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The ergogenic effects of glucose and fructose coingestion during prolonged cycling

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THE ERGOGENIC EFFECTS OF GLUCOSE AND FRUCTOSE COINGESTION DURING PROLONGED CYCLING

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ABSTRACT

The purpose of this investigation was to examine the effects of glucose and fructose coingestion on cycling time trial performance and physiological responses to exercise. Eight trained male cyclists (age: 25 ± 6.2 yrs, height: 180.2 ± 4.3 cm, weight: 76.9 ± 9.2 kg, and VO_{2max}: 61.9 ± 6.2 $mL \cdot kg^{-1} \cdot min^{-1}$) completed the study. Subjects ingested either an artificially-sweetened placebo (PL), a moderate-glucose beverage (MG: 1.0 $g \cdot min^{-1}$), a high-glucose beverage (HG: 1.5 $g \cdot min^{-1}$), or a glucose and fructose beverage (GF: 1.5 $g \cdot min^{-1}$; 2:1 ratio) during ~3 hrs of exercise; consisting of 2 hours of constant load cycling (55% W_{max}, 195 ± 17.3 W), immediately followed by a computer-simulated 30-km time trial. Physiological responses (V_E, VO_2, RER, heart rate, blood glucose, blood lactate, and RPE) and incidences of GI distress were assessed during early- (15-20 min), middle- (55-60 min), and late-exercise (115-20 min), and during the time-trial. Treatment differences were analyzed using qualitative inferences. Time trial performances were 'likely' improved with GF (50.4 ± 2.2 min) and MG (51.1 ± 2.4) versus PL (52.9 ± 3.7 min), while differences between HG (52.0 ± 3.7 min) and PL were 'unclear'. GF resulted in 'likely' (3.0%) improvement versus HG and an 'unclear' (1.2%) benefit relative to MG. MG was 'possibly' beneficial (1.8%) versus HG. Few incidences of GI distress were reported in any trials. GF ingestion appears to enhance performance relative to PL, and HG. However, further study is necessary to determine if GF improves performance versus moderate (currently recommended) doses of glucose.

CHAPTER ONE

INTRODUCTION

Carbohydrate (CHO) ingestion during exercise has generally been shown to enhance performance in prolonged endurance events (>2 hrs) (26, 33, 35, 48, 60, 65, 116, 119). This benefit is likely due to increased CHO availability as a fuel source for working muscles. Indeed, ingesting CHO during exercise maintains blood glucose levels and sustains high rates of CHO oxidation late in exercise (27, 33). Moreover, increased provision of exogenous CHO may result in sparing of endogenous CHO stores such as muscle and/or liver glycogen (11, 80, 152, 158).

There is controversy regarding the 'optimal' dose of CHO to enhance performance. Current recommendations generally advise consuming 30-60 g/hr during prolonged exercise (89, 137), as this range has consistently been shown to improve performance with minimal detrimental effects such as gastrointestinal (GI) distress (26, 33, 35, 48, 60, 65, 116, 119). Conceptually, higher rates of CHO ingestion could elicit larger ergogenic effects by increasing CHO availability to a greater degree. To this end, several studies have analyzed the affects of varied CHO intake rates during prolonged exercise to see if, in fact, 'more is better.' Early studies did not provide evidence supporting a clear CHO dose-response (52, 113, 116, 134), but this may be due to methodological limitations in assessing relatively small, but potentially important differences in performance (i.e. inadequate subject populations). Recent research has provided stronger evidence for a CHO dose-response effect (149, 150). Smith et al. (150), reported that 20km cycling performance (following 2 hrs at 75% VO_2max) improved progressively as the CHO dose increased from 15 g/hr to 60 g/hr. This result was likely

due to increased exogenous CHO oxidation at higher CHO doses, resulting in the sparing of endogenous CHO stores. These results suggest that the ergogenic effects of CHO can be augmented by increasing the CHO dose. However, exogenous CHO oxidation rates may not be increased at intake rates exceeding 60 g/hr because CHO absorption rates are limited.

Exogenous CHO oxidation appears to be limited by rates of absorption from the intestine, as studies have shown that CHO readily empties from the stomach (134, 144). Intestinal absorption of CHO is limited by transporters in the brush-border membrane. The glucose (Glu) transporter, SGLT1, becomes saturated at ingestion rates of ~60 g/hr (76, 163). The fructose (Fru) transporter, GLUT5, is saturated at ~35 g/hr (76). These rates appear to be similar with different feeding schedules. Studies have shown mostly uniform oxidation rates whether CHO is ingested in a single large dose at the onset of exercise (90, 132) or with smaller doses evenly distributed during exercise (16, 102, 124).

The co-ingestion of multiple types of CHO (i.e.. Glu and Fru) can increase maximal exogenous CHO oxidation rates (10, 69). Because Glu and Fru are absorbed via different intestinal transporters (14, 49), there is less competition for transporters, and more total CHO can be absorbed from multiple forms of CHO before transporters become saturated (147). Numerous studies (2, 67–72, 77, 95, 141, 164) have reported exogenous CHO oxidation rates in excess of 72 g/hr (and as high as 105 g/hr) when subjects ingested large doses of Glu + Fru. These rates of exogenous CHO oxidation far exceed those observed from ingesting any single CHO source, (60 g/hr for Glu and 35 g/hr for Fru). Moreover, recent evidence suggests that there may be performance benefits from ingesting multiple forms of CHO at higher rates than recommended with Glu alone

(149). Smith and colleagues (149) recently found that as the dose of a maltodextrin/Glu/Fru beverage increased from 0 to 78 g/hr, performance was likely to improve. However, no further performance enhancement was observed at rates above 78 g/hr. Ingesting multiple forms of CHO has also been reported to enhance performance over isocaloric amounts of Glu. In a study by Currell and colleagues (36), subjects cycled for 2 hrs at 55% Wmax and then performed a ~40 km time trial. During exercise, subjects ingested a solution of 72 g/hr of Glu combined with 36 g/hr of Fru, or an isocaloric amount of Glu (108 g/hr). Ingestion of the mixed-CHO solution resulted in an 8% improvement in 40-km time trial time over the Glu solution. Triplett et al. also reported an 8% performance improvement with high doses of Glu+Fru (144 g/hr) versus an isocaloric amount of Glu in a 100-km cycling time trial (156). These performance enhancements appear to illustrate the dose-dependent effects of increased CHO availability.

GI distress is common in endurance sports (13, 79, 125, 128), and symptoms are frequently reported with the ingestion of CHO during exercise (128). Specifically, GI distress seems to be linked to malabsorption of CHO in the intestinal tract (29, 133, 143). As mentioned previously, exogenous CHO oxidation is likely limited by absorption in the intestine (147). When transporters become saturated, any excess CHO remains in the gut and may cause GI distress. Accordingly, studies investigating high rates of CHO ingestion (i.e. which exceed intestinal absorption capacity) commonly report symptoms of GI distress (67, 69, 71, 72, 77, 156, 164).

Ingesting multiple forms of CHO during exercise is associated with reduced symptoms of GI distress. Higher proportions of ingested CHO can be absorbed and

oxidized with a mixed Glu/Fru solution than with large doses of Glu alone, resulting in less CHO remaining in the intestine, [i.e. increased 'oxidation efficiency' (83)]. As a result, studies comparing oxidation rates between Glu/Fru and isocaloric amounts of Glu have observed fewer symptoms of GI distress in the mixed CHO trials (67, 69, 71, 72, 77, 140, 156, 164). In these studies, the highest prevalence of symptoms of GI distress have been associated with Glu intake rates ≥ ~90 g/hr, likely due to malabsorption.

The effects of CHO-related GI distress on performance have not been fully addressed. Rowlands and colleagues recently reported enhanced cycling performance when subjects ingested a mixed CHO solution (at ~84 g/hr) over an isocaloric amount of glucose (140). In this study, the best performance times in a field-based mountain bike race were negatively correlated with levels of GI distress. Interestingly, the relationship between GI distress and performance were not as clear during laboratory trials. As mentioned previously, Triplett et al. (156) observed improved time trial performance with Glu+Fru ingestion, versus Glu alone. The authors also reported complaints of severe GI distress in 45% of subjects during the glucose trial. This is not surprising considering that subjects were ingesting glucose at a rate of 144 g/hr. Currell and colleagues (36) did not report rates of GI distress in their study, which also reported enhanced performance with Glu+Fru ingestion. However, it is possible that subjects experienced more symptoms of GI distress in the glucose trial (108 g/hr). Thus, ergogenic effects reported with high rates of Glu/Fru ingestion might not be attributable to increased CHO availability (i.e. a dose-response effect), but rather, compromised performance in Glu-only trials resulting from malabsorption of excessive Glu. We are aware of no studies comparing the ergogenic effects of Glu+Fru versus Glu ingested at recommended rates (≤ 60 g/hr). Therefore, the

present study was designed to address the following questions: 1) does ingesting a mixed CHO solution (60G + 30F [GF]) during prolonged cycling result in improved performance versus a moderate dose of glucose (G60); and 2) are the putative differences between GF and G60 smaller than those observed between GF and a high dose of glucose (G90)? We hypothesize that performance times will be faster when subjects ingest GF and G60 solutions versus the G90 beverage and a placebo. Secondarily, we hypothesize that performance times will be slightly faster when subjects ingest GF versus G60.

Assumptions

1) It is assumed that subjects follow instructions throughout the duration of the study. Specifically, subjects will be asked to follow the same dietary habits the day before each trial, maintain consistent training throughout the duration of the study, and to accurately record their diets and physical activity.
2) It is assumed that subjects will give maximal efforts during the time trial portions of each trial.
3) It is assumed that the instruments used are valid measurement tools.

Limitations

1) Participants will be recruited through personal contacts and flyers at local bike shops. The subjects may not represent a random sample of trained cyclists.
2) The results are specific to trained male cyclists and cannot be transferred to other populations.

Delimitations

1) Subjects will be restricted to 18-45 years old.
2) Subjects will be "regular cyclists", as defined by performing a minimum average of 3 days of cycling each week during the preceding 2 months.
3) Subjects will possess a VO_{2peak} of >55 ml/kg/min.
4) Only male subjects will be recruited.

Definition of Terms

Moderate Glucose Dose (60G): Glucose beverage consumed during exercise at a rate of 60 g/hr.

High Glucose Dose (90G): Glucose beverage consumed during exercise at a rate of 90 g/hr.

Mixed CHO Beverage (GF): Beverage consumed during exercise containing glucose and fructose. The beverage will deliver glucose at a rate of 60 g/hr and fructose at a rate of 30 g/hr.

Performance: The time taken to complete a 30km time trial.

Steady State: The portion of the trial in which subjects ride at a constant power output corresponding to 55% W_{max} for 2 hrs.

GI Distress: Prevalence of stomach problems, gastrointestinal cramping, bloated feeling, diarrhea, nausea, dizziness, headache, belching, vomiting, urge to urinate, or urge to defecate as measured by a graded scale.

W_{max}: Peak wattage maintained for a complete stage (2 min.) during VO_{2peak} test.

Placebo (P): A flavor-matched non-caloric beverage.

RPE: Rating of perceived exertion.

VO_{2peak}: A measure of aerobic capacity, the rate that oxygen can be utilized by the working muscles at maximal effort. The unit of measure will be ml/kg/min.

CHAPTER TWO

REVIEW OF LITERATURE

Athletes have a long history of experimentation with nutritional strategies intended to augment athletic performance. Carbohydrates (CHO), in particular, have been heavily researched in this regard. As a result, the effects of CHO ingestion during exercise on metabolism (Table 6), various physiological variables (Table 9), and performance (Table 2, 4) have been well-documented.

Recently, researchers have investigated the effects of ingesting solutions containing more than one type of CHO. For example, the effects of consuming solutions containing varying quantities, concentrations, and ratios of glucose (Glu) and fructose (Fru) on exogenous CHO oxidation rates and performance have been investigated (Table 1, 2). Studies to date have illustrated oxidation rates far exceeding the maximum levels observed when equal amounts of Glu alone are ingested (Table 1). These high rates are likely achieved because Glu and Fru are absorbed in the gut via different transport mechanisms (Table 8).

A few studies have shown a performance enhancement when multiple transportable CHOs are ingested during prolonged cycling exercise (Table 2). The mechanisms for these performance benefits are unclear, as evidence for a CHO dose-response, until recently, was lacking (Table 3). Some suggest that oxidizing exogenous CHO at high rates results in sparing of muscle glycogen and/or reduced hepatic Glu production, (i.e. from liver glycogen or gluconeogenesis) (Table 5). Various other possible mechanisms by which CHOs enhance performance have also been investigated

including enhanced maintenance of muscle energy balance and/or excitation-contraction coupling (Table 7).

Gastrointestinal (GI) distress is common during endurance exercise, and is frequently observed with the ingestion of CHOs during exercise (Table 9). By ingesting multiple transportable CHO, GI distress may be reduced (Table 9). Mixed CHO solutions are more efficiently digested and absorbed than equal amounts of any single source of CHO (Table 8). Indeed, several recent studies in which subjects ingested either a Glu/Fru beverage or a calorically-matched Glu-only beverage reported more severe symptoms of GI distress during the Glu-only trials (Table 9). The effects of GI distress on performance have not been examined thoroughly, yet it is plausible that severe GI distress negatively influences performance. With this in mind, it is possible that reported performance enhancements with multiple transportable CHO ingestion were the result of an ergolytic effect of over-consuming large amounts of Glu, rather than an ergogenic effect derived from maximizing oxidation of exogenous CHO.

Multiple Transportable CHOs Oxidation Rates (Table 1)

Oxidation of exogenous CHOs increases during prolonged exercise and plateaus after around 90 min. As the amount of CHO ingested increases, the rate of exogenous oxidation increases. The highest rate of exogenous oxidation from a single CHO source is around 1 g/min or 60 g/hr. When combining multiple sources of CHOs, oxidation rates can exceed 1 g/min. By combining Glu and/or Maltodextrin (MD) and sucrose (Suc), exogenous CHO can be oxidized at up to 1.25 g/min. The combination of Glu, Suc, and Fru results in oxidation rates of around 1.7 g/min. Finally, combined ingestion of Glu and Fru can result in oxidation rates of up to 1.75 g/min.

Study	Problem	Subjects	Treatments	Protocol	Findings
(169)	Compare low concentration and high concentration CHO drinks with water for oxidation and glycogen use	12 trained male cyclists	-Water -2% MD -5.75% MD + 2.75% Fru -3 mL/kg immediately before, every 15 min. during exercise	-Fasted -2 hr at 48% VO2max	-Oxidation higher for mixed CHOs than water
(2)	Oxidation rate of Glu and Fru during exercise when ingested simultaneously	6 healthy males	-50 g glu -50 g fru -100 g glu -100 g fru - 50 g glu + 50 g fru -Water -500 mL at start	-Standardized Breakfast -2 hours at 60% VO2max	21% more exogenous CHOs oxidized with a 50/50 mix than with 100 g of Glu
(76)	-CHOs can be separated into two groups based on oxidation rates: Glu, Suc, Mal, MD at 1 g/min; Fru, Gal, Amylose at .6 g/min -CHO absorption in the gut seems to be the limiting factor for oxidation -CHO intake at 1 g/min can result in oxidation of ~1g/min; increasing intake further doesn't increase oxidation rate -Liver may also take up Glu making it a limiting factor -Ingesting large amounts of Glu can increase CHO and water absorption				
(136)	Substrate utilization in exercising boys ingesting water, Glu, and Glu plus Fru	12 boys (11-14 yrs)	-water -6% Glu -3% Fru + 3% Glu -25 mL/kg -Drinks ingested at 30 and 15 min. before, every 15 min. during	-Standardized Breakfast -90 min. 55% VO2max – 30 min. cycling with 5 min. rest repeated 3 times -Ride to exhaustion at 90% VO2max	-Oxidation of Glu/Fru is slightly less than Glu -Glu/Fru delays fatigue at 90% VO2max by 40% versus Glu at 25%
(72)	Effects of drinking Glu/Suc and Glu/Maltose versus Glu on oxidation rates	9 trained male cyclists	-1.8 g/min Glu -1.2 Glu + .6 Suc g/min -1.2 Glu + .6 Maltose g/min -Water -600 mL at start, 150 mL every 15 min.	-Fasted -150 min. at 50% Wmax	-Glu/Suc results in exogenous oxidation of ~1.25 g/min -No difference between Glu and Glu/Maltose

(67)	Effect of ingesting Glu, Suc, and Fru simultaneously on oxidation rates	8 trained male cyclists	-Water -2.4 g/min Glu -1.2 Glu + .6 Fru + .6 Suc g/min -600 mL at start, 150mL every 15 min.	-Fasted -150 min. at ~60% VO2max	-2.4 g/min of Glu, Suc, and Fru result in oxidation rates of ~1.7 g/min. -Endogenous CHO oxidation reduced compared to Glu alone
(69)	Whether ingestion of Glu/Fru would result in oxidation rate >1 g/min	8 trained male cyclists	-1.8 g/min Glu -1.2 g/min Glu -1.2 Glu + .6 Fru g/min -Water -600 mL at start 150 mL every 15 min.	-Fasted -120 min. at 50% Wmax	-Peak exogenous oxidation was 55% higher with mix -~1.3 g/min oxidation with mix
(164)	Whether ingestion of MD plus Fru leads to exo oxidation >1.1 g/min.	8 trained male cyclists	-Water -1.8 g/min MD -1.2 MD + .6 Fru g/min. -600 mL at start, 200 mL every 15 min.	-Fasted -150 min. at 55% Wmax	-MD/Fru results in exogenous oxidation rates of ~1.5 g/min.
(70)	Whether ingestion of glu/suc results in higher oxidation rates than Glu alone	8 trained male cyclists	-1.2 g/min glu (8.7%) -1.2 g/min suc (8.7%) -.6 glu + .6 suc g/min(8.7%) -1.2 glu + 1.2 suc g/min (17.5%) -600 mL at start, 150 mL every 15 min.	Fasted 120 min. at 50% Wmax	-.6 glu + .6 suc g/min results in 21% higher exogenous oxidation than isocaloric amount of glu -2.4 g/min of glu/suc results in ~1.2 g/min oxidation
(71)	-Exogenous oxidation and fluid delivery of Glu/Fru versus Glu in the heat. -Muscle glycogen utilization with Glu ingestion in heat.	8 trained, non-acclimated male cyclists	-1.5 g/min Glu -1 Glu + .5 Fru g/min -Water -600 mL at start, 200 mL every 15 min.	-Fasted -120 min. at 50% Wmax -31.9 degrees C	-Glu/Fru resulted in 36% higher exogenous oxidation and greater fluid delivery than Glu -No difference in glycogen utilization

(77)	-Exogenous oxidation rates and Glu kinetics during 5 h of exercise -Effect on oxidation of Glu/Fru	8 endurance trained males	-1.5 g/min Glu -1 Glu + .5 Fru g/min -600 mL at start, 270 mL every 20 min.	-Fasted -5 hrs cycling at 58% VO2max	-Glu/Fru increases exogenous oxidation rates compared to Glu -Glu/Fru maintained RPMs and perception of stomach fullness was lower versus Glu
(68)	Whether Glu/Fru leads to oxidation rates >~1.3 g/min	8 trained male cyclists	-Water -1.2 g/min Glu -1.2 Glu + 1.2 Fru g/min -600 mL at start, 150 mL every 15 min.	-Fasted -150 min. at 50% Wmax	-Glu/Fru at high rates results in ~1.75 g/min exogenous oxidation rates
(139)	Effect of various ratios of Fru to MD on oxidation and performance	10 trained male cyclists and triathletes	-MD .6 g/min (No Fru) -MD .6 + Fru .3 g/min (Low Fru .5) -MD .6 + .5 Fru g/min (Medium Fru .8) - MD .6 + .7 Fru g/min (High Fru 1.2)	-Fasted -2 hrs at 50% Wmax -10 max effort sprints (2-3 min.) with rest at ~40% VO2max (5-6 min.) between each	-Exogenous oxidation highest with Medium Fru -Low and Medium are most efficiently oxidized -Lower perceptions of muscle tiredness, nausea, physical exertion, attenuated fatigue with Medium and High Fru
(64)	Whether moderate amounts of Glu plus Fru results in higher oxidation rate than isocaloric amount of Glu	7 trained male cyclists	-Water -Glu .8 g/min -Glu .54g/min + Fru .26 g/min. -600 mL to start, 150 mL every 15 min.	-Fasted -150 Min. cycling at 65% VO2max	-Peak oxidation rates not significantly different -Ingesting moderate amounts of Glu/Fru does not increase oxidation rates over Glu

(95)	Effect of Glu/Fru on oxidation rates, lactate production, gluconeogenesis from lactate, and gluconeogenesis from Fru	7 trained male cyclists	- 2 g/min Glu -1.2 Glu + .8 Fru g/min -600 mL at start, 280 mL every 20 min.	-Fasted -120 min. at 60% VO2max	-Adding Fru increased exogenous oxidation, lactate production and oxidation, and gluconeogenesis from Fru -Fru oxidation explained by Fru-derived lactate and Glu oxidation
(131)	Oxidation rates between mixed CHO gel and drink	8 trained male cyclists	-Gel (1.2 Glu + .6 Fru g/min.) plus water -Drink – 1.2 Glu + .6 Fru g/min -Water -400 mL of water and 50 g of gel at start, 200 mL and 25 g of gel every 15 min. -400 mL of drink at start, 200 mL every 15 min.	-Fasted -180 min. at 60% VO2max	-Gels and Drink with Glu/Fru are oxidized at similar rates -Oxidation >1 g/min with both methods
(130)	Oxidation rates between mixed CHO solids and drink	8 trained cyclists	- Bar (.67 Glu + .33 Fru g/min) plus water - Drink – 1 MD + .5 Fru g/min -Water -400 mL water + Bar at start, 200 mL water + 32 g of Bar every 15 min. -400 mL drink at start, 200 mL every 15 min.	-Fasted -180 min. at 60% VO2max	-Exogenous oxidation similar between solid food and drink. -Oxidation >1g/min with both methods
(83)	-Ingesting CHOs which use different intestinal transporters results can result in increased oxidation of exogenous CHOs; one can increase exogenous oxidation by up to 65% versus a single CHO source -Increased oxidation is accompanied by enhanced fluid delivery and oxidation efficiency, which may decrease GI distress -Fru and galactose oxidized at 50% lower rate than Glu, Suc, Maltose, and MD -Glu/Fru oxidized as high as 1.75 -MD/Fru as high as 1.5; good be best option because of lower osmolality and reduced sweetness				

(123)	Impact of the ratio of Glu/Fru on oxidation, absorption and performance	10 trained male cyclists	-Placebo Fru and MD 1.8 g/min -4.5% and 9% (.5) -6% and 7.5% (.8) -7.5% and 6% (1.25)	-Fasted -150 min. at 50% peak power -Incremental test to exhaustion	-.8 solution oxidized ~10% more than .5 or 1.25 -Best gut comfort with .8
(129)	CHO oxidation from from a drink in running versus cycling	8 trained male cyclists or triathletes	-Water -1 Glu + .5 Fru g/min -300 mL at start, 150 mL every 15 min.	-Fasted -Running 120 min. at 60% VO2max -Cycling 120 min. at 60% VO2max	-Oxidation rates similar between cycling and running
(10)	Oxidation of Glu/Fru versus Glu at rest in the cold	6 non-acclimatized males	- 0.8 g/min Glu -0.4 Glu + 0.4 Fru g/min -Drinks ingested after 60 min. of exposure	-Fasted -150 min. of cold exposure	-Glu/Fru increases exogenous CHO oxidation by 30% over Glu -16% greater total CHO oxidation with Glu/Fru -Endogenous CHO oxidation not different -Glu/Fru results in increased total CHO oxidation without change in fat oxidation

Multiple Transportable CHOs and Performance (Table 2)

Recent research shows that ingesting Glu combined with Fru can result in enhanced cycling performance versus an isocaloric amount of Glu. However, not all studies confirm this performance enhancement. Ingesting mixed CHOs may also result in lower ratings of perceived exertion, less muscle tiredness and fatigue, and higher self-selected cycling cadences. Lower ratings of perceived exertion have also been observed with ingestion of mixed CHOs prior to resistance exercise. GI distress is common in trials where Glu is ingested at a rate exceeding 1 g/min.

