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P. B. Wilson
University of Nebraska–Lincoln, pwilson@huskers.com

S. J, Ingraham
University of Minnesota, Minneapolis

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Glucose-fructose likely improves gastrointestinal comfort and endurance running performance relative to glucose-only

P. B. Wilson,[1,2] and S. J. Ingraham[2]

1 Nebraska Athletic Performance Laboratory, University of Nebraska–Lincoln, Lincoln, NE, USA,
2 Human and Sports Performance Laboratory, School of Kinesiology, University of Minnesota, Minneapolis, MN, USA

Corresponding author — P. B. Wilson, Nebraska Athletic Performance Laboratory, University of Nebraska-Lincoln, One Memorial Stadium, Lincoln, NE 68588, USA. Tel: 402 472 3490, Fax: 402 472 5594, E-mail: pwilson@huskers.com

Abstract
This study aimed to determine whether glucose-fructose (GF) ingestion, relative to glucose-only, would alter performance, metabolism, gastrointestinal (GI) symptoms, and psychological affect during prolonged running. On two occasions, 20 runners (14 men) completed a 120-min submaximal run followed by a 4-mile time trial (TT). Participants consumed glucose-only (G) or GF (1.2:1 ratio) beverages, which supplied ~1.3 g/min of carbohydrate. Substrate use, blood lactate, psychological affect [Feeling Scale (FS)], and GI distress were measured. Differences between conditions were assessed using magnitude-based inferential statistics. Participants completed the TT 1.9% (−1.9; −4.2, 0.4) faster with GF, representing a likely benefit. FS ratings were possibly higher and GI symptoms were possibly-to-likely lower with GF during the submaximal period and TT. Effect sizes for GI distress and FS ratings were relatively small (Cohen's *d* = ~0.2 to 0.4). GF resulted in possibly higher fat oxidation during the submaximal period. No clear differences in lactate were observed. In conclusion, GF ingestion – compared with glucose-only – likely improves TT performance after 2 h of submaximal running, and GI distress and psychological affect are likely mechanisms. These results apply to runners consuming fluid at 500– 600 mL/h and carbohydrate at 1.0–1.3 g/min during running at 60–70% VO_{2peak}.

Keywords: endurance, exercise, exogenous, nutrition

When consuming a high rate of carbohydrate (> 60 g/h) during prolonged exercise, co-ingesting glucose and fructose has been purported to increase exogenous carbohydrate utilization, reduce gastrointestinal (GI) distress, and enhance performance (Jeukendrup, 2010). Glucose and fructose utilize separate transporters for intestinal absorption (SGLT1 and GLUT5; Wood & Trayhurn, 2003) and have been referred to in the literature as multiple transportable carbohydrates (MTC). When glucose is consumed at a rate above 60 g/h, SGLT1 may become saturated, providing a plausible mechanism for improvements in exogenous carbohydrate oxidation and GI distress (Jeukendrup, 2010). In addition, fructose ingestion increases blood lactate through up-regulation of pyruvate kinase (Macdonald et al., 1978), and this lactate can be oxidized during exercise (Miller et al., 2002). Furthermore, concentrated fructose solutions empty faster from the stomach than glucose solutions (Sole & Noakes, 1989) and may result in more rapid fluid delivery (Jeukendrup & Moseley, 2010; Roberts et al., 2014). These mechanisms provide strong rationale for use of MTC during prolonged exercise, which is supported by studies demonstrating MTC reduce GI distress (O'Brien & Rowlands, 2011; O'Brien et al., 2013; Roberts et al., 2014) and lead to performance improvements as large as 8% (Jeukendrup, 2010; Triplett et al., 2010).

Despite these findings, several limitations to the MTC research need to be addressed. Cycling has been used in all but three studies (Pfeiffer et al., 2009; Clarke et al., 2012; Lee et al., 2014), which is unfortunate given the popularity of running and GI distress is more prevalent during running (Peters et al., 1993). None of the three studies that utilized running demonstrated clear benefits with MTC, but they may have been either too short (Pfeiffer et al., 2009; Lee et al., 2014) or did not feed a high enough rate of carbohydrate (Clarke et al., 2012; Lee et al., 2014). Only two studies provided information on beverage flavor characteristics, both of which reported sweetness differences (Rowlands et al., 2008; O'Brien et al., 2013). Furthermore, previous investigations (Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; Triplett et al., 2010; O'Brien & Rowlands, 2011; Roberts et al., 2014) often used fluid volumes (~1000 mL/h) exceeding ad libitum intakes for field events (Pfeiffer et al., 2012), which suggests these protocols could be difficult to implement during "real-life" events. Finally, studies were often conducted with participants fasted (Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; Triplett et al., 2010; O'Brien & Rowlands, 2011; Roberts et al., 2014) and only three studies included women (Pfeiffer et al., 2009; Rowlands et al., 2012; Lee et al., 2014).

