Oxidation of combined ingestion of glucose and fructose during exercise

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Jentjens, Roy L. P. G., Luke Moseley, Rosemary H. Waring, Leslie K. Harding, and Asker E. Jeukendrup. Oxidation of combined ingestion of glucose and fructose during exercise. J Appl Physiol 96: 1277–1284, 2004. First published December 2, 2003; 10.1152/japplphysiol.00974.2003.—The purpose of the present study was to examine whether combined ingestion of a large amount of fructose and glucose during cycling exercise would lead to exogenous carbohydrate oxidation rates >1 g/min. Eight trained cyclists (maximal O2 consumption: 62 ± 3 ml·kg−1·min−1) performed four exercise trials in random order. Each trial consisted of 120 min of cycling at 50% maximum power output (63 ± 2% maximal O2 consumption), while subjects received a solution providing either 1.2 g/min of glucose (Med-Glu), 1.8 g/min of glucose (High-Glu), 0.6 g/min of fructose + 1.2 g/min of glucose (Fruc+Glu), or water. The ingested fructose was labeled with [U-14C]fructose, and the ingested glucose was labeled with [U-14C]glucose. Peak exogenous carbohydrate oxidation rates were ~55% higher (P < 0.001) in Fruc+Glu (1.26 ± 0.07 g/min) compared with Med-Glu and High-Glu (0.80 ± 0.04 and 0.83 ± 0.05 g/min, respectively). Furthermore, the average exogenous carbohydrate oxidation rates over the 60- to 120-min exercise period were higher (P < 0.001) in Fruc+Glu compared with Med-Glu and High-Glu (1.16 ± 0.06, 0.75 ± 0.04, and 0.75 ± 0.04 g/min, respectively). There was a trend toward a lower endogenous carbohydrate oxidation in Fruc+Glu compared with the other two carbohydrate trials, but this failed to reach statistical significance (P = 0.075). The present results demonstrate that, when fructose and glucose are ingested simultaneously at high rates during cycling exercise, exogenous carbohydrate oxidation rates can reach peak values of ~1.3 g/min.

substrate utilization; carbohydrate absorption; isotopic tracers; metabolism

I t has been shown that carbohydrate (CHO) feedings during prolonged moderate- to high-intensity exercise can postpone fatigue and enhance exercise performance when the exercise duration is ~45 min or longer (2, 17, 41). The observed improvements in performance with CHO ingestion have contributed to better maintenance of plasma glucose concentrations and high rates of CHO oxidation late in exercise (3, 5), when muscle and liver glycogen levels are low.

Studies that have used either stable (16, 21, 29, 36, 40) or radioactive isotopes (3, 11) to quantify exogenous CHO oxidation during exercise have found peak oxidation rates of ~1 g/min (for review, see Refs. 10, 18, 21). Even when CHO was ingested at high rates (up to 3.0 g/min), oxidation rates did not exceed 1 g/min (16, 21, 29, 36, 40). In most of the above-cited studies, glucose or glucose polymer was the type of CHO ingested. Although direct evidence is lacking, it has been suggested that the absorption capacity of glucose in the intestine (31) is a limiting factor for the oxidation of ingested glucose (18, 21).

A number of studies have compared the oxidation rates of various types of ingested CHO with the oxidation of exogenous glucose during exercise (for review, see Ref. 18). From these studies, it appears that the rate of oxidation of ingested maltose (11), sucrose (27, 40), glucose polymer (26), and maltodextrin (32) is fairly similar to the oxidation rate of ingested glucose. However, significantly lower exogenous CHO oxidation rates have been reported for fructose (~20–25% lower) (1, 15, 25, 26) and galactose (~50% lower) (23) compared with glucose. There have been suggestions that the lower oxidation rate of fructose is due to a lower rate of absorption (1, 18). Furthermore, both fructose and galactose have to be converted into glucose in the liver before they can be oxidized, and this may slow down the rate of oxidation.

Intestinal transport of glucose occurs via a sodium-dependent glucose transporter (SGLT1), which is located in the brush-border membrane (8). It is likely that SGLT1-transporters are saturated at a glucose ingestion rate of ~1 g/min, which could explain why higher glucose intake rates do not result in oxidation rates higher than 1.0–1.1 g/min (21, 40). In contrast to glucose, fructose is absorbed from the intestine by GLUT-5, a sodium-independent facilitative fructose transporter (4, 8). It is not unlikely that, when a mixture of glucose and fructose is ingested, there is less competition for absorption compared with the ingestion of an isoenergetic amount of glucose (or fructose), and this may increase the availability of CHO into the bloodstream for oxidation.