Study	Subjects	Treatments	Protocol	GI Distress	Findings
(113)	8 trained male cyclists	-Placebo -5% (MD, Glu) -6% (MD 2.14 g/100mL, Fru 1.88 g/100mL, Suc 1.95 g/100mL) -7.5% (MD 5.55 g/100mL, Fru 2g/100mL) -~170 mL prior to each 12 min. bout	-(7 x 12 min.) at 70% VO2max. 3 min. rest in between -12 min. TT at end	N/A	-No sig. difference in performance between CHO trials
(105)	6 males	-Water -Glu -Fru -Glu/Fru -Glu/Electrolyte -36 g/100mL -100mL ingested at the start and every 10 minutes	TTE at 70% VO2max	"Amounts could not be tolerated"	No differences in performance among CHO drinks
(112)	10 trained male cyclists	-Placebo -6% (Glu) -12% (Glu 8.5%/Fru 3.5%) -18% (Glu 14.5%/Fru 3.5%) -150 mL every 15 min.	-105 min. at 70% VO2max followed by 15 min. all out effort -1 trial consisted of 7 x 15 min. bouts at 70% with 3 min. rest between	N/A	-12% solution results in improved performance over placebo
(36)	8 trained male cyclists	-Placebo -Glu 1.8 g/min -Glu 1.2 g/min + Fru .6 g/min -600mL at start, 150 mL every 15 min.	120 min. cycling at 55% Wmax followed by ~1 hour TT	N/A	-8% faster with Glu/Fru compared to Glu. -19% faster with Glu/Fru compared to placebo.

(139)	10 trained male cyclists and triathletes	-MD .6 g/min (No Fru) -MD .6 + Fru .3 g/min (Low Fru .5) -MD .6 + .5 Fru g/min (Medium Fru .8) - MD .6 + .7 Fru g/min (High Fru 1.2)	-Fasted -2 hrs at 50% Wmax -10 max effort sprints (2-3 min.) with rest at ~40% VO2max (5-6 min.) between each	-Questionnaire – nausea and abdominal cramps -Average nausea reduced in Medium and High Fru trials	-No statistically significant performance differences -Lower perceptions of muscle tiredness, nausea, physical exertion, attenuated fatigue with Medium and High Fru
(78)	Effect of Glu/Fru on fluid delivery, gastic emptying, and hydration	8 males	-Water -1.5 g/min Glu -1 Glu + .5 Fru g/min -600 mL at start, 203 mL every 15 min.	-Fasted -120 min. at 60% VO2max	-RPE legs lower with Glu/Fru
(127)	GI tolerance with high CHO intake during exercise	Endurance trained men and women ~75	-Glu/Fru 1.0 g/min every 3.2 kms (Study 1) -Glu/Fru 1.4 g/min (Study 1) -Glu gels 1.4 g/min (Study 2) -Glu/Fru gels 1.4 g/min (Study 2)	-16 km runs outdoors	-No differences in performance
(156)	9 trained male cyclists	-2.4 g/min Glu -1.2 Glu + 1.2 Fru g/min -250 mL to start, 250 mL every 15 min.	-Fasted -simulated 100 km time trial with intermittent 1 km and 4km sprints	-4 of 9 experienced GI distress in Glu trial -2 episodes of diarrhea, 1 vomiting, 1 sour stomach -no complaints in Glu/Fru	8.1% performance improvement with Glu/Fru versus Glu.

(148)	20 aerobically or strength trained men	-Glu 50g -Glu/Fru 50 g + 15g -400mL 15 min. before	-Fasted -10 sets of 10 reps of half squat (90% 10RM, 165 seconds between sets) -30 min. cycling at midpoint between two ventilatory thresholds	N/A	RPE reduced in strength and endurance exercise with glu/fru versus Glu supplementation before exercise
(123)	10 trained male cyclists	-Placebo Fru and MD 1.8 g/min -4.5% and 9% (.5) -6% and 7.5% (.8) -7.5% and 6% (1.25)	-Fasted -150 min. at 50% peak power -Incremental test to exhaustion	-Stomach fullness, ab cramping, nausea lowest with .8 followed by 1.25 solution. -Best gut comfort with .8	-Performance benefits from .8 and 1.25 (3-4% improved peak power) -Enhanced performance may be due to reduced GI distress
(166)	24 healthy males	-Placebo -Sucrose 50%, Glu 25%, Fru 25% -Solutions – 2%, 4%, and 6% -3 mL/kg immediately before, every 10 min. during	-Fasted (at least 6 hrs) -TTE at 70% VO2max in warm and cool temps	N/A	-In cool temps, TTE longer with 4% and 6% over Placebo -In cool temps, TTE longer with 6% than 2% -In heat, TTE longer with 6% than placebo

(140)	-7 male, 3 female mountain bikers (race) -16 male cyclists (lab)	-Glu+MD ~1.4 g/min -Fru+MD ~1.4 g/min	-Standardized meal evening before race and lab portion, no breakfast (fasted) -Lab portion, subjects consumed cereal bar 10 min. prior to exercise -2.5 hr mtn bike race -~3 hr ride – 94 min. set workload followed by performance test	-Reduced GI distress with Fru+MD -Mean sprint power actually *increased* with increased GI distress in the lab -Performance times in race were associated with lower ratings of GI distress	-Fru+MD outperforms Glu+MD -Gut comfort associated with improved performance

Dose-Response Effect (Table 3)

CHOs have generally been shown to enhance performance although little evidence exists that illustrates this enhancement occurs in a dose-dependent manner. This may be due to methodological limitations that make it difficult to observe subtle differences in performance. Recent research has provided evidence for a dose-response effect on cycling performance.

Study	Participants	Treatments	Protocol	Findings
(51)	9 males	-Placebo -10.75 g of sucrose with 200 mL of water at every 30 min. beginning at min. 0 -21 g of sucrose with 400 mL of water every hr starting at min. 0	-Fasted -4 hrs cycling – 20 min. at 50% VO2max followed by 10 min. of intermittent sprints and rest -Sprint ride to exhaustion at end of trial	-Inconclusive dose response -Performance improved over placebo with 21 g/hr; not improved with 11 g/hr
(52)	8 trained male cyclists	-Water -MD 3 g/100mL -MD 5 g/100mL -MD 7.7g/100mL -Fru 5 g/100mL -High Fru corn syrup 2.3 g/100mL -Glu 2 g/100 mL -150 mL immediately prior to start, 150 mL every 20 min.	-Fasted -2 hr at 90 rpms pushing as hard as possible	-No significant difference in performance -No significant difference in glycogen use
(113)	8 trained male cyclists	-Placebo -33 g/hr - 5% (MD, Glu) -40g/hr - 6% (MD 2.14 g/100mL, Fru 1.88 g/100mL, Suc 1.95 g/100mL) -50 g/hr - 7.5% (MD 5.55 g/100mL, Fru 2g/100mL) -~170 mL prior to each 12 min. bout	-(7 x 12 min.) at 70% VO2max. 3 min. rest in between -12 min. TT at end	-No dose-response -No sig. difference in performance -Beverages containing Fru and/or Suc were empytied better than MD/Glu beverage
(112)	10 trained male cyclists	-Placebo -37 g/hr - 6% (Glu) -74 g/hr - 12% (Glu 8.5%/Fru 3.5%) -111 g/hr - 18% (Glu 14.5%/Fru 3.5%) -150 mL every 15 min.	-105 min. at 70% VO2max followed by 15 min. all out effort -1 trial consisted of 7 x 15 min. bouts at 70% with 3 min. rest between	-Dose response inconclusive -12% solution results in improved performance over placebo -No glycogen sparing

(169)	12 trained male cyclists	-Water -2% MD -5.75% MD + 2.75% Fru -3 mL/kg immediately before, every 15 min. during exercise	-Fasted -2 hr at 48% VO2max	-Inconclusive dose response -8.5% sig. different than water but not 2% for oxidation
(116)	8 healthy males, 2 healthy females	-Placebo - 26 g/hr Glu 6% -52 g/hr Glu 12% -78 g/hr Glu 18% - 2 mL/kg every 15 min. starting at min. 12 of exercise (440 mL/hr)	-Standard breakfast -2 hrs of variable-intensity (50%, 65%, 75% VO2max) -Followed by 4.8km TT	-No dose response -Performance enhanced with 26 g/hr and 78 g/hr
(134)	8 trained male cyclists	-Water -4.5% Glu -17% Glu -17% MD -8 mL/kg at start, 3 mL/kg at 20, 40, and 60 min.	-Fasted -80 min. at 70% VO2max	-No dose response -Oxidation rates similar between concentrations -More CHO emptied from stomach with higher concentration -Gastric emptying and fluid absorption don't limit exogenous oxidation
(53)	6 healthy males	-Placebo -2% Glu -6% Glu -12% Glu -7.14 mL/kg immediately before, 1.43 mL/kg every 10 min.	-Fasted -TTE at 80% VO2max	-Dose response for oxidation -Exogenous oxidation sig. lower in 2% than 6% or 12% trials -No sig. difference between endogenous oxidation
(138)	4 healthy males, 1 healthy female	-Water -3% (1% Glu, 2% Suc) -6% (2% Glu, 4% Suc) -325 mL at start, 165 mL every 10 min.	-Fasted -85 min. at ~65% VO2max -Followed by 3 mile time trial	-No dose response for performance

(165)	8 trained female cyclists	-Water -.5 g/min Glu 3.2% -1 g/min Glu 6.4% -1.5 g/min Glu 9.6% -600mL at start, smaller doses every 15 min.	-Fasted -2 hrs at 60% VO2max	-Dose response up to 1 g/min for oxidation -Highest oxidation rates and endogenous sparing observed with 1 g/min Glu -Muscle glycogen oxidation highest with 1.5 g.min
(82)	-Evidence for dose-response effect is inconclusive -Improvements in performance are likely tied to oxidation rates; higher oxidation rates can be obtained with multiple transportable CHOs			
(150)	12 trained male cyclists	-Placebo -15 g/hr Glu -30 g/hr Glu -60 g/hr Glu -250 mL beginning at min. 15 -No fluid ingested during TT	-Fasted -2 hr at 77% VO2max -Followed by 20km TT	-Dose response -60 g/hr results in mean power output 4.2% and 5.7% higher than 30 g/hr and 15 g/hr respectively -Increasing dose from 15 g/hr to 30 g/hr is less likely to result in performance benefit -Endogenous oxidation reduced with 30 g/hr and 60 g/hr due to inhibition of Glu release from liver
(74)	-Recent evidence (Smith 2010) illustrates dose response			
(166)	24 healthy males	-Placebo -Sucrose 50%, Glu 25%, Fru 25% -Solutions – 2%, 4%, and 6% -3 mL/kg immediately before, every 10 min. during	-Fasted (at least 6 hrs) -TTE at 70% VO2max in warm and cool temps	-Dose response -In cool temps, TTE longer with 4% and 6% over Placebo -In cool temps, TTE longer with 6% than 2% -In heat, TTE longer with 6% than placebo

(149)	51 male cyclists and triathletes	10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, and 120 g/hr CHO (1:1:1 glucose–fructose–maltodextrin)	-Fasted -2 hrs at 95% of power eliciting 4 mmol of lactate -20km TT	CHO beverage ingestion and performance appear to be related in a curvilinear dose–response manner, with the best performance occurring with ingestion rate of 78 g/hr.

CHOs and Performance (Table 4)

Most studies show that CHOs enhance performance. Performance improvements have been observed in prolonged exercise (lasting over 2hrs), high-intensity cycling of ~1 hr duration, and intermittent exercise such as soccer.

Study	Problem	Participants	Treatments	Protocol	Findings
(35)	Whether CHOs fed during exercise delays fatigue	10 trained cyclists (9 male, 1 female)	-Placebo -Glu -Ingested 50% solution after 20 min. of exercise delivering 1 g of CHO/kg of body weight. After 60, 90, 120 min. ingest 6% solution	-Fasted -TTE at ~75% VO2max	-Fatigue is delayed when fed CHOs -Effect seen in subjects whose blood Glu declines in fasted state
(65)	Effect of Glu on walking performance and whether it is related to CNS dysfunction	10 trained males	-Placebo -20% solution containing 30 g of Glu at min. 60, 90, 120, and 150	-Fasted -TTE at 45% VO2max walking	-Glu enhances endurance capacity -Hypoglycemia and/or CNS dysfunction not the cause of exhaustion
(60)	Effect of CHOs on glycogen and performance	10 males	-Placebo -43 g of sucrose, 9 g fat, 3 g protein, with 400 mL of water at hr 0, 1, 2, 3	-Fasted -4 hrs cycling – 20 min. at 50% VO2max followed by 10 min. of intermittent sprints and rest -Sprint ride to exhaustion at end of trial	-CHO feedings enhance sprint performance
(9)	Effect of Glu and Fru on exercise capacity	8 trained cyclists	-Water -Glu 7% -Fru 7% -250 mL every 20 min.	TTE at 70% VO2max	-Performance enhanced with Glu ingestion -Subjects rode longer with Glu
(32)	-Long duration moderate exercise >2 hrs results in liver not being able to keep up with muscle Glu uptake: hypoglycemia -People who are hypoglycemic don't always display symptoms -CHOs delays but does not prevent fatigue -CHO ingestion at low intensities results in hyperinsulemia and endogenous sparing mostly in the liver -CHO improves endurance in moderate intensity long duration exercise by sparing muscle glycogen				

(51)	Effect of different frequencies and dosages of CHOs on glycogen and sprint performance	9 males	-Placebo -10.75 g of sucrose with 200 mL of water at every 30 min. beginning at min. 0 -21 g of sucrose with 400 mL of water every hr starting at min. 0	-Fasted -4 hrs cycling – 20 min. at 50% VO2max followed by 10 min. of intermittent sprints and rest -Sprint ride to exhaustion at end of trial	-CHOs enhance sprint performance -BG levels fluctuate more when fed with less frequency
(33)	Muscle glycogen utilization during exercise when fed CHOs	7 trained male cyclists	-Placebo -Glu- 2 g/kg at min. 20, .4 g/kg every 20 min. thereafter	-Fasted -TTE at 70% VO2max	-CHOs delay fatigue significantly (by 1 hr) -Blood Glu can serve as a major fuel source for exercise
(26)	Effect of CHO on performance after cycling to fatigue	7 trained male cyclists	-Placebo -Glu Polymer 3 g/kg -Glu infusion	-Fasted -TTE at 70% VO2max -20 min. rest -TTE at 70% VO2max	-Fatigue can be reversed with CHO ingestion/infusion -Fatigue partly caused by reduced CHO oxidation; infusion of Glu at a rate of 1 g/min required to maintain 70% intensity
(52)	Effect of different amounts of CHOs on performance and glycogen use	8 trained male cyclists	-Water -MD 3 g/100mL -MD 5 g/100mL -MD 7.7g/100mL -Fru 5 g/100mL -High Fru corn syrup 2.3 g/100mL -Glu 2 g/100 mL -150 mL immediately prior to start, 150 mL every 20 min.	-Fasted -2 hr at 90 rpms pushing as hard as possible	-CHO ingestion does not result in improvement in performance

(119)	Effect of CHO feedings immediately before exercise in fasted and fed state	10 trained male cyclists	-Placebo -Drink – 400mL 8% Glu Polymer, 3.5% Fru (45 g CHO) -Bar – 45 g CHO, 9 g fat, 3 g protein with 400 mL water -Ingested 5 min. prior to exercise	-Fasted -4 hrs after high CHO meal -45 min. at 77% VO2max followed by 15 min. performance ride	-Performance enhanced with CHO prior to exercise -Performance enhanced further when fed a meal 4 hrs prior in combo with solid CHO 5 min. prior
(113)	Effect of CHO feedings on gastric emptying and exercise performance	8 trained male cyclists	-Placebo -33 g/hr - 5% (MD, Glu) -40g/hr - 6% (MD 2.14 g/100mL, Fru 1.88 g/100mL, Suc 1.95 g/100mL) -50 g/hr - 7.5% (MD 5.55 g/100mL, Fru 2g/100mL) -~170 mL prior to each 12 min. bout	-(7 x 12 min.) at 70% VO2max. 3 min. rest in between -12 min. TT at end	-Performance enhanced when fed CHOs
(24)	Effect of CHO feedings during high-intensity exercise	7 trained male cyclists	-Placebo -Glu/Suc (85%, 25%) 1 g/kg in 50% solution after 10 min. of exercise. .6 g/kg in 20% solution every 30 min. thereafter	-Fasted -Alternating bouts of 15 min. at 60% VO2max and 15 min. of 85% VO2max until exhaustion	-Performance enhanced -CHO feedings allow subjects to perform 19% more work -CHO allow subjects to maintain 75% VO2max even in latter stages of prolonged intense exercise
(25)	Effect of single CHO feeding late in exercise	6 trained male subjects	-Placebo -Glu Polymer 3 g/kg in 50% solution at min. 135	-Fasted -TTE at 70% VO2max	-Performance enhanced -Subjects given CHO performed 21% longer

(117)	Effects of ingesting Glu, Suc, and Fru on metabolism and performance	9 healthy males, 3 healthy females	-6% Glu -6% Suc -6% Fru -6 mL/kg immediately before, 3mL/kg during every rest period	-Standard breakfast and lunch -20 min. at 65%, 20 min. at 75%, 15 min. at 80%, 10 min at 80%, 15 min. at 75%, 8 min. at 80%, with 4 min. rest between each -600 rpm TT at end	-Performance enhanced more with Glu and Suc than Fru
(105)	Effects of different CHOs on performance	6 males	-Water -Glu -Fru -Glu/Fru -Glu/Electrolyte -36 g/100mL -100mL ingested at the start and every 10 minutes	-Fasted -TTE at 70% VO2max	-Performance enhanced with Glu ingestion
(112)	Effect of different dosages of CHOs on performance and glycogen use	10 trained male cyclists	-Placebo -37 g/hr - 6% (Glu) -74 g/hr - 12% (Glu 8.5%/Fru 3.5%) -111 g/hr - 18% (Glu 14.5%/Fru 3.5%) -150 mL every 15 min.	-105 min. at 70% VO2max followed by 15 min. all out effort -1 trial consisted of 7 x 15 min. bouts at 70% with 3 min. rest between	-12% solution results in improved performance over placebo
(116)	Effect of different doses of CHOs on performance and metabolism	8 healthy males, 2 healthy females	-Placebo - 26 g/hr Glu 6% -52 g/hr Glu 12% -78 g/hr Glu 18% - 2 mL/kg every 15 min. starting at min. 12 of exercise (440 mL/hr)	-Standard breakfast -2 hrs of variable-intensity (50%, 65%, 75% VO2max) -Followed by 4.8km TT	-Performance enhanced with 26 g/hr and 78 g/hr

(168)	Effect of ingesting CHO before, during, or before and during on metabolism and performance	8 trained male, 1 trained female cyclist	-Placebo 3 hrs prior – 5g/kg of 25% CHO solution (333 g total) During - .2g/kg of 8% solution (175 g CHO total) starting at min. 20 and every 20 min. thereafter	-TTE at 70% VO2max -Every 45 min. subjects performed a TT – time taken to complete 3 min. at 90% VO2max	-Performance enhanced with CHO ingestion; effect of ingesting before and during is additive -Fatigue occurs when oxidation falls below 2 g/min
(115)	Effect of different CHO forms on performance	8 trained male triathletes	-Placebo -Solid bananas -Slurried banana drink	-90 min. run followed by 90 min cycling at 70%VO2max -Incremental cycling test to exhaustion	-CHO in solid or liquid form can be equally utilized to improve performance
(93)	Effect of CHO supplementation on finishing time of simulated 80 mile bicycle time trial in FED state	14 trained male cyclists	-Placebo -MD 5% + Fru 2% (37 g/hr) -Every .5 hrs	-80 mile TT	-CHO ingestion enhances performance (by 5%)
(7)	Effect of fluid and CHO ingestion on performance, core temp., and cardiovascular responses	8 trained male cyclists	-Water and electolytes -6% CHO (Gatorade) 1330 ml -40% MD solution 200 ml -Placebo capsules with electrolytes -Immediately before, at 15, 25, 34 min.	-Fasted -50 min. at 80% VO2max -Followed by ~10 min.	Fluid and CHO improve performance by ~6% and effects are additive.
(104)	Effect of an isotonic and hypotonic Glu solution on exercise and metabolism	12 healthy men	-Water -Glu 200 mmol/L -Glu 90 mmol/L -100 mL immediately before and every 10 min. during	-Fasted -TTE at 70% VO2max	-Performance enhanced by ingestion of Glu even if amount is small

(108)	Effects of CHO ingestion throughout exercise versus feeding late in exercise	8 trained male cyclists	-Water -CHO 7% -CHO 21% -250 mL at start and every 15 min. thereafter -21% solution only given at 90, 105, and 120 min.	-Fasted -2 hrs at 70% -Followed by 15 min. performance ride	-Performance enhanced when CHOs ingested throughout -No performance benefit when CHO ingested late in exercise.
(160)	Effect of CHO ingestion during the first hour of running on endurance capacity	11 recreational male runners	-Water -5.5% CHO -6.9% CHO -8 mL/kg immediately before, 2 mL/kg every 20 min. during	-Fasted -TTE at 70% of VO2max	Ingestion CHO in hour 1 of running improves endurance capacity
(158)	Effect of CHO ingestion on glycogen and performance	8 male recreational runners	-Placebo -5.5% CHO -8 mL/kg immediately before, 2 mL every 20 min.	-Fasted -TTE at 70% VO2max	-Performance in TTE enhances with CHO ingestion (27%)
(38)	Effects of ingesting CHOs on fatigue during intermittent, high-intensity cycling	9 healthy men, 7 healthy women	-Placebo -CHO 4 g/kg -18% solution immediately before, 6% every 20 min. during	-Fasted -1 min. bouts at 120-130% with 3 min. rest in between until fatigue	-Performance enhanced with CHO ingestion -RPE lower and time to fatigue longer with CHOs
(111)	Effects of CHO ingestion before and during 15 km running on metabolism and performance	12 trained male runners	-Water -Glu/Suc 6% -Glu/Fru, Syrup/MD 8% -1000 mL 1 hour before, and ad libitum during breaks	-Fasted -15 km TT with breaks at 7.5 km and 13.4 km	-CHOs enhance performance in final 1.6 km of run
(45)	Effect of CHO ingestion on 1 hr TT performance	8 trained male cyclists	-Placebo -8% CHO -25 min. before 4.5 mL/kg	-Not fasted -As much work as possible in 1 hr	-Performance in 1 hr TT enhance by 1.2% with CHO ingestion

