**Title:**

Pectin-alginate does not further enhance exogenous carbohydrate oxidation in running.

**Authors:**

James F. P. Barber1, Joel Thomas1, Ben Narang1, Aaron Hengist1, James A. Betts1, Gareth A. Wallis2, Javier T. Gonzalez1

**Affiliations:**

1Department for Health, University of Bath, Bath, UK.

2School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, UK

**Author Contributions:**

JFPB, JTG, GAW and JAB designed the research, JFPB, JT, AH, JTG and BN conducted the research, JFPB and JTG analyzed the data, JTG performed the statistical analysis, JFPB and JTG primarily wrote the paper and all authors read and approved the final version of the manuscript.

**Corresponding Author:**

Javier T. Gonzalez, Department for Health, University of Bath, BA2 7AY, United Kingdom. Tel: 0(+44) 1225 38 5518; E-mail: [J.T.Gonzalez@bath.ac.uk](mailto:J.T.Gonzalez@bath.ac.uk)

ORCID ID: 0000-0002-9939-0074.

**Running Title:**

Hydrogel and exogenous carbohydrate oxidation

**Keywords:**

Fructose; Glucose; Hydrogel; Metabolism; Sports Nutrition

**FUNDING**

This work was funded by the University of Bath and the University of Birmingham.

**CONFLICTS OF INTEREST**

J.T.G. has received research funding and/or has acted as a consultant for Arla Foods Ingredients, Lucozade Ribena Suntory, Kenniscentrum Suiker and Voeding, and PepsiCo. J.A.B. has received research funding and/or has acted as a consultant for GlaxoSmithKline, Lucozade Ribena Suntory, Kellogg’s, Nestlé and PepsiCo. G.A.W has received research funding and/or has acted as a consultant for GlaxoSmithKline Ltd, Sugar Nutrition UK, Lucozade Ribena Suntory Ltd, Dairy Management Inc. and Volac International Ltd.

**ABSTRACT**

**PURPOSE:** Maximizing carbohydrate availability is important for many endurance events. Combining pectin and sodium alginate with ingested maltodextrin-fructose (MAL+FRU+PEC+ALG) has been suggested to enhance carbohydrate delivery via hydrogel formation but the influence on exogenous carbohydrate oxidation remains unknown. The primary aim of this study was to assess the effects of MAL+FRU+PEC+ALG on exogenous carbohydrate oxidation during exercise compared to a maltodextrin-fructose mixture (MAL+FRU). MAL+FRU has been well established to increase exogenous carbohydrate oxidation during cycling, compared to glucose-based carbohydrates (MAL+GLU). However, much evidence focuses on cycling, and direct evidence in running is lacking. Therefore, a secondary aim was to compare exogenous carbohydrate oxidation rates with MAL+FRU *versus* MAL+GLU during running. **METHODS:** Nine trained runners completed two trials (MAL+FRU and MAL+FRU+PEC+ALG) in a double-blind, randomised crossover design. A subset (n=7) also completed a MAL+GLU trial to address the secondary aim, and a water trial to establish background expired 13CO2 enrichment. Participants ran at 60% peak for 120 min while ingesting either water only, or carbohydrate solutions at a rate of 1.5 g carbohydrate·min-1. **RESULTS:** At the end of 120 min of exercise, exogenous carbohydrate oxidation rates were 0.9 (SD 0.5) g·min-1 with MAL+GLU ingestion. MAL+FRU ingestion increased exogenous carbohydrate oxidation rates to 1.1 (SD 0.3) g·min-1 (*p*=0.038), with no further increase with MAL+FRU+PEC+ALG ingestion (1.1 (SD 0.3) g·min-1; *p*=1.0). No time x treatment interaction effects were observed for plasma glucose, lactate, insulin or non-esterified fatty acids, nor for ratings of perceived exertion or gastrointestinal symptoms (all *p*>0.05). **CONCLUSION:** To maximise exogenous carbohydrate oxidation during moderate-intensity running, athletes may benefit from consuming glucose(polymer)-fructose mixtures over glucose-based carbohydrates alone, but the addition of pectin and sodium alginate offers no further benefit.

**INTRODUCTION**

Carbohydrate availability is a key determinant of endurance exercise performance. Low muscle and liver glycogen concentrations are strongly associated with fatigue during prolonged, moderate-to-high intensity exercise (1, 2). The ingestion of carbohydrate during exercise provides an additional (exogenous) source of carbohydrate, which can prevent or attenuate the decline in liver (3), and sometimes muscle (4, 5), glycogen contents. Increasing exogenous carbohydrate oxidation via altering the dose or type of carbohydrates ingested can improve endurance performance (6-9). Strategies to maximise the ability to digest, absorb and oxidise ingested carbohydrate are therefore a priority for endurance athletes during competition.

One well-established strategy for increasing exogenous carbohydrate oxidation rates during exercise, is the co-ingestion of glucose-fructose mixtures (10-12). When compared to glucose-based carbohydrates alone, isocaloric co-ingestion of fructose with glucose-based carbohydrates typically increases peak exogenous carbohydrate oxidation rates from ~1 g·min-1 to up to ~1.7 g·min-1 (13), which is thought to be (in part) due to fructose being absorbed by an additional intestinal transport route (GLUT5), and thereby bypassing the limiting step of intestinal glucose transport (primarily SGLT1)(14). A recent innovation in commercial carbohydrate sports drinks is the inclusion of pectin and sodium alginate alongside maltodextrin and fructose (15). When combined with water, this mixture can create a hydrogel upon exposure to a low pH environment such as the stomach (16). It is hypothesized that the hydrogel will allow for greater rates of gastric emptying via a reduction in nutrient sensing and thus increase intestinal carbohydrate delivery and absorption, thereby facilitating improvements in endurance performance (15). Whilst some evidence does indicate that the addition of pectin could accelerate gastric emptying during enteral feeding (17), other studies that have added either pectin to a meal (18) or alginate to meal preloads (19) demonstrate that each of these can *delay* gastric emptying at rest.