To our knowledge, only two studies have attempted to investigate the oxidation of combined ingestion of glucose and fructose (1, 33). The results of these studies are contradictory, which might be due to differences in study design or subject selection. Riddell et al. (33) studied 12 children who ingested 67.5 g of a mixture of glucose and fructose or an isoenergetic amount of glucose during 90 min of exercise at 55% maximal O2 consumption (V˙ O2 max). No difference was found in exogenous CHO oxidation between the two CHO trials, and peak oxidation rates did not exceed 0.36 g/min. In a study by Adopo et al. (1), six trained subjects cycled for 120 min at 61% V˙ O2 max while ingesting 100 g of glucose or fructose or a mixture of 50 g glucose and fructose. The addition of fructose to the glucose drink increased total exogenous CHO oxidation by 27% compared with the isoenergetic glucose drink (0.61 vs.

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0.48 g/min). It should be noted that the amounts of CHO ingested in the study of Adopo et al. were relatively small (~0.8 g/min), and, therefore, glucose (and fructose) transporters were probably not fully saturated. At present, there are no studies available in the literature that have investigated whether combined ingestion of large amounts of glucose and fructose can result in exogenous CHO oxidation rates that exceed 1 g/min. Furthermore, in the study of Adopo et al., it was not possible to determine the oxidation rate of both glucose and fructose in one trial, because only one of the ingested CHO was isotopically labeled. To measure the total oxidation rate of the ingested glucose plus fructose mixture, two separate trials were performed, and this may have confounded the results.

We hypothesized that combined ingestion of a large amount of fructose (72 g) and glucose (144 g) during 2 h of exercise would lead to exogenous CHO oxidation rates higher than 1 g/min. The ingested fructose was labeled with [U-14C]fructose, and the ingested glucose was labeled with [U-13C]glucose, which enabled us to measure the oxidation rates of glucose and fructose when ingested simultaneously.

METHODS

Subjects. Eight trained male cyclists or triathletes, aged 29.0 ± 2.7 yr and with a body mass of 75.1 ± 1.8 kg, took part in this study. Before participation, each of the subjects was fully informed of the purpose and risks associated with the procedures, and a written, informed consent was obtained. All subjects were healthy, as assessed by a general health questionnaire. The study was approved by the South Birmingham Local Research Ethics Committee and the UK administration of Radioactive Substance Advisory Committee.

Preliminary testing. At least 1 wk before the start of the experimental trials, an incremental cycle exercise test to volitional exhaustion was performed to determine the individual maximum power output (Wmax) and VO2 max. This test was performed on an electromagnetically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands), modified to the configuration of a racing bicycle with adjustable saddle height and handlebar position. After the subjects reported to the laboratory, body mass (Seca Alpha, Hamburg, Germany) and height were recorded. Subjects then started cycling at 95 W for 3 min, followed by incremental steps of 35 W every 3 min until exhaustion. Heart rate (HR) was recorded continuously by a radiotelemetry HR monitor (Polar Vantage, Kempele, Finland). Wmax was calculated from the last completed work rate, plus the fraction of time spent in the final, noncompleted work rate, multiplied by the work rate increment. The results were used to determine the work rate corresponding to 50% Wmax, which was later employed in the experimental exercise trials. Breath-by-breath measurements were performed throughout exercise by using an online automated gas analysis system (Oxycon Alpha, Jaeger, Wuerzburg, Germany). The volume sensor was calibrated by using a 3-liter calibration syringe, and the gas analyzers were calibrated by using a 5.03% CO2-94.97% N2 gas mixture. Oxygen consumption (VO2) was considered to be maximal (VO2 max) when at least two of the three following criteria were met: 1) a leveling off of VO2 with increasing workrate (increase of no more than 2 ml·kg\(^{-1} \cdot \text{min}^{-1}\)), 2) a HR within 10 beats/min of predicted maximum (HR 220 minus age), and 3) a respiratory exchange ratio (RER) > 1.05. VO2 max was calculated as the average oxygen uptake over the last 60 s of the test. The VO2 max and Wmax achieved during the incremental exercise test were 62 ± 3 ml·kg\(^{-1} \cdot \text{min}^{-1}\) and 374 ± 12 W, respectively.

