14</sup> (Ingest)	10	8.25% CHO vs. PLA Fasted vs. Fed Artificial sweetener	45 min at 77% of VO <sub>2max</sub> 15 min cycling TT (total work N*m)	24-hr controlled Glycogen lowered Via exercise	12-hr or 4-hr	10 (175204, 159143) 22 (194735, 159143)	Not stated
Anantaraman et al. <sup>6</sup> (Ingest)	5	10% GP vs. PLA Artificial sweetener	1-hr cycling kj in 1-hr	Habitual Diet	4-hr Postabsorptive	7 (599, 560)	Not stated
Carter et al. <sup>10</sup> (Mouth rinse)	9	6.4% MD vs. Water	~ 1-hr cycling Time (min)	24-hr Repeated	4-hr Postabsorptive	2.9 (59.57, 61.37)	4 of 9 Could identify
Whitham et al. <sup>25</sup> (Mouth rinse)	7	6% MD vs. PLA Lemon juice	~ 1-hr running Distance (km)	24-hr repeated Standard breakfast	4-hr Postabsorptive	NS (9.33, 9.31)	1 of 7 Could identify
McConell et al. <sup>22</sup> (Ingest)	13	6% CHO vs. PLA Artificial sweetener	Time to exhaustion Cycling 83% VO <sub>2max</sub>	24-hr controlled Diet and exercise	Fasted 12-hr or 6 - 8-hr	NS (68.1, 69.6)	Not stated
Chambers et al. <sup>11</sup> (Mouth rinse)	8	6.4% CHO vs. PLA Saccharin & aspartame	~ 1-hr cycling Time (min)	Not stated	10-hr or 6-hr	1.9 (60.4, 61.6)	Stated Indistinguishable
Chambers et al. <sup>11</sup> (Mouth rinse)	8	6.4% MD vs. PLA Saccharin & aspartame	~ 1-hr cycling Time (min)	Not stated	10-hr or 6-hr	3.1 (62.6, 64.6)	Stated Indistinguishable
Powers et al. <sup>24</sup> (Ingest)	9	7% CES vs. PLA Saccharin	Time to exhaustion Cycling 85% VO <sub>2max</sub>	Standard 48-hr Diet	6-hr fasted	NS (39.2, 40.2)	Taste matched

Author (Mode)	n	Supplement	Performance Measurement	Meal Standardization	Fed State	Effect %	Indistinguishable Supplement
Carter et al. <sup>9</sup> (Ingest)	8	6.4% CHO vs. Water	Time to exhaustion Cycling 57.5% VO <sub>2max</sub>	24-hr Repeated	Fasted Overnight	15.8 (152.0, 128.0)	Not matched
Carter et al. <sup>9</sup> (Ingest)	8	6.4% MD vs. Water	Time to exhaustion Cycling 57.5% VO <sub>2max</sub>	24-hr Repeated	Fasted Overnight	11.8 (145.1, 128.0)	Not matched
Below et al. <sup>7</sup> (Ingest)	8	6% CES vs. WES	50 min cycling 80% VO <sub>2max</sub> ~ 10 min TT	24-hr Repeated	Fasted Overnight	6 (9.93, 10.51)	Partially disguised
Below et al. <sup>7</sup> (Ingest)	8	40% MDES vs. WES (Pooled CHO vs. none)	50 min cycling 80% VO <sub>2max</sub> ~ 10 min TT	24-hr Repeated	Fasted Overnight	6 (10.23, 10.92)	Partially disguised
Chong et al. <sup>18</sup> (Mouth rinse)	14	6.4% MD vs. 7.1% CHO vs. Water vs. Control	Wingate 30 s sprint test	48-hr Repeated	Fasted Overnight	NS (~856W)	Deceived Re: purpose
Rollo et al. <sup>15</sup> (Mouth rinse)	10	6% CHO vs. PLA Artificial sweetener	30-min running Distance (m)	48-hr Repeated	Fasted Overnight	1.8 (6584, 6469)	2 of 10 could identify
Rollo et al. <sup>33</sup> (Rinse and ingest)	10	6.4% CES vs. PLA Matched (PLA no-CHO) Aspartame	1-hr Run Distance (m)	48-hr Repeated	Fasted overnight 14 - 15-hr	2.3 (14515, 14190)	Not stated
Rollo et al. <sup>33</sup> (Mouth rinse)	10	6.4% CES vs. PLA Matched (PLA no-CHO) Aspartame	1-hr Run Distance (m)	48-hr Repeated	Fasted overnight 14 - 15-hr	NS (14283, 14190)	Not stated

