



Exogenous Oxidation of Isomaltulose Is Lower than That of Sucrose during Exercise in Men^{1,2}

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Abstract

Isomaltulose (ISO) is a disaccharide that is slowly digested, resulting in a slow availability for absorption. The aim of this study was to compare the blood substrate responses and exogenous carbohydrate (CHO) oxidation rates from orally ingested sucrose (SUC) and ISO during moderate intensity exercise. We hypothesized that the oxidation of ISO is lower compared with SUC, resulting in lower plasma glucose and insulin concentrations and subsequent lower CHO and higher fat oxidation rates. Ten trained men [maximal oxygen uptake (VO_2max), 64 ± 1 mL/(kg body mass·min)] cycled on 3 occasions for 150 min at $59 \pm 2\%$ VO_2max and consumed either water (WAT) or 1 of 2 CHO solutions providing 1.1 g/min of CHO in the form of either SUC or ISO. Peak exogenous CHO oxidation rates were higher ($P < 0.05$) during the SUC trial (0.92 ± 0.03 g/min) than during the ISO trial (0.54 ± 0.05 g/min). Total endogenous CHO oxidation over the final 90 min of exercise was lower ($P < 0.05$) in the SUC trial (107 ± 10 g) than in the WAT (137 ± 7 g) and ISO (127 ± 9 g) trials. Fat oxidation was higher during the WAT trial than during the SUC and ISO trials. ISO resulted in a lower plasma insulin response at 30 min compared with SUC, whereas the glucose response did not differ between the 2 CHO. Oxidation of ingested ISO was significantly less than that of SUC, most likely due to the lower rate of digestion of ISO. A lower CHO delivery and a small difference in plasma insulin may have resulted in higher endogenous CHO use and higher fat oxidation during the ISO trial than during the SUC trial. *J. Nutr.* 137: 1143–1148, 2007.

Introduction

The ingestion of carbohydrate (CHO)⁶ during prolonged exercise can increase endurance capacity (1). Although the mechanisms are not completely elucidated, the maintenance of blood glucose concentration and high rates of CHO oxidation are most likely of key importance (2).

Numerous factors appear to affect the efficacy of ingested CHO to delay fatigue, including the timing and amount of CHO ingested. In addition, the type of CHO consumed appears to be an important variable. In a review of the literature, Jeukendrup (3) compared the oxidation rates of different CHO ingested during exercise and concluded that there are 2 categories of CHO: those that are oxidized at high rates (up to 1 g/min) and those that are oxidized at low rates (up to ~ 0.6 g/min). Oxidation rates of di- and polysaccharides like sucrose (4,5), maltose (6), and maltodextrins (7), are all high and comparable to oxidation rates

of monomeric glucose. Fructose (8–11) and galactose (12), in contrast, are oxidized at lower rates. This may be due to a lower intestinal CHO absorption rate or by the fact that these monosaccharides are converted to lactate and glucose by the intestine and liver before they can be oxidized (12). In a series of recent experiments from our laboratory, we showed that exogenous CHO oxidation rates can reach values of ~ 1.7 g/min after consuming a combination of CHO that use different intestinal digestion and transport systems (13–15). These studies further suggest that the rates of digestion and absorption of orally ingested CHO are most likely important factors affecting the rate of its oxidation. The known beneficial effect of CHO ingestion on endurance capacity, through maintenance of glucose availability for muscle and brain, has led to an increased consumption of CHO-containing beverages by athletes.

In this study, we evaluated the metabolic properties of isomaltulose (ISO) [6-0-(α -D-glucopyranosyl)-D-fructofuranose, Chemical Abstract Service 1371 8-94-0]. Animal, human, and in vitro studies have established the digestibility and postprandial blood responses to ISO. The sucrase-isomaltase complex (less commonly called the sucrase-dextrinase complex) located on the outer surface of the brush border membrane of the small intestinal epithelial cells (16) contains a maltase-isomaltase (EC 3.2.1.10) that hydrolyzes isomaltulose and a maltase-sucrase (sucrase glucohydrolase, E.C.3.2.1.48), which, in turn, hydrolyzes sucrose (SUC). Each enzyme subunit of the complex acts

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⁶ Abbreviations used: CHO, carbohydrate; FFA, free fatty acid; ISO, isomaltulose; SUC, sucrose; VCO_2 , volume of carbon dioxide production; VO_2 , volume of oxygen uptake; VO_2max , maximal oxygen uptake; WAT, water.

