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Hydrogel Carbohydrate-Electrolyte Beverage Does Not Improve Glucose Availability, Substrate Oxidation, Gastrointestinal Symptoms or Exercise Performance, Compared With a Concentration and Nutrient-Matched Placebo

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The impact of a carbohydrate-electrolyte solution with sodium alginate and pectin for hydrogel formation (CES-HGel), was compared to a standard CES with otherwise matched ingredients (CES-Std), for blood glucose, substrate oxidation, gastrointestinal symptoms (GIS; nausea, belching, bloating, pain, regurgitation, flatulence, urge to defecate, and diarrhea), and exercise performance. Nine trained male endurance runners completed 3 hr of steady-state running (SS) at 60% $\dot{V}O_2$max, consuming 90 g/hr of carbohydrate from CES-HGel or CES-Std (53 g/hr maltodextrin, 37 g/hr fructose, 16% w/v solution) in a randomized crossover design, followed by an incremental time to exhaustion (TTE) test. Blood glucose and substrate oxidation were measured every 30 min during SS and oxidation throughout TTE. Breath hydrogen (H_2) was measured every 30 min during exercise and every 15 min for 2 hr postexercise. GIS were recorded every 15 min throughout SS, immediately after and every 15-min post-TTE. No differences in blood glucose (incremental area under the curve [mean ± SD]: CES-HGel 1,100 ± 96 mmol·L^{-1}·150 min^{-1} and CES-Std 1,076 ± 58 mmol·L^{-1}·150 min^{-1}; $p = .266$) were observed during SS. There were no differences in substrate oxidation during SS (carbohydrate: $p = .650$; fat: $p = .765$) or TTE (carbohydrate: $p = .466$; fat: $p = .633$) and no effect of trial on GIS incidence (100% in both trials) or severity (summative rating score: CES-HGel 29.1 ± 32.6 and CES-Std 34.8 ± 34.8; $p = .262$). Breath hydrogen was not different between trials ($p = .347$), nor was TTE performance (CES-HGel 722 ± 182 s and CES-Std: 756 ± 187 s; $p = .08$). In conclusion, sodium alginate and pectin added to a CES consumed during endurance running does not alter the blood glucose responses, carbohydrate malabsorption, substrate oxidation, GIS, or TTE beyond those of a CES with otherwise matched ingredients.

Keywords: breath H_2, encapsulated carbohydrate, endurance, gastric emptying, malabsorption, running

It is commonly accepted that during endurance exercise, adequate carbohydrate availability will optimize performance and will reduce the onset of fatigue, and that the use of carbohydrate-electrolyte solutions (CES) is encouraged (Stellingwerff & Cox, 2014). Current carbohydrate ingestion guidelines during prolonged endurance exercise (>2.5 hr) suggest that up to 90 g/hr be consumed by combining glucose and/or its polymers with fructose (Thomas et al., 2016). This approach is recommended to maximize exogenous carbohydrate provision, while aiming to minimize exercise-associated gastrointestinal symptoms (GIS; Jeukendrup, 2014). More recently, there has been a focus on additional ingredients in CES to further improve gastric emptying, minimize GIS, and enhance carbohydrate absorption and oxidation during exercise (Sutehall et al., 2018). Through the addition of alginate and pectin, solutions form a hydrogel structure in the low-pH environment of the stomach, "encapsulating" other beverage constituents, then returning to a liquid consistency in the higher pH environment of the duodenum (George & Abraham, 2007; Lee & Mooney, 2012). Research in pH-sensitive hydrogels began in the 1980s, with the goal to optimize the bioavailability of oral pharmaceuticals (George & Abraham, 2007). In this setting, the delivery of tens or hundreds of milligrams of a substance at rest is required, whereas during exercise, delivery of substantially larger quantities (i.e., tens of grams per hour) of carbohydrate is required. For a hydrogel CES to be considered superior for this purpose, it must either provide the same carbohydrate delivery into circulation with reduced incidence or severity of GIS, or provide greater carbohydrate delivery and oxidation with no additional increase in GIS.

Exercise-induced gastrointestinal syndrome (EIGS) is a term describing the pathophysiological processes during exertional stress, which when exacerbated, increase the risk of GIS (Costa et al., 2017b). Two main mechanisms underpin EIGS: splanchnic hypoperfusion and increased sympathetic drive. Consequences can include damage to the epithelial lining of the gastrointestinal tract, reduced gastric emptying, reduced intestinal motility, and the impaired function of nutrient transporters on the luminal surface of enterocytes. The occurrence of GIS results from any combination of factors, such as increased gastric fullness, nutrient malabsorption (with subsequent bacterial fermentation and gas production), osmotic influx resulting from increased luminal content, translocation of bacterial endotoxins into circulation, and/or the gastric-colonic reflex, which stimulates the onset of defecation (Costa et al., 2017b). Although GIS occurs across a wide range of exercise types and durations, its incidence is substantially greater as the exercise duration increases (Costa et al., 2017b), particularly while running (Pfeiffer et al., 2012) and in hot ambient conditions (Snipe & Costa, 2018; Snipe et al., 2018a, 2018b).