To date, only two studies have been conducted in which ingesting carbohydrate hydrogel has been compared to typical carbohydrate ingestion during exercise. These recent studies indicate no benefit to preloaded incremental time-to-exhaustion during running, or preloaded repeated sprint cycling performance with the ingestion of a maltodextrin-fructose-hydrogel, over maltodextrin-fructose alone (16, 20).It is possible, however, for hydrogels to only be relevant in specific contexts, such as when gastric emptying and carbohydrate availability are both contributing to limiting performance. This scenario may occur with high exercise intensities (>80% peak), combined with a prolonged duration (>90 min), such as elite marathon racing. Methodological limitations mean that it is not yet possible to accurately assess exogenous carbohydrate oxidation at such intensities. Therefore, the current best approach to understand the physiology of carbohydrate hydrogels is likely to be to understand the metabolic responses at moderate-intensity exercise, combined with performance and gut comfort responses at race pace. This approach has been historically fruitful, as the primary principles of glucose-fructose mixtures were developed with data collected at moderate-intensity exercise (12), and have translated well into performances during high-intensity exercise (21).It is yet to be established whether a maltodextrin-fructose-hydrogel can enhance exogenous carbohydrate oxidation during exercise. It is also interesting to note that direct comparisons of exogenous carbohydrate oxidation from glucose plus fructose ingestion *versus* glucose alone have, to date, only been made during cycling-based exercise (13, 22). Given the substantial metabolic differences and the potential for differences in gastrointestinal function with the mechanical action of running compared to cycling (23), evidence derived from cycling cannot necessarily be extrapolated to running.

Therefore, the primary aim of the present study was to assess whether the addition of sodium alginate and pectin to a maltodextrin-fructose mixture enhances exogenous carbohydrate oxidation rates during running. A secondary aim was to assess whether a maltodextrin-fructose mixture enhances exogenous carbohydrate oxidation rates during running, when compared to isocaloric ingestion of glucose-based carbohydrates alone. It was hypothesized that a maltodextrin-fructose mixture would enhance exogenous carbohydrate oxidation rates compared to maltodextrin-glucose ingestion, and that the addition of sodium alginate and pectin to a maltodextrin-fructose mixture would further increase exogenous carbohydrate oxidation rates.

**METHODS**

*Study design*

All participants completed preliminary testing followed by two main trials to address the primary aim, in a randomised, double-blind, crossover design separated by 7-14 days (*n*=9). During main trials, participants ingested a maltodextrin-fructose mixture either without (MAL+FRU), or with pectin and sodium alginate to create a hydrogel (MAL+FRU+PEC+ALG). Trials were conducted at the University of Bath, in accordance with the latest version of the Declaration of Helsinki and following institutional ethical approval (MSES 18/19-001). Participants provided informed written consent prior to participation. Randomisation was performed by JTG with online software (<https://www.randomizer.org>). Blinding and preparation of the test drinks was performed by an assistant who was not involved in the exercise tests.

Two subgroups of participants (*n*=7) also completed an additional trial with the ingestion of either glucose-based carbohydrates alone (MAL+GLU) or water alone (WATER) to address the secondary aim and to determine background 13CO2 breath enrichment for calculation of exogenous carbohydrate oxidation rates, respectively.

*Participants*

Ten trained male runners were recruited to the study (>1 year training in endurance running), but due to dropouts nine participants completed the two main trials (MAL+FRU and MAL+FRU+PEC+ALG), and seven participants completed the MAL+GLU and the WATER trial, respectively (**Table 1**). Exclusion criteria included: metabolic or gastrointestinal disorders, smokers or failure to pass a physical activity readiness questionnaire. Females were excluded on the rationale of studying a homogenous population, since there are potential sex differences in gastric emptying (24).

*Preliminary testing*

Participants’ height (Leicester Height Measure, Seca GmbH, Hamburg, Germany) and mass (Tanita, Tokyo, Japan) were measured. To determine running economy and peak oxygen consumption (peak), participants completed a graded exercise test to exhaustion on a motorised treadmill (Ergo ELG70, Woodway, Weil am Rhein, Germany). Participants initially ran for 4 x 4 mins on a 0% gradient to establish the relationship between O2 uptake and running speed (8-12 km⋅h-1) on a flat treadmill. Following a 5-minute rest, participants then began the exhaustive test, whereby the treadmill speed was fixed (at a speed based on participants perception in the 4-minute stages), and the gradient was increased by 3% every 3 minutes, starting from a 1% gradient, until volitional exhaustion. The running speed which elicited 60% peak was interpolated and used for prescribing running velocity during the experimental visits.

*Replication of usual diet and physical activity*

The approach to replication of usual diet and physical activity was based on the balance between reducing day-to-day variability whilst minimizing participant burden (25). Participants recorded diet and exercise for 2 days prior to the first experimental trial and replicated these prior to subsequent trials. During this time, participants refrained from consuming foods with a high natural abundance of 13C to minimise background shifts in 13C enrichment of expired gas arising from endogenous carbohydrate stores being oxidized during exercise. For 24 h prior to each visit, participants refrained from strenuous exercise, caffeine and alcohol. Participants also fasted for 8 h prior to each experimental visit. Participants were reminded of these protocols 5 days and 3 days prior to trials. Participants were also reminded of the fasting period 24 hours prior to trials. Adherence to these protocols was confirmed verbally with participants prior to each trial. This relatively modest method was thought to be appropriate for the current study design as the primary outcome measure (exogenous carbohydrate oxidation) has been shown to be unaffected by pre-exercise glycogen status (26), that would be influenced by dietary carbohydrate intake and physical activity levels.

