Effects of Pre-Exercise Sucralose Ingestion on Carbohydrate Oxidation During Exercise

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Recent studies have demonstrated a direct link between increased exogenous CHO oxidation (CHO_exog) and enhanced performance. The limiting factor for CHO_exog appears to be at the level of intestinal transporters, with sodium/glucose cotransporter 1 (SGLT1) and glucose transporter Type 5 (GLUT5) responsible for glucose and fructose transport, respectively. Studies in animal models have shown that SGLT1 and intestinal glucose uptake are up-regulated by high carbohydrate diets or noncaloric sweeteners. The aim of this study was to determine the effect of preexercise ingestion of noncaloric sweeteners on CHO_exog during exercise in athletes. In a randomized, crossover, double-blind fashion twenty-three healthy male cyclists (age = 29 ± 7yrs, mass = 73.6 ± 7.4kg, VO2peak = 68.3 ± 9.3 ml/kg/min) consumed 8 × 50ml doses of either placebo (CON) or 1mM sucralose (SUCRA) every 15 min starting 120 min before the onset of exercise. This was followed by 2h of cycling at 48.5 ± 8.6% of VO2peak with continual ingestion of a maltodextrin drink (1.2g/min; 828ml/hr). Average CHO_exog during the first hour of exercise did not differ between SUCRA and CON conditions (0.226 ± 0.081 g/min vs. 0.212 ± 0.076 g/min, Δ = 0.015 g/min, 95%CI -0.008 g/min, 0.038 g/min, p = .178). Blood glucose, plasma insulin and lactate, CHO and fat substrate utilization, heart rate, ratings of perceived exertion, and gastrointestinal symptoms did not differ between conditions. Our data suggest that consumption of noncaloric sweeteners in the immediate period before exercise does not lead to a significant increase in CHO_exog during exercise.

Keywords: exogenous CHO oxidation, SGLT-1, taste receptor, intestinal taste, glucose uptake, endurance exercise

A series of recent studies has consistently observed that a combination of glucose (or maltodextrin) and fructose can result in 20–40% greater exogenous carbohydrate (CHO) oxidation during exercise as compared with a single CHO source (for review see Jeukendrup, 2010). The proposed mechanism is that the rate-limiting step to exogenous CHO delivery and oxidation appears to be at the level of the gastrointestinal (GI) tract due to intestinal CHO transport mechanisms. More specifically, glucose (GLU) and fructose (FRU) have separate and unique transport mechanisms: sodium/glucose cotransporter 1 (SGLT1) for GLU and probably glucose transporter type 5 (GLUT5) for FRU (for reviews see Jeukendrup, 2010; Wright, Martin, & Turk, 2003). Supporting the benefit of greater CHO delivery and oxidation are two recent studies demonstrating an 8% increase in performance when GLU: FRU CHO blends were used at saturating intake rates (>1.8g/min) versus isocaloric GLU only beverages when exercise was longer than 2 hr (Currell & Jeukendrup, 2008; Triplett et al., 2010). Accordingly, a recent CHO-dose response study showed an increase in performance, in combination with increased CHO oxidation, in a dose-dependent manner with 60g CHO/h resulting in greater oxidation and performance than either 30 or 15g CHO/h (Smith et al., 2010). Therefore, recent evidence strongly suggests that CHO delivery and oxidation rates, which appear dependent upon the number and function of the GI transporters SGLT1 and GLUT5, are a central mechanism responsible for the enhanced performance found with CHO supplementation (Jeukendrup, 2010).