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To date, no studies have investigated the effect of a hydrogel CES, consumed during endurance exercise, on the outcomes related to glucose availability and carbohydrate oxidation, markers of EIGS and GIS, or performance. Therefore, the purpose of this study was to assess the impact of a hydrogel-forming CES, compared with a standard CES of the same carbohydrate composition and concentration, during prolonged endurance running. The outcomes included glucose availability and subsequent substrate oxidation, carbohydrate malabsorption as measured by breath hydrogen (H_2) responses, GIS, and performance at high intensities of endurance exercise. We hypothesized that a carbohydrate-electrolyte solution with sodium alginate and pectin for hydrogel formation (CES-HGel) would result in an increased rate of appearance of blood glucose and total carbohydrate oxidation, but with no differences in carbohydrate malabsorption, GIS, or time to exhaustion (TTE).

Methods

Participants

Nine trained male endurance runners, who trained at least 4 days per week and competed in either recreational or elite-level running events, were recruited for this study (mean ± SD: age 36 ± 5 y, weight 76 ± 5 kg, body fat mass 15.0% ± 5.9%, $\dot{V}O_2$max 59 ± 8 ml·kg^{-1}·min^{-1}, training volume 8.9 ± 2.9 hr/wk), which was approved by the Monash University Human Research Ethics Committee (Project No. 15012). Participants with a current injury or diagnosed medical condition that impairs gastrointestinal function, blood glucose homeostasis, or the ability to safely complete the exercise protocol were excluded. The participants were accustomed to consuming carbohydrate during training and/or competition (≥30 g/hr), but no participant was accustomed to consistently consuming 90 g/hr (Miall et al., 2018). Each participant completed two experimental trials, consuming a hydrogel CES (HGel) or standard carbohydrate-electrolyte solution (CES-Std) in a double-blind, randomized crossover design.

Preliminary Measures

One week before the first experimental trial, the height, nude body mass, fat, and fat-free mass were obtained using multifrequency bioelectric impedance analysis (Seca 515 MBCA; Seca Group, Hamburg, Germany). The maximum oxygen uptake ($\dot{V}O_2$max) was estimated by a continuous incremental exercise test to volitional exhaustion (Vmax Encore Metabolic Cart; CareFusion, San Diego, CA) on a motorized treadmill (Forma Run 500; Technogym, Seattle, WA), as previously reported (Costa et al., 2009). Steady-state (SS) running speed for experimental trials was determined as the speed at 1% gradient eliciting 60% of $\dot{V}O_2$max, verified from the oxygen uptake–work–rate relationship (9.9 ± 1.3 km/hr).

Experimental Procedure

The experimental procedure is shown in Figure 1. For 24 hr prior to the first experimental visit, the participants refrained from strenuous exercise and kept a record of all food and fluids consumed (149 ± 35 kJ/kg, 1.6 ± 0.5 g/kg protein, and 4.2 ± 0.9 g/kg carbohydrate), replicating this prior to the second visit. The participants arrived at the laboratory between 08:00 and 09:00 hr, having consumed a standardized breakfast (24 kJ/kg, 1 g/kg carbohydrate, 0.15 g/kg protein, and 12 ml/kg fluid). About 2 hr after breakfast, nude body mass was obtained, and total body water assessed, corrected by regression equation, as previously validated against deuterium dilution in endurance athletes with a constant error of 0.02 L, using multifrequency bioelectric impedance analysis. The experimental protocol consisted of 3 hr of SS running at the speed corresponding to 60% $\dot{V}O_2$max, at ambient temperature 23.6 ± 1.3 °C, 40.6% ± 6.7% relative humidity, and fan airspeed ~10.6 km/hr. Heart rate (HR) was recorded using a chest strap monitor (Polar Electro, Kempele, Finland). Rating of perceived exertion (RPE; 6–20 scale; Borg, 1982) and GIS using a modified visual analog scale (Gaskell et al., 2019a) were recorded every 15 min during SS. Capillary blood glucose concentration was measured before and every 30 min during SS (Accu-Chek Performa; Roche Diagnostics, Indianapolis, IN). Total nonprotein carbohydrate and fat oxidation was measured every 30 min using breath-by-breath indirect calorimetry, averaged over 5 min (Vmax Encore Metabolic Cart; CareFusion, San Diego, CA) and determined from the equations of Péronnet and Massicotte (1991):