(48)	Effect of CHO ingestion before and during exercise on metabolism and performance	7 trained male cyclists	-Placebo -CHO 6.4% 2g/hg -Placebo 30 min. before and CHO during -21% CHO before and placebo during -CHO before and during	-Fasted -2 hrs at 65% VO2max -Followed by 7 kJ TT	-Performance enhanced when CHOs are ingested during exercise -CHOs before only beneficial when CHOs are ingest during exercise with it
(110)	Effect of CHO ingestion on high-intensity ~1 hr exercise	13 trained male cyclists and triathletes	-Placebo -6% Glu -7 mL/kg immediately before, 3.5 mL/kg every 15 min.	-Fasted -TTE at ~83% VO2max	-CHO does not enhance performance in intense ~1 hr exercise -Insufficient CHO gets into blood to affect metabolism
(23)	Effects of pre-exercise CHO meal and CHO solution on running performance	10 trained male runners	-Placebo -CHO meal before and 6.9% drink (dextrose, MD, and Glu) -CHO solution before and water during -5 mL/kg before, 2 mL/kg every 20 min. during	TTE at 70% on treadmill	-CHO meal and drink during had additive positive effect (22%) on TTE performance in runners
(43)	Effect of low and high glycemic CHO intake on performance in 64 km TT	9 trained male cyclists	-Placebo -Low glycemic (Honey 38.5% Fru, 31% Glu, 17% water, 7.2% maltose, 4.2% trisaccharides, 1.5% sucrose, .5% protein) -High glycemic (Dextrose) -15 g gels with 250 mL of water every 16 km	-Meal 4 hrs before TT -64 km TT	-Performance enhanced in final 16 km of TT with low and high glycemic CHOs -No difference between CHO types

(19)	Effect of CHO mouth rinse on ~1 hr TT	9 trained male cyclists (7 male, 2 female)	-Placebo -6.4% MD -Mouth rinse every 12.5% of ride	-Fasted -~60 min. TT	-Performance improved with CHO ingestion by 2.7%
(40)	Effect of CHO on ~60 min. TT	9 trained male cyclists	-Placebo -6% CHO (Gatorade) -8 mL/kg before, 2 mL/kg every 10% of TT starting at 20%	-Standard breakfast 2-hrs before -~60 min. TT	-CHO ingestion has no effect on ~1hr TT performance
(81)	-Performance in events lasting >2hrs and ~1hr enhanced with CHOs although mechanisms unclear -Benefits from small amounts (~15 g/hr) -Most studies conducted using overnight fast, which may produce effects that aren't seen when in fed state -Mechanisms include maintenance of blood Glu, CHO oxidation, endogenous sparing, central effects -Glu, Mal, MD, Suc 1 g/min; Fru, Gal .6 g/min -Intestinal absorption of CHO greatest limiting factor -Multiple transportable CHOs have higher oxidation efficiency				
(88)	Effect of CHO ingestion on running performance	12 trained males	-No supplementation -5% CHO solution every 15 min. during exercise	-TTE at 70% of VO2max	-CHO ingestion improves performance and delays fatigue
(4)	Effect of ingesting CHO solution on subjects with low CHO stores on shuttle running times, soccer passing and shooting performance	16 male college soccer players	-Placebo -6.4% CHO -5 mL/kg before shuttle run, 2 mL/kg every 15 min. during	-Fasted -6 x 15 min. blocks of shuttle runs -Post-exercise soccers skills test	-CHO enables subjects in glycogen depleted states to better maintain skill and sprint performance in soccer
(75)	Effect of CHO ingestion on high-intensity cycling performance of ~25 min.	12 trained male cyclists	-Placebo -6% CHO (Gatorade) -4 mL/kg immediately before, 1.4 mL/kg at 25, 40, and 75% completed of TT	-3 h fast (Not fasted) -16 km time trial	-CHO ingestion during ~25 minute high intensity cycling does not improve performance.
(137)	-CHO intake recommendation of 6-10 g/kg per day -After exercise, 1-1/5 g/kg within 30 min. and again every 2 hrs for 4-6 hrs to replenish glycogen -CHO restriction can be detrimental to performance -Meals consumed 90 to 4hrs prior to competition had no appreciable affect on performance despite hyperglycemia, hyperinsulemia				

(31)	Effects of daily training with CHO ingestion on oxidation rates: trainability of the gut	16 endurance trained male cyclists/triathletes	-High CHO training group -Low CHO training group -During test: CHO 10% Water 5 mL/kg every 20 min.	28 days training -Standard breakfast -Test before and after training – 100 min.65% VO2max -Following by ~30 min. TT	-No clear benefit on performance from training with high or low CHO availability
(89)	-Athletes should consume 5-10 g/kg per day for glycogen resyntheis -CHO meals require 4 hrs to be digested and synthesized into glycogen -CHO snacks consumed 30-60 minutes prior to exercise can increase CHO availability in later stages of exercise -Athletes should consume 1-1.5 g/kg within 30 min and at high CHO meal within 2 hrs to maximize glycogen resynthesis				
(153)	Effect of CHO versus placebo on performance	-Meta Analysis -CHO intakes of ≤8% and between 30-80 g/hr	CHO ingestion enhances performance in TT (2%), submax +TT (7.5%), submax + TTE, and TTE even when subjects optimize endogenous stores before exercise		
(17)	-CHO availability important for training and performance; glycogen replenishment essential -Adding protein to CHO during recovery enhances glycogen storage -For events lasting ~1 hr, very small amounts of CHO or mouth rinsing benefits performance -For longer events, 30-60 g/hr of CHO is beneficial and possibly up to 90 g/hr with mixed CHOs -Benefits of training in a glycogen depleted state are unclear				
(74)	-Glycogen loading can be achieved by athletes without the depletion phase; little benefit of loading in events <90 min. -Pre-exercise feeding may not be detrimental to performance; rebound hypoglycemia early in exercise does not effect performance -CHOs beneficial for intense exercise of ~1 hr (CNS); and over 2 hrs (Metabolic) -Multiple transportable CHOs can increase oxidation rates above 60 g/hr -CHO intake independent of body mass -Training the gut				

Glycogen Sparing (Table 5)

Glycogen sparing is a potential mechanism by which CHOs enhance performance. Many studies show that muscle glycogen is spared when CHO is ingested during prolonged low-intensity exercise (~40% VO2max) and intermittent exercise. During moderate intensity exercise, most research agrees that muscle glycogen sparing occurs during running, but not cycling. Sparing may occur as a result of hyperglycemia and hyperinsulemia, which seems to be more prevalent when CHOs are ingested during running. Liver glycogen sparing and/or reduced hepatic Glu production has also been observed with CHO feedings during exercise.

Study	Participants	Treatment	Protocol	Findings
(98)	4 healthy males, 4 healthy females	-Water -Glu 75 g -Fru 75 g -300 ml 45 min. before,	-CHO rich meal 4 hrs before -30 min. running at 75% VO2max	-Muscle glycogen spared with Fru ingestion prior to exercise
(60)	10 males	-Placebo -43 g of sucrose, 9 g fat, 3 g protein, with 400 mL of water at hr 0, 1, 2, 3	-Fasted -4 hrs cycling – 20 min. at 50% VO2max followed by 10 min. of intermittent sprints and rest -Sprint ride to exhaustion at end of trial	-Muscle glycogen spared with CHO ingestion
(9)	8 trained cyclists	-Water -Glu 7% -Fru 7% -250 mL every 20 min.	TTE at 70% VO2max	-Glu ingestion spares muscle glycogen -Fru does not
(51)	9 males	-Placebo -10.75 g of sucrose with 200 mL of water at every 30 min. beginning at min. 0 -21 g of sucrose with 400 mL of water every hr starting at min. 0	-Fasted -4 hrs cycling – 20 min. at 50% VO2max followed by 10 min. of intermittent sprints and rest -Sprint ride to exhaustion at end of trial	-Inconclusive dose response -Performance improved over placebo with 21 g/hr; not improved with 11 g/hr
(59)	8 males	-Placebo -50 g Glu -50 g Fru -710 mL 45 min. prior to exercise	-Fasted -30 min. cycling at 70% VO2max	-Muscle glycogen usage was *greater* with Glu versus control -Trend towards less glycogen usage with Fru versus Glu
(33)	7 trained male cyclists	-Placebo -Glu- 2 g/kg at min. 20, .4 g/kg every 20 min. thereafter	-Fasted -TTE at 70% VO2max	-Muscle glycogen not spared with CHO ingestion -Blood Glu can serve as a major fuel source for exercise

(91)	27 wistar rats -Glycogen depleted -Non glycogen depleted	-Glu	1 hr running	-In non-depleted rats, Glu infusion spared glycogen in the liver -Glycogen depletion stimulates glycogen synthese; not necessarily Glu infusion -Sources other than Glu infused were used for resynthesis (possibly gluconeogenesis)
(92)	7 trained male cyclists	-25% MD, Fru drink -Encouraged to drink 2 L over 2 hrs 45 min.	-Glycogen depleting ride afternoon before -Standard breakfast -2 min. bouts at 90% Wmax followed by 2 min. at 50% Wmax to exhaustion while drinking water -3 hrs at 40% Wmax (Trial A) -Rest 3 hrs (Trial B)	-Glycogen was synthesis during exercise in Type II fibers (32 mmol/kg) -Resynthesis rate during exercise comparable to maximum rates after exercise
(52)	8 trained male cyclists	-Water -MD 3 g/100mL -MD 5 g/100mL -MD 7.7g/100mL -Fru 5 g/100mL -High Fru corn syrup 2.3 g/100mL -Glu 2 g/100 mL -150 mL immediately prior to start, 150 mL every 20 min.	-Fasted -2 hr at 90 rpms pushing as hard as possible	-No significant difference in glycogen use

(46)	1 female and 4 male trained cyclists	-Placebo -Fru before -Caffeine before -Glu during -Fru/Caff before; Glu during -Every 15 min. starting at min. 15 -240 kcal prior and/or during	-90 min. cycling at ~70% VO2max	-Glu and Caffeine spare muscle glycogen -Ingestion of multiple substances cause greatest variability in glycogen use
(58)	5 trained male cyclists	-Placebo -30 g Glu polymer -250 mL at min. 0, 30, 60, 90	-Fasted -2 hrs cycling at 70% VO2max	-CHO ingestion does not spare muscle glycogen
(112)	10 trained male cyclists	-Placebo -37 g/hr - 6% (Glu) -74 g/hr - 12% (Glu 8.5%/Fru 3.5%) -111 g/hr - 18% (Glu 14.5%/Fru 3.5%) -150 mL every 15 min.	-105 min. at 70% VO2max followed by 15 min. all out effort -1 trial consisted of 7 x 15 min. bouts at 70% with 3 min. rest between	-Muscle glycogen not spared with CHO ingestion at 12% dosage
(169)	12 trained male cyclists	-Water -2% MD -5.75% MD + 2.75% Fru -3 mL/kg immediately before, every 15 min. during exercise	-Fasted -2 hr at 48% VO2max	-Muscle glycogen is spared in the heat with CHO ingestion
(170)	7 trained male cyclists	-Placebo -10% CHO -Solid CHO (25 g MD/Fru) -25% CHO solution 1 g/kg immediately before, 180 mL every 20 min. -Bar consumed with water every 30 min.	-Fasted -200 min. of variable intensity exercise -30 min at 45%VO2max - 6 x 16 min. (8 min. at 75% VO2max, 8 min. at 45% VO2max) -9 x 6 min intervals (3 min. at 75%, 3 min. 45%) -TTE 80% VO2max	-Liquid CHO spares muscle glycogen after 190 min. (35% versus placebo) -CHO drink results in very high blood Glu and insulin -Low intensity or variable intensity with CHO ingestion seems to spare glycogen because it can cause hyperglycemia and hyperinsulemia but not during Moderate intensity

(107)	6 trained cyclists/triathletes	-Placebo -Glu 10% -250 mL at start and every 15 min. during	-Fasted -2 hrs cycling at ~70% VO2max	-CHO intake suppresses hepatic Glu production (51% reduction in HGP)
(12)	14 trained male cyclists (glycogen-loaded)	-Placebo -10% CHO drink -170 mL at start and every 20 min.	-Standard meal 3 hrs before -180 min. cycling at 70% VO2max	-CHO either spares liver glycogen or reduces gluconeogenesis -CHO does not spare muscle glycogen
(159)	7 male recreational runners	-Water -5.5% CHO (Glu, Fru, Maltose, higher saccharides) -8 ml/kg immediately before, 2 ml/kg at min. 20 and 40	-Fasted -60 min. running at 70% VO2max	-CHO ingestion spares glycogen in Type I fibers only (28% sparing)
(158)	8 male recreational runners	-Placebo -5.5% CHO -8 mL/kg immediately before, 2 mL every 20 min.	-Fasted -TTE at 70% VO2max	-CHO ingestion spares glycogen in Type I fibers at time point equivalent to exhaustion in Placebo trial -Muscle ATP and phospocreatine maintained in with CHO ingestion
(157)	-Ingestion of CHOs >45 g/hr accompanied by significant increase in insulin levels could spare muscle glycogen -At low intensities, CHO ingestion can spare muscle glycogen -During moderate intensity cycling, performance enhanced by maintenance of BG and oxidation but not sparing -In moderate intensity running, sparing occurs because insulin and BG is more elevated with CHO ingestion -Glycogen is spared with CHO during intermittent exercise -Fru does not seem to spare glycogen; Glu and sucrose do spare glycogen -Glycogen loading does not appear to inhibit exogenous oxidation, and glycogen loading may spare glycogen during exercise			
(120)	6 male athletes	-Placebo -6.9% CHO (dextrose, Fru, maltose, higher saccarides) -5 mL/kg immediately before, 2mL/kg during rest periods	-Fasted -90 min. of intermittent running (6 x 15 min. bouts with 3 min. rest in between)	-Muscle glycogen spared in Type I and II fibers -Utilization reduced by 22% when ingesting CHO -Glycogen could have been resynthesized during low intensity periods

(80)	6 trained cyclists	-Water -Glu 4% -Glu 22% -Infusion of Glu -8 mL/kg at start, 2 mL/kg every 15 min. during -With low Glu trial – 35 g/hr -With high Glu trial – 175 g/hr	-Fasted -120 min. cycling at 50% VO2max	-Hepatic Glu output completely suppressed with high Glu trial -HGP partially suppressed with low Glu trial -No effect on muscle glycogen
(110)	13 trained male cyclists and triathletes	-Placebo -6% Glu -7 mL/kg immediately before, 3.5 mL/kg every 15 min.	-Fasted -TTE at ~83% VO2max	-Muscle glycogen not spared; usage similar between trials -Only small percentage (26%) of ingested CHO appeared in the blood
(136)	12 boys (11-14 yrs)	-water -6% Glu -3% Fru + 3% Glu -25 mL/kg -Drinks ingested at 30 and 15 min. before, every 15 min. during	-Standardized Breakfast -90 min. 55% VO2max – 30 min. cycling with 5 min. rest repeated 3 times -Ride to exhaustion at 90% VO2max	-Endogenous oxidation was significantly lower at min. in Glu and Glu/Fru trials, but not significantly different from each other
(71)	8 trained, nonacclimated male cyclists	-1.5 g/min Glu -1 Glu + .5 Fru g/min -Water -600 mL at start, 200 mL every 15 min.	-Fasted -120 min. at 50% Wmax -31.9 degrees C	-Glu/Fru resulted in significantly lower endogenous oxidation versus water

(11)	8 healthy males	-Placebo -MD 15% -1 g/kg during exercise	-CHO trial – standard breakfast 2 hrs before -Or Fasted Trial -2 hrs cycling at 75% VO2max	-CHO ingestion combined before and during results in sparing of Type IIa fibers -Glycogen breakdown could have been slowed in Type I early in exercise meaning Type II were not recruited till later -Higher blood insulin, Glu, and lower FFA levels may contribute to increased glycogen synthase activity
(152)	10 trained male cyclists	-Placebo -8% CHO -.7 mL/kg immediately before, 2.5 ml/kg every 20 min. during	-Fasted -180 min. at 50% Wmax	-CHO spares muscle glycogen use during first hour of 3 hrs cycling resulting in significant sparing after 3 hrs -38% and 57% in Type I and II respectively
(165)	8 trained female cyclists	-Water -.5 g/min Glu 3.2% -1 g/min Glu 6.4% -1.5 g/min Glu 9.6% -600mL at start, smaller doses every 15 min.	-Fasted -2 hrs at 60% VO2max	-Muscle glycogen use was 28% lower with Moderate does versus water (Not significant) -CHO at all doses reduces liver Glu output by ~30% -Endogenous oxidation significantly lower.

CHO Metabolism (Table 6)

Glu and Fru provide energy through different pathways. The majority of ingested Glu is absorbed into the circulation. From plasma, this Glu can be taken up by muscle to fuel contraction. This exogenous Glu can represent a large portion of total CHO utilization, 60-90% in some studies. Fru, following absorption in the gut, is mostly taken up by the liver. Although some free Fru remains in the blood to be taken up by muscle, the majority is metabolized in the liver to lactate or converted to Glu. Lactate is either released to be oxidized as a fuel source in active muscles or converted to Glu via gluconeogenesis.

Study	Problem	Participants	Treatments	Protocol	Findings/Mechanisms
(132)	Glu oxidation during prolonged oxidation	7 healthy males	-Glu -100 g in 400 mL of water after 15 min. exercise	-Fasted -4 subjects walked on 10% grade for 2 hrs at 50% VO2max -3 subjects walked for 4 hrs	-Exogenous CHO represented 55% of CHO metabolism and 24% of total energy expenditure -Max exogenous oxidation between .5 and .6 g/min. -Exogenous oxidation increases up to 1-1.5 hrs of exercise
(57)	Fate of Glu ingested during prolonged exercise	6 trained male cyclists	-139 mM of Glu -589 mM of Glu -400 mL consumed after 120 min. of exercise	-Fasted -180 min. cycling at 50% VO2max	-More Glu oxidized from more concentrated solution (Peak contribution of 67% blood Glu) -Oxidation of exogenous low possible because only consumed at start of final hour of exercise
(98)	Substrate utilization after Fru, Glu, and water ingestion during exercise	4 healthy males, 4 healthy females	-Water -Glu 75 g -Fru 75 g -300 ml 45 min. before,	-CHO rich meal 4 hrs before -30 min. running at 75% VO2max	-Blood Glu and insulin do not respond as dramatically with Fru versus Glu -May be because Fru is absorbed and released from liver slower than Glu -Muscle glycogen sparing with Fru

(8)	Absorption rates and metabolism of Glu or Fru ingested in pigs	6 adult Yucatan miniature swine	-1.5 g/kg of Glu -1.5 g/kg of Fru	-Fasted -Observations made every 15 min. during 4 hr period	-More Fru is metabolized in the gut than Glu by intestinal cells (15-20% of lactate) -Small portion of Fru in converted to Glu in gut -Fru taken up by liver more rapidly than Glu -Almost all Glu enters portal vein as Glu, i.e. not metabolized in gut -Fru ingestion increases lactate -12% of Fru absorbed or metabolized was converted to lactate
(90)	Timing of Glu ingestion's effect on exogenous Glu oxidation	9 healthy males	-100 g of Glu after 15 min. of exercise -100 g of Glu after 120 min. of exercise	-Fasted -4 hrs of treadmill at 45% VO2 max	-Oxidation of exogenous Glu is similar if ingested after 15 or 120 min.
(39)	Compare Fru with Glu intake prior to exercise on metabolism	10 trained adults	-Glu -Fru -1 g/kg 1 hr before exercise	-Fasted -45 min. at 60% VO2max -Followed by 15 min. performance test	-Fru oxidized similarly with Glu -Lactate rose more with Fru -Fru has reduced effect on blood Glu and insulin levels versus Glu -Exogenous CHOs represented ~15% of total energy used -No effect on performance with Fru versus Glu

(124)	Percentage of Glu ingested is utilized during exercise	6 healthy males	-200 g Glu in 8 doses every 30 min. -400 g Glu in 8 doses every 30 min.	-Fasted -285 min. at 45% VO2max on treadmill	-100 g/hr of Glu results in exo CHO representing ~90% of total CHO utilization in last hour and permits endogenous sparing
(101)	Metabolic response to Glu and Fru ingestion during exercise	7 healthy males	-Water -Glu (140 g at 7%) -Fru (140 g at 7%) -Ingested every 20 min. starting at min. 0	-Fasted -180 min at 50% VO2max	-Fat utilization greater with Fru than Glu -Less Fru (56%) was oxidized versus Glu (75%) -Blood Glu maintained similarly between Glu and Fru -Lower insulin response with Fru -Endogenous sparing similar between two
(102)	Compare oxidation of Glu, Glu polymer, and Fru during exercise	6 healthy males	-Water -Glu Polymer -Glu -Fru -7% with 235 mL every 20 min. from min. 0 to 100	-Fasted -120 min. cycling 55% VO2max	-Fru less readily oxidation resulting in less sparing than Glu -Fru did not raise plasma insulin higher than water -Water delivery to plasma similar between CHOs
(117)	Effects of ingesting Glu, Suc, and Fru on metabolism and performance	9 healthy males, 3 healthy females	-6% Glu -6% Suc -6% Fru -6 mL/kg immediately before, 3mL/kg during every rest period	-Standard breakfast and lunch -20 min. at 65%, 20 min. at 75%, 15 min. at 80%, 10 min at 80%, 15 min. at 75%, 8 min. at 80%, with 4 min. rest between each -600 rpm TT at end	-Fru ingested resulted in lower plasma Glu and insulin; higher blood Fru, FFAs, cortisol, RPE, and GI distress -Some Fru escaped hepatic metabolism -Fru resulted in lower lactate during performance bout