A diet high in CHO has been shown to up-regulate the expression of the glucose transporter SGLT1 and glucose uptake by enterocytes in many species, including humans (for review see Ferraris, 2001). Recent studies in rodents have shown that this up-regulation is in part mediated by gut-expressed sweet taste receptors (Margolskee et al., 2007). The sweet taste receptor expressed at the surface of taste bud cells in the tongue is a heterodimer of two G-protein coupled receptors, T1R2 and T1R3 (Nelson et al., 2001). Activation of T1R2/T1R3 by sugars or noncaloric sweeteners initiates the sweet taste signal transduction cascade. Interestingly, T1R2 and T1R3 are also expressed in the intestine (Bezencon et al., 2007; Dyer et al., 2005), and intake of noncaloric...
sweeteners, such as 2mM sucralose in drinking water, over two weeks is as effective as sugars in up-regulating intestinal SGLT1 expression and glucose uptake via gut-expressed T1R2/T1R3 in both mice (Margolskee et al., 2007) and piglets (Moran et al., 2010). Furthermore, other ex vivo studies have shown a very rapid effect, in that the glucose absorption rate more than doubled when 1mM of the noncaloric sweetener sucralose was infused into the intestinal lumen of rats, reaching a plateau 45 min postconsumption, concomitant with an increase of GLUT2 protein expression and translocation to the apical membrane (Mace et al., 2007). Others have shown that in rats, intestinal infusion with glucose or saccharin for three hours leads to more than doubling of SGLT-1 protein expression (Stearns et al., 2010). Together these data suggest that there might be acute (over minutes) and chronic (over days) mechanisms of up-regulation of intestinal glucose uptake via intestinal expressed T1R2/T1R3, leading to overexpression of SGLT-1 (Margolskee et al., 2007) or translocation of GLUT-2 to the apical membrane (Mace et al., 2007).

If the rate-limiting step to CHO delivery and oxidation is at the level of the GLU and FRU transporters SGLT-1 and GLUT 5, then increasing the expression levels, or function, of these transporters should theoretically increase CHO delivery and oxidation. Therefore, as has been previously demonstrated in rodent models (Mace et al., 2007; Margolskee et al., 2007), it could be hypothesized that the ingestion of sugars or noncaloric sweeteners in the immediate hours before exercise may improve glucose GI transport during exercise and result in increased exogenous CHO oxidation rates, especially during the first hour of exercise. This was with this rationale that the current double-blind cross-over study was designed to examine the acute effects of preexercise sucralose consumption (SUCRA) compared with a water control (CON) on subsequent exogenous CHO oxidation rates of a glucose drink and metabolism during 2 hr of endurance exercise. Sucralose was chosen instead of sugar to avoid overloading the GI tract with large amounts of nonabsorbable carbohydrates that may lead to abdominal disturbances.

**Methods**

**Subjects**

Twenty-three healthy male cyclists (4–20hr/week of training) participated in this study with the following characteristics (mean ± SD): 29 ± 7yrs, 1.78 ± 0.06m, 73.6 ± 7.4kg, 23.1 ± 1.9 kg/m² and 68.3 ± 9.3 ml/kg/min for age, height, body mass, body mass index and peak oxygen consumption (VO₂peak), respectively. Volunteers were excluded if having allergies, smokers, intestinal disorders, unfit/injuries, on regular medication or having not followed the controlled dietary regimen. Subjects were informed verbally and in writing about the nature and potential risks of the experimental procedures before written informed consent were obtained. The study was approved by the ethics committee of the University of Lausanne, Switzerland (Protocol 125/09) and conducted at the Nestlé Research Center/Metabolic Unit following the principles of International Conference on Harmonization guideline for Good Clinical Practice (GCP).

**Preexperimental Trial Testing, Dietary, and Activity Controls**

At least 7 days before the first familiarization trial, volunteers performed a continuous incremental cycling test on a cycle ergometer (Excalibur-Lode, Groningen, The Netherlands) to exhaustion to determine peak oxygen consumption (VO₂peak; VMax 29C, SensorMedics, Bilthoven, The Netherlands). On the first visit, the cycle ergometer was individually adjusted for each subject and was set accordingly for all subsequent tests. Heart rate (HR) was monitored every 5sec by near infrared telemetry (Polar NV, Polar Electro, Kempele, Finland). The VO₂peak test started at 100W for 5 min, followed by 50W increases every 2.5min until HR > 160 beats/min. Subjects then increased 25W every 2.5 min until exhaustion (RQ > 1.1; HR max; plateau and/or exhaustion). Wmax was then calculated as Wmax = Wstart + (t/150) * 25, where Wstart equaled the last workload (wattage attained), and t was the time (sec) at the last workload (Jeukendrup et al., 1996). At least 7 days before the first experimental session subjects underwent a full familiarization trial (2h cycling at ~50% VO₂peak) consuming only water to measure background ¹³C enrichment of expired air, which was used in subsequent full experimental trials to calculated exogenous CHO oxidation (see below). Subjects were limited to light exercise, and no caffeine or alcohol intake in the 24 h before each trial (familiarization and 2 experimental trials). Subjects also recorded their food intake and exercise activities in the 24 hr before the first trial and repeated this for each subsequent visit. Furthermore, 5 days before each experimental trial, subjects performed an intense training session (glycogen depleting bout) to lower ¹³C-enriched glycogen stores and then instructed not to consume foods with a high natural abundance of ¹³C (e.g., corn and cane sugar) to minimize background ¹³C oxidation.