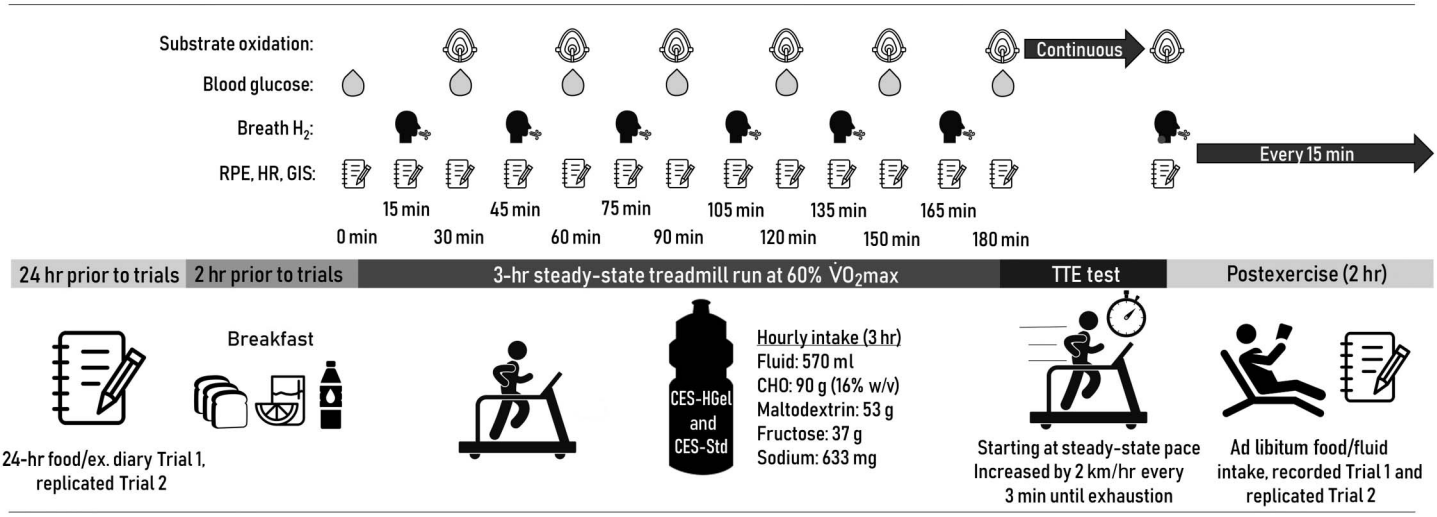

Figure 1 — Schematic description of the experimental design. RPE = rating of perceived exertion; HR = heart rate; GIS = gastrointestinal symptoms; CES-HGel = carbohydrate-electrolyte solution with sodium alginate and pectin for hydrogel; CES-Std = standard CES; TTE = time to exhaustion test.

Total carbohydrate oxidation:

$$(4.585 \times \dot{V}CO_2) - (3.226 \times \dot{V}O_2).$$

Total fat oxidation:

$$(1.695 \times \dot{V}O_2) - (1.701 \times \dot{V}CO_2).$$

Breath samples were obtained every 30 min during SS and analyzed in duplicate for H_2 (BreathTracker Digital MicroLyzer; Quintron, Milwaukee, WI). Following SS, a TTE test was performed, beginning at SS treadmill speed and thereafter increasing by 2 km/hr every 3 min until exhaustion. Substrate oxidation was measured throughout. Following exercise, the participants rested in the laboratory for 2 hr, consuming food and fluids of their choice during the first trial (28 ± 34 kJ/kg, 0.3 ± 0.4 g/kg protein, and 0.8 ± 1.0 g/kg carbohydrate) and recording and replicating this in the second trial. The GIS were recorded and breath samples were collected every 15 min during recovery.

Experimental Beverages

Throughout SS, participants consumed 90 g/hr of carbohydrate in a 16% w/v solution from a commercially available hydrogel CES (CES-HGel) or a standard carbohydrate- and sodium-matched CES (CES-Std) with identical color and similar taste, both hypertonic to plasma, as prepared (Table 1). The beverages were provided in one opaque drink bottle per hour of exercise, with the participants instructed to consume half of the contents every 30 min (i.e., 45 g of carbohydrates every 30 minutes). Additional water was available ad libitum; however, no participant opted to consume this, resulting in a fluid intake of 570 ml/hr in all trials.

In Vitro Beverage Analysis

Beverage analysis was performed in vitro to examine the ability of CES-HGel to form a hydrogel under simulated gastric conditions. About 100 ml of solution, prepared as consumed, simulated a typical fluid bolus ingested during exercise. This was added to 50 ml of acetic acid solution (pH 2.4), the volume chosen to simulate typical gastric juice volume when the stomach is empty (Mudie et al., 2014). Beverage osmolality was measured before and after addition to the acetic acid solution, in triplicate, by freeze point osmometry (Osmomat 030; Gonotec, Berlin, Germany).

Table 1 Composition of Hydrogel (CES-HGel) and Standard (CES-Std) Beverages

	CES-HGel	CES-Std
Fluid (ml)	570	570
Total carbohydrate (g)	90	90
Maltodextrin (g)	53	53
Fructose (g)	37	37
Concentration (% w/v)	16	16
Sodium (mg)	225	225
Osmolality (mOsm/kg)		
As consumed	486	460
With acetic acid solution in vitro	588	577

Statistical Analysis

Data are presented as mean and *SD*, unless indicated otherwise. Single time-point data were analyzed using dependent *t* tests or a nonparametric equivalent (Wilcoxon matched-pairs signed-rank test) after testing normality. Data with multiple time points were analyzed by two-way analysis of variance with repeated measures and Tukey's HSD post hoc analysis. Blood glucose incremental area under the curve (iAUC) was calculated using the trapezoidal method. Analysis was performed using SPSS (version 25.0; IBM Corp., Armonk, NY), with statistical significance accepted at $p \le .05$.

Results

In Vitro Product Analysis

A visual inspection of 100 ml of CES-HGel in 50 ml of acetic acid solution in vitro confirmed hydrogel formation, with no viscosity change in CES-Std (Figure 2). Beverage osmolality, as prepared, was 486 and 460 mOsm/kg, and 588 and 577 mOsm/kg in acetic acid solution, for CES-HGel and CES-Std, respectively.