(3)	Splanchnic and muscle Fru metabolism before and after exercise	12 trained male adults -6 received Fru, 6 Control	-8.5 mmol/min Fru infusion starting at min. 40 till end of rest	-90 min. cycling at 30% VO2max followed by 20 min. rest	-Fru taken up by splanchnic tissue (45%), exercising muscle (28%), and resting muscle (28%) -Glu uptake was unchanged meaning uptake mechanisms are different -Lactate and pyruvate rose with infusion and was taken up by working muscle -Splanchnic release of lactate and pyruvate accounted for 78% of Fru uptake at 90 min. exercise
(22)	Conversion of Fru to Glu in the liver	-Over 90% of the Fru than is converted to Glu derives from cleaving of the Fru carbon skeleton			
(106)	-Fru is rapidly taken up by the liver; majority of Fru taken up by liver meaning very little Fru in blood -Fru enters glycolysis after the phosphofructokinase step allowing for greater flux – increased lactate production -When ingested with Glu, Fru phosporylation largely inhibited by Glu -Major products of Fru in the liver are Glu, glycogen, and lactate -Fru combined with Glu may conserve or synthesize liver glycogen -In the fed state, Fru appears to be predominantly converted to lactate rather than glycogen or Glu				
(144)	Exogenous CHO oxidation during exercise from different sources	8 trained male subjects	-Water -15% Glu, Dextrose -15% Amylose, amylopectin -6 mL/kg immediately before, 2.5mL/kg every 15 min.	-Fasted -150 min. cycling at 60% VO2max	-Soluble CHOs oxidized at higher rate than insoluble

(96)	Oxidation of Glu or galactose during exercise	8 trained male cyclists	-8% galactose -8% Glu -8 mL/kg immediately before, 2 mL/kg every 15 min. during	-Standard breakfast -120 min. at 65% Wmax -60 min. rest -30 min. at 60% Wmax	-Galactose oxidized at .41 g/min at peak -Glu oxidized at .85 g/min at peak -46% of ingested Glu was oxidized; 21% of galactose -Galactose resulted in more endogenous use
(15)	Glu, Fru, and Galactose oxidation during exercise	6 healthy males	-Placebo -Glu -Fru -Galactose -100 g total given via 200 mL every 20 min. starting at min. 0	-Standard breakfast -Snack 2 hrs before -120 min. cycling at 65% VO2max	-Glu and Fru oxidized at similar rates -Galactose oxidized at 60% the rate of Glu and Fru -CHO ingestion reduces endogenous CHO oxidation (9-13%) -Fru and galactose could be preferentially taken up by the liver
(1)	Oxidation of sucrose and isomaltulose during exercise	10 healthy males	-Water -Sucrose 8.5% 1.1 g/min -ISO 8.5% 1.1 g/min	-150 min. cycling at 65% VO2max	-Sucrose oxidized a higher rate than ISO (.92 g/min vs. .54 g/min.)
(161)	Oxidation of trehalose and maltose during exercise	9 trained male cyclists	-Water -Trehalose 1.1 g/min 8.5% -Maltose 1.1 g/min 8.5% -600 mL at start, 150 mL every 15 min.	-Fasted -150 min. of cycling at 55% Wmax	-Maltose had higher oxidation than trehalose (1.01 g/min versus .73 g/min) -Maltose results in greater endogenous sparing

(95)	Effect of Glu and Fru co-ingestion on lactate and Glu fluxes and oxidation compared to Glu alone during exercise	7 trained male cyclists	-Glu/Fru 1.2 g + .8 g/min -Glu 2 g/min -600 mL at start, 280 mL every 20 min.	-Fasted -120 min. cycling at 60% VO2max	-Lactate appearance (~30% higher), disappearance, and oxidation was higher in Glu/Fru versus Glu -Liver may act as carbon reservoir after Fru has been converted to lactate; 40% of labeled carbons not recovered -Oxidation higher in Glu/Fru -Gluconeogenesis from Fru higher in Glu/Fru -Gluconeogenesis from lactate was likely suppressed by hyperinsulemia

Mechanisms (Table 7)

CHOs may enhance performance by maintaining oxidation rates, preventing hypoglycemia, sparing muscle and/or liver glycogen, and/or by providing an important fuel source late in exercise.

Recent research and technological innovation has allowed the examination of cellular mechanisms. CHO ingestion may help maintain muscle energy balance. Studies show that subjects ingesting CHO during exercise have reduced levels of inosine monophospate (IMP) late in exercise. Thus, it is likely that CHO availability leads to reduced metabolism of adenosine diphospate (ADP) and adenosine monophospate (AMP), which occurs when adenosine triphosphate (ATP) is being utilized faster than it is being produced. CHO ingestion also may help to maintain excitation-contraction coupling late in exercise. This may be due to a better maintenance of Na-K-ATPase activity, and therefore membrane potential, which has been observed with CHO ingestion.

Study	Problem	Participants	Treatments	Protocol	Findings/Mechanisms
(35)	Whether CHOs fed during exercise delays fatigue	10 trained cyclists (9 male, 1 female)	-Placebo -Glu -Ingested 50% solution after 20 min. of exercise delivering 1 g of CHO/kg of body weight. After 60, 90, 120 min. ingest 6% solution	-Fasted -TTE at ~75% VO2max	-Delayed fatigue not tied to prevention of hypoglycemia -Blood Glu may be an important fuel source
(32)	-Prolonged moderated intensity exercise reduces blood Glu and depletes glycogen -Hypoglycemic subjects often don't display symptoms; can't fully explain fatigue -CHO during moderate intensity exercise reduces muscle glycogen depletion -During low intensity, CHO causes hyperinsulemia causing increase Glu uptake and oxidation sparing endogenous sources mostly in the liver				
(59)	Effect of Fru ingestion on muscle glycogen usage during exercise	8 males	-Placebo -50 g Glu -50 g Fru -710 mL 45 min. prior to exercise	-Fasted -30 min. cycling at 70% VO2max	-Trend towards less glycogen usage with Fru versus Glu -Less dramatic increase in blood Glu with Fru; also rapid decline during exercise with Glu but not Fru -Increased blood lactate with Fru -Fru may better maintain liver CHO stores because it is more readily taken up by liver
(124)	Percentage of Glu ingested is utilized during exercise	6 healthy males	-200 g Glu in 8 doses every 30 min. -400 g Glu in 8 doses every 30 min.	-Fasted -285 min. at 45% VO2max on treadmill	-100 g/hr of Glu results in exo CHO representing ~90% of total CHO utilization in last hour and permits endogenous sparing

(26)	Effect of CHO on performance after cycling to fatigue	7 trained male cyclists	-Placebo -Glu Polymer 3 g/kg -Glu infusion	-Fasted -TTE at 70% VO2max -20 min. rest -TTE at 70% VO2max	-BG important energy source for CHO availability late in exercise -Fatigue associated with declines in CHO oxidation or reduced CHO availability -Muscles rely on BG late in exercise as glycogen is depleted; Infusion of Glu at a rate of >1 g/min required to maintain 70% intensity -Likely that majority of infused Glu readily oxidized rather than stored
(151)	Effect of CHO ingestion during exercise on IMP accumulation	9 trained cyclists (8 males, 1 female)	-Placebo -Glu/Fru 7.5% (1.8:1) -3.6 mL/kg after 15 min. exercise and every 15 min. thereafter	-Fasted -TTE cycling at 70% VO2max	-CHO increased kreb's cycle intermediates -CHO reduces IMP accumulation; improved muscle energy balance
(163)	Oxidation rates of orally ingested CHOs during exercise	6 trained male cyclists	-Water -MD 4, 8, 12, 16% -Sucrose 8% -8 mL/kg immediately before; 2mL/kg every 15 min. during	-Standard breakfast -120 min. cycling at 60% VO2max	-No difference in oxidation between MD and Sucrose; close to 1 g/min -Oxidation rates plateau at 90-120 min. -CHO maintains oxidation rates late in exercise; 50% of all CHO oxidation in last 30 min. -Maximal oxidation and sparing with 8%

(12)	Influence of CHO intake during exercise on substrate turnover and oxidation	14 trained male cyclists (glycogen-loaded)	-Placebo -10% CHO drink -170 mL at start and every 20 min.	-Standard meal 3 hrs before -180 min. cycling at 70% VO2max	-CHO provided at a rate (.83 g/min) closely matched by exogenous oxidation (.7 g/min) -CHO did not cause hyperglycemia; plasma insulin remained low -Glu oxidation increased to minute 90 -BG as fuel source: Blood Glu oxidation reached 65% of total late in exercise
(61)	Effects of hyperglycemia and Euglycemia on Glu kinetics	12 trained male cyclists	-Glu (25% Dextrose)	-2 hrs cycling at 70% VO2max	-Liver Glu output completely suppressed by hyperglycemia
(107)	Effect of CHO ingestion during exercise on Glu kinetics	6 trained cyclists/triathletes	-Glu 10% -Placebo -250 mL every 15 min. starting at min. 0	-Fasted -2 hrs cycling at 70% VO2max	-Liver Glu production reduced by 51% -Plasma Glu uptake is enhanced with CHO ingestion, i.e. uptake is increased with increased availability -Exogenous Glu accounted for ~15% of TEE -Glycogenolysis does not inhibit BG uptake due to hyperglycemia

(80)	Effect of CHO on endogenous CHO production	6 trained cyclists	-Water -Glu 4% -Glu 22% -Infusion of Glu -8 mL/kg at start, 2 mL/kg every 15 min. during -With low Glu trial – 35 g/hr -With high Glu trial – 175 g/hr	-Fasted -120 min. cycling at 50% VO2max	-Hepatic Glu output completely suppressed with high Glu trial -HGP partially suppressed with low Glu trial -No effect on muscle glycogen -CHO oxidation may be limited by rate of appearance in the gut -Insulin levels were significantly increased during High Glu trials; possibly inhibits HGP -Max oxidation rate - .94 g/min.; limited by intestinal absorption -Ingested Glu nearly completely oxidized (close to 98%)
(109)	Effect of CHO ingestion during exercise on IMP levels	8 trained male cyclists	-Placebo -CHO 8% -250 mL at start and every 15 min.	-Fasted -TTE cycling at 70% VO2max	-CHO ingestion resulted in lower levels of IMP at end of exercise – CHO improves muscle energy balance -Levels lower despite exercising for longer
(110)	Effect of CHO ingestion on high-intensity ~1 hr exercise	13 trained male cyclists and triathletes	-Placebo -6% Glu -7 mL/kg immediately before, 3.5 mL/kg every 15 min.	-Fasted -TTE at ~83% VO2max	-HGP partially suppressed with CHO ingestion -Only 26% of CHO enters blood; intensity causes less absorption
(81)	-CHOs improve performance in short ~1hr intense exercise possibly my central mechanisms -Proposed mechanism – maintaining blood Glu and oxidation, sparing liver and/or muscle glycogen, synthesizing glycogen during low intensity exercise, or central effects				

(56)	Effects of Glu on Na-K-ATPase pump activity in response to exercise	14 healthy males, 1 healthy female	-Placebo -Glu 6% -240 mL at min. 30, every 15 min. during	-Fasted -TTE cycling at 52% VO2peak	-Na-K-ATPase activity was higher at min. 90 with Glu -Exercise regardless of duration did not result in a decrease activity -Glu may help to maintain membrane excitability -Glu resulted in higher insulin and lower catacholamines -Pump activity up despite lower catacholamines; mechanism independent of catacholamines -These pumps appear to prefer CHO for ATP meaning low levels of CHO availability may inhibit function
(42)	Exercise's effect with or without Glu on sarcoplasmic reticulum Ca++ handling properties	14 males, 1 female	-Placebo -Glu 6% -240 mL starting at min. 30, every 15 min. thereafter	-Fasted -TTE cycling at 60% VO2max	-Glu ingestion has no effect on SR-Ca++ handling, endogenous glycogen, or muscle metabolic responses -Glu increases insulin, reduces catacholamines -Exercise reduces Ca++-ATPase activity
(82)	-Mechanisms responsible for ergogenic effects – maintenance of CHO oxidation, glycogen sparing, prevention of hypoglycemia, central mechanisms via oralpharyngeal receptors (high intensity)				

(86)	-Mechanisms for ergogenic effect – attenuation of central fatigue; maintenance of oxidation rates; muscle glycogen sparing; changes in muscle metabolite levels; reduced exercise-induced strain; better maintenance of excitation-contraction coupling -Evidence shows CHO does not reduce muscle glycogen use -Little evidence for dose-response effect -CHO may maintain muscle function late in exercise by maintaining Na-K-ATPase activity -Glu may blunt serotonin release (via blunting of free tryptophan), which may be responsible for central fatigue -Hypoglycemia does not necessarily negatively affect performance in prolonged exercise -CHO reduces IMP and results in increased PCr levels following exercise -CHO may reduce stress hormones and cytokines which lead to central fatigue -CHO may reduce oxidative stress

CHO Digestion and Fluid Delivery (Table 8)

CHO oxidation does not seem to be limited by gastric emptying. Although emptying slows as the CHO concentration increases, delivery of CHO to the intestine actually increases with increasing concentration. Moreover, emptying does not slow at a rate that limits absorption. Small doses of CHOs may actually enhance emptying and fluid delivery via solvent drag; however, larger doses of CHO typically slow fluid delivery and gastric emptying, as mentioned. The slowing of gastic emptying and fluid delivery may be attenuated by mixing different forms of CHOs. Mixtures of Glu or MD and Fru result in improved gastric emptying and fluid delivery versus an isocaloric amount of Glu or MD.

The limiting factor for exogenous CHO utilization is likely absorption in the gut. Absorption into the circulation requires transport across two membranes in intestinal cells, first the apical followed by the basolateral membrane. At the apical membrane, Glu is primarily transported via the active transporter, SGLT1. However, it can also be transported via GLUT2. Fru is primarily transported via GLUT5 at the apical membrane, but can also be transported, to a smaller extent, via GLUT2. Interestingly, Glu ingestion has been shown to upregulate GLUT2 translocation to the apical membrane. This may explain why coingesting Glu with Fru stimulates Fru absorption. Both Glu and Fru are transported across the basolateral membrane primarily via GLUT2.

The primary limiting factors for CHO absorption are intensity of exercise and CHO content. High-intensity exercise results in reduced blood flow to the gut which reduces CHO transport. Highly concentrated doses of CHO often result in malabsorption because transporters become saturated. Because Glu and Fru do not share transporters, by coingesting Glu and Fru, more CHO can be absorbed before saturation of transporters occurs.

Study	Problem	Participants	Treatments	Protocol	Findings
(34)	Gastric emptying rates for various sports drinks	3 healthy women, 9 healthy men	-Water -Gatorade -Braketime -Body Punch -400 mL	-Stomach aspiration	-High concentration of CHOs slows gastric empyting -Gatorade emptied slowest, but it delivers most CHOs in 15 min.
(122)	Gastric emptying of CHO drinks during exercise in heat	5 trained male runners	-Placebo -10% Glu -10% Glu Polymer -200mL every 20 min.	-Fed -2 hrs running at 65% VO2max	-No difference in gastric emptying - Trend for Glu drink to empty slower than water-placebo (not significant)
(143)	Capacity to absorb Fru	10 healthy adults	-15, 20, 25, 37.5, 50 g of Fru 10% -100, 75, 50 Suc 10% -50 g Glu, 50 g Fru 10% -50 g Fru, 25 g Glu 10% -50 g Fru, 12.5 g Glu 10%	N/A	-Fru alone isn't absorbed as well as Glu or Suc -Fru and Glu combined absorbed well -Glu stimulates Fru uptake in dose-dependent manner
(113)	Effects of different CHO concentrations on gastic emptying and performance	8 trained male cyclists	-Placebo -5% (MD, Glu) -6% (MD 2.14 g/100mL, Fru 1.88 g/100mL, Suc 1.95 g/100mL) -7.5% (MD 5.55 g/100mL, Fru 2g/100mL) -~170 mL prior to each 12 min. bout	-(7 x 12 min.) at 70% VO2max. 3 min. rest in between -12 min. TT at end	-Beverages containing Fru and/or Suc were empytied better than MD/Glu beverage
(103)	-GE is slowed by CHOs with more slowing occurring the higher the concentration and osmolality -With increasing CHO intake fluid delivery is decreased, but CHO delivery is increased -Passive water absorption is stimulated by active Glu and sodium absorption				

(14)	Fru transporter – GLUT 5	-GLUT5 is the Fru transporter -GLUT5 shows little ability to transport Glu -Uptake up Fru by GLUT2 inhibited by Glu and Galactose			
(134)	Gastric emptying, absorption, and oxidation of CHO during exercise	8 trained male cyclists	-Water -4.5% Glu -17% Glu -17% MD -8 mL/kg at start, 3 mL/kg at 20, 40, and 60 min.	-Fasted -80 min. at 70% VO2max	-More CHO emptied from stomach with higher concentration -Gastric emptying and fluid absorption don't limit exogenous oxidation
(28)	Effect of CHO composition on plasma volume and gastric emptying	10 trained male cyclists	-Placebo -Glu/Suc 6% -8.3% High Fru CS -6.3% HFCS + 2% Glu Polymer -Consumed every 15 minutes	-105 min. cycling at 70% VO2max -Followed by 15 min. performance ride	-No differences in gastric emptying or plasma volume -Highly concentrated drinks deliver more CHOs
(13)	-30 to 50% of people participating in exhaustive exercise experience 1 or more symptoms of GI distress -Ingesting foods high in fiber, fat, protein, or highly concentrated CHOs can cause symptoms -Dilute CHO solutions do not cause GI distress -Reduced blood flow to GI tract during intense exercise causes distress -Exercising training can attenuate the reduction in blood to gut				
(114)	Responses of intestinal Glu transporters to different levels of dietary sugars	-High Glu diet increases SGLT1 and GLUT2 mRNA -Galactose and Fru increase GLUT2 mRNA -GLUT5 mRNA was only increased by Fru			
(118)	-Gastric emptying and fluid absorption is reduced with increasing CHO concentration -Small concentrations of CHO can actually stimulate net intestinal absorption				
(162)	Effect of osmolality and CHO content on gastric emptying	6 healthy males	-Glu 40g/L -Glu polymer 40 g/L -Glu 188 g/L -Glu polymer 188 g/L -600 mL	-Fasted -Gastric aspiration	-CHO content has more effect on gastric emptying than osmolality

(147)	Effect of CHO type and concentration on water absorption	8 healthy males	-Glu -MD -Glu + Fru -Glu + Suc -All varied from 6-8%; osmolalities 268-314 mOsm/kg	-75 min. rest	--Highest CHO absorption occurred with Glu and Fru -Mixed solution had greater water absorption despite increased osmolalities -Effect of osmolality on water absorption is related to CHO type -Water absorption may be limited by CHO transport -When CHOs are mixed, higher concentration does not effect absorption
(49)	-Diet influences up or downregulation of intestinal transporters; trainability of the gut? -Reserve of unutilized transporters exists because of unpredictability of diet and physiological responses to environment -Hyperglycemia increases turnover of transporters perhaps by turning on inactive ones -High CHO diet can increase Glu absorption rates via increased transport sites within 24 hrs, takes 48hrs to lose these adaptations; same for GLUT5 and Fru although increases take 48 hrs -Increased transport activity is more sensitive to Fru than Glu (GLUT5) -High fat diets enhances Glu uptake -Starvation/fasting causing increased absorption of nutrients per milligram without an upregulation in transporters; causes higher ratio of mature transporters as fewer new transporters will be made because of lack of energy – thus efficient transporters -Thus, starvation can lead to increased sugar transport -Exercise causes reduced Fru uptake capacity -GLUT5 highly specific to Fru; upregulation is transcriptional -SGLT 1 transports Glu and other sugars -GLUT 2 Glu, Galactose, and Fru?				

(146)	Mechanisms of Fru transport	7 healthy men	-Fru/Glu -Fru/Glu/Acarbose -Fru/Mannitol -Suc/Acarbose -Suc - perfused 15 mL/min.	-triple lumen	-Fru/Glu and Fru/Glu/Acarbose absorbed fastest -Fru transported via facilitated diffusion -Paracellulary, transported via Glu-drag
(48)	Effect of CHO ingestion before and during exercise on metabolism and performance	7 trained male cyclists	-Placebo -CHO 6.4% 2g/hg -Placebo 30 min. before and CHO during -21% CHO before and placebo during -CHO before and during	-Fasted -2 hrs at 65% VO2max -Followed by 7 kJ TT	-Rate of exogenous Glu oxidation is limited by digestion, absorption, and rate of appearance in blood -Higher oxidation with pre-exercise feeding likely tied to hyperinsulemia
(110)	Effect of CHO ingestion on high-intensity ~1 hr exercise	13 trained male cyclists and triathletes	-Placebo -6% Glu -7 mL/kg immediately before, 3.5 mL/kg every 15 min.	-Fasted -TTE at ~83% VO2max	-Only 26% of CHO enters blood; intensity causes less absorption
(76)	-CHOs can be separated into two groups based on oxidation rates: Glu, Suc, Mal, MD at 1 g/min; Fru, Gal, Amylose at .6 g/min -CHO absorption in the gut seems to be the limiting factor for oxidation -CHO intake at 1 g/min can result in oxidation of ~1g/min; increasing intake doesn't increase oxidation rate -Liver may also take up Glu making it a limiting factor -Ingesting large amounts of Glu can increase CHO and water absorption				
(135)	-Fluid delivery increases with increasing ingestion although the percentage of total fluid ingested drops with increasing ingestion -Increased fluid intake is associated with increased GI distress -High intensity limits absorption -CHO enhances fluid delivery				

(97)	-The majority of CHO absorption occurs in the small intestine meaning absorption depends on the rate at which CHO is emptied from the stomach -Gastric emptying is slowed by increasing the energy content. Although low concentrations (~2%) of CHO are emptied at roughly the same rate as water, increasing the content above this slows the rate. However, more CHO is delivered the more the energy content. -Energy density is the limiting factor for empyting, not osmolality. -High intensity exercise results in reduced emptying -Absorption is also negatively correlated to intensity -CHO can stimulate water absorption unless the concentration is very high; high concentrations can cause body water to move into the intestine before reaching equilibrium and being reabsorbed with the solute -Intestinal transporters can be separated into two categories: active transporters and diffusion facilitated transporters -Active transports function via the electrochemical gradient of a co-transported molecule like Na -Diffusion facilitated transporters function via concentration gradients of a particular solute -Glu is mainly actively transported with sodium via SGLT1 -Fru is transported via the sodium-independent GLUT5 -Suc is hydrolyzed to Glu and Fru in the intestine				
(81)	-CHOs improve performance in short ~1hr intense exercise possibly my central mechanisms -Single CHO sources can be absorbed at a max rate of 1 g/min (Glu, Suc, MD, Maltose 1 g/min; Fru, Galactose ~.6 g/min.) -Using multiple CHOs can increase absorption by 20-50% -Proposed mechanism – maintaining blood Glu and oxidation, sparing liver and/or muscle glycogen, synthesizing glycogen during low intensity exercise, or central effects				
(142)	High molecular weight versus low molecular weight Glu polymers on substrate oxidaton	8 trained male cyclists	-water - 1.8 g/min HMW 11.25% - 1.8 g/min LMW 11.25% -600 mL at start, 250 mL every 15 min.	-Fasted -150 min. cycling at 65% VO2max	-Molecular weight has no influence on absorption and oxidation -Maximum oxidation Glu 1 g/min (52% of what was ingested)
(138)	Whether lowering the concentration of a CHO drink influences gastric empyting or CHO absorption	4 healthy males, 1 healthy female	-Water -3% (1% Glu, 2% Suc) -6% (2% Glu, 4% Suc) -325 mL at start, 165 mL every 10 min.	-Fasted -85 min. at ~65% VO2max -Followed by 3 mile time trial	-Gastric emptying, water absorption, and time trial performance not different -CHO absorption and blood Glu highest with 6%