**Experimental Trials**

Each subject underwent two experimental trials separated by at least two weeks in a randomized, two-period crossover design. Subjects were randomized in balanced order, with 13 subjects starting with control trial. As outlined in Supplementary Figure 1, subjects arrived in the laboratory for each trial at the same time (~8:00am), to avoid circadian variability, after an overnight fast (10–12h) and completed a 24-hr food/beverage/activity questionnaire to confirm dietary and exercise compliance. A Teflon catheter (B/BRAUN 18 gauge, Melsungen A.G.) was inserted into the antecubital vein for repeated blood sampling, which was kept patent by flushing with 1.0–1.5 mL of isotonic saline (0.9%). Before each breath, blood,
HR and ratings of perceived effort (RPE) sampling point, inspired and expired gases were collected via a metabolic cart and were used to calculate oxygen consumption (VO₂), carbon dioxide production (VCO₂) and respiratory exchange ratio (RER) over a 3-min period. Within the last 60 s of each 3 min period, vacutainer tubes were filled in triplicate for measurement of breath ¹³C/¹²C ratio as described below. The baseline blood sample was drawn 2 hr before exercise and expired breath sample was collected into a vacutainer tube (blood time point = -120min). Immediately after, starting 2h before cycling exercise, subjects consumed 8 “priming” doses in randomized fashion every 15 min of either: 1) 50ml of 1mM sucralose solution (SUCRA; 19.9mg of sucralose/50ml; Tate & Lyle PLC, London, UK) or 2) sucralose mouthwash (not swallowed) with 50ml of water consumption (CON; Supplementary Figure 1). 1mM sucralose is intensely sweet, and was shown in ex vivo studies to be effective in up-regulating intestinal glucose absorption. Because the timing of glucose uptake up-regulation is unknown in humans, we chose to give sucralose over a period of two hours, in a reasonable amount of fluid. The sucralose mouthwash was intended to exclude a possible cephalic phase effect due to the sweet taste of sucralose.

Two hours after the first blood and breath sample, and 15 min after the last “priming” dose, subjects commenced with 2 hr of steady-state cycling (time point = 0min). During cycling the power output on the cycle ergometer was set to elicit 48.5% ±8.6% of VO₂peak. For each trial, subjects were given the same maltodextrin drink over the exercise period at the following rates: an initial 391ml bolus (34g CHO; ~8.7% solution) at the onset of exercise and then 115 ml (10g CHO; ~8.7% solution) every 10 min until the cessation of exercise (11 doses), resulting in an average intake rate of 1.2g maltodextrin/min (72g/hr; 828ml/h). This intake rate was selected to ensure saturation of glucose transport via SGLT-1 and for comparison with previous studies (for review see Jeukendrup, 2010). The drink was made up with 87g maltodextrin/L (GLUCIDEX 19, Roquette, Sugro AG, Basel, Switzerland) with 800mg/L of sodium chloride (NaCl; 13.7 mmol/L) and was spiked with 200 mg/L [U¹³C]-glucose (99 atom %, Cambridge Isotopes Laboratories, Andover, Massachusetts, USA). Continuous blood and breath samples (n = 10) were taken every 10min during the first hour of cycling, and every 20 min during the second hour. All exercise tests were performed under normal and standard environmental conditions (16–24 °C temperature and 50–60% relative humidity). During the exercise trials, subjects were cooled with standing floor fans to minimize thermal stress. After the completion of cycling, a standardized gastrointestinal (GI) questionnaire was given for all subjects to complete. As fully described by Pfeiffer et al. (Pfeiffer et al., 2009; Pfeiffer et al., 2012), this questionnaire asked 16 graded questions on a 10-point scale from 0 (none) to 9 (worst experienced) and grouped questions to upper abdominal, lower abdominal and systemic outcomes.