*Main trials*

Participants arrived at the laboratory following pre-trial standardisation (confirmed by verbal questioning) and at a similar time of day within participants (±1 h). After a 5-min flush period (to washout dead space in tubing and familiarise participants), a 5-min sample of expired breath was taken using the Douglas bag method, and an additional breath sample was collected into an exetainer for analysis of 13C enrichment. A cannula was then inserted into an antecubital vein and a resting blood sample was drawn. Participants then ran for 2 h at a speed eliciting 60% peak. The run was performed in standard environmental conditions (17-22 °C dry bulb temperature, 40-65% relative humidity), and participants were fan cooled throughout.

*Carbohydrate drinks*

On all trials other than the WATER trial, participants ingested 140 mL of a 16% w/v solution upon initiating running, and then every 15 min until 105 min providing an average intake of 1.5 g carbohydrate⋅min-1. The rate of carbohydrate intake was chosen to align with guidelines for prolonged exercise. As the solution concentration may affect the ability to form a hydrogel in the stomach this meant that fluid intake could not be tailored to expected sweat losses. This may have resulted in a slight hypohydration on all trials. The MAL+GLU drink provided 0.87 g maltodextrin⋅min-1 and 0.63 g dextrose⋅min-1, whereas both the MAL+FRU and MAL+FRU+PEC+ALG drinks provided 0.87 g maltodextrin⋅min-1 and 0.63 g fructose⋅min-1. The ratio of fructose/glucose to maltodextrin was dictated by that present in the commercially available product at the time of testing. Systematic review indicates that a ratio closer to unity might be more optimal for balancing exogenous oxidation, gut comfort, and performance (14). MAL+GLU and MAL+FRU had 1 g sodium chloride⋅L-1 added to match the MAL+FRU+PEC+ALG drink. Consistent with manufacturer’s instructions, all drinks were made with low-calcium water (<40 mg⋅L-1).

In order to quantify exogenous carbohydrate oxidation, carbohydrates with a high natural abundance of 13C were used. The natural 13C abundance of the MAL+GLU, MAL+FRU and MAL+FRU+PEC+ALG were -11.37, -11.20 and -11.86 δ‰ vs. Pee Dee Bellemnitella (PDB), respectively. Maltodextrin, dextrose (both MyProtein, Cheshire, UK) and fructose (PeakSupps, Bridgend, UK) were purchased as raw materials and mixed accordingly while the MAL+FRU+PEC+ALG, was purchased as a commercially available finished product (Maurten, Gothenburg, Sweden).

*Expired breath analysis*

Expired breath samples were analyzed using the Douglas bag method to establish rates of oxygen consumption and carbon dioxide production. At rest, a 5-min sample was collected after a 5-min equilibration period. During exercise, 1-min samples were taken after 1-min equilibration periods. Concurrently, ambient O2 and CO2 concentrations were measured to account for changes in inspired gas concentrations (27). Concentrations of O2 and CO2 were measured in a known volume of sample (Mini MP 5200, Servomex Ltd., Crowborough, UK), and the total volume of expired gas determined by evacuation using a dry gas meter (Harvard Apparatus, Holliston, USA). To determine 13C enrichment of expired CO2, breath samples were collected in 10 mL exetainers (Labco Ltd, Lampeter, UK), filled in duplicate by 10 s exhalation into a discard bag (Quintron Inc, Milwaukee, USA). At rest, participants exhaled for 20 s to ensure sufficient collection of expired gas.

Whole-body substrate oxidation was calculated from and according to stochiometric equations (28, 29). The 13C/12C ratio of expired CO2 was determined by continuous flow isotope ratio mass spectrometry, and the enrichment expressed as δ per mil difference between the 13C/12C ratio of the sample and a known standard (30). The δ13C was related to an international standard from which exogenous carbohydrate oxidation was calculated according to the following equation (31):

Where is the 13C enrichment of expired CO2, is the 13C enrichment of the drink, and is the 13C enrichment of expired CO2 during the WATER trial. For participants who did not complete a WATER trial, the group mean of the other participants was used for . *k* is the with the oxidation of 1 g of glucose (0.7467 L CO2·g-1).

Some 13C can be trapped within the bicarbonate pool with implications for the quantification of exogenous carbohydrate oxidation. However, during exercise, the increase in CO2 production results in a rapid equilibration of expired 13CO2 with the 13CO2/H13CO3- pool and recovery of 13CO2 from oxidation approaches 100% after 20 min of exercise at ~60 %peak (unpublished observations). Therefore, calculations on substrate oxidation were performed on data from 30 mins of exercise onwards.

*Blood sampling and analysis*

Venous blood samples (10 mL) were taken at rest and at 15, 30, 60, 90 and 120 min of exercise. Samples were collected into EDTA-containing tubes (Sarstedt, Germany) and centrifuged for 10 min at 4000 *g* and 4 ºC. Aliquots of plasma were stored at -80 ºC before analysis. Due to cost implications, only blood samples from the trials that related to the primary aim were analyzed (MAL+FRU and MAL+FRU+PEC+ALG trials). Plasma was analyzed for glucose and lactate using an automated analyzer (RX Daytona, Randox, UK). Insulin (IBL International, Hamburg, Germany), and non-esterified fatty acid concentrations (NEFA, WAKO Diagnostics, Richmond, VA) were analyzed by ELISA and colorimetric assays, respectively. For all analyses, intra- and inter-assay coefficients of variation were below 10%.