(71)	-Exogenous oxidation and fluid delivery of Glu/fru versus Glu in the heat. -Muscle glycogen utilization with Glu ingestion in heat.	8 trained, nonacclimated male cyclists	-1.5 g/min Glu -1 Glu + .5 Fru g/min -Water -600 mL at start, 200 mL every 15 min.	-Fasted -120 min. at 50% Wmax -31.9 degrees C	-Glu/Fru resulted in greater fluid delivery than Glu -No difference in glycogen utilization
(94)	Fluid tolerance while running	5 female, 2 male trained runners	-Glu 4% - ad libitum every 10 min. -Glu 4% - Match sweat rate every 10 min.	-Fasted -90 min. at 65% VO2max	-No differences observed in gastric emptying
(37)	Fluid delivery with mixed carb beverage versus Glu	6 males	-Water -75 g Glu 12.5% - 50 g Glu, 25 g Fru 12.5% -Taken in 600 mL bolus	-Fasted -Drink -Sit for 180 min.	-Glu/Fru results in higher fluid delivery than Glu -Fluid delivery for water and Glu/Fru not different
(82)	-Oxidation rates - ~1 g/min – Glu, Suc, Maltose, MD, Amylopectic, High molecular weight Glu polymer; .5-.6 g/min – Fru, Galactose, Isomaltulose, Trehalose, Amylose -Oxidation increased with multiple sources and has higher oxidation efficiency -Body size/mass has little effect on oxidation rates				
(78)	Effects of ingesting Water, Glu,, and Glu/Fru on gastric emptying and fluid delivery	8 healthy males	-Water -1.5 g/min Glu -1 Glu + .5 Fru g/min -600 mL at start, 203 mL every 15 min.	-Fasted -120 min. cycling at 50% Wmax	-Ingesting Glu/Fru results in increased gastric emptying and fluid delivery versus Glu
(87)	-Glu is primarily transported via the active transporter SGLT1; however, Glu ingestion results in movement of GLUT2 to the apical membrane which facilitates Glu transport also -Glu travels across the basolateral membrane via GLUT2 -Fru is transported through the apical membrane via GLUT5 but shares GLUT2 with Glu for transport from the basolateral membrane -Fru transport through apical membrane can be increased with Glu coingestion as it results in GLUT2 moving to apical membrane				
(83)	-Absorption rate not affected by body mass -Oxidation rates similar if large bolus of CHO is ingested at the onset of exercise or with frequent smaller feedings				

(84)	-Fru is transported across the apical membrane of intestinal epithelial cell by GLUT5 and possibly by GLUT2 -Fru is transported across the basolateral membrane is via GLUT2 and GLUT5 -Upregulation of GLUT5 and GLUT2 mRNA occurs with increases in dietary Fru; GLUT2 also upregulated by dietary Glu -Glu seems to stimulate Fru absorption possibly because of the upregulation of GLUT2 (particularly at the apical membrane) by the presence of Glu

GI Distress (Table 9)

Gastrointestinal (GI) distress is often reported during endurance exercise. Symptoms include nausea, abdominal cramping, urge to urinate or defecate, bloating, belching, flatulence, etc. GI distress is often observed with the ingestion of CHO during exercise. The cause of these symptoms may be inefficient gastric emptying or absorption of CHO. Indeed, studies show that GI distress is associated with unabsorbed CHO remaining in the gut. Multiple transportable CHOs have been shown to be digested and/or absorbed more efficiently than isocaloric amounts of Glu. Moreover, more symptoms of GI distress have been observed when subjects ingest large amounts of any single CHO source. However, there are individual differences in terms of GI distress. Some can tolerate higher CHO intake rates than others. In fact, one may be able to 'train' his/her gut to absorb more CHOs by training with high CHO availability. The effect of 'training the gut' on the occurrence of GI distress is yet to be examined.

Study	Problem	Subjects	Treatments	Protocol	GI Distress
(85)	Effect of diet on Glu transport in mice	Adult swiss Webster mice	-CHOW diet (High in CHOs) -MEAT diet (negligible CHOs)	Measurements on excised everted sleeves	-Intestinal transport of Glu increases nearly 2-fold with high Glu diets -Most likely because of stimulation of unused transporters rather than formation of new ones
(133)	Absorption of Fru	16 healthy adults	Various amounts of Fru	N/A	-Malabsorption associated with GI distress
(143)	Capacity to absorb Fru	10 healthy adults	-15, 20, 25, 37.5, 50 g of Fru 10% -100, 75, 50 Suc 10% -50 g Glu, 50 g Fru 10% -50 g Fru, 25 g Glu 10% -50 g Fru, 12.5 g Glu 10%	N/A	-Unabsorbed CHO could cause GI distress
(29)	Effect of sorbitol ingestion on GI distress	30 healthy men and women	-20 g 8% -10 g 4% -5 g 2%	N/A	-Malabsorption can cause GI distress
(117)	Effects of ingesting Glu, Suc, and Fru on metabolism and performance	9 healthy males, 3 healthy females	-6% Glu -6% Suc -6% Fru -6 mL/kg immediately before, 3mL/kg during every rest period	-Standard breakfast and lunch -20 min. at 65%, 20 min. at 75%, 15 min. at 80%, 10 min at 80%, 15 min. at 75%, 8 min. at 80%, with 4 min. rest between each -600 rpm TT at end	-Fru ingested resulted in more GI distress
(114)	Responses of intestinal Glu transporters to different levels of dietary sugars	-High Glu diet increases SGLT1 and GLUT2 mRNA -Galactose and Fru increase GLUT2 mRNA -GLUT5 mRNA was only increased by Fru			

(13)	-30 to 50% of people participating in exhaustive exercise experience 1 or more symptoms of GI distress -Ingesting foods high in fiber, fat, protein, or highly concentrated CHOs can cause symptoms -Dilute CHO solutions do not cause GI distress -Reduced blood flow to GI tract during exercise causes distress -Exercising training can attenuate the reduction in blood to gut				
(49)	-Diet influences up or downregulation of intestinal transporters; trainability of the gut? -Reserve of unutilized transporters exists because of unpredictability of diet and physiological responses to environment -Hyperglycemia increases turnover of transporters perhaps by turning on inactive ones -High CHO diet can increase Glu absorption rates via increased transport sites within 24 hrs, takes 48hrs to lose these adaptations; same for GLUT5 and Fru although increases take 48 hrs -Increased transport activity is more sensitive to Fru than Glu (GLUT5) -High fat diets enhances Glu uptake -Starvation/fasting causing increased absorption of nutrients per milligram without an upregulation in transporters; causes higher ratio of mature transporters as fewer new transporters will be made because of lack of energy – thus efficient transporters -Thus, starvation can lead to increased sugar transport -Exercise causes reduced Fru uptake capacity -GLUT5 highly specific to Fru; upregulation is transcriptional -SGLT 1 transports Glu and other sugars -GLUT 2 Glu, Galactose, and Fru?				
(125)	Prevalence of GI distress symptoms in runners, cyclists, triathletes	606 trained endurance athletes	Various	Questionnaire	-Most symptoms reported by cyclists -GI distress during exercise correlates with GI distress issues when at rest -Runners experience more lower GI distress -Cyclists upper and lower GI symptoms

(79)	Whether gastrointestinal problems are related to endotoxemia in ironman triathletes	29 male triathletes, 1 female triathlete	Various	-Blood samples immediately after and 1, 2, and 16 hrs after competition	-93% of participants experienced GI distress; 7% had to quit because of them -Endotoxin LPS does leak into the circulation and may be responsible for cytokine release and GI distress -68% of subjects had endotoxemia
(136)	Substrate utilization in exercising boys ingesting water, Glu, and Glu plus Fru	12 boys (11-14 yrs)	-water -6% Glu -3% Fru + 3% Glu -25 mL/kg -Drinks ingested at 30 and 15 min. before, every 15 min. during	-Standardized Breakfast -90 min. 55% VO2max – 30 min. cycling with 5 min. rest repeated 3 times -Ride to exhaustion at 90% VO2max -Stomach fullness scale	-Similar in all trials
(145)	Effect of intravenous Glu infusion on gastric motility	Adult male Sprague-Dawley rats	25%Glu at 2 mL/hr	N/A	-Gastric motility inhibited by Glu infusion, but only when rats were hypoglycemic to begin with. -Site of inhibition is in CNS not periphery
(67)	Effect of ingesting Glu, Suc, and Fru simultaneously on oxidation rates	8 trained male cyclists	-Water -2.4 g/min Glu -1.2 Glu + .6 Fru + .6 Suc g/min -600 mL at start, 150mL every 15 min.	-Fasted -150 min. at ~60% VO2max	-More severe complaints in Glu trial -1 subject in Glu trial vomited after 120 min.

(72)	Effects of drinking Glu/Suc and Glu/Maltose versus Glu on oxidation rates	9 trained male cyclists	-1.8 g/min Glu -1.2 Glu + .6 Suc g/min -1.2 Glu + .6 Maltose g/min -Water -600 mL at start, 150 mL every 15 min.	-Fasted -150 min. at 50% Wmax	-More subjects reported severe problems in Glu and Glu/Maltose trials
(69)	Whether ingestion of Glu/Fru would result in oxidation rate >1 g/min	8 trained male cyclists	-1.8 g/min Glu -1.2 g/min Glu -1.2 Glu + .6 Fru g/min -Water -600 mL at start 150 mL every 15 min.	-Fasted -120 min. at 50% Wmax	-Severe GI complaints in high Glu trial -Questionnaire used
(164)	Whether ingestion of MD plus Fru leads to exo oxidation >1.1 g/min.	8 trained male cyclists	-Water -1.8 g/min MD -1.2 MD + .6 Fru g/min. -600 mL at start, 200 mL every 15 min.	-Fasted -150 min. at 55% Wmax	-4 severe complaints in MD trial -1 sever complaint in MD/Fru
(18)	Role of tension receptors in gastric perception	6 healthy men, 8 healthy women	N/A	-Induce gastric contraction or relaxation -Scale of fullness and hunger	-Stomach volume and subsequent stretch is more likely the cause of fullness -Tension receptors do not signal fullness
(70)	Whether ingestion of glu/suc results in higher oxidation rates than Glu alone	8 trained male cyclists	-1.2 g/min glu (8.7%) -1.2 g/min suc (8.7%) -.6 glu + .6 suc g/min(8.7%) -1.2 glu + 1.2 suc g/min (17.5%) -600 mL at start, 150 mL every 15 min.	Fasted 120 min. at 50% Wmax	-No obvious differences between trials -More distress with CHOs

(77)	-Exogenous oxidation rates and Glu kinetics during 5 h of exercise -Effect on oxidation of Glu/Fru	8 endurance trained males	-1.5 g/min Glu -1 Glu + .5 Fru g/min -600 mL at start, 270 mL every 20 min.	-Fasted -5 hrs cycling at 58% VO2max	-Perception of stomach fullness lower with Glu/Fru compared to Glu
(71)	-Exogenous oxidation and fluid delivery of Glu/fru versus Glu in the heat. -Muscle glycogen utilization with Glu ingestion in heat.	8 trained, nonacclimated male cyclists	-1.5 g/min Glu -1 Glu + .5 Fru g/min -Water -600 mL at start, 200 mL every 15 min.	-Fasted -120 min. at 50% Wmax -31.9 degrees C	-2 severe complaints in Glu trial -No severe complaints in Glu/Fru or water
(154)	Effect of ingestion of high fat energy supplements on gastric distress	9 trained male cyclists	-2 week diet high in esterified oils -2 week diet high in long-chain fatty acids During: 1) CHO + esterified oils 2) Placebo following long chain fatty acid diet 3) CHO only following long chain fatty acid diet	-Fasted -3 hrs cycling at 50% VO2max -Followed by 10 min. maximal sprints	-Some attenuation of gastric distress with CHOs and esterified oils, but detrimental effect on performance
(68)	Whether Glu/Fru leads to oxidation rates >~1.3 g/min	8 trained male cyclists	-Water -1.2 g/min Glu -1.2 Glu + 1.2 Fru g/min -600 mL at start, 150 mL every 15 min.	-Fasted -150 min. at 50% Wmax	-No difference in number of complaints or number of subjects complaining between trials -1 subject in Glu/Fru trial had severe problem

(139)	Effect of various ratios of Fru to MD on oxidation and performance	10 trained male cyclists and triathletes	-MD .6 g/min (No Fru) -MD .6 + Fru .3 g/min (Low Fru .5) -MD .6 + .5 Fru g/min (Medium Fru .8) - MD .6 + .7 Fru g/min (High Fru 1.2)	-Fasted -2 hrs at 50% Wmax -10 max effort sprints (2-3 min.) with rest at ~40% VO2max (5-6 min.) between each -Questionnaire – nausea and abdominal cramps	-Average nausea reduced in Medium and High Fru trials
(94)	Fluid tolerance while running	5 female, 2 male trained runners	-Glu 4% - ad libitum every 10 min. -Glu 4% - Match sweat rate every 10 min.	-Fasted -90 min. at 65% VO2max	-Drinking to match sweat rate results in fewer complaint of GI distress
(127)	GI tolerance with high CHO intake during exercise	Endurance trained men and women ~75	-Glu/Fru 1.0 g/min every 3.2 kms (Study 1) -Glu/Fru 1.4 g/min (Study 1) -Glu gels 1.4 g/min (Study 2) -Glu/Fru gels 1.4 g/min (Study 2)	-16 km runs outdoors	-No significant differences between trials for GI distress -Few had severe complaints meaning individualized feeding strategies may be required
(131)	Oxidation rates between mixed CHO gel and drink	8 trained male cyclists	-Gel (1.2 Glu + .6 Fru g/min.) plus water -Drink – 1.2 Glu + .6 Fru g/min -Water -400 mL of water and 50 g of gel at start, 200 mL and 25 g of gel every 15 min. -400 mL of drink at start, 200 mL every 15 min.	-Fasted -180 min. at 60% VO2max	-No severe GI symptoms -No difference in stomach fullness

(130)	Oxidation rates between mixed CHO solids and drink	8 trained cyclists	- Bar (.67 Glu + .33 Fru g/min) plus water - Drink – 1 MD + .5 Fru g/min -Water -400 mL water + Bar at start, 200 mL water + 32 g of Bar every 15 min. -400 mL drink at start, 200 mL every 15 min.	-Fasted -180 min. at 60% VO2max	-No severe symptoms in any trial -Stomach fullness highest with bar
(156)	Effect of Glu/Fru versus isocaloric Glu on performance	9 trained male cyclists	-2.4 g/min Glu -1.2 Glu + 1.2 Fru g/min -250 mL to start, 250 mL every 15 min.	-Fasted -simulated 100 km time trial with intermittent 1 km and 4km sprints	-4 of 9 experienced GI distress in Glu trial -2 episodes of diarrhea, 1 vomiting, 1 sour stomach -no complaints in Glu/Fru
(31)	Effects of daily training with CHO ingestion on oxidation rates: trainability of the gut	16 endurance trained male cyclists/triathletes	-High CHO training group -Low CHO training group -During test: CHO 10% Water 5 mL/kg every 20 min.	28 days training -Standard breakfast -Test before and after training – 100 min.65% VO2max -Following by ~30 min. TT	-Training with high CHO availability resulted in increased Glu oxidation during submaximal exercise and increased citrate synthase activity -This occurred despite no increase in GLUT4 content -No clear benefit on performance
(129)	CHO oxidation from from a drink in running versus cycling	8 trained male cyclists or triathletes	-Water -1 Glu + .5 Fru g/min -300 mL at start, 150 mL every 15 min.	-Fasted -Running 120 min. at 60% VO2max -Cycling 120 min. at 60% VO2max	-No severe problems recorded in either trial

(128)	Nutritional and fluid intake of endurance athletes and GI symptoms	221 ironman triathletes, marathon runners, or professional cyclists	N/A	-Post-race questionnaires for intake and GI symptoms	-High CHO intake related to more GI symptoms, but also better performance -GI distress most prevalent in Ironman -GI distress correlated with history of problems -Triathletes ingest more CHOs than runners
(123)	Impact of the ratio of Glu/Fru on oxidation, absorption and performance	10 trained male cyclists	-Placebo Fru and MD 1.8 g/min -4.5% and 9% (.5) -6% and 7.5% (.8) -7.5% and 6% (1.25)	-Fasted -150 min. at 50% peak power -Incremental test to exhaustion	-Stomach fullness, ab cramping, nausea lowest with .8 followed by 1.25 solution.
(140)		-7 male, 3 female mountain bikers (race) -16 male cyclists (lab)	-Glu+MD ~1.4 g/min -Fru+MD ~1.4 g/min	-Standardized meal evening before race and lab portion, no breakfast (fasted) -Lab portion, subjects consumed cereal bar 10 min. prior to exercise -2.5 hr mtn bike race -~3 hr ride – 94 min. set workload followed by performance test	-Reduced GI distress with Fru+MD -Mean sprint power actually *increased* with increased GI distress in the lab -Performance times in race were associated with lower ratings of GI distress

Physiological Variables (Table 10)

The effect of CHO on various physiological variables has been reported on extensively. CHO ingestion during exercise generally does not alter VO_2 or VE compared to placebo or water ingestion. RER and blood glucose typically rise with CHO ingestion. Moreover, as a result of increased CHO availability, RER is maintained late in exercise with CHO ingestion compared to water or placebo. HR is not affected at the onset or during the early stages of exercise. However, late in exercise, via the enhanced ability to maintain intensity, HR is often higher with CHO ingestion. Ratings of perceived exertion (RPE) are lower with CHO ingestion, particularly late in exercise. These differences may be due to depletion of endogenous CHO stores. Recent studies have reported lower RPE with ingestion of a Glu/Fru beverage versus a Glu beverage. The authors have speculated that this may be due to greater CHO availability when subjects ingest Glu/Fru. It may also be due to reduced GI distress with Glu/Fru relative to Glu.

The effect of CHO ingestion on blood lactate (LA) and blood glucose seems to be dependent on the CHO type. When comparing Glu to placebo or water, there is no difference in LA. Fru ingestion results in increased LA versus Glu and placebo/water. This is likely due to differences in metabolism between Glu and Fru. Glu is readily available to be taken up and oxidized by the muscle after being absorbed; Fru is diverted to the liver where is it converted either to LA or Glu via gluconeogenesis. These differences are also likely responsible for the effect of Fru on blood glucose. There is a delay in the rise of blood glucose with Fru ingestion. This is likely due to the time it takes to convert Fru to Glu via gluconeogenesis.

Glu and Fru coingestion results in enhanced CHO oxidation versus ingestion of an isocaloric Glu beverage. This is due to enhanced absorption via separate intestinal transporters for Glu and Fru. Not surprisingly, this enhanced CHO oxidation results in higher RER values with Glu/Fru versus Glu and placebo/water. LA is also higher with Glu/Fru because of the above-mentioned nature of Fru metabolism.

Study	Problem	Participants	Treatments	Protocol	Findings
(57)	Fate of Glu ingested during prolonged exercise	6 trained male cyclists	-139 mM of Glu -589 mM of Glu -400 mL consumed after 120 min. of exercise	-Fasted -180 min. cycling at 50% VO2max	-Plasma glucose rises within 5 min. of exercise and plateaus after 20 min.
(35)	Whether CHOs fed during exercise delays fatigue	10 trained cyclists (9 male, 1 female)	-Placebo -Glu -Ingested 50% solution after 20 min. of exercise delivering 1 g of CHO/kg of body weight. After 60, 90, 120 min. ingest 6% solution	-Fasted -TTE at ~75% VO2max	-CHO ingestion leads to blood glucose level being maintained at higher than pre-exercise levels throughout exercise -RER was not different between trials
(39)	Compare Fru with Glu intake prior to exercise on metabolism	10 trained adults	-Glu -Fru -1 g/kg 1 hr before exercise	-Fasted -45 min. at 60% VO2max -Followed by 15 min. performance test	-Fructose results in lower RER, blood glucose, and LA (in hour rest before exercise)
(59)	Effect of Fru ingestion on muscle glycogen usage during exercise	8 males	-Placebo -50 g Glu -50 g Fru -710 mL 45 min. prior to exercise	-Fasted -30 min. cycling at 70% VO2max	-No differences in RER -Blood glucose decline more rapidly with Glu than Fru with onset of exercise -Blood glucose elevated more with Glu than Fru
(101)	Metabolic response to Glu and Fru ingestion during exercise	7 healthy males	-Water -Glu (140 g at 7%) -Fru (140 g at 7%) -Ingested every 20 min. starting at min. 0	-Fasted -180 min at 50% VO2max	-Blood glucose remains stable with Glu and Fru -HR rose more with Water -Fructose has delayed affect on Glu availability—increase in blood glucose and RER occurs after 40 min. rather than 20 min with Glu

(33)	Muscle glycogen utilization during exercise when fed CHOs	7 trained male cyclists	-Placebo -Glu- 2 g/kg at min. 20, .4 g/kg every 20 min. thereafter	-Fasted -TTE at 70% VO2max	-Blood glucose and RER maintained with Glu -LA the same -RPE higher with placebo late in exercise
(26)	Effect of CHO on performance after cycling to fatigue	7 trained male cyclists	-Placebo -Glu Polymer 3 g/kg -Glu infusion	-Fasted -TTE at 70% VO2max -20 min. rest -TTE at 70% VO2max	-Glu ingestion or infusion raises blood glucose and RER -LA similar between trials -RPE lower with CHO
(102)	Compare oxidation of Glu, Glu polymer, and Fru during exercise	6 healthy males	-Water -Glu Polymer -Glu -Fru -7% with 235 mL every 20 min. from min. 0 to 100	-Fasted -120 min. cycling 55% VO2max	-Plasma glucose rose with Glu ingestion only -HR maintained with CHO
(117)	Effects of ingesting Glu, Suc, and Fru on metabolism and performance	9 healthy males, 3 healthy females	-6% Glu -6% Suc -6% Fru -6 mL/kg immediately before, 3mL/kg during every rest period	-Standard breakfast and lunch -20 min. at 65%, 20 min. at 75%, 15 min. at 80%, 10 min at 80%, 15 min. at 75%, 8 min. at 80%, with 4 min. rest between each -600 rpm TT at end	-Plasma glucose lower with Fru than Suc or Glu -Lower LA and HR during TT with Fru compared to Suc and Glu
(3)	Splanchnic and muscle Fru metabolism before and after exercise	12 trained male adults -6 received Fru, 6 Control	-8.5 mmol/min Fru infusion starting at min. 40 till end of rest	-90 min. cycling at 30% VO2max followed by 20 min. rest	-RER rose with Fru infusion -Lactate rose 2-fold with Fru infusion

(68)	Whether Glu/Fru leads to oxidation rates >~1.3 g/min	8 trained male cyclists	-Water -1.2 g/min Glu -1.2 Glu + 1.2 Fru g/min -600 mL at start, 150 mL every 15 min.		-No differences between VO2 -RER was higher with CHO -RER higher with Glu/Fru than Glu -Plasma glucose higher with CHO -LA higher with Glu/Fru than Glu or water
(139)	10 trained male cyclists and triathletes	-MD .6 g/min (No Fru) -MD .6 + Fru .3 g/min (Low Fru .5) -MD .6 + .5 Fru g/min (Medium Fru .8) - MD .6 + .7 Fru g/min (High Fru 1.2)	-Fasted -2 hrs at 50% Wmax -10 max effort sprints (2-3 min.) with rest at ~40% VO2max (5-6 min.) between each	-Questionnaire – nausea and abdominal cramps -Average nausea reduced in Medium and High Fru trials	-Lower perceptions of muscle tiredness, nausea, physical exertion, attenuated fatigue with Medium and High Fru
(78)	Effect of Glu/Fru on fluid delivery, gastic emptying, and hydration	8 males	-Water -1.5 g/min Glu -1 Glu + .5 Fru g/min -600 mL at start, 203 mL every 15 min.	-Fasted -120 min. at 60% VO2max	-RPE legs lower with Glu/Fru
(148)	20 aerobically or strength trained men	-Glu 50g -Glu/Fru 50 g + 15g -400mL 15 min. before	-Fasted -10 sets of 10 reps of half squat (90% 10RM, 165 seconds between sets) -30 min. cycling at midpoint between two ventilatory thresholds	N/A	RPE reduced in strength and endurance exercise with glu/fru versus Glu supplementation before exercise

(95)	Effect of Glu and Fru co-ingestion on lactate and Glu fluxes and oxidation compared to Glu alone during exercise	7 trained male cyclists	-Glu/Fru 1.2 g + .8 g/min -Glu 2 g/min -600 mL at start, 280 mL every 20 min.	-Fasted -120 min. cycling at 60% VO2max	-LA higher with Fru -Plasma glucose not different between CHO trials -Plasma fructose increased with Fru -RER was higher with Glu/Fru than Glu -HR the same

CHAPTER THREE

METHODOLOGY

Subjects

Approximately 10-12 endurance-trained male cyclists will be recruited from James Madison University and the surrounding area. A minimum of 10 subjects will ensure adequate statistical power. Subjects will be recruited through personal contacts and flyers posted at local bike shops. Information provided to potential subjects will include the following: basic criteria for inclusion in the study, a brief description of the study demands, and benefits of participation.