Author (Mode)	n	Supplement	Performance Measurement	Meal Standardization	Fed State	Effect %	Indistinguishable Supplement
Rollo et al. <sup>16</sup> (Mouth rinse)	10	6.4% CES vs. PLA Matched (PLA no-CHO) Aspartame	1-hr Run Distance (m)	48-hr Repeated	Fasted overnight 13 - 15-hr	1.5 (14298, 14086)	0 of 10 Could identify
Present study (Mouth rinse)	12	6.4% MD vs. PLA Lemon juice	1-hr cycling Distance (km)	24-hr Repeated	Fasted overnight 12-hr Standard meal 2-hr	NS (27.5, 27.4) NS (27.8, 28.1)	1 of 12 Could identify

Table 2. Individual and mean distance covered (km) and SD for all four conditions.

subject (n=12)	FastC (km)	FedC (km)	FedP (km)	FastP (km)	CV
1	27.4	26.7	27.6	27.7	1.6
2	25.5	26.2	25.8	24.7	2.4
3	29.0	26.4	27.3	27.6	3.9
4	31.7	31.9	32.2	32.7	1.4
5	24.3	25.8	26.2	22.7	6.4
6	24.2	24.1	25.4	24.2	2.4
7	25.3	26.0	25.3	25.7	1.4
8	23.8	24.0	27.3	25.3	6.5
9	33.6	33.4	32.9	33.2	0.8
10	27.9	29.3	28.3	28.2	2.2
11	27.6	29.2	28.8	28.4	2.3
12	29.6	30.5	30.2	28.8	2.4
AV	27.5	27.8	28.1	27.4	2.8
SD	3.1	3.0	2.5	3.2	

Table 3. Data from participants who deviated from their diet in exercise trails. \* Participant 5 consumed a cereal product containing a large (59 g) amount of dietary fiber before trial 1 which is contributing to the calculated carbohydrate and caloric discrepancy.

Participant		kcal	protein(g)	carbohydrate (g)	Fat (g)
1	T1,T3,T4	4401	179	605	146
	T2	4173	179	545	146
	Ave	4287	179	575	146
	Range	228	0	60	0
2	T1	4060	142	476	178
	T2	4205	142	513	178
	T3 & T4	4377	147	544	181
	Ave	4214	144	511	179
	Range	317	6	68	3
3	T1	2813	118	331	113
	T2-T4	3113	122	367	127
	Ave	2963	120	349	120
	Range	300	4	36	14
4	T1	1880	82	239	67
	T2	2150	87	292	71
	T3 - T4	1900	83	240	67
	Ave	1977	84	257	69
	Range	270	5	53	4
5	T1	2463	110	370*	86
	T2-T4	2397	101	322	84
	Ave	2430	106	346	85
	Range	66	9	48*	2