*Subjective ratings*

Ratings of gastrointestinal distress were measured on a 7-point scale adapted from the Gastrointestinal Symptoms Rating Scale (GSRS; (32)). Four questions related to upper, three to central, and two to lower gastrointestinal symptoms. The GSRS has adequate internal consistence (α > 0.61), construct and discriminant validity, and is suitable for comparisons over 6 weeks (32). Since these ratings are subjective and cannot therefore be readily compared between groups of people, only data for the primary comparison (MAL+FRU vs MAL+FRU+PEC+ALG) are presented.

*Statistical analysis*

An *a priori* sample size estimate was performed based on the effect size (Cohen’s *d*) of exogenous carbohydrate oxidation rates in response to glucose-fructose co-ingestion compared to glucose alone based on the following equations:

where

Peak exogenous carbohydrate oxidation rates from glucose ingestion alone have been reported to be 1.06 (SD 0.11) g·min-1, compared to 1.75 (SD 0.31) g·min-1 with glucose-fructose co-ingestion (*n* = 8, in a crossover design)(12). Using this effect size (*d* = 2.49), 5 participants should provide power >95% to detect a difference with a two-tailed test and an α-level of 0.05. To ensure adequate power with the potential for dropouts, we aimed to recruit at least 7 participants.

Data were analyzed using Prism (v 8.2.1, GraphPad, San Diego, CA, USA) and SPSS (v24, IBM, Armonk, NY, USA). Data expressed over time (e.g. expired 13CO2 enrichment, exogenous carbohydrate oxidation rates, , , RER, plasma metabolite and hormone concentrations, RPE, and gastrointestinal symptom ratings) were analyzed by repeated measures ANOVA or mixed-effects model as appropriate. Summary statistics (e.g. peak exogenous carbohydrate oxidation rates, the percentage contribution of substrates to total energy expenditure) were analyzed by one-way ANOVA or two-tailed, paired *t*-tests with Bonferroni correction, as appropriate. An exploratory analysis was performed to assess whether baseline differences in NEFA concentrations were driving differences in whole-body substrate use by ANCOVA analysis on whole-body fat oxidation rates with baseline plasma NEFA concentrations as the covariate. Furthermore, data were checked for order effects by repeated measures ANOVA (trial order x time interaction) and one-way ANOVA (trial order) as appropriate. All data are expressed as means (SD) in the text and tables, and as means ± 95%CI in figures, other than subjective data, which are presented as medians ± 95%CI. Differences were considered significant if *p* 0.05.

**RESULTS**

*Substrate oxidation and gas exchange*

No order effects were detected for either expired 13CO2 enrichments (trial order: *p* = 0.59; trial order x time interaction effect: *p* = 1.0) or exogenous carbohydrate oxidation rates (trial order: *p* = 0.61; trial order x time interaction effect: *p* = 1.0). Furthermore, no order effects were detected for the total amount of fat (*p* = 0.62), endogenous carbohydrate (*p* = 0.38), or exogenous carbohydrate oxidised (*p* = 0.93). Expired 13CO2 enrichments increased during exercise (time effect, *p* < 0.001), and were higher during MAL+FRU compared to MAL+GLU (treatment effect, *p* < 0.001, *post-hoc* comparison *p* < 0.001), with no further increase seen with MAL+FRU+PEC+ALG compared to MAL+FRU (*p* = 0.11; **Figure 1A**). Differences across time were detected between the WATER trial and the carbohydrate drink treatments (time x treatment interaction, *p* < 0.001). Exogenous carbohydrate oxidation rates increased over time (time effect, *p* < 0.001), and to a greater extent with both of the fructose-containing drinks compared to MAL+GLU (time x treatment interaction, *p* < 0.001; **Figure 1B**). At the end of exercise, exogenous carbohydrate oxidation rates were higher with MAL+FRU, compared to MAL+GLU (*p* = 0.04), but not further increased by MAL+FRU+PEC+ALG (*p* = 1.0). The exogenous oxidation rate expressed relative to ingestion rate at this timepoint equated to 59 (SD 19)%, 70 (SD 19)%, and 71 (SD 21)% with MAL+GLU, MAL+FRU MAL+FRU+PEC+ALG, respectively. Peak exogenous carbohydrate oxidation rates were 0.92 (SD 0.29) g⋅min-1, 1.08 (SD 0.26) g⋅min-1 and 1.11 (SD 0.31) g⋅min-1 with MAL+GLU, MAL+FRU MAL+FRU+PEC+ALG, respectively (all *p* > 0.05).

During MAL+GLU and MAL+FRU trials, fat oxidation was 234 (SD 50) kcal·h-1 and 165 (SD 83) kcal·h-1 respectively (*p* = 0.14). Fat oxidation was 255 (SD 120) kcal·h-1 during the MAL+FRU+PEC+ALG trial, which was higher than MAL+FRU (*p* = 0.04). During MAL+GLU and MAL+FRU trials, endogenous carbohydrate oxidation was 525 (SD 89) kcal·h-1 and 530 (SD 99) kcal·h-1 respectively (*p* = 0.93). During the MAL+FRU+PEC+ALG endogenous carbohydrate oxidation was lower compared to MAL+FRU (434 (SD 112) kcal·h-1, *p* = 0.05). During MAL+GLU, exogenous carbohydrate oxidation was 165 (SD 60) kcal·h-1. MAL+FRU increased exogenous carbohydrate oxidation to 201 (SD 66) kcal·h-1 (*p* = 0.05), with no further increase from MAL+FRU+PEC+ALG ingestion (193 (SD 66) kcal·h-1;*p* = 0.66).