Experimental design. Each subject performed four exercise trials, which consisted of 120 min of cycling at 50% Wmax, while ingesting an 8.7% glucose drink (Med-Glu), a 13.1% glucose drink (High-Glu), an isoinertgenic fructose plus glucose drink (Fruc+Glu) (the ingested fructose-to-glucose ratio was 1:2), or plain water (Wat). To quantify exogenous CHO oxidation, the ingested fructose was enriched with [U-13C]fructose, and the ingested glucose was labeled with [U-14C]glucose. The order of the experimental drinks was counterbalanced in a crossover design. Experimental trials were separated by at least 7 days.

Diet and activity before testing. Subjects were asked to record their food intake and activity pattern 2 days before the first exercise trial and were then instructed to follow the same diet and exercise activities before the other three trials. In addition, 5–7 days before each experimental testing day, they were asked to perform an intense training session (“glycogen-depleting” exercise bout) in an attempt to empty any 13C-enriched glycogen stores. Subjects were further instructed not to consume any food products with a high natural abundance of 13C (CHO derived from C4 plants: corn, sugar cane) at least 1 wk before and during the entire experimental period to reduce the background shift (change in 13CO2) from endogenous substrate stores.

Protocol. Subjects reported to the Human Performance Laboratory in the morning (between 7:00 and 9:00 AM) after an overnight fast (10–12 h) and having refrained from any strenuous activity or drinking any alcohol in the previous 24 h. For a given subject, all trials were conducted at the same time of the day to avoid any influence of circadian variance. On arrival in the laboratory, a flexible 21-gauge Teflon catheter (Quickcath, Baxter BV, Norfolk, UK) was inserted in an antecubital vein of an arm and attached to a three-way stopcock (Sims Portex, Kingsmead, UK) to allow for repeated blood sampling during exercise. The catheter was kept patent by flushing with 1.0–1.5 ml of isotonic saline (0.9% Baxter) after each blood sample collection. After voiding, subjects were weighed in cycling shorts to the nearest 0.1 kg by using a platform scale (Seca Alpha, Hamburg, Germany).

The subjects then mounted a cycle ergometer, and a resting breath sample was collected in 10-ml Extainer tubes (Labco Brow Works, High Wycombe, UK), which were filled directly from a mixing chamber in duplicate to determine the 13C-to-12C ratio (13C/12C) in the expired air. A second resting breath sample was collected for later determination of 14CO2-specific activity. The expired air of each second breath sample was collected in a 6-liter anesthetic gas bag by using a two-way Hans Rudolph valve and subsequently passed through a CO2 trapping solution, containing 1 ml of hyamine hydroxide in 1 M methanol (Zinsser Analytic, Berkshire, UK), 2 ml of 96% ethanol (BD Laboratory Supplies, Poole, UK), and one to two drops of phenolphthalein (Riedel-de Haën, Seez, Germany). The expired air was bubbled for 2–3 min through the pink-colored CO2 trapping solution until the solution became clear, at which point exactly 1 mmol of CO2 was trapped (37). Seventeen milliliters of liquid scintillation cocktail (Ready Gel, Beckman Coulter, High Wycombe, UK) was then added to the solution, and 14CO2 radioactivity in disintegrations/min (dpm, later converted to dpm/mmol) was subsequently counted in a liquid scintillation counter (Beckman, LS 1800).

Next, a resting blood sample (10 ml) was taken and stored on ice until centrifugation. Subjects then started a 120-min exercise bout at a work rate equivalent to 50% Wmax (63 ± 2% VO2 max). Additional blood samples were drawn at 15-min intervals during exercise. Expired breath samples were collected every 15 min until the end of exercise. VO2, carbon dioxide production (VCO2), and RER were measured every 15 min for periods of 4 min by using an online automated gas analysis system, as previously described.