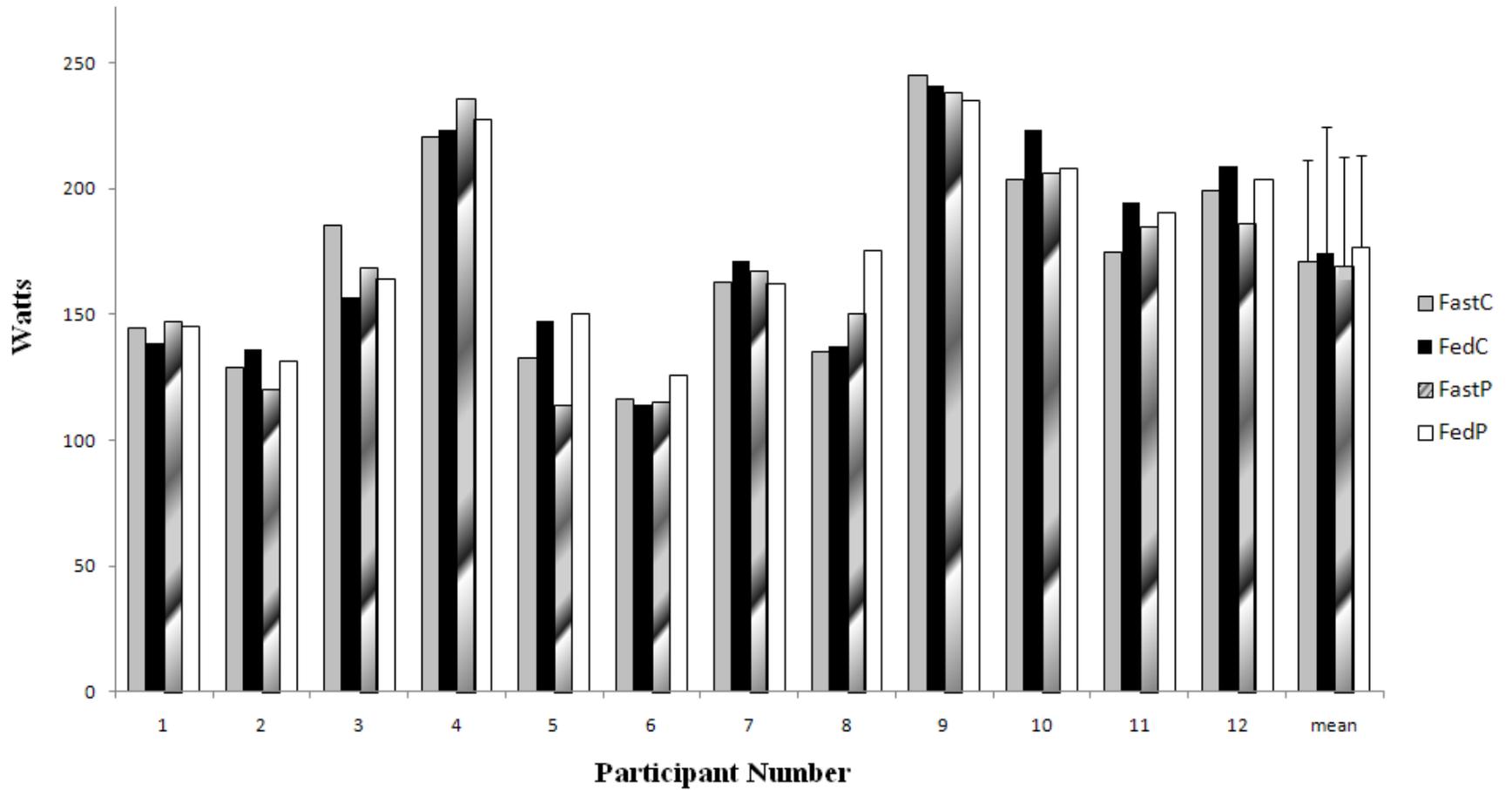


Figure 1. Individual Watt comparison for each participant. Mean watts  $\pm$  standard deviations are shown on the right.