Hydration Status, HR, Perceived Exertion, and TTE

No differences were observed between the trials for pre exercise nude body mass (CES-HGel 75.8 ± 4.7 kg and CES-Std 75.8 ± 4.8 kg; $p = 1.00$) or total body water (CES-HGel 44.5 ± 2.5 L and CES-Std 44.6 ± 2.6 L; $p = .513$). Body mass loss throughout exercise was not different between trials (CES-HGel 2.7% ± 0.7% and CES-Std 2.0% ± 0.9%; $p = .468$). A main effect of time ($p < .001$) but not trial ($p = .520$) was observed for HR during SS, with greater values from 90 to 105 min ($p < .05$) and 120 to 180 min ($p < .01$) compared with 15 min in both trials. Similarly, a main effect of time ($p < .001$) but not trial ($p = .531$), was observed for RPE, with greater perceived effort at 120 min ($p < .05$) and 135–180 min ($p < .01$) compared with 15 min in both trials. There was no significant difference between trials for TTE performance (CES-HGel 744 ± 182 s and CES-Std 756 ± 187 s; $p = .080$) (Figure 3).

Blood Glucose Responses and Substrate Oxidation

Preexercise blood glucose was similar between trials (CES-HGel 5.5 ± 0.4 mmol·L^{-1} and CES-Std 5.2 ± 0.4 mmol·L^{-1}; $p = .128$). A main effect of time ($p < .05$) was observed for blood glucose during SS ($p < .05$), with blood glucose greater at 30, 60, and 90 min compared with that at preexercise (Figure 4). The blood glucose incremental area under the curve was not different between trials (CES-HGel 1,100 ± 96 mmol·L^{-1}·150 min^{-1} and CES-Std 1,076 ± 58 mmol·L^{-1}·150 min^{-1}; $p = .266$). An effect of time was observed for both carbohydrate ($p = .001$) and fat ($p = .002$) oxidation during SS, with carbohydrate oxidation lower at 180 min compared with 30 min ($p < .05$). However, differences between individual time points could not be determined for fat oxidation. No effect of trial was observed for carbohydrate ($p = .650$) or fat ($p = .765$) oxidation during SS.

Substrate oxidation during the four completed intervals of TTE is shown in Figure 5. The exercise intensity at each interval, across both trials, was 63.4% ± 6.6%, 71.9% ± 9.1%, 80.5% ± 5.1%, and 90.5% ± 6.0% of $\dot{V}O_2$max. Only four participants completed a fifth interval (corresponding to 94.3% ± 7.0% of $\dot{V}O_2$max), and none completed a sixth interval; these data were excluded from further analysis. A main effect of time was observed for both carbohydrate