When expressed as the contribution to total energy expenditure, fat oxidation contributed ~20-25% of total energy expenditure during MAL+GLU and MAL+FRU trials and increased to ~30% of total energy expenditure during MAL+FRU+PEC+ALG (*p* = 0.02; **Figure 2**). However, this increase in fat oxidation as a contribution to total energy expenditure between MAL+FRU and MAL+FRU+PEC+ALG (mean difference: 10.7%, 95%CI: 0.2 to 21.1%), did not remain after baseline NEFA concentrations were added as a covariate (adjusted mean difference: 7.8%, 95%CI: -0.6 to 16.1%, *p* = 0.07). Endogenous carbohydrate oxidation contributed ~60% of total energy expenditure during MAL+GLU and MAL+FRU trials, and decreased to ~50% of total energy expenditure during MAL+FRU+PEC+ALG (*p* = 0.03; **Figure 2**). Exogenous carbohydrate oxidation contributed ~18% of total energy expenditure during MAL+GLU, and increased to ~22% of total energy expenditure during MAL+FRU (*p* = 0.05; **Figure 2**). Exogenous carbohydrate oxidation was not further increased with MAL+FRU+PEC+ALG compared to MAL+FRU (*p* = 0.71; **Figure 2**).

, and RER all displayed main effects of time (all *p* < 0.05), but no treatment effects were detected (all *p* > 0.29; *p* = 0.08 for RER), and no differences over time were detected (time x treatment interaction effects, all *p* > 0.45; **Figure 3**).

*Plasma insulin and metabolite concentrations*

Plasma glucose, lactate and insulin concentrations all rose slightly at the onset of exercise (time effect for all, *p* < 0.01), to a similar extent across time in both MAL+FRU and MAL+FRU+PEC+ALG trials (treatment effect and time x treatment interaction, all *p* > 0.20; **Figures 4A, 4B and 4C,** respectively). Plasma NEFA concentrations were ~0.13 mmol⋅L-1 higher at baseline in the MAL+FRU+PEC+ALG trial compared to the MAL+FRU trial (*p* = 0.03; **Figure 4D**). During exercise, plasma NEFA concentrations declined (time effect, *p* < 0.001), to a similar level across time in both trials (treatment effect and time x treatment interaction, both *p* = 0.12).

*Subjective ratings*

RPE, upper, central and lower gastrointestinal symptom ratings all increased throughout exercise (time effect, all *p* < 0.01), to a similar extent across time in both trials (treatment effect and time x treatment interaction, all *p* > 0.07; **Figures 5A, 5B, 5C and 5D**, respectively).

**DISCUSSION**

The present data demonstrate that, when ingesting carbohydrates at 90 g per hour during running, the addition of pectin and sodium alginate to ingested glucose-fructose does not further enhance exogenous carbohydrate oxidation rates, when compared to a glucose-fructose mixture alone. However, ingestion of glucose-fructose mixture can enhance exogenous carbohydrate oxidation during running, when compared to isocaloric ingestion of glucose-based carbohydrates alone.

Maximizing carbohydrate availability during exercise is a key goal for many endurance athletes (22). A novel nutrient blend of sodium alginate and pectin, combined with a maltodextrin-fructose mixture has recently been developed, and has been proposed to further enhance exogenous carbohydrate oxidation during exercise (15). This combination purports to produce a hydrogel when exposed to the acidic environment of the stomach, thereby encapsulating the carbohydrate (15). It is expected that this hydrogel may attenuate the reduction in gastric emptying rates seen with large amounts of carbohydrate ingestion, thereby facilitating high exogenous carbohydrate oxidation rates during exercise. To the best of the authors’ knowledge, there are currently only two randomised, controlled trials that have examined the effects of co-ingesting pectin and sodium alginate with carbohydrates during exercise. Both of these studies demonstrated no changes in whole-body metabolism, ratings of gut discomfort or perception of effort, or performance during running (16), or cycling (20). Consistent with this, we also observed no differences in ratings of gut discomfort or perception of effort. However, it is possible that increased exogenous carbohydrate availability above that seen with maltodextrin-fructose mixtures only enhances performance during very specific contexts. Therefore, further insight about the potential for this nutritional strategy to influence performance could be gained from establishing whether pectin and sodium alginate co-ingestion with carbohydrate affects exogenous carbohydrate oxidation.

In the present study, exogenous carbohydrate oxidation rates were not further increased by the co-ingestion of pectin and sodium alginate with a maltodextrin-fructose mixture, compared to a maltodextrin-fructose mixture alone. If the mechanism by which pectin and alginate are proposed to enhance carbohydrate delivery is via accelerating gastric emptying, then the lack of effect on exogenous carbohydrate oxidation is perhaps not surprising, as gastric emptying rates are not thought to be limiting to exogenous carbohydrate oxidation when large amounts of carbohydrate are ingested during exercise (33). These data demonstrate that there is no increase in exogenous carbohydrate availability with the co-ingestion of alginate and pectin with a maltodextrin-fructose mixture, and thereby can explain why recent studies have demonstrated a lack of effect on endurance performance (16, 20).