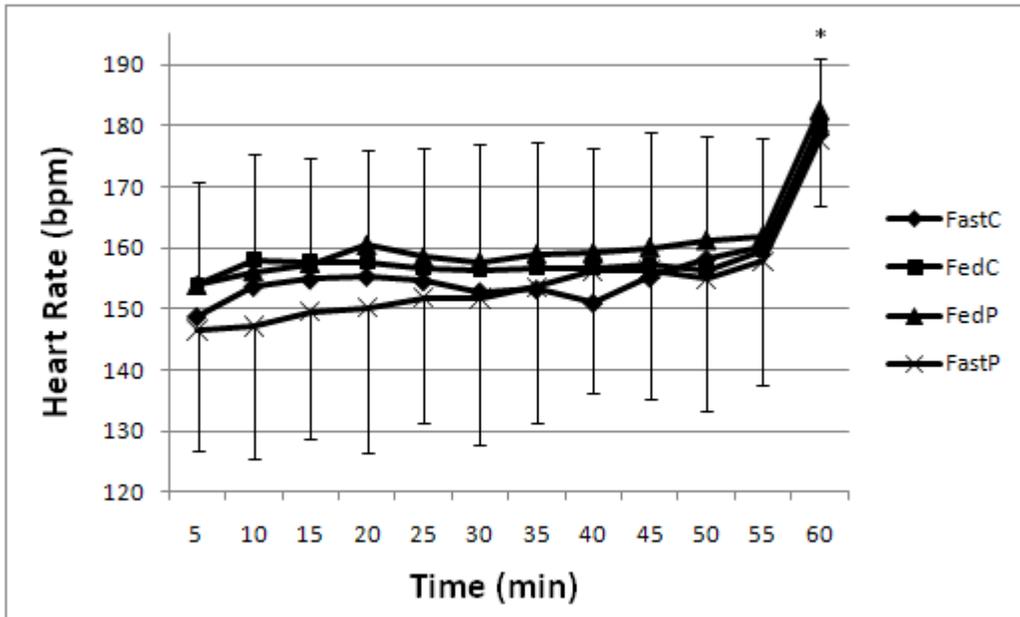


Figure 2. There was no difference between treatments for heart rate. Data are displayed as mean of participants for each treatment  $\pm$  SD. \* indicates significance ( $P < 0.05$ )

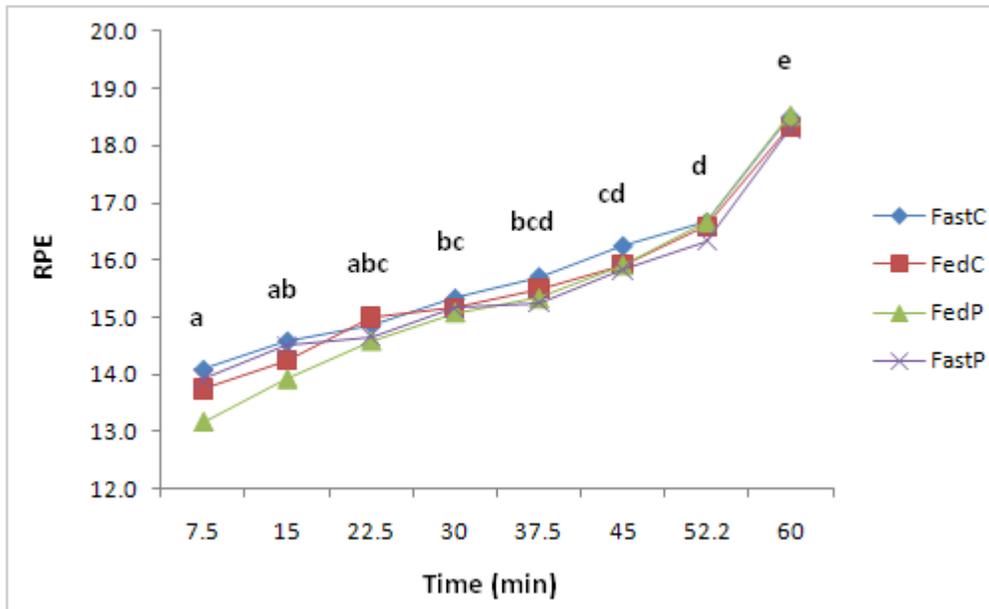


Figure 3. Rating of perceived exertion (RPE). There was no difference between treatments. Letters indicate significant differences in RPE over time.