**Blood and Breath Analysis**

Eleven breath and blood samples (~10 ml) were taken at -120, 0, 10, 20, 30, 40, 50, 60, and then 80, 100, 120 min throughout the experimental trial. All blood samples were collected into prechilled lithium heparin containing tubes and centrifuged at 1000 × g at 4 °C for 10 min. Aliquots of 0.5ml of plasma were frozen and stored at -80 °C until further analysis is completed for blood glucose, lactate and insulin. Glucose and lactate were assessed enzymatically by a Siemens Dimension clinical chemistry system (Siemens Healthcare Diagnostics Inc, Newark, USA), while insulin was quantified by an immunoassay.
ELISA test Kit (Insulin Elecsys kit; Roche Diagnostics, Germany). Breath samples were collected using a Quintron breath collection system utilizing a dual bag system collecting 750 mL of expired air. Three aliquots of air were drawn from the bag and injected into gas analysis vacutainers for analysis. Breath samples were analyzed for $^{13}$CO$_2$/^{12}$CO$_2$ ratio by gas chromatography continuous flow-isotope ratio mass spectrometer (GC-IRMS, Thermo Fischer, Bremen, Germany). The reference gas used was normalized with calibration gases of known isotopic ratio (Eurisotope, France). $^{13}$C isotopic enrichment of ingested CHO solution was determined and measured by liquid chromatography coupled to isotope ratio mass spectrometer (LC-IRMS, Thermo Fisher, Bremen, Germany; Godin et al., 2011)

**Calculations**

Oxidation rates of total fat, total CHO and exogeneous CHO oxidation were calculated from indirect calorimetry (VO$_2$ and VCO$_2$) and stable isotope measurements of breath CO$_2$ and drink CHO solution. VO$_2$ and VCO$_2$ were recorded on a breath-by-breath basis over a 3- to 5-min period before sampling time, and from these respiratory measures, total fat and carbohydrate oxidation rates were calculated using the nonprotein respiratory quotient (Peronnet & Massicotte, 1991):

Total fat oxidation rate = $1.695 \text{ VO}_2 - 3.22 \text{ VCO}_2$

Total CHO oxidation rate = $4.585 \text{ VCO}_2 - 3.22 \text{ VO}_2$

with VO$_2$ and VCO$_2$ in liters per minute (L/min) and oxidation rates being reported in grams/minute (g/min). The $^{13}$C/$^{12}$C isotopic ratio was first expressed as $\delta^{13}$C values calibrated against the international standard (Vienna Pee Dee Belemnite, VPDB; Slater et al., 2001). The delta notation is defined as $\delta^{13}$C/$^{12}$C$_{\text{sample}}$ = $(R_s / R_{\text{st}} - 1) \times 1000$, where $R_s$ is the ratio of $^{13}$C/$^{12}$C in the sample and $R_{\text{at}}$ is the ratio of the international standard used (Craig, 1957). The result of this calculation is a relative delta ($\delta$) calibrated against the international standard. The rate of exogenous CHO oxidation was then calculated via the following formula (Pirnay et al., 1977):

$$\text{exogenous CHO oxidation} = \text{VCO}_2 \cdot \frac{\delta_{\text{Exp}} - \delta_{\text{Exp bkg}}}{\delta_{\text{Ing}} - \delta_{\text{Exp bkg}}} \left( \frac{1}{k} \right)$$

where $\delta_{\text{Exp}}$ is the $^{13}$C enrichment of expired air during exercise at different time points, $\delta_{\text{Ing}}$ is the $^{13}$C enrichment of the ingested CHO solution, $\delta_{\text{Exp bkg}}$ is the $^{13}$C enrichment of expired air in the water only familiarization trial (background) at different time points, and $k$ is the amount of CO$_2$ (in liters) produced by the oxidation of 1 g of glucose ($k = 0.7467$ L of CO$_2$ per gram of glucose). Endogenous CHO oxidation was calculated by subtracting exogenous CHO oxidation from total CHO oxidation.

**Statistics**

Exogenous CHO oxidation between 10 and 60 min was the primary outcome. To show a 20% treatment difference as significant with a power of 80%, power calculations required 24 subjects to be enrolled. From published data, the within subject standard deviation (SD) was estimated at 0.21 ml/minute (32%). A repeated measurement analysis was performed for all time points and measurements via a mixed model correcting for period and sequence (fixed effects) with subjects as random effects. For the GI questionnaire, each subscore was computed as the mean of items belonging to each scale and the overall score as the mean of all items. Overall score and subscales scores were compared between groups using paired t tests. All analyses were performed using the statistical program SAS (SAS, Cary, NC), with significance set to $p < .05$ and data are reported as mean ± SD.