This study aimed to determine whether ingestion of a glucose-fructose beverage, under fed conditions, would alter performance, metabolism, GI symptoms, and psychological affect during prolonged running. Beverages supplied carbohydrate at 1.3 g/min in a double-blind, crossover fashion, with goals of matching sweetness and providing realistic fluid and carbohydrate feeding rates. Beverages supplied carbohydrate as glucose-fructose or glucose-only during 120 min of steady-state running, which was followed by a 4-mile time trial (TT). We hypothesized that glucose-fructose ingestion would improve performance, improve psychological affect, reduce GI distress, increase blood lactate, and increase end-exercise carbohydrate oxidation.

Materials and methods

Participants

Participants were recruited from the Minneapolis-St. Paul area. Eligibility criteria included completion of at least one marathon within the past year (men < 210 min; women < 225 min), running ≥ 30 miles/week, and completion of at least two 20-mile runs over the past 2 months. Participants went through an informed consent process prior to signing a University of Minnesota Institutional Review Board approved consent form. A total of 17 men and nine women were enrolled in the study. Fourteen men [35.8 ± 2.2 years; body mass index (BMI), 22.9 ± 0.5 kg/m; personal record marathon time, 182 ± 2 min; VO_{2peak}, 58.7 ± 1.9 mL/kg/min] and six women (31.3 ± 2.9 years; BMI, 21.8 ± 0.5 kg/m; PR marathon time, 201 ± 6 min; VO_{2peak}, 55.0 ± 2.4 mL/kg/min) completed all visits; reasons for not completing are presented in Fig. 1.

Procedures

Each participant underwent two, ~2.5 h runs during which they consumed the beverages. The initial 120 min consisted of submaximal running at a constant velocity, after which participants completed a 4-mile TT to assess performance. Data collection began October 2013 and was completed by March 2014.

Participants were assigned to beverages using a randomized, double-blind, counterbalanced, crossover design. Beverages supplied carbohydrate at ~1.3 g/min during the submaximal period, since a rate of < 0.8–1.0 g/min has failed to elicit metabolic and performance differences in past research (Jeukendrup, 2010). Although we considered standardizing the carbohydrate feeding rate to body size, we decided against this since there is little evidence to suggest that carbohydrate absorption capacity is significantly influenced by body size. In addition, fluid volume was not standardized against body size since it would have resulted in different beverage concentrations between participants.

The glucose-fructose beverage (GF) was a 10.3% carbohydrate mixture (103 g per 1 kg tap water) containing maltodextrin (Star-Dri® 10, Tate & Lyle, Decatur, Illinois, USA) and crystalline fructose (Krystar® 300, Tate & Lyle). Glucose and fructose were supplied in a 1.2:1 ratio (5.61% maltodextrin and 4.66% fructose) because previous studies have indicated it may be optimal (Rowlands et al., 2008; O'Brien & Rowlands, 2011; O'Brien et al., 2013). The glucose-only beverage (G) supplied carbohydrate as 5.61% maltodextrin (Star-Dri® 10, Tate & Lyle) and 4.66% dextrose anhydrous (Cerelose®, Ingredion, Westchester, Illinois, USA). Concentrations of 10.3% were chosen because fluid intakes for runners during events lasting 1–3 h rarely exceed 600 mL/h (Pfeiffer et al., 2012), and 1000 mL/h of a 6% beverage would be necessary to supply carbohydrate at ≥ 1.0 g/min. Both beverages contained sodium chloride (540 mg/kg water) and lemon juice (9 g/kg water), and since fructose is sweeter than glucose, G was treated with aspartame (90 mg/kg water). To ensure researcher blinding, one investigator mixed beverages in two identical containers, labeled them, and left the room. An individual not involved with data collection subsequently chose one of the beverages by drawing assignments from sex-specific envelopes.