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## Summary and Conclusion

This dissertation has reviewed the literature pertaining to carbohydrate administration during endurance exercise with a specific focus on high intensity exercise bouts lasting less than 1.5 hours. This document, also, has presented results from two original studies regarding carbohydrate gel ingestion and carbohydrate mouth rinsing. The body of literature and the studies herein suggest that it is not necessary to ingest large amounts of carbohydrates during high intensity exercise bouts lasting less than 1.5 hours to maintain or increase performance. This is especially true when pre-exercise nutritional status is optimized, as the addition of carbohydrate ingestion or mouth rinsing tends not to further increase performance when athletes are exercising in an adequately fed state (2 hours postprandial). Nonetheless, there are still circumstances during which athletes may want to ingest and/or swish carbohydrates during endurance exercise to attain optimal performance. Athletes engaging in exercise bouts that include a warm-up resulting in a total exercise duration extending beyond 1.5 hours will likely benefit from carbohydrate ingestion due to continued availability of carbohydrate as a substrate for oxidation. Additionally, ingestion of carbohydrate beverages of appropriate and commonly used dosages or concentrations during exercise have not shown a decrease in performance compared to placebo and often result in a significant performance benefit. Considering the potential benefit of fluid ingestion, carbohydrate ingestion providing continued substrate availability, and the potential positive effects of mouth rinsing a carbohydrate beverage, carbohydrate ingestion and mouth rinsing are recommended for the greatest likelihood of an ergogenic effect.

Conversely, there also are circumstances where carbohydrate mouth rinsing may be a better choice than carbohydrate ingestion. Some athletes experience gastrointestinal problems

during endurance exercise with ingestion of carbohydrates during exercise. Simply rinsing the mouth with carbohydrate without ingestion may benefit these athletes. Additionally, athletes who are exercising in the fasted state during training who are also attempting to limit total caloric intake may benefit from carbohydrate mouth rinsing. These athletes may be able to continue to work at a higher rate without an increased rate of perceived exertion without increasing caloric intake. Further studies are needed to examine this possibility.

# BRIAN S. SNYDER

**Address:** 2604 S. Brookglen Cir.  
Manhattan, KS 66502

Phone: (785) 317-2267  
Office: (785) 532-0170  
Email: bsnyder@ksu.edu

## EDUCATION

<u>Institution</u>	<u>Degree</u>	<u>Year</u>	<u>Major</u>
Kansas State University Manhattan, KS	PhD	ABD	Human Nutrition, Mark Haub

**Dissertation:** Carbohydrate ingestion and mouth rinsing on metabolism and endurance exercise performance

Kansas State University Manhattan, KS	MS	2006	Human Nutrition, Mark Haub
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**Thesis:** Human skeletal muscle protein metabolism: The effects of amino acids and resistance exercise

Loras College Dubuque, IA	BS	2001	Biological Research Major Prof. David Shealer
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**Project:** Effect of temperature on desaturation of cell membrane in *Eurosta solidaginis* and *Mordellistena unicolor*

## EXPERIENCE

- 2010 Graduate Teaching Assistant- Kansas State University: Co-taught HN132 Basic Nutrition, the 400 student introductory nutrition course.
- 2005-2010 Graduate Research Assistant- Metabolism and Sports Science Lab, Kansas State University: Assisting with numerous research projects, VO<sub>2</sub>max (treadmill and cycle ergometer) and resting metabolic rate tests using a ParvoMedics metabolic cart, Luminex multiplex assays (cytokines, insulin, gut hormones), muscle biopsies and tissue analysis, phlebotomy, antioxidant assays, DEXA testing, YSI glucose/lactate analyzer, dietary analysis using Nutritionist Pro, glycemic index testing, as well as data management.