Subjects will undergo initial screening to ensure they meet inclusion criteria. Subjects must be "regular cyclists" (i.e. perform cycling a minimum of 3 times per week for the preceding two months). Each subject needs to possess a VO_{2peak} of $\geq$55 ml/kg/min or 4.5 L/min in pre-trial physical assessments. Subjects will be asked to complete a health history questionnaire. To ensure the subjects' safety, all subjects must be characterized as "low risk" for exercise complications using criteria from the American College of Sports Medicine's Guidelines for Exercise Testing and Prescription (7^{th} Ed., ACSM, 2006). Finally, prior to any testing, subjects will be required to read and sign informed consent forms, which provide details describing the study, the risks and benefits of the study, and confidentiality of the study. IRB approval will be obtained before proceeding with the study.

Experimental Design

Subjects who meet the above criteria will complete 6 total trials, each separated by 5-7 days. Specifically, subjects will complete 1 pre-testing trial, 1 familiarization trial,

and 4 experimental trials. During the 4 experimental trials, subjects will ingest a carbohydrate solution or a flavored placebo.

Preliminary Testing

Subjects will report to the Human Performance Laboratory where their height (nearest 0.5 cm) and weight (nearest 0.1 kg) will be recorded. Their VO_{2peak} and associated W_{max} will be assessed using a graded exercise test on an electronically braked cycle ergometer. Subjects will ride at a self-selected workload estimated as "a comfortable, but not easy pace for a 1-hour ride." The workload will be increased by 25 watts every 2 minutes until subjects voluntarily request to stop due to fatigue or are unable to continue at a cadence >50 rpms. Metabolic measurements will be assessed at each stage during this test using a Moxus Modular Metabolic System (Bastrop, TX). Heart rate will be assessed throughout using a Suunto heart rate monitor (Vaanta, Finland).VO_{2peak} and W_{max} will be determined from data obtained during the test and used to establish intensities for subsequent exercise protocols as well as to establish inclusion criteria as described above.

Familiarization Trial

Before performing the experimental trials, subjects will complete one familiarization trial. The familiarization trial will be identical to experimental trials, with the exception that subjects will consume only water during the trial.

Experimental Trials

Subjects will complete 4 separate experimental trials on an electronically braked cycle ergometer (Velotron, Inc.). Trials will be double-blind, randomly counterbalanced, and placebo controlled. Each trial will consist of two exercise phases. The first phase will

consist of 120 min. of steady-state cycling at 55% W_{max}. The steady-state portion will be immediately followed by a simulated 30-km TT (~50 min.).

All trials will be conducted at ambient room temperature (72-76^{o}F). Subjects will be asked to void their bladders prior to all trials. A fan will be utilized on "high" speed setting and placed 2 meters from the handlebars for uniform cooling during trials. Subjects will be encouraged to treat the TT portion of each trial as a competitive event and provide a maximal effort. Subjects will receive no feedback regarding performance during the TT except for distance completed and distance remaining. Researchers will provide no verbal encouragement during the TT.

Treatments

As outlined above, subjects will perform 4 experimental trials. During these trials, subjects will consume 4 different solutions. Subjects will receive 60 g/hr of glucose (MG), 90 g/hr of glucose (HG), 60 g/hr of glucose + 30 g/hr of fructose (GF), or a non-caloric artificially sweetened placebo (P). Immediately prior to each trial, subjects will receive 600 ml of an experimental beverage. Thereafter, subjects will receive 150 ml every 15 min. during the steady state portion of the trial. Another 150 ml will be provided at 3 points during the 30 km TT (TT), (7.5, 15, and 22.5 km).

Dietary and Exercise Controls

Subjects will be asked to record food intake 24 hours prior to their first experimental trial. The subjects will then be provided with a copy of their initial dietary log, which they will be asked to use in order to replicate their food intake for the 24 hrs preceding each subsequent experimental trial. Subjects will be asked to refrain from heavy exercise for 48 hrs prior to each experimental trial. Moreover, subjects will be

asked to record all physical activity performed during the 72-hr preceding each experimental trial and be instructed to maintain consistent exercise habits between trials. Additionally, subjects will be asked to abstain from any alcohol and caffeine for 24 hrs and 12 hrs prior to the experimental trials, respectively.

Subjects will perform the trials in the fed state. On the night prior to each trial (7-9 hrs prior), subjects will consume a liquid meal replacement (Ensure® Shakes) at an amount corresponding to 20-25% of their daily caloric intake. 2 hrs prior to all experimental trials, subjects will consume a standardized breakfast consisting of ~500 kcals. Consuming the meal replacement shakes and standardized breakfast will standardize the nutritional intake leading up to each trial. Two previous studies, (Currell et al. 2008; Triplett et al. 2010), standardized pre-trial nutrition by having subjects perform after an overnight fast. During pilot testing, fasted subjects became severely hypoglycemic and, in some cases, could not complete the trial without consuming CHOs. Exercising in the post-prandial state will help to prevent hypoglycemia and better emulate real-world racing conditions.

Measurement of Performance and Physiological Data

Performance – Exercise performance will be measured using cycling time and mean power output (watts) for the simulated 30-km TT.

Metabolic Measurements – Metabolic measurements will be assessed using a Moxus Modular Metabolic System (Bastrop, TX) at the following time points: minutes 15, 35, 55, 75, 95, and 115 of the 120-min steady state phase, and at 20-km into the 30-km time trial (TT). At each of these points, 5 minutes of expired gas collection will be performed and an average of the last three minutes will be recorded. Dependent

measurements obtained/derived from expired gases will include *oxygen uptake (VO_2)*, *ventilation rate (VE)*, and *respiratory exchange ratio* (*RER*; indicating relative contributions of fat and carbohydrate to energy expenditure).

Blood Glucose and Lactic Acid – Finger-stick blood samples (~0.5 ml) will be obtained at the following time points: minutes 20, 40, 60, 80, 100, and 120 of the 120-min steady state phase, and at 20-km into the 30-km TT. Glucose and lactate levels will be determined immediately from whole blood using an automated analyzer (YSI 2300 STAT glucose/lactate analyzer).

Heart Rate – Heart rate will be recorded at the time-points above (Blood glucose and lactic acid time points) using a Suunto heart rate monitor. In addition, average heart rate for the 30-km TT will be recorded.

Ratings of Perceived Exertion (RPE) – Subjective ratings of exertion will be obtained by having subjects point to a corresponding level of exertion (rated numerically from 6-20) on a Borg RPE scale. RPE will be obtained at the time-points indicated (Blood glucose and lactic acid time points). Subjects will receive instructions regarding how to utilize the RPE scale during the familiarization trial, consisting of the following: *"Please describe your current level of exertion using the following scale. This level should represent your overall perception of effort, and not localized to a specific group of muscles, etc. For reference, a 6 would represent your effort when you are resting or watching TV, while 20 would represent the highest level of exertion you are capable of producing during exercise".*

Gastrointestinal Distress Scale – Subjects will be asked to complete a questionnaire (verbally) at minutes 30, 60, 90, and 120 of the 120-min steady state phase

of the exercise trials. Subjects will also be asked to complete the questionnaire at 20 and 30-km of the 30-km TT. The questionnaire contains questions regarding the presence of GI problems at that moment and addresses the following complaints: stomach problems, GI cramping, bloated feeling, diarrhea, nausea, dizziness, headache, belching, vomiting, and urge to urinate or defecate. The items will be scored on a 10-point scale (1 = not at all, 10 = very, very much). The severity of the GI symptoms will be divided into two categories, severe and nonsevere symptoms. Symptoms will only be registered as severe symptoms when a score of ≥5 out of 10 is reported. When a score of <5 is given, they will be registered as nonsevere.

Statistics

Univariate ANOVAs (randomized complete block design) were used to determine differences between treatment conditions for all variables unless otherwise stated. Simple contrasts between treatment conditions were used to generate *P* values for subsequent analysis as has been done previously (67). Residuals from ANOVA analyses were visually inspected for non-uniformity of variance. In cases of heteroscedasticity, variables were log-transformed prior to analysis. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

Due to limitations in examining performance-related measurements with traditional null hypothesis testing, magnitude-based inferences about the data were made using methods described by Hopkins and colleagues (25). 90% confidence intervals (CI) are presented to illustrate uncertainly in treatment effects. Threshold values for a substantial change were calculated as 0.2 × SD (from PL trial) , while thresholds for log-

transformed data were held constant at 0.2; as described previously (1, 67).. A published spreadsheet (26) was used to classify treatment effects as beneficial/positive, harmful/negative, or trivial/neglible. Likelihoods were classified as <1% almost certainly no chance, 1-5% = very unlikely, 5-25% = unlikely, 25-75% = possible, 75-95% = likely, 95-99% = very likely, and >99% = almost certain (67). If confidence intervals overlapped, effects were classified as unclear. Effects were described as trivial/negligible when the majority of the CI lay between the threshold for a substantially positive and negative effect (67). All data was presented as means ± SD.

GI distress scores were analyzed with a frequency table for severe symptoms (a score of ≥ 5), as described previously (32).

CHAPTER FOUR

MANUSCRIPT

THE ERGOGENIC EFFECTS OF GLUCOSE AND FRUCTOSE COINGESTION DURING PROLONGED CYCLING

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Running head: carbohydrate, glucose, fructose, and cycling performance

ABSTRACT

The purpose of this investigation was to examine the effects of glucose and fructose coingestion on cycling time trial performance and physiological responses to exercise. Eight trained male cyclists (age: 25 ± 6.2 yrs, height: 180.2 ± 4.3 cm, weight: 76.9 ± 9.2 kg, and VO_{2max}: 61.9 ± 6.2 $mL \cdot kg^{-1} \cdot min^{-1}$) completed the study. Subjects ingested either an artificially-sweetened placebo (PL), a moderate-glucose beverage (MG: 1.0 $g \cdot min^{-1}$), a high-glucose beverage (HG: 1.5 $g \cdot min^{-1}$), or a glucose and fructose beverage (GF: 1.5 $g \cdot min^{-1}$; 2:1 ratio) during ~3 hrs of exercise; consisting of 2 hours of constant load cycling (55% W_{max}, 195 ± 17.3 W), immediately followed by a computer-simulated 30-km time trial. Physiological responses (V_E, VO_2, RER, heart rate, blood glucose, blood lactate, and RPE) and incidences of GI distress were assessed during early- (15-20 min), middle- (55-60 min), and late-exercise (115-20 min), and during the time-trial. Treatment differences were analyzed using qualitative inferences. Time trial performances were 'likely' improved with GF (50.4 ± 2.2 min) and MG (51.1 ± 2.4) versus PL (52.9 ± 3.7 min), while differences between HG (52.0 ± 3.7 min) and PL were 'unclear'. GF resulted in 'likely' (3.0%) improvement versus HG and an 'unclear' (1.2%) benefit relative to MG. MG was 'possibly' beneficial (1.8%) versus HG. Few incidences of GI distress were reported in any trials. GF ingestion appears to enhance performance relative to PL, and HG. However, further study is necessary to determine if GF improves performance versus moderate (currently recommended) doses of glucose.

INTRODUCTION

Carbohydrate ingestion is recommended during prolonged exercise (37, 47) because it maintains blood glucose levels (9, 10), spares endogenous carbohydrate stores (2, 32, 55, 58), sustains high rates of carbohydrate oxidation late in exercise (7, 44), enhances motor output (5), and improves performance (9, 14, 16). Recent evidence suggests that the ergogenic effects of carbohydrate are dose-dependent. Smith and colleagues reported progressive improvements in prolonged cycling performance with increasing glucose dosages up to 60 $g \cdot hr^{-1}$ (54); and up to 78 $g \cdot hr^{-1}$ with co-ingestion of glucose, maltodextrin, and fructose (53).

The dose-response effects of carbohydrate ingestion likely results from augmented exogenous carbohydrate oxidation, which is limited by intestinal absorption (46, 51). Glucose is absorbed via the SGLT1 transporter at a peak rate of ~60 $g \cdot hr^{-1}$; while fructose is absorbed via GLUT5 at rates up to ~35 $g \cdot hr^{-1}$ (29, 51). When glucose (and/or glucose polymers) and fructose are consumed simultaneously, absorption and oxidation rates increase up to ~90 $g \cdot hr^{-1}$ (23, 59) likely as a result of non-competitive intestinal transport (3, 15, 52). This enhanced oxidation may be responsible for reported improvements in cycling performance with glucose and fructose co-ingestion (11, 48, 57).

Two studies have reported that glucose+fructose ingestion during prolonged cycling augments performance by a substantial degree (~8%) in comparison to isocaloric amounts of glucose (11, 57). However, the volume of glucose consumed in these studies (90-122 $g \cdot hr^{-1}$) exceeded maximal intestinal uptake rates (60 $g \cdot hr^{-1}$), likely resulting in considerable glucose malabsorption. Carbohydrate malabsorption often results in

gastrointestinal distress (45, 50). This supposition is supported by observations from Triplett (57), that 4 of their 9 subjects reported substantial GI symptoms during the glucose trial. Alternatively, numerous studies have reported fewer incidences of GI distress with glucose+fructose ingestion during cycling versus isocaloric amounts of glucose presumably as a result of enhanced absorption of glucose and fructose (24, 30, 48, 57). Thus, it is plausible that the reported performance benefits of glucose+fructose were larger than would be expected if compared to recommended amounts of glucose ($\leq$ 60 $g \cdot hr^{-1}$). Furthermore, subjects in the previous studies completed all cycling trials following an overnight fast, which might magnify performance benefits of carbohydrate ingestion in comparison to trials conducted in the post-prandial state (1).

The purpose of the current study was to examine the effects of glucose+fructose ingestion on prolonged cycling performance under conditions that were consistent with current sports nutrition recommendations. Specifically, we tested cyclists in the post-prandial state, and examined the efficacy of glucose+fructose in comparison to a moderate dose of glucose, an isocaloric high-dose of glucose, as well as a placebo beverage.

MATERIALS AND METHODS

Subjects

Ten male endurance trained cyclists and triathletes (VO_{2max} >55 $ml \cdot kg^{-1} \cdot min^{-1}$) from James Madison University and the Harrisonburg area volunteered to participate in this study. Two subjects withdrew prior to completion because of circumstances unrelated to the study, resulting in complete data from eight subjects. Subjects were provided written and oral information about experimental procedures and potential risks prior to giving informed consent. All procedures were approved by the James Madison University Institutional Review Board prior to any testing.

Cardiorespiratory Fitness

Subjects performed an incremental exercise test to exhaustion on a bicycle ergometer (Velotron, Racermate, Inc., Seattle, WA, USA) to determine VO_{2max}. Subjects began the test at a self-selected workload estimated as "a comfortable, but not easy pace for a 60-min ride". Power was then increased by 25 W every two-min until the subject reached volitional exhaustion. Metabolic measurements were assessed throughout each stage of the test using a Moxus Modular Metabolic System (AEI Technologies, Pittsburgh, PA, USA). VO_{2max} was determined by the highest 30-sec mean oxygen uptake value. Peak power at VO_{2max} (W_{max}) was defined by the power corresponding to the final completed stage, and was used to prescribe exercise intensity for the 120-min constant-load segment of subsequent trials.

Exercise Trials

Subjects completed five trials (one familiarization trial, followed by four experimental trials) on the aforementioned cycle ergometer. Trials consisted of 120 min of constant-load cycling at 55% W_{max} (195 ± 6 W) followed by a simulated 30-km TT, each separated by 6-14 days. The familiarization trial was identical to the experimental trials (see below), except that no blood samples were obtained, and subjects received only water while cycling. Subjects were asked to void their bladder prior to all trials. A pedestal fan was placed ~2 m from the handlebars and utilized on high speed setting for uniform cooling during each trial. Subjects were encouraged to treat the TT portion of each trial as a competitive event and provide a maximal effort. Subjects did not receive performance feedback during the TT other than elapsed- and remaining distance, and no verbal encouragement was provided during the TT.

Treatments

A randomly counterbalanced, double-blind, placebo-controlled design was implemented to compare the effects of four separate treatment conditions on performance, cardiovascular, and metabolic physiology. The treatments were: 1) glucose+fructose (GF): 80 $g \cdot L^{-1}$ glucose + 40 $g \cdot L^{-1}$ fructose (Tate and Lyle, Decatur, IL, USA), 2) a moderate-dose of glucose (MG): 80 $g \cdot L^{-1}$glucose, 3) a high-dose of glucose, calorically-matched to GF (HG): 120 $g \cdot L^{-1}$ glucose, 4) non-caloric artificially sweetened placebo (Splenda, Fort Washington, PA, USA) (PL). Each solution also contained 470 $mg \cdot L^{-1}$ sodium chloride (Morton Salt, Chicago, IL, USA) and 200 $mg \cdot L^{-1}$ potassium chloride (NOW Foods, Bloomingdale, IL, USA). Immediately prior to each trial, subjects

received 600 ml of treatment beverage. Thereafter, subjects received a 150 ml feeding every 15 minutes during the constant-load portion of the trial, and at three points during the 30 km TT (7.5, 15, and 22.5 km). The MG ingestion rate of 60 $g \cdot hr^{-1}$ (1.0 $g \cdot min^{-1}$) was chosen as it falls at the upper end of recommended ranges for carbohydrate intake rates (47). A carbohydrate delivery rate for GF and HG of 90 $g \cdot hr^{-1}$ (1.5 $g \cdot min^{-1}$) was chosen for comparison with studies using similar amounts (26, 30, 31).

30-km TT Performance

Finishing time and mean power output (watts) during the pre-loaded 30-km TT were used as performance criteria. We have previously assessed the reproducibility of cycling time/power measurements using identical equipment in our laboratory. Using a similar performance trial (20-km of cycling over a simulated hilly course) and a comparable set of male subjects (n=10; 28 ± 8 y, 73 ± 6 kg, 65 ± 9 $ml \cdot kg^{-1} \cdot min^{-1}$), the coefficient of variation (CV) between repeated trials (under placebo conditions, following a familiarization trial) was 1.4% for time, and 2.6 % for power output (18). Similarly, we obtained repeatability data from three pilot subjects, who performed repeated trials using the exact trial utilized in this study (i.e. 30-km trial, following two hours of constant-load cycling), and obtained CV's of ~3%.

Physiological Measurements

Oxygen uptake (VO_2), expired ventilation (VE) and respiratory exchange ratio (RER) were assessed using a Moxus Modular Metabolic System (AEI Technologies, Pittsburgh, PA, USA) at the following time points: minutes 15-20, 55-60, and 115-120 of

the constant-load phase, and at 20-km of the TT. These time points were selected to correspond with early, middle, and late exercise, and a representative value from the TT. Aggregates of the final 3 minutes of each phase were recorded.

Heart rate (Suunto, Vaanta, Finland) and ratings of perceived exertion (RPE; Borg Scale) were recorded at minutes 20, 60, and 120 of constant-load cycling, and at 20-km of the TT. Finger-stick blood samples (~0.5 ml) were obtained at rest, and at the time points indicated above. Glucose and lactate levels were determined immediately from whole blood using automated instrumentation (YSI 2300 STAT glucose/lactate analyzer, Yellow Springs, OH, USA).

Total carbohydrate oxidation during the time trial was analyzed as described previously (33).

Gastrointestinal Distress Scale

Subjects verbally indicated their perceived level of upper-GI distress at minutes 30, 60, and 120 of constant-load cycling and at 20-km of the TT. Utilizing a 10-point scale (1 = not at all, 10 = very, very much), subjects rated the following symptoms: stomach problems, GI cramping, bloated feeling, diarrhea, nausea, dizziness, headache, belching, and vomiting (28).

Dietary and Exercise Controls

Subjects were instructed to: 1) Maintain consistent dietary habits for 72 hours prior to each trial, 2) Record food intake 24 hours prior to their first experimental trial, 3) Replicate their exact food intake for the 24 hours preceding each subsequent

experimental trial, 4) Refrain from heavy and/or unaccustomed exercise for 48 hours prior to each experimental trial, 5) Maintain consistent exercise habits between trials and record all physical activity performed during the 72 hours preceding each experimental trial, and 6) Abstain from alcohol and caffeine for 24 hours and 12 hours prior to the experimental trials, respectively. Subjects performed all trials in the fed state. Specifically, subjects consumed 20-25% of their estimated daily caloric expenditure (Harris-Benedict equation) in the form of a liquid meal replacement (Ensure® Shakes, Abbott Laboratories, Abbott Park, IL, USA) in the evening prior to each trial (8-10 hours prior). Two hours prior to all exercise trials, subjects consumed a standardized meal consisting of ~500 kcals (cereal with milk, orange juice, and strawberry yogurt).