It is well-established that the co-ingestion of fructose with glucose can enhance exogenous carbohydrate oxidation rates during cycling-based exercise, when compared to the co-ingestion of glucose-based carbohydrates alone (13, 34). However, the ability to extrapolate findings from cycling to other modes of exercise is uncertain. When compared to cycling, running typically results in higher rates of fat oxidation and a concomitant decrease in whole-body carbohydrate oxidation rates (35, 36). Furthermore, running is thought to pose a greater mechanical stress on the gastrointestinal system, potentially altering the capacity for intestinal absorption and thus limiting the rate of digestion, absorption and oxidation of exogenous carbohydrate (35). Nevertheless, the only direct comparison to date of prolonged running *versus* cycling reported equivalent exogenous carbohydrate oxidation rates with the ingestion of a glucose-fructose mixture (35). However, in that study, participants exercised at the same relative intensity during both trials (60% peak), resulting in a ~5% higher absolute exercise intensity (based on oxygen consumption and energy expenditure) with running *versus* cycling (35). The higher absolute energy cost of exercise could have driven a higher exogenous carbohydrate oxidation rate in the running trial and offset any potential reduction in exogenous carbohydrate oxidation rates seen with running. Therefore, whilst the present data demonstrate that a glucose-fructose mixture can increase exogenous carbohydrate oxidation during running, it remains to be established whether running *versus* cycling alters the efficiency or capacity for digestion, absorption and oxidation of exogenous carbohydrate.

Unexpectedly, during the trial where pectin and sodium alginate were co-ingested with a maltodextrin-fructose mixture, we observed a higher rate of fat oxidation compared to ingestion of a maltodextrin-fructose mixture alone. Since there was no change in exogenous carbohydrate oxidation, this resulted in a reduction in endogenous carbohydrate oxidation. It is tempting to speculate that this could be a direct effect of the test drink. For example, it has been suggested that hydrogels may attenuate nutrient-sensing in the proximal gastrointestinal tract (15), which would result in higher gastric emptying rates and lower insulin secretion (37). However, plasma insulin concentrations were unaffected by the addition of pectin and sodium alginate to carbohydrate in the present study. Additionally, a baseline difference was observed in plasma NEFA concentrations, which was higher in the MAL+FRU+PEC+ALG trial. Elevated baseline NEFA is one possible explanation for the higher whole-body fat oxidation in that trial (38). Indeed, when baseline NEFA concentrations are added as a covariate, the difference in fat oxidation between trials is no longer statistically significant. The reasons for this baseline difference in NEFA concentrations are not clear. Whilst participants were asked to replicate diet and activity in the days before trials, this was only checked by verbal confirmation, and it is possible that this was not fully adhered to. Differences in carbohydrate intake and/or physical activity levels could have caused baseline glycogen concentrations to be lower in the MAL+FRU+PEC+ALG trial. Fortunately, this is unlikely to have implications for our primary and secondary aims, as exercising with low glycogen contents does not alter exogenous carbohydrate oxidation rates (26). This highlights the importance of considering pre-trial standardization with respect to the specific aims and methods of a study. If a study design requires tighter control of pre-exercise carbohydrate availability, then researchers should consider requesting participants to report back on the accuracy of diet and physical activity replication and/or provide food packages to facilitate adherence (25).

A potential limitation with the present study is that it was not confirmed whether the addition of pectin and sodium alginate to carbohydrate resulted in hydrogel formation within the stomach or therefore altered gastric emptying. Nevertheless, the product was made accordingly to manufacturer’s instructions, and this method has been recently shown to produce a hydrogel within a low pH environment *in vitro* (16). Furthermore, the measurement of exogenous carbohydrate oxidation encapsulates the integrated sum of gastric emptying, intestinal absorption and oxidation of the ingested carbohydrate. Therefore, if a carbohydrate hydrogel is to enhance carbohydrate delivery and thereby performance, an increase in exogenous carbohydrate oxidation is most likely a requirement. Whilst the study was powered for the outcome of exogenous carbohydrate oxidation with the specified comparisons, the relatively small sample size has the potential to be underpowered for some of our other outcome measures reported. Inadequate power for some outcomes has the potential to result in either a type II error (false negative), but also overestimate the true effect size when an effect is detected. It should also be acknowledged that the exercise intensity employed in the present study is not relevant to elite-level marathon running, which occurs at ~90% peak (39). Given the differences in gastric emptying rates at high- *versus* moderate-intensity exercise (40), it is not possible to directly extrapolate the findings of the present study to exercise intensities above ~80% peak. However, the measurement of exogenous carbohydrate oxidation also becomes problematic at high exercise intensities, and therefore it is unlikely that measurements of exogenous carbohydrate oxidation can be made at elite-level marathon race with the current methods available.

In conclusion, when carbohydrates are ingested at rates recommended for prolonged endurance-type exercise (*i.e.* 90 grams per hour), maltodextrin-fructose mixtures increase exogenous carbohydrate oxidation compared to the ingestion of glucose-based carbohydrates alone. The additional ingestion of pectin and sodium alginate with a maltodextrin-fructose mixture does not further increase exogenous carbohydrate oxidation, or alter the perception of effort or ratings of gastrointestinal symptoms during moderate-intensity running. Given the technical difficulties in assessing exogenous carbohydrate oxidation at exercise intensities reflective of elite marathon racing, decisions on the use of hydrogels in elite sport should be based on the total balance of evidence from mechanistic studies at moderate-intensity exercise, performance studies at race pace, combined with careful observations in elite athletes during hard training and racing.