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independently on its respective substrates. The resulting monosaccharides, glucose and fructose, are efficiently taken up into the portal blood. Because disaccharides with α -1,6-glycosidic bonds are hydrolyzed at very low rates, the absorption of ISO is much slower and only 20–25% of that of SUC (17). The absorption of ISO is also interesting from the perspective of studies in oral health, which have found a causal relation between sports drink consumption and dental erosion or plaque formation (18–21). ISO is not fermented in the oral cavity and does not reduce oral pH (22,23).

The aim of the present study was to compare exogenous CHO oxidation rates of orally ingested SUC (a rapidly absorbed and high insulinemic CHO) and ISO (low glycemic and low insulinemic CHO) during moderately intense endurance exercise. We hypothesized that the oxidation of ISO is slower than that of SUC, resulting in lower plasma glucose and insulin concentrations and, consequently, lower CHO and higher fat oxidation rates.

Methods

Subjects. Ten healthy, moderately trained men were recruited in this study, which was approved by the Ethics Subcommittee of the School of Sport and Exercise Sciences, University of Birmingham, and complied with the Helsinki declaration as revised in 1983. The health of the subjects was assessed by a general health questionnaire and each volunteer gave his written informed consent. The subjects were all club/county standard endurance athletes with a training background of at least 3 y. The subject characteristics were: age 27 ± 2 y, body mass 74.7 ± 2.5 kg, BMI 22.6 ± 1.0 kg/m², maximal oxygen uptake (VO₂max) 62.7 ± 1.1 mL (kg · min).

General design. Subjects were asked to visit the laboratory on 3 different occasions after a 10 to 12-h overnight fast, when they were asked to cycle for 150 min at 50% of their maximal work rate (Wmax). During each test, the subjects received a drink containing water (WAT), SUC, or ISO, the latter 2 containing CHO with naturally high ¹³C abundance. During the test, expired gas analyses were performed and breath and blood samples were collected at regular intervals. The tests were performed 5–7 d apart, and the order of the tests was randomly assigned in a crossover design.

Preliminary testing. Before the start of the experiments, the subjects were familiarized with the equipment and the procedures. Approximately 1 wk before the start of the experimental trials, subjects were asked to perform a graded exercise test to volitional exhaustion on an electromagnetically braked cycle ergometer (Lode Excalibur Sport) as previously described (15). Breath-by-breath measurements were performed throughout the exercise using an online gas analysis system (Oxycon Pro, Jaeger).

Diet and activity prior to testing. Subjects were asked to record their food intake and activity patterns 2 d before the 1st exercise trial and were then instructed to follow the same diet and activities before the 2 subsequent trials. Records of food intake and activity patterns were collected prior to the 2nd and 3rd trials to verify that these were similar to the records before the 1st trial. In addition, 5–7 d before each experimental testing day, subjects were asked to perform an intense training session (a glycogen-depleting exercise bout) in an attempt to empty any ¹³C-enriched glycogen stores. Subjects were further instructed not to consume food products with a high natural abundance of ¹³C (CHO derived from C4 plants such as corn and sugar cane) at least 1 wk before and during the entire experimental period to minimize the background shift (change in ¹³CO₂) from endogenous substrate stores.

Experimental trials. To avoid circadian variance, all experiments were performed in the morning and at the same time for each subject. After arrival in the laboratory, a teflon catheter (Quickcath, Baxter) was introduced into an antecubital arm vein and maintained patent with isotonic saline (Baxter). Before the start of the experiment, resting breath samples were collected in exetainers (Labco Brow Works) from a mixing chamber to determine the ¹³C to ¹²C ratio in expired air. In addition, a

blood sample was collected, after which subjects consumed a 600 mL bolus of either water or one of the 8.5% CHO beverages. After consuming the bolus, which was consumed within a 5-min period, subjects started cycling at 50% Wmax ($59 \pm 2\%$ VO₂max). Blood and breath samples were collected at 15-min intervals and expired gas analysis was performed for 4 min at the end of each 15-min interval. After completing the blood collection, subjects were provided with 150 mL of experimental beverage. Ratings of perceived exertion were measured every 30 min using the 6–20 Borg scale.