During the first 3 min of exercise, subjects drank an initial bolus (600 ml) of one of the four experimental drinks: Med-Glu, High-Glu, Fruc+Glu, or Wat. Thereafter, every 15 min, a beverage volume of 150 ml was provided. The total fluid provided during the 120-min exercise bout was 1.65 liters. The average rate of glucose intake in the Med-Glu and High-Glu trial was 1.2 and 1.8 g/min, respectively. In the Fruc+Glu trial, subjects ingested, on average, 0.6 and 1.2 g/min of fructose and glucose, respectively.
Subjects were asked every 30 min to fill in a questionnaire to rate (possible) gastrointestinal (GI) problems. Immediately after exercise, subjects voided and were weighed again wearing cycling shorts only. All exercise tests were performed under normal and standard environmental conditions (20–23°C dry bulb temperature and 50–60% relative humidity). During the exercise trials, subjects were cooled with standing floor fans in order minimize thermal stress.

**Experimental drinks.** The fructose used in the Fruc+Glu trial was a corn-derived crystalline fructose (Krystal 300, A. E. Staley Manufacturing), which has a high natural abundance of $^{13}$C ($\sim 11.9 \%^{\text{vs}}$ PDB). To increase the $^{13}$C content of the fructose even further, a trace amount of uniformly labeled $^{13}$C fructose was added ($\sim 0.083 \text{ g [U-13 C]fructose/l (\geq 99\%; Cambridge Isotope Laboratories)}$). The fructose provided to the subjects in the Fruc+Glu trial had a $^{13}$C enrichment of 134.7 $\%^{\text{vs}}$ vs. PDB. The $^{13}$C enrichment of the corn-derived fructose and the experimental fructose solution was determined by elemental analyzer-isotope ratio mass spectrometry (Europa Scientific GEO 20–20, Crewe, UK).

In all three CHO trials, a wheat-derived glucose (Amylum, London, UK) was used that has a $^{13}$C enrichment of $\sim 27.5 \%^{\text{vs}}$ vs. PDB. The glucose (+fructose) beverages were labeled with a trace amount of 0.45 MBq [U-13C]glucose (Amersham Pharmacia Biotech, Little Chalfont, UK), leading to a dose rate of 0.37 MBq/h. Furthermore, to all drinks, 20 mmol/l of sodium chloride were added to stimulate fluid absorption.

**Questionnaires.** Subjects were asked to fill out a short questionnaire every 30 min during the exercise trials. The questionnaire contained questions regarding the presence of GI problems at that moment and addressed the following complaints: stomach problems, GI cramping, bloated feeling, diarrhea, dizziness, headache, belching, vomiting, and urge to urinate or defecate. While subjects were on the cycle ergometer and continued their exercise, each question was answered by simply ticking a box on the questionnaire that corresponded to the severity of the GI problem addressed. The items were scored on a 10-point scale (1 = not at all, 10 = very, very much). The severity of the GI symptoms was divided into two categories, severe and nonsevere symptoms, as was previously described by Jeukendrup et al. (20). Severe complaints included nausea, stomach problems, bloated feeling, diarrhea, urge to vomit, and stomach and intestinal cramps, because these are symptoms that commonly impair performance and may bring with them health risks. The above symptoms were only registered as severe symptoms when a score of $\geq 5$ out of 10 was reported. When a score $< 5$ was given, they were registered as nonsevere. All other symptoms were registered as nonsevere, regardless of the score reported.

**Analyses.** Blood samples were collected into prechilled tubes containing potassium oxalate and sodium fluoride (Beckton Dickinson, Plymouth, UK) and were centrifuged at 2,300 $\times$ g for 10 min. Aliquots of plasma were immediately frozen in liquid nitrogen and stored at $\sim 70^\circ$C until analyses of glucose and lactate. Glucose (glucose HK kit, Sigma-Aldrich, Dorset, UK) and lactate (lactate kit, Sigma-Aldrich) were analyzed on a Cobas Bio semiautomatic analyzer (La Roche, Basel, Switzerland).

Breath samples were analyzed for $^{13}$CO$_2$ by gas chromatography continuous flow isotope ratio mass spectrometry (Europa Scientific, Crewe, UK). Furthermore, a second series of breath samples was measured for $^{14}$CO$_2$ radioactivity. These breath samples were counted for 10 min in a liquid scintillation counter, and all counts were corrected for differences in quench and background. From indirect calorimetry (Vo$_2$ and VCO$_2$), stable isotope measurements (breath $^{13}$CO$_2$/$^{12}$CO$_2$), and radioactive isotope measurements (breath $^{13}$CO$_2$ activity), oxidation rates of total fat, total CHO, and exogenous glucose and fructose were calculated.