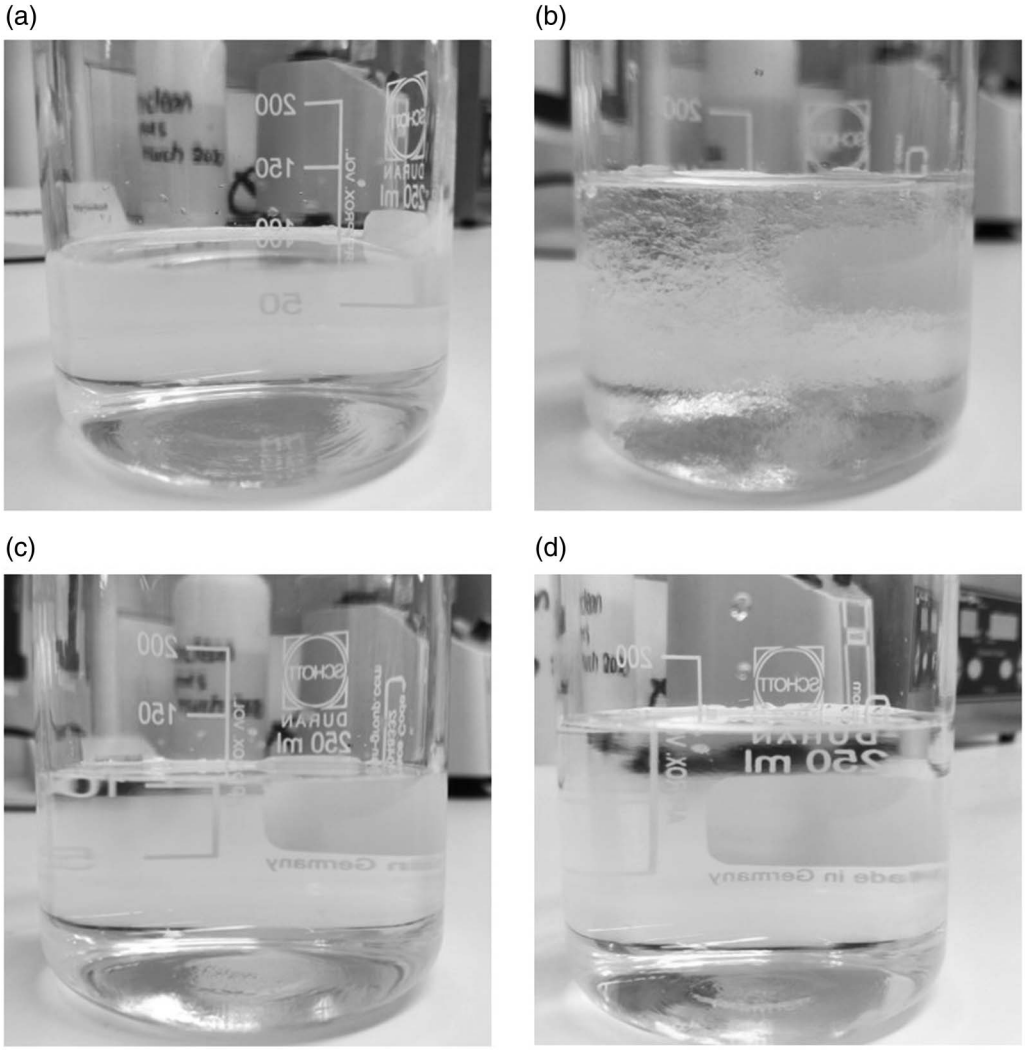

Figure 2 — 100-ml hydrogel solution (CES-HGel), before (a) and after addition to 50-ml acetic acid solution (pH 2.4) (b) and standard carbohydrate-electrolyte solution (CES-Std) before (c) and after addition to 50-ml acetic acid solution (d). A visible hydrogel formation is observed after addition of CES-HGel to the acetic acid solution, with no change in viscosity of CES-Std.

($p < .001$) and fat oxidation ($p < .001$), with carbohydrate oxidation significantly greater at the third ($p < .05$) and fourth ($p < .01$) compared with the first interval, and fat oxidation lower at the third ($p < .05$) and fourth ($p < .01$) compared with the first interval. No effect of trial was observed for carbohydrate ($p = .466$) or fat ($p = .633$) oxidation.

GIS and Breath H_2 Responses

The data for GIS are presented in Table 2. Although the GIS incidence was 100% in both trials, the incidence of severe symptoms (≥5 on the 0–10 modified visual analog scale) was 11% during CES-HGel and 22% during CES-Std. Gut discomfort, total GIS (summative score), upper and lower GIS, and nausea scores were not different between trials ($p > .05$). Breath H_2 from the samples taken during exercise was 1.0 ± 0.7 ppm, regardless of the trial. During the postexercise period, no main effect of trial ($p = .347$) or time ($p = .127$) was observed, and the mean H_2 values remained below 10 ppm throughout, indicating clinically insignificant carbohydrate malabsorption (Bate et al., 2010).

Discussion

The aim of this study was to investigate the addition of sodium alginate and pectin to a CES, compared with a standard carbohydrate- and sodium-matched CES. Both beverages were consumed in a 16% w/v solution providing 90 g/hr of multiple transportable carbohydrates, during 3 hr of running at 60% $\dot{V}O_2$max, followed by an incremental running exercise task. CES-HGel was assessed in vitro under conditions likely to simulate an ingested fluid bolus and gastric juice volume of the stomach during exercise, and formation of a pH-sensitive hydrogel was confirmed visually. In accordance with our hypothesis, CES-HGel did not influence GIS incidence or severity, or breath H_2 as an indicator of carbohydrate malabsorption. Contrary to our hypothesis, CES-HGel also did not influence blood glucose availability, total carbohydrate, or fat oxidation at multiple exercise intensities, nor did it influence TTE performance during the incremental running exercise task. To the best of our knowledge, this is the first published study whereby athletes have ingested a hydrogel-forming CES during exercise, matched to a standard CES of the same concentration and

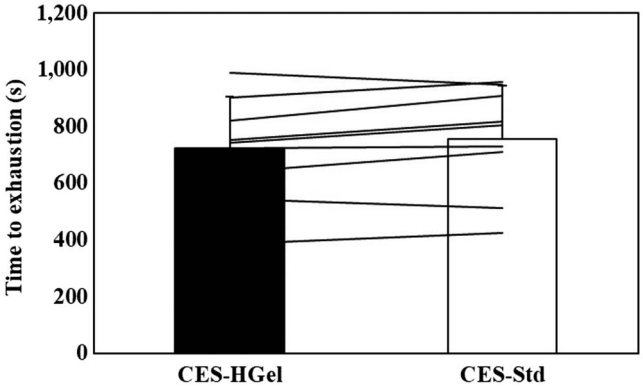

Figure 3 — Mean ± *SD* (bars) and individual participant time to exhaustion at increasing exercise intensity, following 3-hr steady-state running at 60% $\dot{V}O_2$max. ■ indicates CES-HGel, □ indicates CES-Std; CES-HGel = carbohydrate-electrolyte solution with sodium alginate and pectin for hydrogel; CES-Std = standard CES.

carbohydrate composition, and assessed outcomes related to glucose appearance in circulation, total carbohydrate oxidation, GIS, and exercise performance.