Test carbohydrates and experimental beverages. To quantify exogenous CHO oxidation, 8.5% CHO solutions were prepared. The ¹³C-enrichment of the experimental beverages was determined by elemental analyzer isotope ratio MS (Europa Scientific). The measured natural abundance of ¹³C in sucrose and isomaltulose was -11.17 and -11.42 ‰, respectively, compared with Pee Dee Bellemnitella.⁷ The total carbohydrate supply was 165 g dissolved in water up to a volume of 1950 mL. Sodium chloride was added (2.28 g) to create a 20 mmol/L solution. The carbohydrate ingestion rate from the beverages was set at 1.1 g/min.

Analysis. At all time points, 8 mL blood was collected in prechilled tubes with 200 μ L of 0.2 mol/L ethylenediaminetetraacetic acid (Sigma). The samples were immediately centrifuged at $1500 \times g$ for 10 min at 4°C and aliquots of plasma were frozen at -80°C . Plasma glucose, lactate, and free fatty acid (FFA) concentrations were determined enzymatically (glucose HK and lactic acid 10, ABX Diagnostics and NEFA-C, Alpha Labs) on a semiautomatic analyzer (Cobas Mira S plus, ABX). Insulin was determined using an enzyme-linked immuno specific assay (IDS). Breath samples were analyzed for ¹³C to ¹²C ratio by gas chromatography continuous flow isotope ratio mass spectrometry (GC-IRMS) (Europa Scientific).

Calculations. From VO₂ and VCO₂ (L/min), total CHO and fat oxidation rates were calculated using stoichiometric equations for moderate to high intensity exercise by Jeukendrup and Wallis (24), with the assumption that protein oxidation was negligible:

$$\text{CHO oxidation} = 4.210 \text{ VCO}_2 - 2.962 \text{ VO}_2$$

$$\text{Fat oxidation} = 1.695 \text{ VO}_2 - 1.701 \text{ VCO}_2$$

The isotopic enrichment was expressed as $\delta\%$ difference between ¹³C to ¹²C ratio of the sample and a known laboratory reference standard according to the formula of Craig (25):

$$\delta^{13}\text{C} = \left[\frac{^{13}\text{C}/^{12}\text{C}_{\text{sample}}}{^{13}\text{C}/^{12}\text{C}_{\text{standard}}} - 1 \right] \cdot 10^3 \text{ per mil.}$$

The $\delta^{13}\text{C}$ was then related to the international standard of Pee Dee Bellemnitella.

Exogenous CHO oxidation was calculated using the following formula (26):

$$\text{Exo CHO oxidation} = \text{VCO}_2 \cdot \frac{[\delta \text{Exp} - \delta \text{Exp}_{\text{bkg}}]}{[\delta \text{Ing} - \delta \text{Exp}_{\text{bkg}}]} \left(\frac{1}{k} \right),$$

in which VCO₂ is the volume of expired CO₂/min (L/min), δExp is the ¹³C enrichment of expired air during exercise with CHO ingestion at different time-points, δIng is the enrichment of the CHO in the experimental beverages, $\delta \text{Exp}_{\text{bkg}}$ is the ¹³C enrichment of expired air in the WAT trial (background) at different time-points, and k is the amount of CO₂ (in L) produced by the oxidation of 1 g of glucose ($k = 0.7467$ L of CO₂/g of glucose). Endogenous CHO oxidation was calculated as the difference between total CHO oxidation and exogenous CHO oxidation.

All calculations on substrate oxidation were performed over the last 90 min of exercise (60–150 min) to take the temporary trapping of ¹³CO₂ into the bicarbonate pool into account, as discussed previously (27,28).

Statistics. Experimental data are expressed as means \pm SEM. Before statistical analysis, the variables were tested for normality at all

⁷ Pee Dee Bellemnitella is derived from marine fossil material that has a higher ¹³C to ¹²C ratio than nearly all other natural carbon-based substances.

time-points. A 2-way general linear model for repeated measures (treatment \times time) was used to identify differences between the 3 trials. In the event that sphericity was violated, the analyses were adjusted using a Greenhouse-Geisser correction. When a significant F-ratio was obtained for the interaction, the Tukey post-hoc test was used to locate the differences. Where appropriate, a comparison of variables between 2 conditions was conducted using a Student's *t* test for paired samples. For all statistical analyses, significance was accepted at $P < 0.05$.