Statistical Analyses

Univariate ANOVAs (randomized complete block design) were used to determine differences between treatment conditions for all variables unless otherwise stated. Simple contrasts between treatment conditions were used to generate *P* values for subsequent analysis as has been done previously (60). Residuals from ANOVA analyses were visually inspected for non-uniformity of variance. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

Due to limitations in examining performance-related measurements with traditional null hypothesis testing, magnitude-based inferences about the data were made using methods described by Hopkins and colleagues (20). 90% confidence intervals (CI) are presented to illustrate uncertainly in treatment effects. Threshold values for a

substantial change were calculated as 0.2 × SD (from PL trial). A published spreadsheet (21) was used to classify treatment effects as beneficial/positive, harmful/negative, or trivial/negligible. Likelihoods of reaching the substantial change threshold were classified as <1% almost certainly no chance, 1-5% = very unlikely, 5-25% = unlikely, 25-75% = possible, 75-95% = likely, 95-99% = very likely, and >99% = almost certain (60). If confidence intervals overlapped, effects were classified as unclear. Effects were described as trivial/negligible when the majority of the CI lay between the threshold for a substantially positive and negative effect (60). All data was presented as means ± SD.

GI distress scores were analyzed with a frequency table for severe symptoms (a score of ≥ 5), as described previously (27).

RESULTS

Subject Characteristics

Eight trained male cyclists and triathletes (Age: 25 ± 6.2 yrs, Height: 180.2 ± 4.3 cm, Weight: 76.9 ± 9.2 kg, and VO_2max: 61.9 ± 6.2 $ml \cdot kg^{-1} \cdot min^{-1}$) participated in this study.

30-km Time Trial Performance

Time trial performance data is shown in Figure 4.1 and qualitative inferences regarding time trial performance and power output are summarized in Table 4.1. Respectively, GF and MG resulted in 'very likely' and 'likely' improvements in TT finishing time of 4.7% and 3.5% versus PL, while differences between HG and PL were 'unclear' (1.7%). GF also resulted in a 'likely' 3.0% improvement versus HG. Differences between GF and MG (1.2%) were 'unclear.' Finally, performance with MG was 'possibly beneficial' (1.8%) versus HG.

Metabolic Measurements

VO_2 and V_E data are displayed in Figures 4.2 and 4.3. There were no systematic differences between treatments during the constant-load portion of the trials. Differences in VO_2 during the TT closely matched performance differences. Specifically, VO_2 during all carbohydrate treatments were 'likely' (MG and HG) or 'very likely' (GF) higher than PL. VO_2 during GF was also 'likely' higher versus MG/HG. VO_2 differences between MG and HG were 'unclear.' V_E during the TT was 'likely higher' with all carbohydrate treatment versus PL. Among the carbohydrate treatments, a 'possibly trivial' increase in

V_E with GF versus MG during the TT was the only apparent difference between beverages.

RER data are displayed in Figure 4.4. Carbohydrate ingestion (all treatments) resulted in higher RER values versus PL at 55 min and 115 min of steady-state cycling. 'Unclear' differences were observed in late-exercise (115 min) of the constant-load portion between GF and MG as well as between MG and HG. There was a 'possibly trivial' increase in RER with GF versus HG at the same time point. During the TT, all carbohydrate treatments resulted in 'most likely' higher RER values than PL. Differences between carbohydrate treatments were 'unclear.'

All carbohydrate treatments, (MG = 2.74 ± 0.69 $g \cdot min^{-1}$; HG = 2.57 ± 0.58 $g \cdot min^{-1}$; and GF = 2.79 ± 0.34 $g \cdot min^{-1}$), resulted in 'most likely' higher total carbohydrate oxidation versus PL (1.77 ± 0.46 $g \cdot min^{-1}$) during the time trial. Differences between carbohydrate treatments were 'unclear.'

Heart Rate and Ratings of Perceived Exertion

Heart rate data are displayed in Figure 4.5. There was no evidence of any systematic differences between treatments during the constant-load portion of the trials. All carbohydrate treatments resulted in 'likely' higher heart rate values during the TT. Differences in heart rate between carbohydrate treatments was 'unclear.' No 'likely' differences were observed between treatments for ratings of perceived exertion.

Blood Glucose and Lactate

Blood glucose data are displayed in Figure 4.6. With all carbohydrate treatments, blood glucose was ‘very likely’ increased versus PL during both constant-load cycling and the TT. HG was ‘very likely’ and ‘likely’ to increase late-exercise blood glucose (120 min) relative to MG and GF, respectively. However, differences in blood glucose with HG versus MG and GF were ‘unclear’ during the TT. Differences in late-exercise blood glucose were ‘unclear’ between GF and MG. However, blood glucose was ‘likely’ increased with GF versus MG during the TT.

Blood lactate data are presented in Figure 4.7. There were no systematic differences observed between treatments throughout constant-load cycling, with one exception: late-exercise blood lactate was ‘likely’ higher with GF and MG versus HG. During the TT, lactate was ‘likely’ higher with GF versus HG, and ‘likely’ higher with GF and MG versus PL. All other differences were unclear.

GI Distress Symptoms

Reported symptoms of GI distress were generally low in all trials (average values were ≤ 1.75 for all individual symptoms, evaluated at all individual time-points). Only two subjects reported any GI distress symptoms ≥ 5 (‘severe’ or higher) in the constant-load portion of any of the trials. These included symptoms in the following areas: stomach problems, stomach cramping, nausea, dizziness, headache, and vomiting (no ratings ≥ 5 were reported for: bloated feeling, diarrhea, and belching). During the TT portion of the trials, three subjects (including the two aforementioned participants) reported GI distress symptoms ≥ 5. These ratings were observed for the same symptoms as those reported during constant-load cycling, with the exception that no

moderate/severe ratings were observed in the category of stomach cramping. Individual GI distress ratings are displayed for representative symptoms for the three individuals who reported moderate-severe symptoms (Table 4.3). No systematic differences in GI distress ratings were observed between individual treatments during constant-load cycling. Similarly, no systematic differences in symptoms were observed during the TT, other than the observation that dizziness ratings during the PL trial were higher than baseline levels in all three subjects.

DISCUSSION

Several recent studies have examined the effects of glucose+fructose coingestion on cycling performance, versus isocaloric amounts of glucose (11, 48, 57). The present investigation was the first to compare the ergogenic effects of a glucose+fructose beverage (GF) to a recommended moderate dose of glucose (MG; 60 $g \cdot hr^{-1}$). GF was also compared to an isocaloric glucose beverage (HG) and a placebo (PL). Unlike previous studies (11, 48, 57), all trials were performed in the postprandial state in order to replicate the conditions in which athletes typically compete. The primary finding of the current study was that GF 'very likely' and 'likely' improved performance versus PL (4.7%) and HG (3.0%), respectively, while potential performance benefits for GF versus MG (1.2%) were 'unclear.'

Our finding of a 'likely' 3.0% improvement with GF versus HG is in general agreement with prior studies investigating cycling performance with glucose+fructose consumption. Currell and colleagues (11) reported that high rates of glucose and fructose co-ingestion (108 $g \cdot hr^{-1}$; 2:1 ratio) resulted in 8% faster completion times during a 40-km time trial (following 2 hours of constant-load cycling) in comparison to a calorically-matched glucose-only beverage. Similarly, Triplett et al. (2010) observed 8% improvements in power output during 100 km of intermittent cycling with glucose+fructose intake (144 $g \cdot hr^{-1}$; 2:1 ratio) versus isocaloric amounts of glucose (57). These performance enhancements have been primarily attributed to augmented exogenous carbohydrate oxidation, which is influenced by intestinal absorption (46, 51). Glucose transport occurs predominantly via the sodium-dependent SGLT1 transporter, at rates up to ~60 $g \cdot hr^{-1}$; whereas fructose is transported predominantly by GLUT5 at peak

rates of ~35 g·hr^{-1} (29, 51). Co-ingestion of glucose and fructose at high rates have resulted in exogenous oxidation rates exceeding 90 g·hr^{-1} (23, 59), likely as a result of non-competitive intestinal transport (52). These rates are considerably higher than those reported with isocaloric amounts of glucose alone (22, 24, 30).

It is possible that the ergogenic effects of GF ingestion are derived from increased total carbohydrate oxidation, allowing for greater energy turnover. However, despite the 'likely' enhancement in time-trial performance with GF versus HG in the present study, treatment differences in total carbohydrate oxidation were 'unclear' (GF = 2.79 ± 0.34 g·min^{-1}, HG = 2.57 ± 0.58 g·min^{-1}). Similarly, Triplett et al. (2010), found no differences in total carbohydrate oxidation during an intermittent 100-km time trial. Despite these findings, there is other evidence to suggest that total carbohydrate oxidation increases with glucose+fructose coingestion versus glucose alone (22, 38). The source of this added carbohydrate oxidation is somewhat unclear, but could be the result of endogenous carbohydrate sparing in early-exercise, allowing greater contributions from hepatic/muscle glycogen stores (and higher total carbohydrate availability) in late-exercise. Although a majority of studies have reported no muscle glycogen sparing with carbohydrate ingestion during constant-load cycling (9, 16, 19, 41), there is some recent evidence that it occurs (2, 55). Furthermore, hepatic glucose output can be completely suppressed with high rates of carbohydrate ingestion (i.e. liver glycogen sparing) (32). The higher exogenous carbohydrate oxidation rates achieved with glucose+fructose ingestion should logically result in a concomitant sparing of endogenous carbohydrate reserves. However, there is little evidence at present to directly support this conclusion. Although a prior study reported a trend towards decreased endogenous carbohydrate

utilization with glucose+fructose intake (24), most have reported no differences versus isocaloric glucose beverages (22, 26, 59). It is worth noting that these studies examined carbohydrate oxidation, but not performance, during 2-2.5 hours of constant-load (55% W_{max}) cycling. Conceivably, the added duration and intensity of a time trial (as in the present study, and others reporting performance benefits with glucose+fructose) might increase total carbohydrate utilization to an extent that could reveal meaningful differences in carbohydrate sparing between beverages. However, Currell et al. (2008) and Triplett et al. (2010) did not measure liver/muscle glycogen levels, nor was it assessed in the current study.

Another possible candidate for increased total carbohydrate oxidation is increased lactate production and metabolism, which has been shown to be elevated with fructose ingestion (24, 25, 38). Fructose phosphorylation in the liver increases pyruvate production (via increased concentrations of fructose-1-phosphate), resulting in increased lactate production (38). Fructose-derived lactate is released from the liver, and the majority is subsequently oxidized in active skeletal muscle (38). We observed late-exercise blood lactate with GF was "very likely" higher than the HG trial, which could have contributed to augmented performance. However, it should be noted that lactate in the MG trial was also "very likely" higher than HG at this time point. An alternative explanation for added total carbohydrate oxidation could be enhanced gluconeogenesis, either from lactate or fructose. We found 'unclear' differences in blood glucose between GF and HG during the time trial. Nevertheless, this may be explained by the combination of enhanced hepatic output with glucose+fructose, combined with increased muscular uptake in response to increased energy demand (36).

Although generally consistent with previous studies, the 3.0% improvement in TT performance observed with our GF treatment (versus the isocaloric HG beverage) is notably lower than the 8% improvements reported by Currell et al. (2008) and Triplett et al. (2010). Additionally, our novel finding of a 1.2% benefit of GF versus MG ('unclear') indicates that the ergogenic effects of glucose+fructose ingestion may be more modest than previously reported (11, 57). One explanation for the reduced benefit observed in the current study is the lower total carbohydrate intake rate compared to the above studies (90 $g \cdot hr^{-1}$ vs. 108-144 $g \cdot hr^{-1}$). Enhanced delivery of carbohydrate via non-competitive glucose and fructose transport results in increased oxidation of exogenous carbohydrate (23, 59), which appears to be dose-dependent (53, 54). Perhaps the larger doses of glucose+fructose administered by Currell et al. (2008) and Triplett et al. (2010) resulted in greater absorption and subsequent oxidation of carbohydrate, resulting in a larger performance improvement. However, Smith and colleagues (2013), reported a curvilinear dose-response effect with maltodextrin/glucose/fructose, with optimal performance occurring at intake rates of ~78 $g \cdot hr^{-1}$. Moreover, oxidation efficiency (i.e. proportion of ingested carbohydrate that are oxidized) likely decreases at high carbohydrate ingestion rates ($\geq$ 80 $g \cdot hr^{-1}$) (35, 43, 49). Thus, our chosen carbohydrate delivery rate of 90 $g \cdot hr^{-1}$ would seem to approximate theoretically optimal levels.

Differences in the magnitude of benefits between the current study and prior studies (11, 57) could also be attributed to GI distress. Prior studies used higher rates of carbohydrate ingestion in their glucose-only trials (108 and 144 $g \cdot hr^{-1}$ [11, 53]), which exceeded the presumed maximal absorption rates of glucose (60 $g \cdot hr^{-1}$) (34). This likely resulted in greater carbohydrate accumulation in the gut, which has been associated with

GI distress (45, 50). High incidences of substantial GI distress in glucose-only trials reported by Triplett and colleagues (4 out of 9 subjects, versus 0 of 8 subjects registering 'severe' symptoms in our HG trials) support this notion (57). Assuming severe GI distress limits performance (48, 56), the large performance differences reported by Currell and Triplett (8%) may be partly explained by GI distress related to 'excess' glucose in the glucose-only comparison beverages. This hypothesis is supported by findings of Rowlands and colleagues (2012), who reported 1.4 - 1.8% performance enhancements with maltodextrin+fructose (versus an isocaloric maltodextrin+glucose beverage), after statistically eliminating the effects of GI distress (48). These values are similar to our observed differences between GF and MG treatments (1.2% 'unclear' effect).

The potentially negative influences of excess glucose on performance likely explain why the ergogenic effects of GF were larger versus HG (compared to GF versus MG). It may also explain why differences between HG and PL beverages (1.7%) were 'unclear.' However, very few symptoms of severe GI distress were reported in our HG trials, possibly as a result of lower intake rates (90 $g \cdot hr^{-1}$) versus previous studies (11, 57). Thus, the 'possible/likely harmful' effects of HG on performance in our study (compared to MG/GF, respectively) cannot be directly attributed to GI distress symptoms per se. However, we cannot dismiss the possibility that our subjects anticipatorily selected lower time-trial intensities during the HG trial, in order to prevent severe GI distress. Furthermore, others (43) have speculated that nausea, [presumably caused by carbohydrate malabsorption (8, 45)], may blunt motor output via stimulation of receptors in the gut. To this end, gut receptors that respond to distension (4) and taste (13) have

been identified. Moreover, the appearance of GLUT2 transporters in the intestine seem to increase in response to highly concentrated amounts of glucose, presumably the result of chemoreceptors (39). This raises the possibility that receptors in the gut (responding to glucose concentration) may have preemptively blunted motor drive during the HG trials, contributing to the larger differences between GF/HG beverages ('likely' 3.0%), versus those observed between GF/MG ('unclear' 1.2%), although this idea is purely speculative.

Another factor which may have affected the magnitude of our treatment effects was that our trials were conducted in the postprandial state. Previous studies have reported that the ergogenic effects of carbohydrate observed in high-intensity cycling trials (i.e. ~60 min at > 85% VO_{2max}) were likely the result of improved motor output via stimulation of oral carbohydrate receptors (6, 17). As others have speculated (48), beverages containing fructose may produce greater stimulation of oral carbohydrate receptors, possibly contributing to performance enhancements with glucose+fructose ingestion. However, the influence of carbohydrate on the CNS appears to be blunted in the postprandial state (1), which could have reduced potential performance benefits from glucose+fructose in the current study. Furthermore, the ingestion of a pre-exercise meal would likely have an impact on endogenous carbohydrate stores at the onset of exercise (42), and potentially influence substrate utilization (12, 40). Collectively, it is possible these factors could explain the larger treatment effects reported in prior studies reporting ergogenic effects with glucose+fructose, which were conducted following an overnight fast, (11, 57).

In summary, ingesting a beverage containing glucose and fructose at a rate of 90 gCHO·hr^{-1} was 'very likely'/'likely' beneficial for enhancing prolonged cycling performance versus placebo/isocaloric glucose solutions, respectively. However, differences in performance for glucose+fructose versus a glucose beverage containing 60 gCHO·hr^{-1} were 'unclear'. Current sports nutrition guidelines recommend ingesting 30 - 60 g of carbohydrate per hour during exercise lasting ≥ 2 hrs (47). Recent studies reporting performance enhancements with glucose+fructose coingestion at rates ≥ 80 g·hr^{-1} (11, 48, 49, 57) have led some to argue for revisions in the current recommendations (39). Our findings suggest that the ergogenic effects of glucose+fructose ingestion may be more modest than previously reported, particularly in the postprandial state and when compared to moderate doses of glucose. Notably, our observed performance benefit for GF versus MG (1.2%) is also in line with recent findings (48) which have statistically corrected for differences in GI tolerance. Despite our reported statistical inference that this is an 'unclear' effect, further study of the ergogenic effects of glucose+fructose beverages is warranted, as this would be deemed a functionally meaningful improvement to athletes if upheld in future studies.

Table 4.1. Treatment Effects on Time-Trial Performance with Qualitative Inferences.

	30 km TT Performance		Difference in Performance (min)*		
	Time (min)	Power (W)	MG	HG	GF
PL	52.9 ± 3.7	217 ± 40	-1.88, -0.6 to -3.2 (1.3); 93.1% likely beneficial, P = 0.029	-0.92, -2.4 to 0.5 (1.4); unclear, P = 0.263	-2.48, -3.6 to -1.3 (1.2); 98.8% very likely beneficial, P = 0.005
MG	51.1 ± 2.4	237 ± 30		0.96, 2.4 to 0.5 (1.4); possibly harmful, P = 0.247	-0.61, -2.4 to 0.9 (1.5); unclear, P = 0.458
HG	52.0 ± 3.7	229 ± 38	-0.96, -2.4 to 0.5 (1.4); possibly beneficial, P = 0.245		1.56, -2.8 to 0.3 (1.2); likely beneficial, P = 0.065
GF	50.4 ± 2.2	244 ± 27	0.61, 0.9 to -2.4 (1.5); unclear, P = 0.458	1.56, 0.3 to 2.8 (1.2); likely harmful, P = 0.065	

Data is presented as mean ± SD for performance times and power output during the 30km time trials with ingestion of PL, MG, HG, and GF. Time differences between treatments are presented as mean differences (min.), 90% confidence interval (effect size), % chance and qualitative inference, and exact P value from means comparisons).

* Performance differences not shown for power output, but inferences were identical in all cases.

Table 4.2: Ventilation (VE), Oxygen Uptake (VO2), Respiratory Exchange Ration (RER), and heart rate (HR) during constant load exercise and the time trial.

	15 min.	60 min.	120 min.	TT
V_E (L/min.)				
PL	68.1 ± 5.8	69.5 ± 5.5	72.2 ± 6.5	79.0 ± 20.9
MG	67.8 ± 5.6	70.4 ± 5.0	71.6 ± 5.1	88.9 ± 20.0*
HG	68.4 ± 8.3	70.7 ± 8.5	72.6 ± 9.2	88.5 ± 23.8*
GF	67.3 ± 6.8	71.9 ± 7.0	70.8 ± 5.3	92.0 ± 14.6**$^{\#}$
VO_2 (L/min.)				
PL	2.8 ± 0.3	2.9 ± 0.3	3.0 ± 0.3	3.2 ± 0.6
MG	2.8 ± 0.2	2.9 ± 0.2	2.9 ± 0.2	3.4 ± 0.4*
HG	2.9 ± 0.4	2.9 ± 0.3	3.0 ± 0.4	3.4 ± 0.6*
GF	2.8 ± 0.2	2.9 ± 0.3	2.9 ± 0.3	3.6 ± 0.4**$^{+}$
RER				
PL	0.91 ± 0.03	0.87 ± 0.03	0.84 ± 0.03	0.84 ± 0.02
MG	0.94 ± 0.02	0.91 ± 0.02§	0.89 ± 0.02§	0.90 ± 0.04§
HG	0.92 ± 0.02	0.90 ± 0.03**	0.88 ± 0.02§	0.89 ± 0.02§
GF	0.94 ± 0.02	0.92 ± 0.02§	0.89 ± 0.02$^{\S\#}$	0.89 ± 0.02§
HR (bpm)				
PL	118 ± 8	122 ± 10	129 ± 12	140 ± 13
MG	124 ± 8	126 ± 9	130 ± 11	150 ± 14§
HG	125 ± 10	128 ± 12	133 ± 13	152 ± 15**
GF	121 ± 9	124 ± 8	127 ± 10	149 ± 14*

* denotes "likely" positive versus PL.
** denotes "very likely" positive versus PL.
$^{\#}$ denotes "possibly trivial" higher value versus HG.
$^{+}$ denotes "likely" positive versus MG and HG.
§ denotes "most likely" positive versus PL.

Table 4.3: Individual Ratings of GI Distress during Cycling

	Constant-Load Exercise*				Time-Trial			
Stomach Problems	PL	MG	HG	GF	PL	MG	HG	GF
Subject 3	6	1	3	1	3	1	3	1
Subject 5	1	5	1	4	1	1	1	1
Subject 7	1	1	1	1	1	6	1	1
Nausea								
Subject 3	7	1	1	1	7	1	3	1
Subject 5	1	1	1	1	1	1	1	1
Subject 7	1	1	1	1	1	7	1	1
Dizziness								
Subject 3	1	1	1	1	4	1	1	1
Subject 5	1	1	1	1	5	1	1	1
Subject 7	2	1	1	1	3	6	1	3

Ratings shown only for subjects reporting ratings ≥ 5 during any of the trials.