**Calculations.** From VCO$_2$ and Vo$_2$ (l/min), total CHO and fat oxidation rates (g/min) were calculated by using stoichiometric equations of Frayn (9), with the assumption that protein oxidation during exercise was negligible.
Fruc+Glu trial, there was a significant increase \((P < 0.001)\) in the \(^{13}\)C enrichment of expired breath, reaching an enrichment difference of \(-17.8\%e\) vs. PDB toward the end of the 120-min exercise (compared with corresponding resting breath sample). During the Wat trial, there was a small but significant increase in \(^{13}\)C enrichment of the expired air \((P < 0.05)\). The rise in breath \(^{13}\)CO\(_2\) enrichment during the Wat trial was relatively small \((<4\%)\) compared with the increase in breath \(^{13}\)CO\(_2\) enrichment observed during the Fruc+Glu trial. However, although the background shift was small in the present study, a background correction was made for the calculation of EFO in the Fruc+Glu trial by using the data from the Wat trial.

The \(^{14}\)CO\(_2\) radioactivity of expired breath samples (corrected for background) is shown in Fig. 1B. In all three CHO trials, the \(^{14}\)C activity of the expired CO\(_2\) increased significantly \((P < 0.001)\) during exercise and leveled off after 90 min of exercise.

**Exogenous and endogenous CHO oxidation.** Peak exogenous CHO oxidation rates were reached at the end of exercise \((120\) min) and were significantly higher \((P < 0.001)\) in the Fruc+Glu trial \((1.26 \pm 0.07 \text{ g/min})\) compared with the Med-Glu and High-Glu trials \((0.80 \pm 0.04 \text{ and } 0.83 \pm 0.05 \text{ g/min, respectively})\) (Fig. 2). No difference was found in peak oxidation rates between Med-Glu and High-Glu. The average EGO rates over the 60- to 120-min exercise period were 0.75 \pm 0.04, 0.75 \pm 0.04, and 0.77 \pm 0.04 \text{ g/min for Med-Glu, High-Glu, and Fruc+Glu, respectively \((P > 0.05)\)} (Table 1). There were no significant differences in EGO among the three CHO trials.

In the Fruc+Glu trial, the average EFO rate during the final 60 min of exercise was 0.38 \pm 0.02 \text{ g/min, and this resulted in a total exogenous CHO oxidation rate (EGO + EFO)} of 1.16 \pm 0.06 \text{ g/min. Exogenous CHO oxidation in the Fruc+Glu trial was \sim55\% higher \((P < 0.001)\) compared with that in the isoenergetic glucose trial (High-Glu) and the Med-Glu trial (Table 1 and Fig. 2).}

Endogenous CHO oxidation was calculated by subtracting exogenous CHO oxidation from total CHO oxidation (Table 1 and Fig. 3). There were no significant differences in endogenous CHO oxidation rates among trials. However, there was a trend for a lower endogenous CHO oxidation in Fruc+Glu compared with Med-Glu and High-Glu \((P = 0.075)\).

**\(\text{V}_\text{O}_2\), RER, total CHO, and fat oxidation.** Data for \(\text{V}_\text{O}_2\), RER, total CHO, and fat oxidation over the 60- to 120-min exercise period were 0.84 \pm 0.01, 0.90 \pm 0.01, 0.91 \pm 0.01, \text{ and } 0.90 \pm 0.01 \text{ for Med-Glu, High-Glu, and Fruc+Glu, respectively \((P > 0.05)\)} (Table 1 and Fig. 3). There were no significant differences in respiratory exchange ratio among trials. However, there was a trend for a lower respiratory exchange ratio in Fruc+Glu compared with Med-Glu and High-Glu \((P = 0.01)\). Total CHO and fat oxidation over the 60- to 120-min exercise period were 1.85 \pm 0.02, 1.92 \pm 0.18, 2.11 \pm 0.19, \text{ and } 2.77 \pm 0.15 \text{ for Med-Glu, High-Glu, and Fruc+Glu, respectively \((P = 0.01)\)} (Table 1). There were no significant differences in fat oxidation among trials.