Results

Heart rate, oxygen uptake, and perceived exertion. The work rate during the 3 trials was 174 ± 3 Watt. The VO_2 and heart rate during exercise did not differ among the 3 trials. The rating of perceived exertion also did not differ and were 11.9 ± 0.4 , 11.4 ± 0.5 , and 11.7 ± 0.3 during the WAT, SUC, and ISO trials, respectively.

Total carbohydrate and fat oxidation. There was a significant decrease in the CHO oxidation rate (Fig. 1A) and a concomitant increase in fat oxidation rate (not shown) over the course of the WAT trial. Total CHO oxidation rates were lower throughout the ISO trial than the SUC trial ($P < 0.05$); however, the difference was significant only at the 2nd phase of exercise at 60, 75, and 150 min. Total CHO oxidation during the WAT trial was significantly lower than the SUC trial from 30 min onwards and from 60 min onwards, compared with the ISO trial. Fat oxidation rates did not differ between the WAT and ISO trials, whereas fat oxidation was significantly higher during the WAT trial than during the SUC trial at 60, 90, 135, and 150 min (data not shown). Fat oxidation rates did not differ between the 2 CHO trials, except at 150 min when the rate was significantly higher during the ISO than during the SUC trial. The total amount of fat oxidized was significantly higher during the ISO trial compared with the SUC trial.

Exogenous carbohydrate oxidation. After 30 min of exercise, exogenous sucrose oxidation was significantly higher than exogenous ISO oxidation and remained higher throughout the exercise period (Fig. 1B). During the 60–150 min period, 78 ± 3 g of exogenous CHO was oxidized during the SUC trial whereas 40 ± 4 g was oxidized during the ISO trial ($P < 0.05$). Peak rates of exogenous SUC and ISO oxidation were 0.92 ± 0.03 and 0.54 ± 0.05 g/min, respectively ($P < 0.05$).

Endogenous carbohydrate oxidation. Endogenous CHO oxidation decreased over time in all trials (Fig. 1C). The rate of endogenous CHO oxidation was higher during the water (WAT) trial compared with the SUC trial between 45 and 120 min of exercise. The rate of endogenous CHO oxidation generally was lower during the SUC trial compared with the ISO trial, with differences at 60, 90, and 105 min ($P < 0.05$). The total amount of endogenous CHO oxidized during the final 90 min of the exercise bout was lower in the SUC trial (107 ± 10 g) compared with the WAT (137 ± 7 g) and ISO trials (127 ± 9 g). The total amount of endogenous CHO oxidized during the final 90 min of exercise did not differ between the ISO and WAT trials.

Energy expenditure. During the SUC trial, 35% of energy was provided by endogenous CHO oxidation, less than during the ISO (40%) and WAT (45%) trials ($P < 0.05$). Less energy was derived from exogenous CHO sources in the ISO trial ($13 \pm 1\%$) than in the SUC trial ($25 \pm 3\%$, $P < 0.05$). Furthermore, energy derived from fat oxidation during the ISO trial was higher than