The causal mechanisms of gastrointestinal perturbations during exercise are multifactorial and stem primarily from splanchnic hypoperfusion and increased sympathetic drive (Costa et al., 2017b). The significance of these perturbations can include GIS, which is likely to influence exercise performance (Costa et al., 2017a; Miall et al., 2018), reduce food and fluid intake (Costa et al., 2016), and reduce absorption of nutrients from ingested food and/or fluids (Costa et al., 2017b). This study sought to investigate not only GIS incidence and severity, but also key markers of the process, whereby exogenous carbohydrate begins with ingestion and ends with substrate oxidation. This was achieved by measuring blood glucose responses and carbohydrate malabsorption through breath H_2 responses. As no significant differences were observed between CES-HGel and CES-Std for either marker, it appears the same quantity of carbohydrate was absorbed from the gastrointestinal tract, at the same rate. Exogenous carbohydrate oxidation was not specifically assessed in the current study, and therefore, it cannot be concluded with certainty that no differences in the rate of exogenous versus endogenous carbohydrate oxidation occurred between CES-HGel and CES-Std. It is important to note that the end point of the current exertional load (i.e., 3-hr SS, plus incremental exercise test to volitional exhaustion) is synonymous with stressed muscle glycogen stores, at which point exogenous carbohydrate would be the predominant carbohydrate energy substrate contributing toward oxidative phosphorylation (Costa et al., 2017a). No differences in total carbohydrate or fat oxidation were observed between trials following 3 hr of continuous exercise; however, total carbohydrate oxidation declined significantly over the exercise duration. Combined with no difference in the blood glucose rate of appearance or incremental area under the curve, we speculate that the depletion of endogenous carbohydrate stores and, therefore, the relative contribution of endogenous and exogenous carbohydrate to the total oxidation rate, was not different between trials. Future studies of hydrogel-forming CES should aim to assess the contribution of exogenous carbohydrate oxidation specifically, using standardized isotope tracer techniques (e.g., ^{13}C), to confirm this observation. Researchers, however, should be mindful of the potential issues in using such techniques on oxidation rate

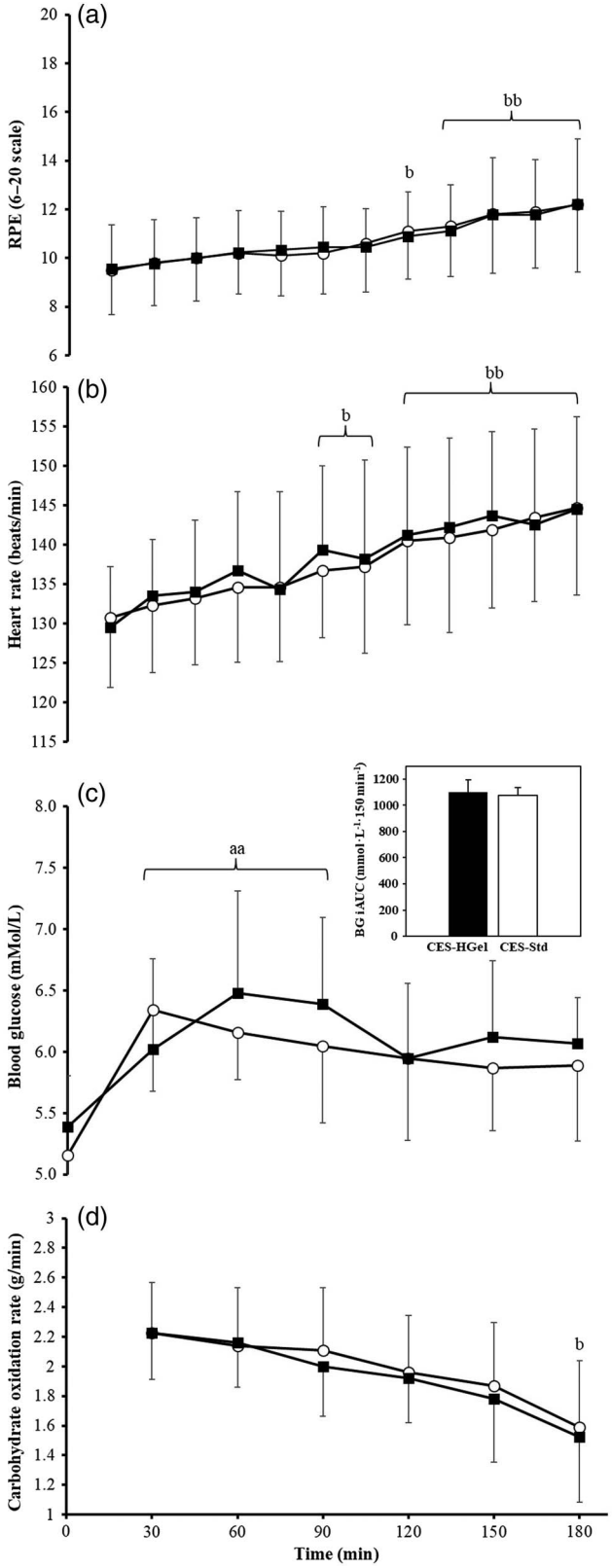

Figure 4 — RPE, heart rate, blood glucose, blood glucose incremental area under the curve (BG iAUC), and total carbohydrate oxidation during steady-state running. ■ indicates CES-HGel; ○ indicates; CES-Std; RPE = rating of perceived exertion; CES-Std = standard; CES-HGel = carbohydrate-electrolyte solution with sodium alginate and pectin for hydrogel. Mean ± *SD*. $^{aa}p < .01$ and $^{a}p < .05$ versus 0 min. $^{bb}p < .01$ and $^{b}p < .05$ versus 15 min.