*Ratings represent the highest values reported during constant-load cycling

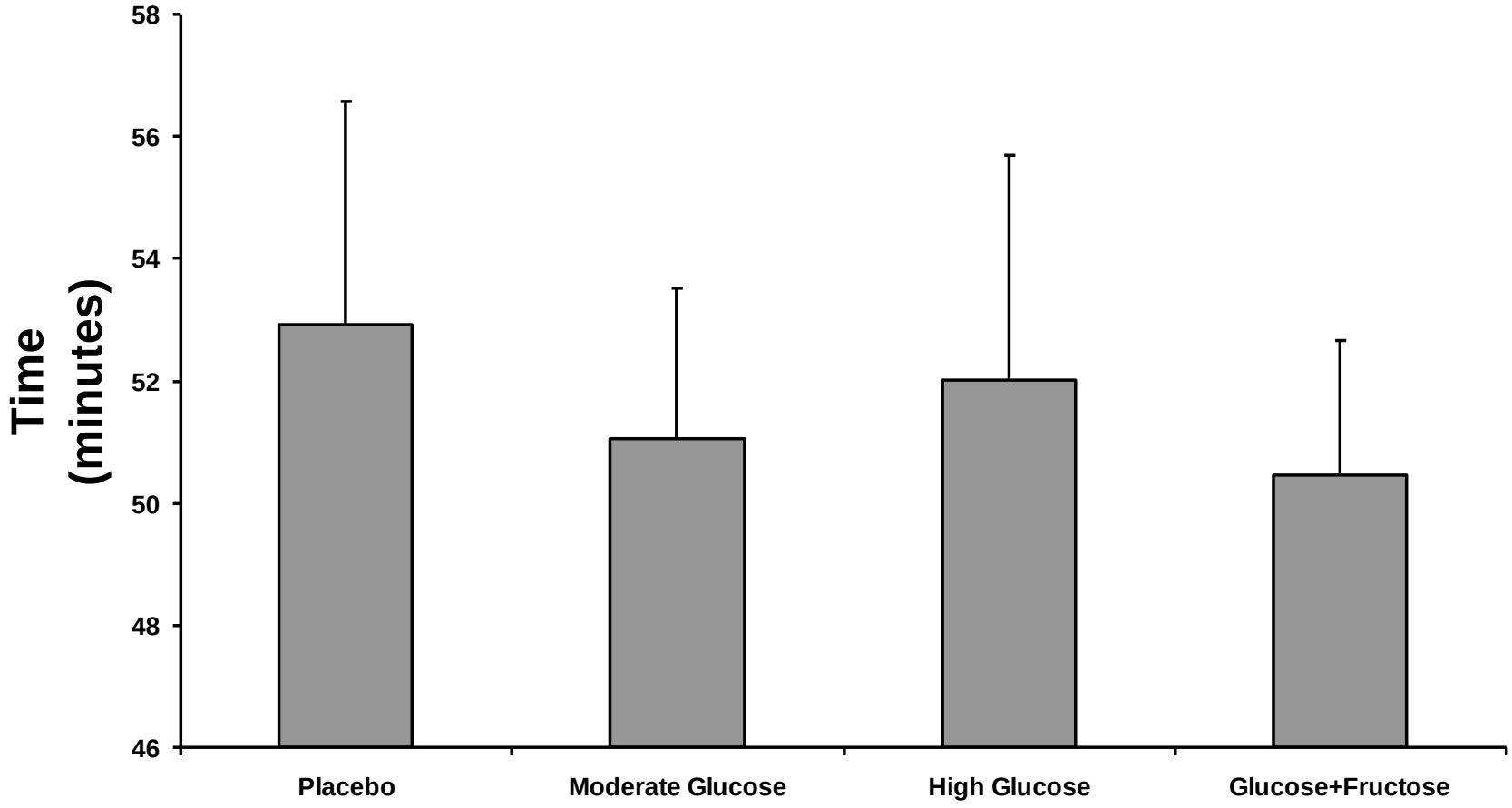

Figure 4.1. Mean time trial completion times. Data is presented as Mean + SD.

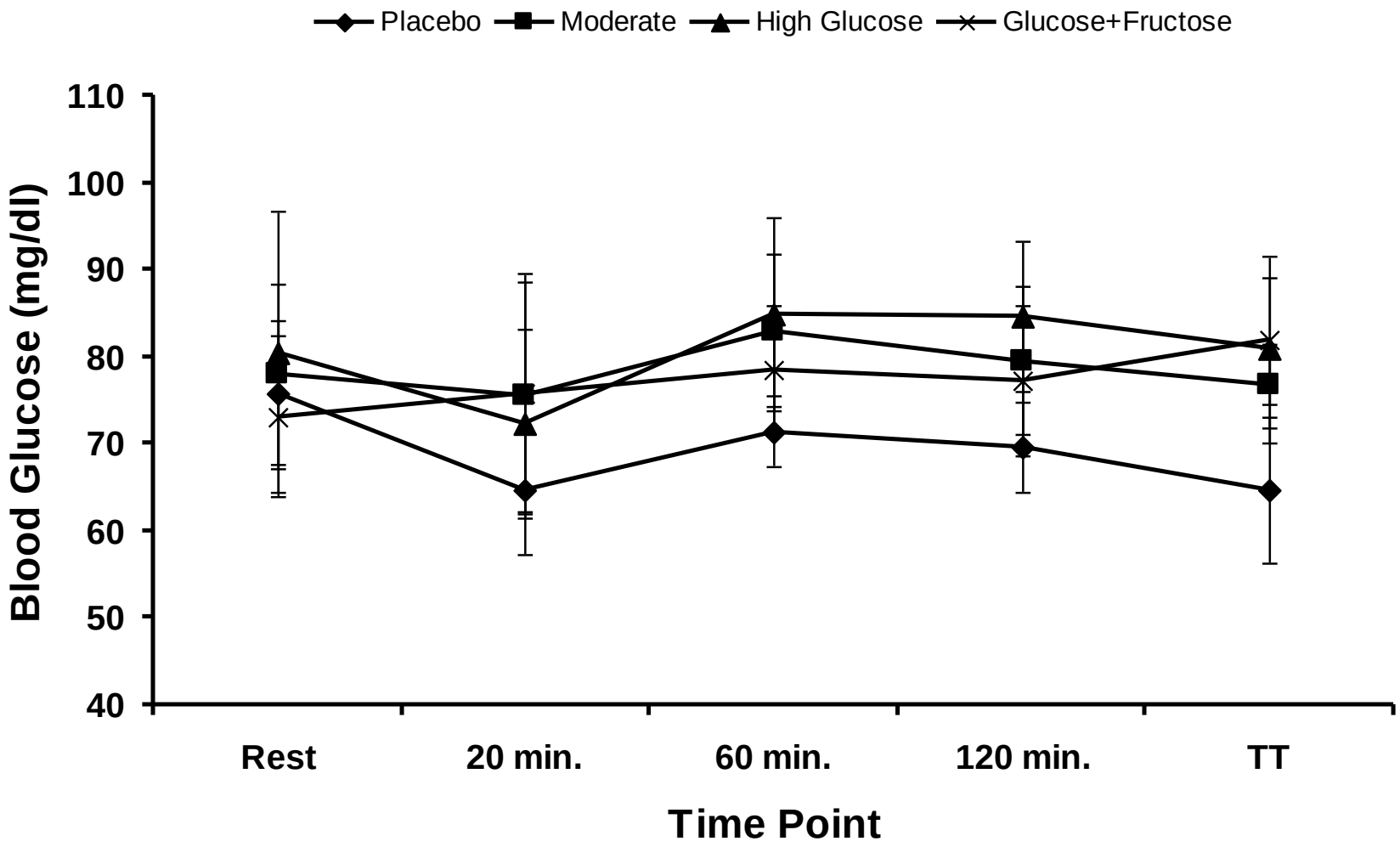

Figure 4.2. Blood glucose over time with PL, MG, HG, and GF. Data is presented as Mean + SD.

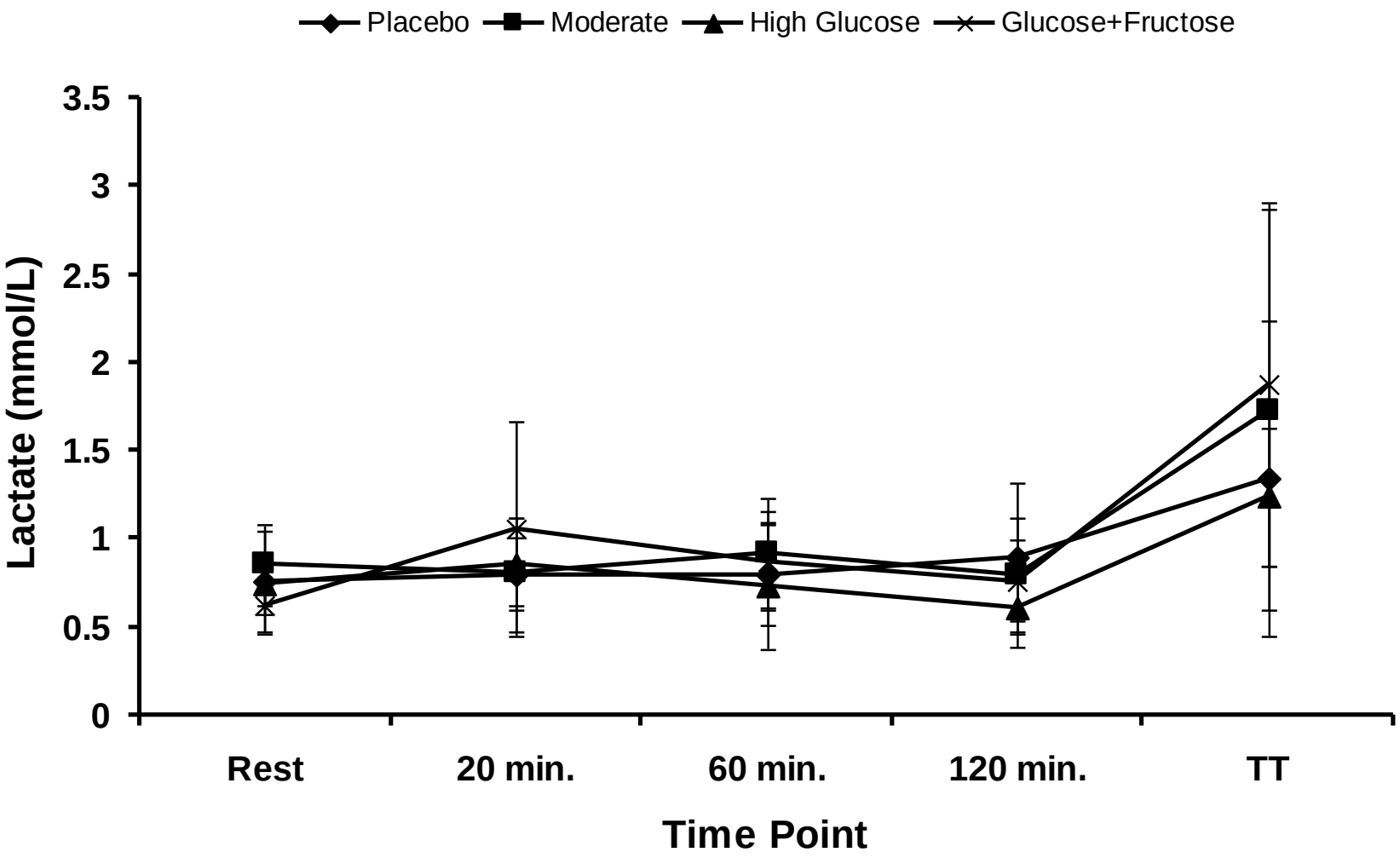

Figure 4.3. Blood lactate over time with PL, MG, HG, and GF. Data is presented as Mean + SD.

James Madison University

Department of Kinesiology
Informed Consent

Purpose

You are being asked to volunteer for a research project conducted by Dr. Mike Saunders, Dr. Nick Luden, Dan Baur, Adam Schroer, Katie Gorman, and Sarah Smyth from James Madison University titled "Influence of Mixed Carbohydrate Solutions on Performance during Prolonged Cycling".

The primary goal of this study is to determine the effectiveness of different carbohydrate sports beverages on cycling performance.

Experimental Procedures

You will be asked to report to James Madison University's Human Performance Laboratory (Godwin 209) on six occasions. Specifically, you will be asked to participate in one preliminary trial, one familiarization trial, and four experimental exercise trials, each separated by 5 to 7 days. The preliminary trial will require approximately 45 minutes, whereas the familiarization trial and each experimental exercise trial will require approximately 3 hrs each, for a total time commitment of 15 hrs 45 min. Detailed information for each of these trials is provided below:

<u>Preliminary Trial – Visit 1 – 45 minutes</u>

Prior to any data collection, you will be asked to complete health history and screening questionnaires to ensure that you meet the study criteria and that you do not have any risk factors that would prevent you from performing heavy exercise. In the process of completing these forms, you will be asked to share information regarding your general health and lifestyle with the researchers. If you meet the criteria for the study, the researchers will measure your height and body weight and you will then be asked to perform a cardiovascular fitness test on a bicycle ergometer to determine your peak oxygen consumption (VO_{2peak}). At the beginning of the test, you will be asked to ride the stationary bicycle ergometer at an initial workload that is 'fairly easy'. The workload will be increased every two minutes during the test. You will be encouraged to continue to cycle until you request to stop due to fatigue or are unable to continue at a cadence of >50 revolutions per minute.

<u>Familiarization Trial and Experimental Exercise Trials – Visits 2, 3, 4, and 5 – 3 hrs each</u>

You will be asked to complete each trial on a stationary bicycle ergometer. Each trial will consist of two distinct exercise phases. Specifically, each trial will include an initial steady-state segment of 120 min at 55% W_{max} ('moderate intensity'). The steady-state ride will be immediately followed by a simulated 30-km time trial (~50 minutes). Total exercise time will be approximately 3 hrs. During each of these five trials, you will

receive water or a carbohydrate sports beverage at various time-points. Each of the trials will be separated by a minimum of 5-7 days. A different beverage will be provided during each trial. You will consume the beverages according to the following schedule:

- 600 ml of the assigned beverage will be provided in a bottle immediately prior to exercise.
- 150 ml will be provided every 15 min during the steady state portion of the trial.
- 150 ml will also be provided at 7.5, 15, and 22.5 km of the time trial.

You will be instructed to consume the beverages within 2 minutes during exercise. The beverages will have slightly different ingredients during each trial (see *Study Treatments* below).

You will be asked to void your bladder prior to each trial. You will also be encouraged to treat all time trials as a competitive event, and provide a maximal effort. You will receive no feedback regarding performance during the time-trials, except for the distance completed and distance remaining in the trial. The researchers will not provide any verbal encouragement.

You will be asked to complete the following procedures during each protocol:

Exercise Performance

Performance will be measured by your finishing times (and average power output) in the 30-km time trial. Again, these are to be approached as competitions.

Metabolic Measurements

Metabolic measurements such as oxygen uptake, ventilation, etc. will be measured with a metabolic cart at the following time points: minutes 15, 35, 55, 75, 95, and 115 of the 120-min steady state phase, and at 20-km into the 30-km time trial. At each of these points, 5 minutes of expired gas will be collected. To do this, you will be asked to breathe through a mouthpiece/breathing apparatus that collected your expired breath. This apparatus will NOT be worn during exercise other than at the indicated time points.

Blood Glucose and Lactic Acid

A total of 8 finger-stick blood samples (~0.5 ml) will be obtained at the following time points: minutes 20, 40, 60, 80, 100, and 120 of the 120-min steady state phase, and at 20-km into the 30-km time trial. Each of these samples will be obtained by puncturing your fingertip with a small lancet. A very small amount of blood (~2 drops) will be collected at each time point.

Heart Rate

You will be asked to wear a heart rate monitor around your chest. Heart rate will be monitored throughout each exercise session.

Ratings of Perceived Exertion (RPE)

You will be asked to provide subjective ratings of your exertion level. You will do this by pointing to a corresponding level of exertion (rated numerically from 6-20) on a Borg RPE scale.

Gastrointestinal Distress Scale

You will be asked to complete a questionnaire (verbally) at several points throughout the exercise session. The questionnaire contains questions regarding the presence of GI problems at that moment and addresses the following complaints: stomach problems, GI cramping, bloated feeling, diarrhea, nausea, dizziness, headache, belching, vomiting, and urge to urinate or defecate.

Dietary and Exercise Controls

You will be asked to complete a diet record for the 24-hr preceding each treatment trial. You will also be asked to bring your initial diet record with you to the laboratory on the morning of your first experimental trial (diet record from previous day). You will be provided with a copy of this dietary log, which is to be used as a template when replicating your dietary habits for the 24-hrs leading up to each of the following trials. You are also asked to refrain from heavy exercise for 48-hours prior to each trial. You will be asked to keep a record all physical activity performed during the 72-hr preceding each treatment trial and to maintain consistent exercise habits between each of these trials. You are to consume your final 'self-selected' meal no less than 12 hours prior to the start of the exercise trials (i.e. dinner on the evening prior to testing). Approximately 7-9 hrs prior to each trial (the night before), you will consume a liquid meal replacement (Ensure® Shakes) at an amount corresponding to 20-25% of daily caloric intake. 2 hrs prior to all experimental trials, you will consume a standardized breakfast consisting of ~500 kcals (provided by the researchers). Finally, you will be asked to abstain from alcohol for 24 hrs preceding each trial and caffeine for 12 hrs preceding each trial.

Risks

Participants are expected to be honest about disclosing all known risk factors to the researchers.
According to the American College of Sports Medicine, the risks associated with maximal exercise/testing for healthy individuals are very minimal. To be included in this study, you will need to meet the criteria for "low risk". In the unlikely event of cardiac or

other complications during exercise, an emergency plan is in place. This includes immediate access to a phone to call emergency personnel. In addition, at least one investigator present at all testing sessions will be CPR certified.

The exercise protocol may result in minor-moderate levels of muscle soreness and fatigue for 1-2 days following each exercise session. However, the level of muscle soreness is expected to be lower than levels normally experienced when you perform other 'normal' activities that are not part of your regular exercise routine (i.e. if a cyclist played a game of basketball with friends for 2 hours).

The consumption of relatively large amounts of sports drinks can increase the risk of digestive issues; include symptoms such as nausea, stomach cramping, bloated feeling, vomiting, dizziness, and diarrhea. These symptoms may cause mild discomfort for a short-term period, but are not life-threatening. Digestive symptoms will be monitored throughout testing, and tests will be terminated if your symptoms become severe enough to require you to cease exercise.

The risks of finger stick blood sampling include possible mild bruising, and the risk of transfer of blood-borne pathogens. This risk is considered to be very minimal, and all safety precautions for handing blood samples will be followed according to OSHA protocols. The investigators have been trained in phlebotomy and completed JMU blood-borne pathogen training.

Benefits

The benefits associated with this project include a free VO_{2peak} assessment, and a $125 payment for study completion. In the case of withdrawal, payments will be pro-rated such that you will receive $25 for the completion of each exercise trial (steady-state + TT). Participation in this novel research project will also contribute to our understanding of nutritional influences on recovery from endurance exercise.

Inquiries

If you have any questions or concerns, please contact Dr. Mike Saunders at saundemj@jmu.edu and (540) 568-8121 or Dr. Nicholas Luden at ludennd@jmu.edu and (540) 568-4069.

Questions about Your Rights as a Research Subject

Dr. David Cockley
Chair, Institutional Review Board
James Madison University
(540) 568-2834
cocklede@jmu.edu

Confidentiality

All data and results will be kept confidential. You will be assigned an identification code. At no time will your name be identified with individual data. The researchers retain the right to use and publish non-identifiable data. All data will be kept secured in a locked cabinet. Upon completion of the study, all information that matches up individual respondents with their answers will be destroyed. Final aggregate results will be made available to you upon request.

Freedom of Consent

Your participation is entirely voluntary. You are free to choose not to participate. Should you choose to participate, you can withdraw at any time without consequences of any kind.

I have read this consent form and I understand what is being requested of me as a participant in this study. I freely consent to participate. I have been given satisfactory answers to my questions. The investigator provided me with a copy of this form. I certify that I am at least 18 years of age.

Name of Subject (Printed)	Name of Researcher (Printed)
Name of Subject (Signed)	Name of Researcher (Signed)
Date	Date

CYCLISTS WANTED FOR CARBOHYDRATE STUDY

The Human Performance Laboratory at JMU will be conducting a study examining the effects of ingesting carbohydrate on cycling performance.

Who Are We Looking For?

- 18-45 years old
- Experienced cyclists (performing cycling exercise on a regular basis)

What Will You Be Asked to Do?

- Complete preliminary fitness testing/screening
- Participate in five exercise protocols, each of which will consist of 3 hrs of cycling on a computerized bicycle ergometer. Carbohydrate beverages will be provided during each session
- Receive laboratory assessments (including finger stick blood sampling) during each session
- Each of the 5 exercise protocols above will be separated by 5-7 days

What are the benefits of participation?

- Free evaluation of aerobic capacity (VO_{2peak}) and physiological data from a race simulation
- $125 for study completion

For more information, please contact Dr. Mike Saunders at saundemj@jmu.edu ((540) 568-8121), or Dan Baur at baurda@dukes.jmu.edu ((540)-460-7122).

Subject Prescreening Information

Age: ____

Height: _____ Weight: _____

Average Exercise Habits over the Past 2 Months:

Avg. # days of exercise per week: _____

Avg. # of days of aerobic exercise per week: _____

Avg. # of days of cycling per week: _____

Do you have a muscle or joint injury/condition that precludes the completion of exercise protocol?

Do you have any food allergies?

AHA/ACSM Health/Fitness Facility Pre-participation Screening Questionnaire

Assess your health status by marking all *true* statements

History

You have had:

_____ a heart attack
_____ heart surgery
_____ cardiac catheterization
_____ coronary angioplasty (PTCA)
_____ pacemaker/implantable cardiac
_____ defibrillator/rhythm disturbance
_____ heart valve disease
_____ heart failure
_____ heart transplantation
_____ congenital heart disease

If you marked any of these statements in this section, consult your physician or other appropriate health care provider before engaging in exercise. You may need to use a facility with a ***medically qualified staff***.

Symptoms

_____ You experience chest discomfort with exertion
_____ You experience unreasonable breathlessness
_____ You experience dizziness, fainting, or blackouts
_____ You take heart medications

Other Health Issues

_____ You have diabetes
_____ You have asthma or other lung disease
_____ You have burning or cramping sensation in your lower legs when walking short distances
_____ You have musculoskeletal problems that limit your physical activity
_____ You have concerns about the safety of exercise
_____ You take prescription medication(s)

If you marked that you have diabetes but did not mark any other statements, physician's approval will be necessary before engaging in the study.

Cardiovascular risk factors

_____ You are a man older than 45 years
_____ You are a woman older than 55 years, have had a hysterectomy, or are postmenopausal
_____ You smoke, or quit smoking within the previous 6 months
_____ Your blood pressure is > 140/90 mmHg
_____ You do not know your blood pressure
_____ You take blood pressure medication
_____ Your blood cholesterol level is > 200 mg/dl
_____ You do not know your cholesterol level
_____ You have a close blood relative who had a heart attack or heart surgery before age 55 (father or brother) or age 65 (mother or sister)
_____ You are physically inactive (i.e. you get < 30 minutes of physical activity on at least 3 days of the week)
_____ You are > 20 pounds overweight

If you marked two or more of the statements in this section, you should consult your physician or other appropriate health care provider before engaging in exercise. You might benefit from using a facility with a ***professionally qualified exercise staff*** to guide your exercise program.

_____ None of the above

You should be able to exercise safely without consulting your physician or other appropriate health care provider in a self-guided program or almost any facility that meets your exercise program needs.

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