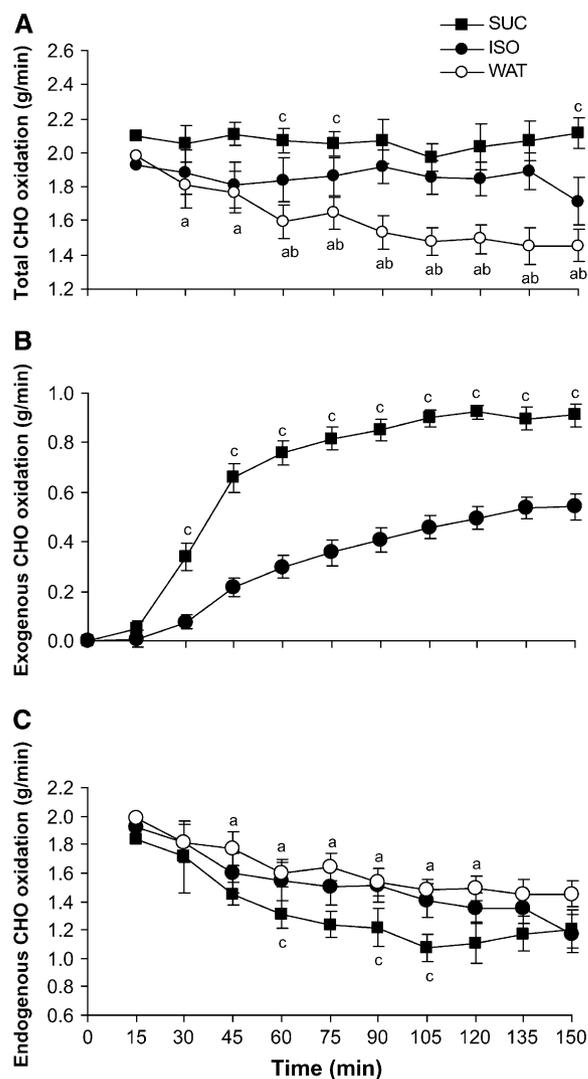


FIGURE 1 Total CHO (A), exogenous CHO (B), and endogenous CHO (C) oxidation in men during the WAT, SUC, and ISO trials. Values are means \pm SEM, $n = 10$; ^aWAT vs. SUC, $P < 0.05$; ^bWAT vs. ISO, $P < 0.05$; ^cSUC vs. ISO, $P < 0.05$.

during the SUC trial. The energy derived from fat oxidation was higher during the WAT trial (2.8 ± 0.1 MJ/90 min) compared with both the SUC (2.1 ± 0.1 MJ/90 min) and ISO trials (2.4 ± 0.1 MJ/90 min) (Fig. 2).

Plasma substrates. The plasma glucose concentration did not change during the WAT trial (Fig. 3A). The ingestion of the bolus of SUC significantly increased the glucose concentration from 5.06 ± 0.24 mmol/L at rest to 6.43 ± 0.48 mmol/L after 15 min. Ingestion of SUC and ISO resulted in higher glucose concentrations than WAT at some time points (15, 75, 105, and 150 min for SUC; 45, 60, 75, and 120 min for ISO). Concentrations did not differ between the SUC and ISO trials.

The plasma insulin concentration was significantly higher throughout the SUC trial compared with the WAT trial (Fig. 3B). It did not change during the first 60 min of the ISO trial but increased rapidly during the SUC trial, resulting in a difference between the SUC and ISO trials at 30 min ($P < 0.05$). Subsequently, this difference disappeared because insulin returned

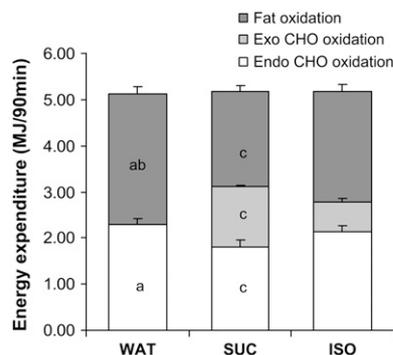


FIGURE 2 Source of energy in men during the WAT, SUC, and ISO trials during the final 90 min of exercise. Values are means \pm SEM, $n = 10$; ^aWAT vs. SUC, $P < 0.05$; ^bWAT vs. ISO, $P < 0.05$; ^cSUC vs. ISO, $P < 0.05$.

to lower levels in the SUC trial. The difference between ISO and WAT was significant only at 60 min of exercise.

The plasma FFA concentration rose significantly above fasting levels in the WAT trial after 90 min of exercise (Fig.