**Results**

**Exogenous CHO Oxidation and Whole-Body Substrate Utilization**

Exogenous CHO oxidation rates increased over time (Figure 1) with continuous glucose consumption during exercise (72g/h). Peak exogenous CHO oxidation rates were reached at the end of 120 min of exercise and were not significantly different between SUCRA and CON (0.64 ± 0.10 vs. 0.64 ± 0.10 g/min, respectively). Mean exogenous CHO oxidation rates during the first hour of exercise were not significantly different between groups SUCRA and CON (0.226 ± 0.081 g/min vs. 0.212 ± 0.076 g/min, $\Delta = 0.015$ g/min, 95%CI -0.008 g/min, 0.038 g/min, $p = .178$, Figure 1). This corresponds to 7% effect; note the trial was powered to show a 20% effect. Total exogenous CHO oxidation during the first hour of exercise, estimated by calculating the area under the curve, was not significantly different between groups SUCRA (11.19 ± 0.89g) vs. CON (10.40 ± 0.82g). For isotopic ratios see Supplementary Figure 2. The relative contribution of fat, exogenous and endogenous carbohydrate oxidation

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**Supplementary Figure 2**—Isotopic ratios during 2h cycling at ~50% of VO$_{\text{peak}}$ with either preexercise ingestion of sucralose (SUCRA) or water (CON). Values are means ± SD ($n = 23$). Exercise and carbohydrate intake started at $t = 0$ min.
to total energy expenditure during exercise is shown in Figure 2. The major contributor to energy expenditure at exercise onset was endogenous CHO (glycogen), which progressively decreased throughout exercise. There was a significant increase in exogenous CHO oxidation throughout exercise. On average, CHO contributed 65 ± 7% and fat provided 35 ± 7% to total energy expenditure throughout exercise (Figure 2). There was no significant difference between SUCRA pretreatment and CON for any of the energy expenditure values.

**Plasma Metabolites**

Plasma glucose, insulin, and lactate concentrations at rest and during 120 min of exercise are shown in Figures 3A, B, and C, respectively. Resting plasma glucose, insulin, and lactate concentrations before the onset of exercise were similar between the two conditions. Due to the initial CHO bolus consumed at the onset of exercise (34g CHO; 391ml), plasma glucose and insulin significantly increased, with blood glucose peaking at 30 min and insulin peaking at 45 min into exercise, respectively (Figure 3A and B). Plasma lactate increased significantly in the first 10 min during the two trials (*p* < .05; Figure 3C). Following their peak, blood glucose, plasma insulin and lactate declined progressively throughout exercise, but were still elevated (*p* < .05) above baseline at the end of exercise. There were no significant differences for these three parameters between pretreated SUCRA and CON trials (Figure 3).

**Cardiovascular and Metabolic Responses**

VO$_2$, VCO$_2$, RER, total CHO, and fat oxidation rates, HR and RPE during the 120 min exercise period are shown in Table 1. VO$_2$, VCO$_2$ and RER all increased significantly at the onset of exercise, with VO$_2$, VCO$_2$ continuing to gradually increase throughout the 120 min of exercise. There were no significant differences between treatments on any parameter. HR and RPE increased significantly and steadily throughout exercise, but there was no significant difference between SUCRA and CON treatments (Table 1).

**Gastrointestinal Symptoms**

Few GI or systemic symptoms were reported after the trials, with all individual responses of minor or lower severity (<4) and all mean results below 0.2. There was no difference in GI or systemic symptoms between treatments (Table 2).
Discussion

This study examined the effects of preexercise consumption of noncaloric sweetener on subsequent exogenous CHO oxidation during exercise in humans. Our data suggest that consumption of noncaloric sweeteners in the immediate period before exercise does not lead to a significant increase in exogenous CHO oxidation during submaximal steady-state exercise.