**ACKNOWLEDGEMENTS**

The authors thank the volunteers for participating in this study. The study was funded by the University of Bath and University of Birmingham. J.T.G. has received research funding and/or has acted as a consultant for Arla Foods Ingredients, Lucozade Ribena Suntory, Kenniscentrum Suiker and Voeding, and PepsiCo. J.A.B. has received research funding and/or has acted as a consultant for GlaxoSmithKline, Lucozade Ribena Suntory, Kellogg’s, Nestlé and PepsiCo. G.A.W has received research funding and/or has acted as a consultant for GlaxoSmithKline Ltd, Sugar Nutrition UK, Lucozade Ribena Suntory Ltd, Dairy Management Inc. and Volac International Ltd. The results of the study do not constitute endorsement by the American College of Sports Medicine.

**REFERENCES**

1. Casey A, Mann R, Banister K et al. Effect of carbohydrate ingestion on glycogen resynthesis in human liver and skeletal muscle, measured by (13)C MRS. *Am J Physiol Endocrinol Metab*. 2000;278(1):E65-75.

2. Bergstrom J, Hermansen L, Hultman E, Saltin B. Diet, muscle glycogen and physical performance. *Acta Physiol Scand*. 1967;71(2):140-50.

3. Gonzalez JT, Fuchs CJ, Smith FE et al. Ingestion of glucose or sucrose prevents liver but not muscle glycogen depletion during prolonged endurance-type exercise in trained cyclists. *Am J Physiol Endocrinol Metab*. 2015;309(12):E1032-9.

4. Tsintzas OK, Williams C, Boobis L, Greenhaff P. Carbohydrate ingestion and glycogen utilization in different muscle fibre types in man. *J Physiol*. 1995;489 ( Pt 1):243-50.

5. Stellingwerff T, Boon H, Gijsen AP, Stegen JH, Kuipers H, van Loon LJ. Carbohydrate supplementation during prolonged cycling exercise spares muscle glycogen but does not affect intramyocellular lipid use. *Pflugers Arch*. 2007;454(4):635-47.

6. Smith JW, Pascoe DD, Passe DH et al. Curvilinear dose-response relationship of carbohydrate (0-120 g.h(-1)) and performance. *Med Sci Sports Exerc*. 2013;45(2):336-41.

7. Smith JW, Zachwieja JJ, Peronnet F et al. Fuel selection and cycling endurance performance with ingestion of [13C]glucose: evidence for a carbohydrate dose response. *J Appl Physiol (1985)*. 2010;108(6):1520-9.

8. Currell K, Jeukendrup AE. Superior endurance performance with ingestion of multiple transportable carbohydrates. *Med Sci Sports Exerc*. 2008;40(2):275-81.

9. Newell ML, Wallis GA, Hunter AM, Tipton KD, Galloway SDR. Metabolic Responses to Carbohydrate Ingestion during Exercise: Associations between Carbohydrate Dose and Endurance Performance. *Nutrients*. 2018;10(1).

10. Hulston CJ, Wallis GA, Jeukendrup AE. Exogenous CHO oxidation with glucose plus fructose intake during exercise. *Med Sci Sports Exerc*. 2009;41(2):357-63.

11. Wallis GA, Wittekind A. Is there a specific role for sucrose in sports and exercise performance? *Int J Sport Nutr Exerc Metab*. 2013;23(6):571-83.

12. Jentjens RL, Jeukendrup AE. High rates of exogenous carbohydrate oxidation from a mixture of glucose and fructose ingested during prolonged cycling exercise. *Br J Nutr*. 2005;93(4):485-92.

13. Gonzalez JT, Fuchs CJ, Betts JA, van Loon LJ. Glucose Plus Fructose Ingestion for Post-Exercise Recovery-Greater than the Sum of Its Parts? *Nutrients*. 2017;9(4).

14. Rowlands DS, Houltham S, Musa-Veloso K, Brown F, Paulionis L, Bailey D. Fructose-Glucose Composite Carbohydrates and Endurance Performance: Critical Review and Future Perspectives. *Sports Med*. 2015;45(11):1561-76.

15. Sutehall S, Muniz-Pardos B, Bosch AN, Di Gianfrancesco A, Pitsiladis YP. Sports Drinks on the Edge of a New Era. *Curr Sports Med Rep*. 2018;17(4):112-6.

16. McCubbin AJ, Zhu A, Gaskell SK, Costa RJS. Hydrogel carbohydrate-electrolyte bervarage does not improve glucose availability, substrate oxidation, gastrointestinal symptoms or exercise performance, compared with a concentration and nutrient-matched placebo. *Int J Sport Nutr Exerc Metab*. 2019. doi: 10.1123/ijsnem.2019-0090.

17. Shimoyama Y, Kusano M, Kawamura O et al. High-viscosity liquid meal accelerates gastric emptying. *Neurogastroenterol Motil*. 2007;19(11):879-86.

18. Sanaka M, Yamamoto T, Anjiki H, Nagasawa K, Kuyama Y. Effects of agar and pectin on gastric emptying and post-prandial glycaemic profiles in healthy human volunteers. *Clin Exp Pharmacol Physiol*. 2007;34(11):1151-5.

19. Georg Jensen M, Kristensen M, Belza A, Knudsen JC, Astrup A. Acute effect of alginate-based preload on satiety feelings, energy intake, and gastric emptying rate in healthy subjects. *Obesity (Silver Spring)*. 2012;20(9):1851-8.

20. Baur DA, Toney HR, Saunders MJ, Baur KG, Luden ND, Womack CJ. Carbohydrate hydrogel beverage provides no additional cycling performance benefit versus carbohydrate alone. *Eur J Appl Physiol*. 2019; 119: 2599-608.

21. Rowlands DS, Swift M, Ros M, Green JG. Composite versus single transportable carbohydrate solution enhances race and laboratory cycling performance. *Appl Physiol Nutr Metab*. 2012;37(3):425-36.