**Table 1. Oxygen uptake, respiratory exchange ratio, total carbohydrate oxidation, total fat oxidation, endogenous carbohydrate oxidation, and exogenous glucose and fructose oxidation during the 60- to 120-min period of exercise**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Med-Glu</th>
<th>High-Glu</th>
<th>Fruc+Glu</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{V}_\text{O}_2), l/min</td>
<td>3.09 \pm 0.12</td>
<td>3.09 \pm 0.10</td>
<td>3.08 \pm 0.12</td>
</tr>
<tr>
<td>RER</td>
<td>0.91 \pm 0.01*</td>
<td>0.91 \pm 0.01*</td>
<td>0.90 \pm 0.01*</td>
</tr>
<tr>
<td>CHO(_\text{tot}), g/min</td>
<td>1.85 \pm 0.23</td>
<td>2.67 \pm 0.18*</td>
<td>2.86 \pm 0.18*</td>
</tr>
<tr>
<td>Fat(_\text{tot}), g/min</td>
<td>0.15 \pm 0.06*</td>
<td>0.13 \pm 0.06*</td>
<td>0.11 \pm 0.06*</td>
</tr>
<tr>
<td>EGO, g/min</td>
<td>0.75 \pm 0.04*</td>
<td>0.75 \pm 0.04*</td>
<td>0.77 \pm 0.04*</td>
</tr>
<tr>
<td>EFO, g/min</td>
<td>0.38 \pm 0.02</td>
<td>0.47 \pm 0.00</td>
<td>0.47 \pm 0.00</td>
</tr>
</tbody>
</table>

Values are means \pm SE; \(n = 8\) subjects; \(\text{V}_\text{O}_2\), oxygen uptake; RER, respiratory exchange ratio; CHO, carbohydrate; CHO\(_\text{tot}\), total CHO oxidation; Fat\(_\text{tot}\), total fat oxidation; EGO, exogenous glucose oxidation; EFO, exogenous fructose oxidation; Wat, plain water; Med-Glu, medium glucose; High-Glu, high glucose; Fruc+Glu, fructose plus glucose. *Significantly different from Wat, \(P < 0.05\).
period are shown in Table 1. There was no difference in $V_{O2}$ among the four trials. RER in the Wat trial was significantly lower ($P < 0.01$) compared with that in the three CHO trials (Table 1). CHO oxidation was significantly higher ($P < 0.01$) after CHO ingestion compared with Wat ingestion. No significant differences in total CHO oxidation were found among CHO trials. Total fat oxidation was markedly suppressed with lactate concentrations were found among the three lactate levels increased ($P < 0.01$) at values around 4.9–5.4 mmol/l for the entire duration of exercise. Plasma glucose concentrations during Wat decreased from 4.6 ± 0.1 mmol/l at the start of exercise to 4.0 ± 0.1 mmol/l by the end of exercise ($P < 0.01$). Plasma glucose concentrations were higher throughout exercise in the CHO trials compared with the Wat trial, although Med-Glu failed to reach statistical significance between time = 30 and 60 min ($P > 0.05$).

In addition, during the second hour of exercise, plasma glucose concentrations were significantly lower in Med-Glu compared with High-Glu ($P < 0.05$). No other differences in plasma glucose concentrations were found among the three CHO trials.

Resting concentrations of plasma lactate were not different among trials (on average, 0.8 ± 0.1 mmol/l) (Fig. 4B). Plasma lactate levels increased ($P < 0.05$) during the first 15 min of exercise in all four trials. Thereafter, plasma lactate concentrations gradually declined until the end of exercise. At all time points during exercise, plasma lactate concentrations were significantly higher ($P < 0.05$) compared with lactate concentrations at rest. During the first 75 min of exercise, plasma lactate concentrations were significantly higher ($P < 0.05$) in Fruc+Glu compared with Med-Glu and Wat.

GI discomfort. GI and related complaints were registered by a questionnaire. The results of the questionnaires obtained during the four experimental trials are presented in Table 2. The most frequently reported complaints were bloated feeling, nausea, belching, flatulence, and urge to urinate and vomit. More subjects reported severe GI discomfort (bloated feeling, urge to vomit) in the High-Glu trial compared with the Med-Glu and the Fruc+Glu trial. None of the subjects vomited or suffered from diarrhea during the exercise trials.

Body mass loss. Body mass losses during exercise were not different among the four experimental trials (on average, 2.0 ± 0.1 kg).