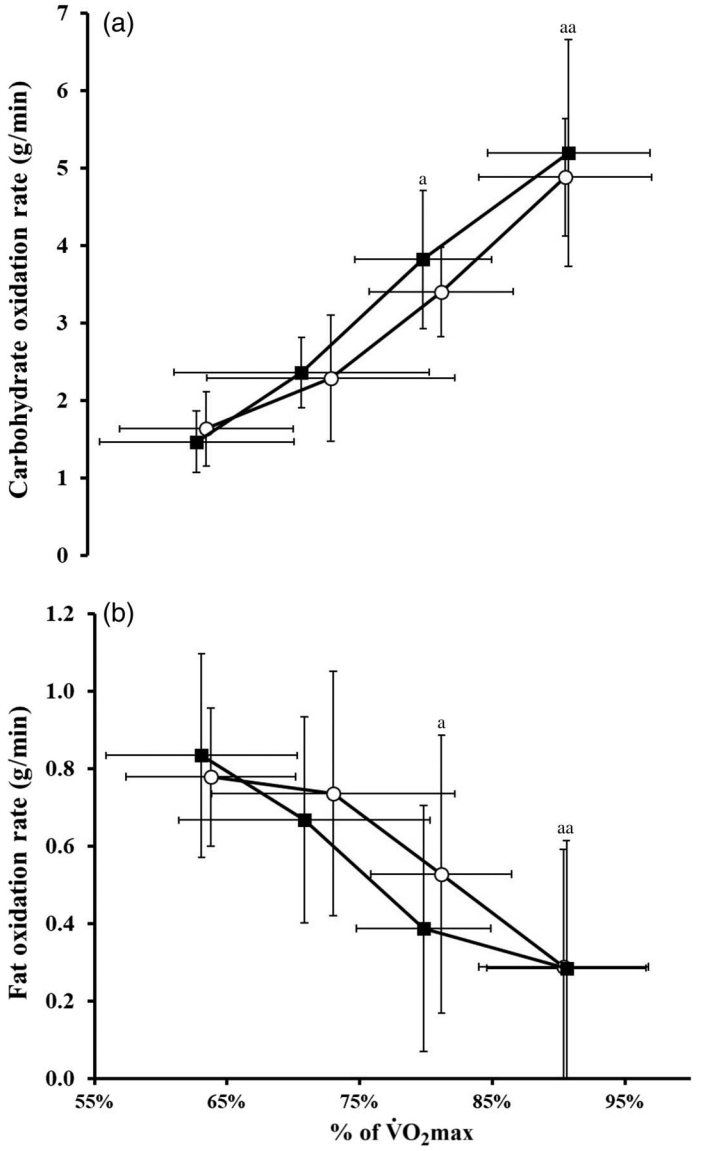

Figure 5 — Total carbohydrate and fat oxidation during incremental time to exhaustion test. Values are represented by mean (SD). $^{aa}p < .01$ and $^{a}p < .05$ versus first increment.

Table 2 Gastrointestinal Symptom (GIS) Incidence and Severity Scores (Summative Accumulation of Rating Scale Point Score at Measured Time Periods) During Steady-State Running at 60% $\dot{V}O_2$max While Consuming 90 g/hr Carbohydrate (16% w/v) From Hydrogel (CES-HGel) or Standard (CES-Std) Beverage

	CES-HGel	CES-Std	*p* value
GIS incidence			
Total (%)	100	100	NA
Severe (≥5/10) (%)	11	22	NA
GIS score (summative)			
Gut discomfort	15 (1–39)	18 (2–37)	.310
Total GIS	29 (1–79)	35 (2–90)	.262
Upper GIS	14 (0–38)	19 (0–59)	.674
Lower GIS	11 (0–51)	12 (0–38)	.610
Nausea	2 (0–18)	3 (0–26)	.317

Note. Mean (range within individual participants).

accuracy, including measures taken to deplete ^{13}C glycogen stores prior to ^{13}C-free glycogen reloading, and prolonged dietary control of ^{13}C-free foods to ascertain a ^{13}C-free glycogen load prior to the experimental protocol, both of which have previously been reported as technique limitations (Jentjens et al., 2004, 2006).

CES-HGel has been proposed to reduce the incidence and/or severity of GIS through the increase of gastric emptying and the uptake of carbohydrate from the ingested beverage (Sutehall et al., 2018). Although gastric emptying and the orocecal transit time were not measured in the current study, the outcomes of significance to athletes, which are at least partially based on gastric emptying and intestinal transit rates, are upper GIS and glucose appearance in circulation. These findings suggest no beneficial effect of CES-HGel for either of these measures. Future studies may seek to measure gastrointestinal function, either through the assessment of gastric emptying specifically or through the orocecal transit time. Methods for assessing gastric emptying (e.g., gastric aspiration and fluoroscopy) are impractical during prolonged running exercise and are likely to independently influence the incidence and severity of GIS in response to external manipulations (e.g., introducing a foreign object and fluctuating changes in intragastric pressures; Maughan & Leiper, 1996; Strid et al., 2011). Furthermore, the exhalation of ^{13}C-acetate during a challenge test may not provide an accurate reflection of gastric emptying due to the increased respiration of exercise (van Nieuwenhoven et al., 1999a). Instead, gastric myoelectrical activity assessed by electrogastrography preexercise and immediately postexercise (Parkman et al., 2003), in conjunction with an orocecal transit time assessment through a lactulose challenge test toward the end stage of the exercise bout (e.g., 30 min prior to cessation, then observing the time course of the breath H_2 turning point and peak), may provide a more practical and accurate depiction of upper gastrointestinal activity and tolerance (van Nieuwenhoven et al., 1999b). Interpreting gastric emptying rates in isolation is limited without the determination of intestinal activity (e.g., transit of the nutrient bolus along the duodenum into the jejunum and ileum, which is inclusive of the segment along the gastrointestinal tract where nutrient absorption occurs). Therefore, the global assessment of gastric emptying, intestinal transit, and absorption is warranted for a clearer understanding of the intake tolerance and fuel availability of a respective CES provided during exercise.