Participants reported to the Human and Sport Performance Laboratory (HSPL) 1–4 weeks before their first run. Participants completed a cardiorespiratory test on a treadmill (Pro XL, Woodway USA, Waukesha, Wisconsin, USA). The protocol began with a 3-min walk at 5.0 km/h and 0% grade. Subsequently, 1-min stages at 1% grade with 0.64 km/h speed increases were used to achieve a speed equal to the participant's 5 km pace by the 11th

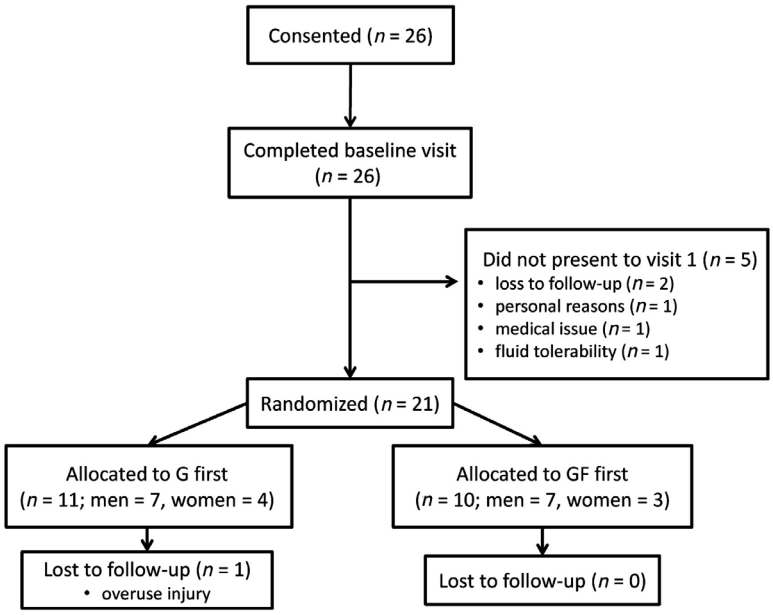

Figure 1. The flow of participants through the study.

minute. Grade was increased 1.5% every minute thereafter until volitional exhaustion.

Participants recorded training for 5 days prior to each run, while diet was recorded with prospective records for 2 days. Intakes of energy, carbohydrate, fat and protein were calculated based on manufacturer information (if available) or the USDA Food Database (U.S. Department of Agriculture, 2012). Participants were asked to avoid strenuous activity and alcohol for 48 h and caffeine for 12 h before visits. For their second run, participants were instructed to match training and diet from their first run. To further standardize nutrition, participants were supplied meals for the night before (between 5–7 p.m.) and morning of runs (2 h before). The meals provided were between 140–210 and 75–115 g of carbohydrate for dinner and breakfast, depending on body mass.

Physiological outcomes

A metabolic cart (Ultima, Medical Graphics, St. Paul, Minnesota, USA) measured breath-by-breath exchange of oxygen and carbon dioxide. Oxygen consumption ($VO_{2)}$ and carbon dioxide expiration (VCO_2) were calculated automatically by the software Breeze (Medical Graphics). Rates of carbohydrate and fat oxidation were estimated using stoichiometric equations from Jeukendrup and Wallis (2005): (carbohydrate = 4.210 VCO_2 – 2.962 VO_2 – 2.37 N; fat = 1.695 VO_2 – 1.701 VCO_2 – 1.77 N). VCO_2 and VO_2 were in L/min and N (nitrogen excretion) was considered to be negligible.

Capillary blood lactate was assessed using a handheld analyzer (Lactate Plus, Nova Biomedical, Waltham, Massachusetts, USA). The finger was cleaned with an alcohol swab, and a damp cotton pad removed excess alcohol. The finger was dried for 1 min, after which the treadmill was stopped and the participant's finger was pricked with a lancet. Heart rate (HR) was recorded with a chest strap monitor (Polar, Kempele, Finland).

Psychometric outcomes

The Feeling Scale (FS), an 11-point scale ranging from +5 to −5, assessed pleasure and displeasure (Hardy & Rejeski, 1989). To assess GI distress, a 7-point scale with anchors ranging from "no discomfort" at 1 to "very severe discomfort" at 7 was adapted from the validated Gastrointestinal Symptom Rating Scale (Revicki et al., 1998). Nausea, belching/regurgitation/reflux, bloating/fullness, gas/flatulence, lower abdominal cramps, and urge to defecate were assessed. To assess blinding, participants rated beverage sweetness and overall likability on a labeled hedonic scale (LHS; Lim et al., 2009). Sweetness scores ranged from 0 to +100 ("neutral" to "most sweet sensation imaginable") while overall likability ranged from −100 to +100 ("most disliked sensation imaginable" to "most liked sensation imaginable").

Submaximal protocol

Constant-velocity, 120-min runs were separated by at least 14 days. A median of 23 (15–33) days elapsed between runs for men, while women completed runs within 26–29 days to control for menstrual cycle. Participants reported to HSPL between 6 and 9 a.m. for their first run and within 1 h of that time for their second run. Upon arrival, participants voided and were weighed.

Participants' GI symptoms, FS ratings, and HR were recorded 25 min before starting the submaximal protocol. Ten minutes before, participants completed a 5-min warm-up, after which they rested for 5 min. Treadmill velocity for the submaximal protocol was set at 90% of the average pace from the participant's most recent marathon.