Enhancing Endurance Performance Via Increased Exogenous CHO Oxidation

Since the early studies by Coyle et al. (Coyle, 1992a; Coyle & Coggan, 1984) it has become well established that the intake of CHO can significantly improve prolonged endurance capacity and performance (Jeukendrup, 2004). Although there are many factors to prolonged endurance exercise fatigue, one of the primary proposed mechanisms for this improved performance is due to an enhanced maintenance of plasma glucose (prevention of hypoglycemia), which results in augmented exogenous CHO oxidation by the muscles during exercise (Coyle, 1992b; Jeukendrup, 2004). In support of this, a recent study has shown that increased exogenous CHO oxidation significantly correlated with improved endurance performances in a dose-dependent manner, with 60 g of consumed CHO/h resulting in greater exogenous CHO oxidation and enhanced endurance performance than either 15 or 30 g CHO/hr (Smith et al., 2010). Furthermore, many studies have consistently found that GLU:FRU CHO blends result in 30–50% greater exogenous CHO oxidation during exercise as compared with GLU alone (for review see Jeukendrup, 2010), most likely due to separate GI CHO transporters for GLU (SGLT1) and FRU (GLUT5; Wright et al., 2003), which have been shown to significantly improve endurance performance (Currell & Jeukendrup, 2008; Triplett et al., 2010). Taken together, the delivery of CHO to the muscles is of paramount importance to optimal endurance performance.

Impact of Noncaloric Sweeteners on Exogenous CHO Oxidation

Recent findings from in vivo and in vitro animal studies showed that the intestinal glucose transporter SGLT-1 is up-regulated in acute and chronic fashion by gut expressed sweet taste receptor T1R2-T1R3 upon stimulation of this receptor by sugars or noncaloric sweeteners (Mace et al., 2007; Mace et al., 2009; Margolskee et al., 2007; Miyamoto et al., 1993; Moran et al., 2010). Thus, we sought to examine whether our approach of preexercise GI CHO transporter priming, via acute preexercise noncaloric sweetener consumption, could further increase CHO oxidation in humans.

We hypothesized that the impact of improving exogenous CHO oxidation during exercise via acute preexercise supplementation of noncaloric sweeteners would have the largest impact during the first hour of exercise. At the onset of exercise, exogenous CHO oxidation rates are lowest due to time for gastric emptying (Carrio et al., 1989), potentially due to GI CHO transporter expression being nonoptimal and time for muscle glucose uptake and oxidation (Stearns et al., 2010). In the subsequent hours of exercise we hypothesized that the concomitant ingestion of high carbohydrate drink would lead to intestinal glucose transport reaching a plateau, with prior ingestion of sucralose having a small or no impact.

Ex vivo studies have shown a very rapid effect of sucralose on intestinal glucose uptake, in that the glucose absorption rate more than doubled when the noncaloric sweetener sucralose was infused into the intestinal lumen of rats, reaching a plateau 45 min post consumption (Mace et al., 2007; Mace et al., 2009). In rats, intestinal infusion with glucose or saccharin for three hours leads
to more than doubling of SGLT-1 protein expression (Stearns et al., 2010). Further, we would not expect any acute changes to muscle glucose uptake (GLUT4) and oxidation between treatments (Cox et al., 2010). So any changes in exogenous CHO oxidation would presum-
ably be due to increased intestinal transport and uptake of CHO, via optimized CHO transporter expression, function, or density.

The dose of sucralose effective in up-regulating intestinal glucose uptake in humans is unknown. Concentra-
tions of 1mM and 2mM were effective in rats (acute ex vivo; Mace et al., 2007), and in mice (chronic; Mar-
golskee et al., 2007), respectively, but no dose-response studies have been reported. A concentration of 1mM was chosen for this study because it is intensely sweet and therefore highly effective in activating the T1R2/T1R3 receptors. Higher concentrations might also activate gut-expressed bitter receptors with possible confound-
ing effects.

Contrary to our hypothesis, this study demonstrated no acute effect of sucralose on exogenous carbohydrate oxidation, which suggests no significant change to CHO transporter function or density. Future studies should test higher concentrations, or combinations of sweet-
eners and undertake a more prolonged (several days to weeks) consumption period of noncaloric sweeteners, as perhaps a repeated exposure to CHO and/or noncal-
loric sweeteners could potentially increase intestinal

### Table 1
Mean Values (± SD; n = 23) for Respiratory Responses, Heart Rate, Ratings of Perceived Effort, and Whole-Body Fat and Carbohydrate Oxidation During 2-hr Cycling at ~50% of VO\textsubscript{2peak} with either Preexercise Ingestion of Sucralose (SUCRA) or Water (CON). Exercise and Carbohydrate Intake Started at t = 0 min

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<th>Measure</th>
<th>Trial</th>
<th>0 min</th>
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<th>40 min</th>
<th>60 min</th>
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</tbody>
</table>

**Note:** VO\textsubscript{2}: oxygen uptake (l/min), CO\textsubscript{2}: carbon dioxide production (l/min). RER: respiratory exchange ratio. CHO: whole-body carbohydrate oxidation (g/min). HR: heart rate. Fat: whole-body fat oxidation (g/min). RPE: ratings of perceived effort.