DISCUSSION

To our knowledge, this study is the first to report exogenous CHO oxidation rates during cycling exercise >1.1 g/min (1.26 ± 0.07 g/min). Previous studies that have investigated exogenous CHO oxidation during cycling exercise have re-
ported peak oxidation rates of ~1.0 g/min (3, 11, 21, 36, 40) for exercise durations up to 180 min. Another interesting finding was that a mixture of glucose and fructose when ingested at a high rate resulted in ~55% higher exogenous CHO oxidation rates compared with ingestion of an isoenergetic amount of glucose only.

In the present study, exogenous CHO oxidation rates did not increase when the rate of glucose ingestion was increased from 1.2 to 1.8 g/min (Table 1 and Fig. 2). Peak oxidation rates were 0.80 ± 0.04 and 0.83 ± 0.05 g/min for Med-Glu and High-Glu, respectively. These results are in close agreement with the findings of a study by Wagenmakers et al. (40), who investigated the effect of four different doses of maltodextrin ingestion on exogenous CHO oxidation. Calculated average CHO ingestion rates during 120 min of cycling exercise were 0.6, 1.2, 1.8, and 2.4 g/min. Exogenous CHO oxidation was higher when maltodextrin was ingested at a rate of 1.2 g/min compared with 0.6 g/min (0.87 ± 0.13 vs. 0.53 ± 0.17 g/min). However, a further increase in the rate of maltodextrin ingestion did not lead to a significant increase in exogenous CHO oxidation, and oxidation rates leveled off at 1.0–1.1 g/min. Interestingly, in the present study, combined ingestion of fructose and glucose resulted in peak oxidation rates of 1.26 ± 0.07 g/min (Fig. 3), and average oxidation rates during the final 60 min of exercise were 1.16 ± 0.06 g/min (Table 1). Furthermore, ingestion of fructose in combination with glucose resulted in ~55% higher exogenous CHO oxidation rates compared with the ingestion of glucose only (Med-Glu and High-Glu) (Table 1 and Fig. 2). EGO in the Fruc+Glu trial was similar compared with EGO in the Med-Glu and High-Glu trial, and hence the higher exogenous CHO oxidation rate in Fruc+Glu could be fully attributed to the oxidation of ingested fructose (Table 1, Figs. 2 and 3).

When large amounts of glucose or glucose polymer are ingested (>1.0 g/min) during exercise, intestinal absorption and/or disposal by the liver may be limiting factors for exogenous CHO oxidation (18, 21). Glucose is absorbed from the intestine by SGLT1 (8), and suggestions have been made that the upper limit for glucose absorption (at rest) is ~1.0 g/min (31). However, others have suggested slightly higher values (1.3–1.7 g/min) (7). Although speculative, SGLT1 transporters may become “saturated” at a glucose ingestion rate of 1.0–1.2 g/min, and, therefore, no increase in EGO is observed when glucose intake is further increased (Ref. 40 and present results). Fructose is absorbed from the intestine by GLUT-5 transporters (4, 8), and this differs from intestinal glucose transport (SGLT1). Interestingly, a study by Shi et al. (38) showed that beverages containing two or three transportable CHOs (fructose, glucose, and/or sucrose) may increase CHO and water absorption. A solution that contained glucose and fructose especially was found to result in almost 65% higher CHO oxidation rates compared with an isoenergetic glucose solution. This effect was attributed to the fact that glucose and fructose are absorbed by separate intestinal transport mechanisms. Furthermore, it has been shown that fructose absorption is stimulated by the presence of glucose (13, 35), and hence this may further contribute to a faster intestinal CHO absorption rate when glucose and fructose are ingested simultaneously. A faster intestinal CHO absorption might increase the availability of exogenous CHO in the bloodstream, and this might have caused the higher exogenous CHO oxidation rates in Fruc+Glu. Adopo et al. (1) also reported higher oxidation rates when a mixture of glucose and fructose was ingested compared with the ingestion of an isoenergetic amount of glucose. However, the rate of CHO intake in the study of Adopo et al. was relatively low (~0.8 g/min), and intestinal CHO transporters were probably not saturated. As a result of this exogenous CHO oxidation, rates did not exceed 1 g/min. The present data show that, when fructose and glucose are ingested simultaneously at high rates during cycling exercise, exogenous CHO oxidation rates can reach peak values of ~1.3 g/min.