At 25 min before the start, participants consumed their first beverage dose supplying 55.4 g of carbohydrate (~600 mL). This pre-exercise feeding was given so that modest boluses could be used during running, as large boluses (200–250 mL every 15–20 min) would have been required to supply carbohydrate at 1.3 g/min with the exclusive use of during-exercise feedings. Notably, runners reported during pilot testing that they were not accustomed to consuming large fluid boluses (200–250 mL). Participants consumed additional doses after 20, 40, 60, 80, and 100 min of running, and immediately after the submaximal protocol. Feedings at 20, 40, 60, and 80 min provided 18.4 g of carbohydrate (~180 mL) while feedings at 100 min and the finish provided 14.7 (~140 mL) and 11 g (~110 mL), respectively. Volumes decreased over time because it was the most tolerable strategy during pilot testing. Treadmill velocity was slowed to 75% of marathon pace for up to 2 min while participants consumed boluses. Beverages were kept at 2.8–4.0 °C until 15 min before the first bolus. The weight of remaining beverage was recorded immediately after the last dose was administered, with a consumption goal of 1682 g.

At specified intervals, respiratory gases (5, 91, 117 min), HR/FS/GI symptoms (−25, 10, 30, 50, 70, 90, 110 min), and LHS ratings (−25, 20, 60, 100 min) were collected. Lactate was taken at 55 and 115 min. A fan was placed adjacent to the treadmill and set at medium velocity. Treadmill velocity was verified every 2 weeks with a tachometer (RPM33, Extech Instruments, Nashua, New Hampshire, USA).

Time trial performance

After the 120 min submaximal protocol, the treadmill was stopped for 2 min to allow participants to consume the last beverage dose, allow participants to void, and repeat instructions. Participants were instructed to complete 4 miles as fast as possible and were told they could change velocity as frequently as desired. As GI symptoms are purported to be a mechanism responsible for performance benefits with MTC, participants were told they could use the restroom, if necessary, but that it would count toward finishing time (as it would in a race). The restroom was located in proximity to the treadmill (~15 ft). Participants were unable to view time elapsed but were able to see distance covered. Investigator and participant interactions were limited to soliciting FS and GI ratings. FS ratings and HR were recorded at miles 0.5, 1.5, 2.5, 3.5, and 4. GI symptoms were solicited at miles 0.5 and 3.5.

Statistical analyses

A magnitude-based inferential statistics approach that reports uncertainty of outcomes as 90% confidence limits (CL) was utilized to evaluate treatment effects. This approach calculates effects with 90% CL and interprets them in relation to the smallest worthwhile effect (Batterham & Hopkins, 2006). Interpretation is done using probabilities that the true (population) effect is greater, trivial, or lower in relation to the smallest worthwhile effect. Effects, 90% CL, and chances that effects were positive, trivial, or negative were calculated using a spreadsheet for crossover trials (Hopkins, 2006b). The smallest worthwhile effects for performance were set at +0.8% and −0.8%, using the recommendation of 0.3 times the coefficient of variation (~2.5%) for endurance running performance (Hopkins & Hewson, 2001; Hopkins, 2004). For physiological measures, GI distress, and FS ratings, differences were interpreted using a Cohen effect, with thresholds set at +0.2 and –.02 (Cohen, 1988). Chance thresholds for variables were accompanied by qualitative descriptors: < 0.5%, almost certainly not; 0.5–5%, very unlikely; 5–25%, unlikely; 25–75%, possibly; 75–95%, likely; 95–99.5%, very likely; > 99.5%, almost certain. If chances of positive and negative effects were both >5%, the effect was considered unclear.

Performance times and physiological measures were natural log transformed (Hopkins, 2003), and performance times were back transformed to obtain percentage differences. Peak GI and LHS

ratings were percentile rank transformed because of resistance to log transformation. Nadir (low) and change (rest – 110 min) FS ratings were used for the submaximal protocol to limit the number of inferences. To account for order or learning effects, differences in finishing time (G minus GF) were analyzed separately based on randomization sequence (G/GF and GF/G). The independent effects were then combined using a spreadsheet that accounts for order effects (Hopkins, 2006a).

TT data for two participants were excluded. One participant experienced hip pain preventing running during the latter half of his second TT, whereas a treadmill malfunction occurred during another participant's second TT. Additionally, one participant's first TT value was truncated to a value equal to two standard deviations from the mean because it appeared to be a possible outlier, thus preserving the order of the data but reducing the influence of the data point (Field, 2009). Gas exchange for one participant was unavailable because of a computer malfunction. Lactate values were not available for two participants at 55 min and five participants at 115 min because of inadequate sample volume, which occurs for up to 10% of Lactate Plus readings. To simplify interpretation, untransformed means (±standard errors) are presented for variables that were transformed for inferences. Normality was assessed via the Shapiro-Wilk test. Descriptive statistics were generated using SPSS version 22 (IBM, Armonk, New York, USA).