### Table 2
Gastrointestinal Questionnaire Scores Immediately Post 2-hr Cycling at ~50% of VO\textsubscript{2peak} with Either Preexercise Ingestion of Sucralose (SUCRA) or Water (CON) (Mean ± SD; n = 23)

<table>
<thead>
<tr>
<th></th>
<th>SUCRA</th>
<th>CON</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI overall score</td>
<td>0.10 ± 0.12</td>
<td>0.13 ± 0.26</td>
<td>.63</td>
</tr>
<tr>
<td>A. Upper abdomen</td>
<td>0.19 ± 0.29</td>
<td>0.20 ± 0.45</td>
<td>.96</td>
</tr>
<tr>
<td>B. Lower abdomen</td>
<td>0.04 ± 0.1</td>
<td>0.08 ± 0.26</td>
<td>.61</td>
</tr>
<tr>
<td>C. Systemic</td>
<td>0.07 ± 0.19</td>
<td>0.08 ± 0.18</td>
<td>.44</td>
</tr>
</tbody>
</table>

**Note:** p-value of a paired t test adjusting for the period.
CHO transporter expression and enhance CHO delivery and oxidation during exercise. In support of this, a 4-week endurance training study featuring two groups consuming either a high-CHO (~8.5 g CHO/kg/day) vs. lower-CHO (~5.3 g CHO/kg/day) diet, including ~100 g CHO/h/training in the high CHO group, showed significant 16% increase in exogenous CHO oxidation post training in the high-CHO vs. low CHO group (Cox et al., 2010). Interestingly, this study did not show differences in muscle GLUT4 expression, but suggested the role of the gut and its possible trainability in determining CHO oxidation rates as the primary mechanism for their finding. Furthermore, this study demonstrated that chronically ingesting CHO during training (~4 weeks) may offer an advantage to athletes in events where exogenous CHO oxidation is the principal fuel source during prolonged competition (Pfeiffer et al., 2012; Saris et al., 1989).

**Gastrointestinal Side Effects During Endurance Exercise**

During high intensity prolonged exercise the consumption of fluids and CHO can result in adverse GI problems, with ~15–40% of athletes in the field having negative GI side-effects (Pfeiffer et al., 2009; Pfeiffer et al., 2012), which has been suggested to be partially related to nonabsorbed CHO in the GI tract during exercise (Brouns et al., 1987). It is thought that having a high uptake and oxidation efficiency of supplemented CHO fluid beverages should reduce the accumulation of CHO in the GI tract and in turn reduce the potential for GI distress during exercise (Jeukendrup, 2004). This point is not trivial in that even minor GI distress is associated with negative endurance performance outcomes (O’Brien & Rowlands, 2011; Rowlands et al., 2012). Interestingly, the current study found a very low GI side-effect rate (mean of 0.2 out of 10) probably due to the low-exercise intensity, which was a much lower rate than found in the field with athletes utilizing the same questionnaire at higher exercise intensities (~15–40% adverse GI side-effects (Pfeiffer et al., 2009; Pfeiffer et al., 2012). Therefore, more data are required to determine whether a gut adaptation phase in athletes, via increased exposure to fluids, CHO, and/or noncaloric sweeteners, can decrease the number of GI side effects. At least one study has shown improved GI tolerance to fluids within just five practice sessions (Lambert et al., 2008), and a field base case-study report demonstrated exemplary GI tolerance after a gut-adaptation phase to high CHO and fluid intake rates in three world-class marathoners (Stellingwerff, 2012).

In summary ingestion of 400 ml of 1mM sucralose starting 2 hr before exercise onset does not impact exogenous carbohydrate oxidation during exercise. Future studies should explore a more prolonged (several days to weeks) consumption period of noncaloric sweeteners on subsequent exercise exogenous CHO oxidation, and eventually, whether this favorably impacts upon exercise GI symptoms and performance.

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**References**