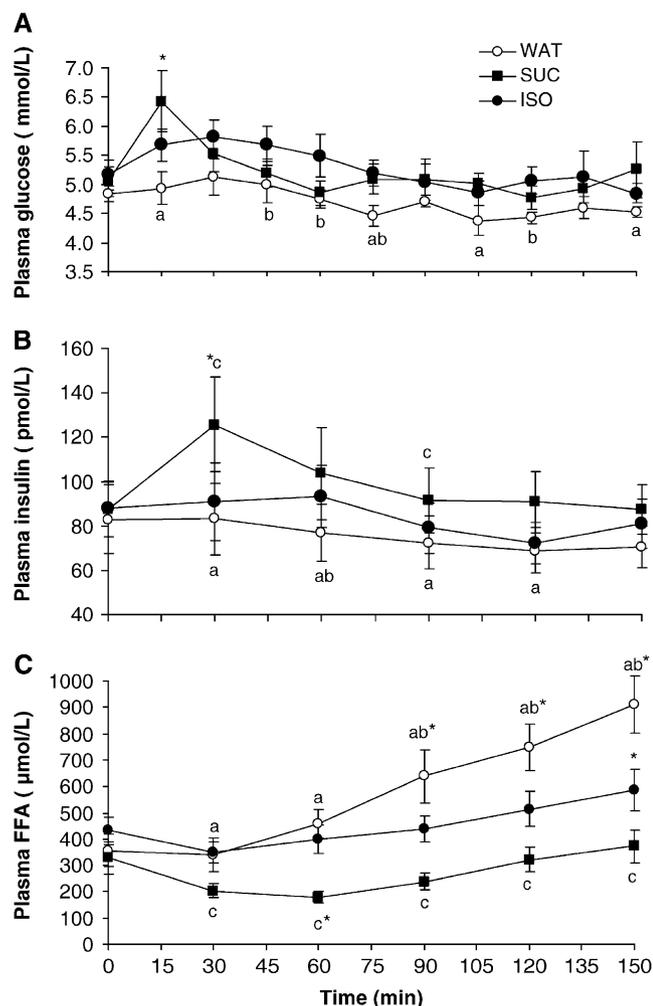


FIGURE 3 Plasma glucose (A), plasma insulin (B), and plasma FFA (C) concentration in men during the WAT, SUC, and ISO trials. Values are means \pm SEM, $n = 10$; ^aWAT vs. SUC, $P < 0.05$; ^bWAT vs. ISO, $P < 0.05$; ^cSUC vs. ISO, $P < 0.05$; ^{*}Different from 0 min, $P < 0.05$.

3C). During the ISO trial, the plasma FFA concentration was greater than the fasting concentration only after 2.5 h of cycling. The FFA concentration decreased after 60 min in the SUC trial after which it returned to concentrations that did not differ from baseline. However, the plasma FFA concentration was significantly higher during the entire exercise bout, after WAT and ISO ingestion than after SUC.

The time \times trial interaction did not significantly affect the plasma lactate concentration. However, the concentration increased as subjects began to exercise ($P < 0.05$), at which point it remained stable.

Discussion

The ingestion of CHO during prolonged exercise has been known for many years to increase endurance capacity. As a result, the consumption of commercially available sports beverages has risen dramatically. Many types of carbohydrates have been well studied and documented for their metabolic and performance effects. However, whereas many chemical and biochemical characteristics of isomaltulose are well documented, no information appears available on the impact of oral isomaltulose during endurance exercise on carbohydrate and fat oxidation. Therefore, the primary goal of the present study was to compare the blood substrate responses and the exogenous oxidation rates of 2 oral disaccharides, sucrose and isomaltulose, during moderately intense exercise.

The main findings of the present study were that the mean and peak oxidation rates of isomaltulose were 50 and 42% lower than the oxidation rates of sucrose when ingested at the same rate (1.1 g/min), which may reflect a reduced rate of digestion and absorption with ISO compared with SUC.

Furthermore, endogenous CHO stores were utilized significantly less when SUC was ingested compared with the ingestion of water and ISO, which can be explained by a higher rate of absorption, and availability for oxidation of SUC. Although oxidation of oral ISO increased slowly and steadily over time, no significant endogenous CHO sparing occurred when ISO was ingested.

When the oxidation efficiency was calculated (exogenous CHO oxidation expressed as a percentage of CHO ingestion), only 28% of the ingested isomaltulose was oxidized whereas \sim 63% of the ingested sucrose was oxidized. This percentage of SUC oxidation is slightly higher than that found by Wagenmakers et al. (5) (\sim 55%). The difference could be explained by differences in the duration of the trials; subjects cycled for 120 min in the study by Wagenmakers et al. (5), whereas the duration of the present study was 150 min. During the first 120 min of exercise in the present study, 59% of the SUC ingested over that time period was oxidized. Moodley et al. (4) reported that of 90 g of SUC ingested in their study, only 30% was oxidized. Jeukendrup et al. (29) showed that 90–95% of all glucose appearing in the circulation is taken up and oxidized, whereas Hawley et al. (6) showed that exogenous CHO oxidation rates could rise above 1.1 g/min when glucose was directly infused into the circulation.