Results

Randomization was counterbalanced among study completers, with 10 participants randomized to G first and 10 participants to GF first. Intakes of energy (5319 ± 256 vs 5300 ± 204 kcal), carbohydrate (11 ± 0.5 vs 10.9 ± 0.4 g/kg body mass), fat (159 ± 11 vs 155 ± 12 g) and protein (208 ± 14 vs 223 ± 17 g) were similar for G and GF over 2 days before the runs.

Finishing times for the TT ranged from 23:50 to 35:37 min, and finishing times for G and GF were 28:46 ± 0:44 and 28:11 ± 0:44 min (Table 1). Participants completed the TT 1.9% (−1.9; −4.2, 0.4) faster with GF compared with G, and there was 79% chance that the true population effect was −0.8% or lower. The effect was similar after accounting for order effects (−2.2%; −4.3, −0.1). Effect sizes for men and women were −1.6% (−4.2, 1.2) and −2.6% (−8.1, 3.1), respectively.

Participants exercised, on average, at 65% of VO_{2peak} during the submaximal protocols. Mean oxygen uptake during G was 2.64 ± 0.1 L/min for all time points, while values during GF were 2.68 ± 0.1, 2.67 ± 0.1, and 2.68 ± 0.1 L/min at 5, 91, and 117 min, respectively. Table 2 presents data for physiological variables hypothesized to be different between conditions. Median (IQR) lactate concentrations at 55 min were 2.3 (1.6–3.4) and 1.9 (1.4–3.3) mmol/L for G and GF. Lactate concentrations were 1.9 (1.3–2.7) and 1.7 (1.4– 3.0) mmol/L for G and GF at 115 min. Mean HR over the submaximal protocol was 145.4 ± 2.3 and 144.8 ± 2.1 b/min for G and GF. During the TT, mean HR was 167.9 ± 2.6 and 168.3 ± 2.5 b/min for G and GF.

Contrary to our hypothesis, carbohydrate oxidation was not higher with GF at the end of the submaximal protocol. In fact, there was a 32% chance that carbohydrate oxidation was lower with GF. At both 5 and 117 min, GF resulted

Table 1. Inferential statistics for 4-mile time trial performance

	G†	GF†	% Difference (90% CL)‡	Chances of GF being higher, trivial, and lower relative to G§	Interpretation
Finishing time* (min:s)	28:46	28:11	−1.9 (−4.2, 0.4)	3%, 18%, 79%	Likely lower

* Excludes two participants because of a treadmill malfunction and hip pain (n = 18).
† Means (min:s) prior to transformation
‡ Based on natural log transformation
§ Based on smallest worthwhile differences of +0.8% and −0.8%
CL, confidence limits; G, glucose-only; GF, glucose-fructose

Table 2. Inferential statistics for substrate use and physiological markers

	G*	GF*	Difference expressed as Cohen (90% CL)†	Chances of GF being higher, trivial, and lower relative to G‡	Interpretation
CHO oxidation (g/min)					
5 min	2.41	2.32	−0.19 (−0.44, 0.07)	1%, 52%, 47%	Possibly lower
91 min	2.05	2.08	0.06 (−0.16, 0.28)	13%, 84%, 3%	Likely trivial
117 min	1.91	1.83	−0.14 (−0.36, 0.08)	1%, 68%, 32%	Possibly lower
Fat oxidation (g/min)					
5 min	0.34	0.40	0.33 (−0.15, 0.80)	67%, 29%, 4%	Possibly higher
91 min	0.49	0.49	−0.04 (−0.36, 0.28)	10%, 70%, 20%	Unclear
117 min	0.54	0.60	0.18 (−0.05, 0.41)	45%, 55%, 0%	Possibly higher
Lactate (mmol/L)					
55 min	2.68	2.39	−0.19 (−0.63, 0.25)	7%, 44%, 49%	Unclear
115 min	2.07	2.12	−0.02 (−0.50, 0.45)	21%, 53%, 26%	Unclear

* Means prior to transformation
† Based on natural log-transformation
‡ Based on Cohen effect sizes of +0.2 and −0.2. CHO and fat oxidation unavailable for one participant (n = 19). Lactate unavailable for two participants at 55 min (n = 18) and five participants at 115 min (n = 15)
CHO, carbohydrate; CL, confidence limits; G, glucose-only; GF, glucose-fructose

in possibly higher fat oxidation relative to G. Lactate effects were unclear at both time points.