The lack of differences in GIS or glucose appearance in circulation in the current study, even if the initial gastric emptying rates were greater with CES-HGel, may be explained by a neuroendocrine negative feedback loop, characteristic of the enteric nervous system (i.e., submucosal and myenteric plexus) and enteroendocrine response (i.e., gut hormone) partnership. As the gastric-originated acidic chyme (containing the ingested CES) initiates entry into the duodenum, bicarbonate released from the common hepatopancreatic duct immediately serves to increase the pH of the emptied chyme. Although this increase in pH may serve to dissociate the hydrogel and release the constituent carbohydrate and sodium, the hepatopancreatic stimulation and subsequent secretions are likely to result in negative feedback to pylorus activity, duodenal peristalsis, and intestinal transit thereafter, in response to the nutrient load (Layer et al., 1990; van Avesaat et al., 2015; Van Citters & Lin 2006). Therefore, irrespective of the

gastric emptying rate, the nutrient density of the ingested CES, as present in the duodenum, is likely to influence the intestinal transit rate, with the aim of optimizing nutrient absorption.

One potential criticism of our study design is that gastric emptying is reported to be reduced ≥70% $\dot{V}O_2$max (Horner et al., 2015), an exercise intensity greater than SS in the current study. However, published data suggest that in general, only elite athletes can sustain exercise intensities ≥70% $\dot{V}O_2$max for periods much longer than 2–3 hr (Gillum et al., 2006; O'Brien et al., 1993; Sims et al., 2007,). Given that the reported incidence of GIS during competitive events of ≤3 hr duration is <10%, despite a greater sympathetic response to the increased exercise intensity, it would appear that strategies to reduce GIS during exercise of ≥70% $\dot{V}O_2$max will appeal to a small minority of athletes. The current exercise intervention targeted runners training and competing in events >3-hr duration, in which the GIS incidence is consistently >60%, and the participants ran at an exercise intensity typical of such events (Costa et al., 2016). During the current study, 100% of the participants experienced at least one mild GIS, and >10% experienced severe symptoms during both trials. These outcomes are in accordance with Costa et al. (2017a), reporting 100% GIS with a 90 g/hr carbohydrate gel disc gut challenge (2-hr running at 60% $\dot{V}O_2$max in temperate conditions, followed by 1-hr distance trial). Together, these findings suggest that carbohydrate feeding, in longer duration exercise at 60% $\dot{V}O_2$max, is sufficient to provoke GIS incidence similar to that observed in competitive events typically performed at ≥70% $\dot{V}O_2$max (Pfeiffer et al., 2012; ter Steege et al., 2008). As this study cannot categorically dismiss an effect of CES-HGel on gastric motility and carbohydrate absorption during SS at higher exercise intensities, such research warrants further investigation.

Prevention and management strategies studied to date in relation to EIGS and associated GIS have shown that those targeting the primary causal mechanisms (i.e., splanchnic hypoperfusion and sympathetic drive) are generally successful in reducing EIGS outcomes (Costa et al., 2017b, 2019a). To date, only one strategy that seeks to reduce the secondary outcomes of EIGS, through a reduction in the dietary fermentable oligosaccharides, disaccharides, monosaccharides and polyol (FODMAP) content in the 24-hr preceding exercise, led to reductions in GIS severity, but not incidence, during exercise (Gaskell et al., 2019b). Multiple studies of amino acids (Buchman et al., 1999a; Lambert et al., 2001; Pugh et al., 2017; van Wijck et al., 2014), antioxidants (Ashton et al., 2003; Buchman et al., 1999b), and probiotics (Gill et al., 2016; Roberts et al., 2016; Shing et al., 2014) have failed to show reduced GIS incidence and/or severity during exercise. As the purpose of CES-HGel is to enhance the gastric emptying rate, this also represents a strategy that attempts to address secondary outcomes, rather than the primary causal mechanisms of EIGS and associated GIS. Furthermore, the prevention and management strategies for exercise-associated GIS should be targeted to the specific primary causal mechanism(s) that affects an individual (Costa et al., 2017b). As there are multiple risk factors for these mechanisms, including hydration status, body temperature, blood flow to the splanchnic region, and individual tolerance to food and fluids (Costa et al., 2017b; Costa et al., 2019a), it is perhaps not surprising that a single nutrition strategy, especially one that acts on secondary outcomes, does not have a significant impact on reducing GIS during exertional stress. Instead, we suggest that athletes experiencing GIS during exercise undergo a comprehensive assessment to determine the specific cause(s) and implement tailored prevention and management strategies accordingly (Costa et al., 2017a, 2017b).

Conclusion

When consumed during prolonged running in temperate ambient conditions at typical ultramarathon intensity, the addition of sodium alginate and pectin to a maltodextrin and fructose CES, providing 90 g/hr of carbohydrate in a concentration of 16% w/v, does not alter the blood glucose availability, breath H_2 response, total substrate oxidation, GIS incidence or severity, or subsequent incremental TTE performance, compared with a matched CES without alginate or pectin. Additional research in athletes during higher intensity exercise scenarios is warranted, as is the specific assessment of gastrointestinal function during exercise and the contribution of exogenous versus endogenous carbohydrate to total oxidation rates.

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