The observed difference in oxidation rates between sucrose and isomaltulose in the present study may be due to the various factors involved from ingestion to tissue uptake and oxidation: 1) gastric emptying, 2) digestion absorption, 3) postabsorptive effects of the liver, and 4) tissue uptake.

Several studies suggest that gastric emptying is not a limiting factor for exogenous CHO oxidation. Rehrer et al. (30) showed that during 80 min of exercise at 70% VO_2max , only 38 g of

glucose was oxidized, whereas 120 g was emptied from the stomach. Wagenmakers et al. (5) and Saris et al. (31) obtained similar data for sucrose, maltodextrins, and starch. To our knowledge, data are not available regarding the gastric emptying rate of ISO. It is possible that the difference in oxidation rate between ISO and SUC is caused by a reduced rate of gastric emptying of ISO.

However, it is more likely that the key difference is the low rate of intestinal ISO digestion and subsequent absorption. Several studies compare the rate of hydrolysis of SUC and ISO. In rats, the hydrolytic activity of the disaccharidase for sucrose was ~85% higher than for isomaltulose in all parts of the intestine (32). Dahlqvist et al. (33) studied the hydrolysis activity of sucrase and isomaltase in human small intestine mucosa. The addition of SUC resulted in a 6-fold higher glucose release than after the addition of an equimolar amount of ISO (33). These results indicate that, in humans, the hydrolysis of ISO also is significantly slower than that of sucrose. After hydrolysis, the glucose and fructose released from SUC and ISO follow the same metabolic pathway (34). Based on the data discussed above, it is likely that the slow hydrolysis of ISO reduces the absorption rate of glucose and fructose from it and hence lowers their rate of oxidation.

Further evidence for this hypothesis comes from studies showing that ingestion of ISO during resting conditions leads to slower rises in blood glucose and insulin levels than with the ingestion of SUC in both healthy and diabetic individuals (34–36). In this study, glycemic responses were similar and insulin responses tended to be slightly lower after ingesting ISO than after ingesting SUC. It is likely that exercise masked some of the responses that occurred at rest. There was, however, a small increase in plasma glucose in the SUC trial from 0 to 15 min that did not occur in the ISO trial, and plasma insulin was slightly higher at 30 min after ingesting SUC than after ingesting ISO.

The ingestion of both CHO resulted in the maintenance of total CHO oxidation rates late in exercise as opposed to the significant decrease that occurred during the WAT trial. In line with this, we found that the contribution of total CHO oxidation to energy expenditure was significantly lower in the WAT trial than in the ISO trial and was highest in the SUC trial. Concomitantly, the contribution of fatty acid oxidation to total energy expenditure was significantly lower in both CHO trials compared with the WAT trial. Decreased availability of fatty acids, due to insulin's inhibition of lipolysis, may be partly responsible for decreased rates of fat oxidation after CHO consumption (37). In the present study, a blunted increase in FFA concentration occurred during both CHO trials compared with WAT.

The ingestion of SUC resulted in a lower oxidation of whole body glycogen compared with the WAT trial. With the methods used in the present study we were unable to determine whether reduced glycogen utilization occurred in liver or muscle glycogen, or in both compartments. Jeukendrup et al. (38) showed that liver glucose output is greatly, if not completely, reduced when CHO is ingested. These data suggest that the reduction of endogenous CHO oxidation in the SUC trial was likely due to a reduction in liver glycogen utilization.

In summary, oxidation rates of ingested ISO were only 59% of the oxidation rates of ingested SUC, presumably because of a lower rate of digestion of ISO. Ingestion of ISO resulted in a slightly lower insulin response compared with that of SUC, whereas the glucose concentrations did not differ after consuming the 2 CHO. A lower CHO delivery and small difference in insulin may have resulted in higher glycogen use and a greater fat oxidation in the ISO trial than in the SUC trial.

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