GI distress incidence is shown in Table 3, expressed as frequencies of experiencing any symptoms (>1) and at least mild symptoms (≥ 3). Table 4 shows inferential statistics for GI symptoms and other psychometric variables. During the submaximal period, belching/regurgitation/reflux, bloating/fullness, and gas/flatulence were all likely lower with GF (Cohen's ranging from −0.37 to −0.45), while effects for abdominal cramps and urge to defecate were unclear. Similar

Table 3. Incidence of gastrointestinal distress

	No. reporting > 1 (%)		No. reporting ≥ 3 (%)	
	G	GF	G	GF
Submaximal (*n* = 20)				
Nausea	3 (15%)	1 (5%)	1 (5%)	1 (5%)
Belching/regurgitation/reflux	13 (65%)	9 (45%)	2 (10%)	1 (5%)
Fullness/bloating	14 (70%)	10 (50%)	6 (30%)	3 (15%)
Lower abdominal cramps	9 (45%)	8 (40%)	3 (15%)	1 (5%)
Gas/flatulence	7 (35%)	4 (20%)	3 (15%)	0 (0%)
Urge to defecate	4 (20%)	3 (15%)	3 (15%)	0 (0%)
Time trial (*n* = 18)				
Nausea	4 (22%)	1 (6%)	1 (6%)	1 (6%)
Belching/regurgitation/reflux	4 (22%)	4 (22%)	0 (0%)	0 (0%)
Fullness/bloating	5 (28%)	4 (22%)	3 (17%)	1 (6%)
Lower abdominal cramps	7 (39%)	5 (28%)	3 (17%)	3 (17%)
Gas/flatulence	5 (28%)	4 (22%)	2 (11%)	1 (6%)
Urge to defecate	4 (22%)	2 (11%)	3 (17%)	1 (6%)

GI symptoms rated from "no discomfort" = 1 to "very severe discomfort" = 7. Based on peak values reported.
G, glucose-only; GF, glucose-fructose.

Table 4. Inferential statistics for psychometric scales

	G*	GF*	Difference expressed as Cohen (90% CL)†	Chances of GF being higher, trivial, and lower relative to G‡	Interpretation
FS (−5 to +5)					
Submax nadir	2.15	2.55	0.22 (−0.05, 0.49)	55%, 44%, 1%	Possibly higher
Change (rest – 110 min)	2.35	1.90	−0.25 (−0.49, −0.01)	0%, 35%, 65%	Possibly lower
TT average	−0.06	0.32	0.15 (−0.17, 0.48)	40%, 56%, 4%	Possibly higher
Submaximal GI symptoms§ (1 to 7)					
Belching/regurgitation/reflux	1.75	1.50	−0.38 (−0.81, 0.04)	1%, 22%, 77%	Likely lower
Bloating/fullness	2.20	1.70	−0.45 (−0.79, −0.10)	0%, 11%, 89%	Likely lower
Abdominal cramps	1.60	1.50	−0.16 (−0.55, 0.23)	6%, 50%, 43%	Unclear
Gas/flatulence	1.50	1.20	−0.37 (−0.78, 0.04)	1%, 22%, 76%	Likely lower
Urge to defecate	1.35	1.15	−0.16 (−0.54, 0.21)	6%, 51%, 43%	Unclear
Time trial GI symptoms (1 to 7)					
Nausea	1.28	1.11	−0.44 (−1.01, 0.14)	4%, 21%, 76%	Likely lower
Belching/regurgitation/reflux	1.22	1.22	0.00 (−0.55, 0.55)	27%, 46%, 27%	Unclear
Bloating/fullness	1.67	1.33	−0.16 (−0.52, 0.20)	5%, 52%, 43%	Possibly lower
Abdominal cramps	1.72	1.56	−0.20 (−0.56, 0.16)	4%, 47%, 50%	Possibly lower
Gas/flatulence	1.50	1.33	−0.14 (−0.60, 0.33)	11%, 48%, 41%	Unclear
Urge to defecate	1.67	1.22	−0.29 (−0.78, 0.19)	5%, 32%, 63%	Possibly lower
LHS ratings (0 to 100)					
Sweet rest	25.1	24.0	−0.08 (−0.48, 0.31)	12%, 58%, 30%	Unclear
Sweet 20 min	22.8	27.1	0.23 (−0.16, 0.63)	56%, 41%, 4%	Possibly higher
Sweet 60 min	26.4	24.3	−0.12 (−0.44, 0.21)	6%, 62%, 33%	Unclear
Sweet 100 min	21.8	22.4	0.07 (−0.39, 0.53)	32%, 52%, 16%	Unclear
Likability rest	12.0	10.8	−0.11 (−0.46, 0.24)	7%, 59%, 33%	Unclear
Likability 20 min	16.0	15.1	−0.04 (−0.33, 0.25)	8%, 74%, 18%	Unclear
Likability 60 min	16.3	18.6	0.04 (−0.32, 0.39)	22%, 65%, 13%	Unclear
Likability 100 min	13.7	21.3	0.30 (−0.02, 0.61)	69%, 30%, 1%	Possibly higher