It should be noted that, over the 2-h exercise period, the percentage of ingested CHO that was not oxidized was much larger in High-Glu (68 ± 2%) compared with Fruc+Glu (49 ± 3%) and Med-Glu (51 ± 3%) (data not shown). This suggests that, in the High-Glu trial, more CHO was accumulating in the body, most likely in the stomach or gut. Malabsorption of CHO during exercise may increase the risk of GI complications (32). The higher prevalence of severe GI discomfort in the High-Glu trial compared with the Fruc+Glu trial may indicate that less CHO is leaving the GI tract and further supports the hypothesis that exogenous CHO oxidation in High-Glu was limited at the level of intestinal absorption.

In the present study, CHO ingestion suppressed fat oxidation (Table 1) compared with fasting (Wat). The contribution of fat oxidation to total energy expenditure was 54 ± 4% during Wat, and this value decreased to 34 ± 4, 29 ± 4, and 31 ± 3% during Med-Glu, High-Glu, and Fruc-Glu, respectively (P < 0.01) (Fig. 3). A decreased fat oxidation with CHO ingestion during exercise has been found in several other studies (1, 19, 21, 24, 40). When CHO is ingested during prolonged low-
moderate-intensity exercise, plasma insulin concentrations may increase (19, 21). Insulin has been shown to be a potent inhibitor of lipolysis and the rate of appearance of free fatty acids (FFA) (14). Although plasma insulin and FFA concentrations were not measured in the present study, it is likely that higher plasma insulin concentrations and a decreased FFA availability have contributed to lower fat oxidation rates in the CHO trials compared with the Wat trial. CHO ingestion also resulted in higher plasma glucose concentrations (Fig. 4A) and higher rates of CHO oxidation (Table 1) compared with Wat. In a study by Jeukendrup et al. (19), it was shown that, when large amounts of CHO are ingested during exercise, plasma glucose oxidation can contribute to ~40% of total energy expenditure and fully accounts for the increase in total CHO oxidation. In the present study, we did not measure plasma glucose oxidation, liver-derived glucose, and muscle glycogen oxidation, and hence we can only speculate what might have caused the higher CHO oxidation rates. It is, however, more than likely that an increased plasma glucose oxidation has contributed to the higher CHO oxidation rates in the CHO trials (19). Of note, endogenous CHO oxidation tended to be lower in the Fruc + Glu trial compared with the two glucose trials (P = 0.075), and this might be due to lower muscle and/or liver glycogen oxidation. More studies are required to assess the effect of combined glucose and fructose ingestion on liver and muscle glycogen oxidation.

In the present study, plasma lactate concentrations during the first 75 min of exercise were significantly higher in the Fruc + Glu trial compared with the Med-Glu and Wat trial. This is in agreement with the findings of a study by Koivisto et al. (22) who found 20–25% higher lactate concentrations during exercise when fructose was ingested in the hour before exercise. Fructose is rapidly phosphorylated in the liver to fructose-1-phosphate, a reaction catalyzed by the enzyme fructokinase (12). It has been suggested that the activity of fructokinase is higher than the activity of hexokinase and glucokinase, which phosphorylate glucose. Therefore, after ingestion of fructose, there is a large increase in the fructose-1-phosphate concentration, which will enhance the activation of pyruvate kinase, and hence this will stimulate the formation of pyruvate and lactate (12, 39). In addition, fructolysis can occur without passing through the main rate-controlling step in glycolysis catalyzed by phosphofructokinase. Therefore, fructose is rapidly phosphorylated, resulting in increased concentrations of glycolytic intermediates, which will lead to an increased glycolytic flux, evidenced by elevated plasma lactate concentrations.

In summary, this is the first study to show that exogenous CHO oxidation rates during cycling exercise can reach values >1.1 g/min when a mixture of glucose and fructose is ingested. Furthermore, combined ingestion of glucose and fructose resulted in ~55% higher exogenous CHO oxidation rates compared with the ingestion of an isocaloric amount of glucose. The present data suggest that, when high exogenous CHO oxidation rates (>1.1 g/min) are required during exercise, ingestion of multiple-transportable CHO is preferred above that of large amounts of a single CHO. More studies are needed to determine the combination of CHO that would lead to maximal exogenous CHO oxidation rates.

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