- 2008            Personal Trainer- Maximum Performance, Manhattan, KS: Provided personal training and exercise plans for clients with a variety of needs.
- 2005            Graduate Teaching Assistant- Kansas State University: Co-taught a 300 level exercise physiology course with lab.
- 2003-2004      Graduate Teaching Assistant- Kansas State University: Assisted with teaching HN132 Basic Nutrition course.
- 2001-2003      QA/QC Technician- Nestle Clinical Nutrition, Hopkins Park, IL: Responsible for analysis of food products, data management, and regulatory record keeping.
- 2000-2001      Undergraduate Research Assistant- Loras College, Dubuque, IA: Collected and analyzed field samples using GC/MS for undergraduate project.

## PUBLICATIONS AND PRESENTATIONS

### Peer-reviewed journal articles:

Al-Tamimi, E.K., Seib, P.A., **Snyder, B.S.**, Haub, M.D. (2010) Consumption of cross-linked resistant starch (RS4XL) on glucose and insulin responses in humans. *Journal of Nutrition and Metabolism*, 2010.

Copp, S.W., Ferreira, L.F., Herspring, K.F., Hirai, D.M., **Snyder, B.S.**, Poole, D.C., Musch, T.I. (2009). The effects of antioxidants on microvascular oxygenation and blood flow in skeletal muscle of young rats. *Experimental Physiology*, 94, (9), 961-971.

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### Book chapters:

**Snyder B.S.**, Haub M.D. (2009). Proteins (Chapter 4) in Judy A. Driskell (editor) – *Nutrition and Exercise Concerns of Middle Age*. CRC Press, Taylor and Francis Group, Boca Raton, FL.

**Snyder B.S.**, Haub M.D. (2007). Whey, Casein, and Soy Proteins (Chapter 8) in Judy A. Driskell (editor) – *Sports Nutrition: Fats and Proteins*. CRC Press, Taylor and Francis Group, Boca Raton, FL.

In Progress:

**Snyder, B.S.**, Lattimer, J.A., Haub, M.D. Comparison of carbohydrate or caffeine supplements on 10-km cycling time trial performance following 1 hour of cycling. Draft completed, to be submitted.

**Snyder, B.S.**, Sitaraman, K., Haub, M.D. Exercise on Postprandial Lipemia and Inflammation in Overweight Men. Draft completed, to be internally reviewed and submitted.

**Snyder, B.S.**, Haub, M.D. No Effect of Carbohydrate Mouth Rinsing in the Fed or Fasted State. Draft in progress.

Presentations:

**Snyder, B.S.**, Sitaraman, K., Haub, M.D. (2008) Exercise on Postprandial Lipemia and Inflammation in Overweight Men. *Medicine and Science in Sports and Exercise*, 40, (5), S56-57. Oral presentation at ACSM national Conference in Indianapolis, 2008.

Grants Awarded/Assisted with submission:

**Snyder, B.S.** (project manager), Drouillard, J., Haub, M.D. Kansas Beef Council. Submission was funded for \$24,000 as part of a larger Flax Canada (Ag Food Canada AAFC) project. Presented to the Kansas Beef Council. Funding was not dispersed due to economic issues with the Flax Canada grant. 2008

**Snyder, B.S.** (project manager), Drouillard, J., Haub, M.D. Flax Canada (Ag Food Canada AAFC) Submission was funded for \$125,000. Funding was not dispersed due to economic issues with the Flax Canada grant. 2008

Professional meetings attended:

American College of Sports Medicine (ACSM) annual meeting 2004 – 2008

University of Kansas Annual Conference on the Prevention and Treatment of Overweight and Obesity 2003, 2004, 2008, and 2009

American College of Sports Medicine (ACSM) Central States