***** Means prior to transformation
† LHS ratings and peak GI symptoms were based on percentile rank transformation.
‡ Based on smallest worthwhile Cohen effect sizes of +0.2 and −0.2
§ Submaximal nausea was not examined because of low overall incidence. Submaximal, *n* = 20; TT, *n* = 18
CL, confidence limits; FS, Feeling Scale; G, glucose-only; GF, glucose-fructose; GI, gastrointestinal; LHS, labeled hedonic scale; TT, time trial

patterns for GI distress emerged during the TT, but effect sizes were generally smaller. Relative to a Cohen threshold of 0.2, nadir FS ratings during the submaximal protocol were possibly higher with GF (55% chance), and FS ratings possibly showed a smaller reduction from rest to 110 min (65% chance). FS ratings averaged over the TT were possibly higher with GF (40% chance). Effects for beverage sweetness and likability were unclear, with the exception of possibly higher sweetness with GF at 20 min (Cohen = 0.23; −0.16, 0.63) and higher likability with GF at 100 min (Cohen = 0.30; −0.02, 0.61).

Weights of beverage consumed for G and GF were 1660 ± 2 g and 1659 ± 2 g, respectively. Body weight decreased by 1.8 ± 0.1 kg for both conditions.

Discussion

The primary finding of this investigation was that ingestion of a glucose-fructose beverage (ratio of 1.2:1) likely improved 4-mile TT performance after 2 h of submaximal running. This finding should be interpreted within the context of the study design, with factors including a carbohydrate feeding rate of 1.3 g/min, a carbohydrate concentration of 10%, and exercise intensity of 60–70% VO_{2peak}. In addition, participants completed trials in a fed state, which increases the generalizability of findings relative to previous studies (Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; Triplett et al., 2010; O'Brien & Rowlands, 2011; Roberts et al., 2014). The direction and magnitude of performance benefits were similar for men and women, with magnitudes ranging from 1.6% to 2.6%.

Notably, this is the first study to find a likely performance benefit with MTC during running. Previously, Pfeiffer et al. (2009) and Lee et al. (2014) examined the effects of glucose-only or glucose-fructose ingestion on endurance running performance. In Pfeiffer et al. (2009), gels supplied carbohydrate at 1.4 g/min during 16 km outdoor running, and finishing times were not different between conditions (1:14:25 for glucose vs 1:14:41 for glucose-fructose). Lee et al. (2014) utilized half-marathon treadmill running, and carbohydrate was supplied at roughly 1.0 g/min in three forms (6% glucose-only beverage, glucose-only gels, and glucose-fructose gels). No significant perceptual or performance differences were found, although effect sizes between the conditions were modest (glucose-fructose gel resulted in 2.7–3.0% slower finishing times). The fact that our study used a protocol of sustainably longer duration may partly explain the discrepant findings with these two studies. The other running-based study had 11 men complete a 90-min soccer protocol while ingesting carbohydrate at 1.0 g/min from glucose or a 2:1 glucose-fructose mix (Clarke et al., 2012). After the protocol, participants ran to exhaustion on a treadmill at 12.8 km/h and 20% grade. Time-to-exhaustion (83 ± 3 vs 77 ± 7.2 s) was not significantly different, but there was a trend for longer time-to-exhaustion with glucose-fructose ($P = 0.06$). Given the inconsistencies between studies, further research is needed to delineate the effects of MTC for a range of running-based tasks.

The GI effects of fructose may partly explain the performance benefit in this study, as previous investigations indicate that GI distress can negatively impact performance. Rowlands et al. (2012) and O'Brien et al. (2013) used statistical modeling to assess the magnitude of performance benefit attributable to reductions in GI symptoms and found that abdominal cramps significantly mediated cycling performance outcomes. Moreover, one of the only MTC studies to utilize a pure TT clearly showed that GI distress can substantially impair performance. Specifically, participants finished a 100-km cycle TT 8% faster when consuming a glucose-fructose beverage compared with glucose-only, and of nine participants, two experienced diarrhea and one experienced vomiting with glucose-only (Triplett et al., 2010). These observations seem to be supported by our data, as GI distress was possibly-to-likely lower with GF for most symptoms.

Several mechanisms may be responsible for the observed GI effects. Under resting conditions, concentrated fructose-containing solutions empty faster from the stomach than glucose solutions (Sole & Noakes, 1989), and these differences are best explained by the inhibitory feedback effects of glucose on intestinal afferents (Zittel et al., 1994). Inhibition of gastric emptying with glucose would explain the likely higher ratings of bloating/fullness observed with G during the present study. Additionally, SGLT1 transporters may become saturated with large, rapid glucose feedings, which could cause carbohydrate malabsorption and osmotic fluid shifts into the intestine (Jeukendrup, 2010). These effects could explain the possibly higher ratings of abdominal cramping and gas in this and previous studies.

In terms of psychological affect, it is possible the GF resulted in higher FS ratings. These positive effects were apparent when expressing FS ratings as nadir and change values, as well as average values during the TT. In light of the multiple physiological effects of fructose, we are not able to delineate precisely which mechanisms were responsible for the possible differences. Interestingly, a recent blinded study found that glucose and fructose activate different brain regions and may have differential effects on reward and motivational processing (Page et al., 2013). Others have argued that sweetness partially mediates the performance benefit of glucose-fructose ingestion (O'Brien et al., 2013), but sweetness differences were not generally apparent in this study (with the exception of a small possible difference at 20 min). Beverage likability was similar between conditions, but ratings for GF were likely higher at 100 min despite no differences in sweetness. It will be important for future studies to assess beverage sensory characteristics in order to help delineate whether metabolic or psychometric properties of fructose are primarily responsible for performance benefits with MTC ingestion.

Despite the apparent confirmation of performance, GI, and psychological benefits, our hypotheses that glucose-fructose would result in higher lactate and carbohydrate oxidation were not supported. Previous studies found higher lactate concentrations with fructose feeding compared with glucose, but timing of ingestion may mediate this effect. Fructose ingestion prior to exercise elevates blood lactate during the postprandial period, but lactate falls with the onset of exercise, at least in comparison to glucose (Hargreaves et al., 1985). Thus, feeding a substantial amount of fructose 25 min prior to exercise possibly minimized elevations in lactate 80 min later. In regards to carbohydrate oxidation, some (Lecoultre et al., 2010; Roberts et al., 2014) but not all studies (Jeukendrup & Moseley, 2010) have found differences in total carbohydrate oxidation with MTC. Interestingly, fat oxidation was possibly higher for GF at 5 and 117 min. Lower fat oxidation with G, especially at 5 min, could have been due to a greater insulin release, leading to insulin-associated fat oxidation suppression (Koivisto et al., 1981). Given the lack of support for our hypotheses related to carbohydrate and lactate metabolism, it would seem the performance benefits were more likely a result of GI and psychological effects.

There are several novel approaches and strengths to this study. Unlike much of the previous literature, this investigation was double-blinded with data on participant blinding. The majority of previous studies were conducted with participants fasted, but participants in our study received two meals to ensure nutrition was similar between participants and trials. Furthermore, the beverage volume was similar to intakes observed in the field (Pfeiffer et al., 2012), and since many of the previous investigations used volumes (~1000 mL/h) exceeding ad libitum intakes, generalizability of previous data may be limited.

Despite this study's strengths, limitations need to be acknowledged. We did not use a non-carbohydrate control, mainly because participant burden would have been increased to three runs. Recruitment was likely enhanced, however, by requiring only two runs, which was evidenced by the relatively large sample size. Another limitation is the lack of data on exogenous carbohydrate oxidation, which requires tracers; the use of invasive and time-consuming testing was avoided to maximize recruitment. Finally, the amount of fluid and carbohydrate ingested were not according to participant preference. Competitors that experience GI distress often adjust intake to mitigate symptoms, but our participants were required to drink a prescribed rate regardless of symptoms experienced.

Perspectives

This study showed that ingestion of glucose-fructose in a ratio of 1.2:1 – compared with glucose-only – likely improved performance, possibly reduced GI distress, and possibly improved psychological affect during prolonged running. The performance benefits observed were most likely attributable to GI and psychological effects of glucose-fructose co-ingestion. These results apply to competitive runners consuming fluid and carbohydrate at relatively aggressive rates (500–600 mL/h and 1.0–1.3 g/min) during running at an intensity of 60–70% VO_{2peak}. Performance benefits were similar for men and women alike, and thus, this study provides evidence – albeit tentative – that ingestion of MTC can be useful for female athletes. To build upon these findings, additional studies are needed to determine whether MTC improve performance, GI distress, and psychological affect for a wide range of running-based activities.

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