22. Fuchs CJ, Gonzalez JT, van Loon LJC. Fructose co-ingestion to increase carbohydrate availability in athletes *Journal of Physiology*. 2019; 597: 3549-60.

23. Gottschall JS, Palmer BM. The acute effects of prior cycling cadence on running performance and kinematics. *Med Sci Sports Exerc*. 2002;34(9):1518-22.

24. Mori H, Suzuki H, Matsuzaki J et al. Gender Difference of Gastric Emptying in Healthy Volunteers and Patients with Functional Dyspepsia. *Digestion*. 2017;95(1):72-8.

25. Jeacocke NA, Burke LM. Methods to standardize dietary intake before performance testing. *Int J Sport Nutr Exerc Metab*. 2010;20(2):87-103.

26. Margolis LM, Wilson MA, Whitney CC et al. Exercising with low muscle glycogen content increases fat oxidation and decreases endogenous, but not exogenous carbohydrate oxidation. *Metabolism*. 2019;97:1-8.

27. Betts JA, Thompson D. Thinking outside the bag (not necessarily outside the lab). *Med Sci Sports Exerc*. 2012;44(10):2040; author reply 1.

28. Frayn KN. Calculation of substrate oxidation rates in vivo from gaseous exchange. *J Appl Physiol Respir Environ Exerc Physiol*. 1983;55(2):628-34.

29. Jeukendrup AE, Wallis GA. Measurement of substrate oxidation during exercise by means of gas exchange measurements. *Int J Sports Med*. 2005;26 Suppl 1:S28-37.

30. Craig H. Isotopic standards for carbon and oxygen and correction factors for mass-spectrometric analysis of carbon dioxide. *Geochimica et Cosmochimica Acta*. 1957;12:133-49.

31. Pirnay F, Scheen AJ, Gautier JF, Lacroix M, Mosora F, Lefebvre PJ. Exogenous glucose oxidation during exercise in relation to the power output. *Int J Sports Med*. 1995;16(7):456-60.

32. Revicki DA, Wood M, Wiklund I, Crawley J. Reliability and validity of the Gastrointestinal Symptom Rating Scale in patients with gastroesophageal reflux disease. *Qual Life Res*. 1998;7(1):75-83.

33. Rehrer NJ, Wagenmakers AJ, Beckers EJ et al. Gastric emptying, absorption, and carbohydrate oxidation during prolonged exercise. *J Appl Physiol (1985)*. 1992;72(2):468-75.

34. Fuchs CJ, Gonzalez JT, Beelen M et al. Sucrose ingestion after exhaustive exercise accelerates liver, but not muscle glycogen repletion compared with glucose ingestion in trained athletes. *J Appl Physiol (1985)*. 2016;120(11):1328-34.

35. Pfeiffer B, Stellingwerff T, Zaltas E, Hodgson AB, Jeukendrup AE. Carbohydrate oxidation from a drink during running compared with cycling exercise. *Med Sci Sports Exerc*. 2011;43(2):327-34.

36. Achten J, Venables MC, Jeukendrup AE. Fat oxidation rates are higher during running compared with cycling over a wide range of intensities. *Metabolism*. 2003;52(6):747-52.

37. Holst JJ. The physiology of glucagon-like peptide 1. *Physiol Rev*. 2007;87(4):1409-39.

38. Robinson SL, Chambers ES, Fletcher G, Wallis GA. Lipolytic Markers, Insulin and Resting Fat Oxidation are Associated with Maximal Fat Oxidation. *Int J Sports Med*. 2016;37(8):607-13.

39. Hagerman FC. Energy metabolism and fuel utilization. *Med Sci Sports Exerc*. 1992;24(9 Suppl):S309-14.

40. Leiper JB. Fate of ingested fluids: factors affecting gastric emptying and intestinal absorption of beverages in humans. *Nutr Rev*. 2015;73 Suppl 2:57-72.

**Figure legends**

**Figure 1**. Breath 13CO2 enrichment (A), and exogenous carbohydrate oxidation rates (B) during 120 min of running at 60% peak with the ingestion of water (WATER; *n*=7), or 1.5 g⋅min-1 of carbohydrate in the form of maltodextrin plus glucose (MAL+GLU; *n*=7), maltodextrin plus fructose (MAL+FRU; *n*=9), or maltodextrin plus fructose with pectin and sodium alginate (MAL+FRU+PEC+ALG; *n*=9). Data are means (error bars: 95%CI). \**p*<0.05 for MAL+GLU *versus* MAL+FRU.

A screenshot of a cell phone

Description automatically generated

**Figure 2**. Whole-body fat (FAT), endogenous carbohydrate (ENDO CHO) and exogenous carbohydrate oxidation rates (EXO CHO) during 120 min of running at 60% peak with the ingestion of 1.5 g⋅min-1 of carbohydrate in the form of maltodextrin plus glucose (MAL+GLU; *n*=7), maltodextrin plus fructose (MAL+FRU; *n*=9), or maltodextrin plus fructose with pectin and sodium alginate (MAL+FRU+PEC+ALG; *n*=9). Data are means (error bars: 95%CI). \**p*<0.05 for differences between treatments. Data were calculated from minutes 30-120 of exercise.

A screenshot of a cell phone

Description automatically generated

**Figure 3**. Oxygen consumption (**A**), carbon dioxide production (**B**), and respiratory exchange ratio (**C**) during 120 min of running at 60% peak with the ingestion of 1.5 g⋅min-1 of carbohydrate in the form of maltodextrin plus glucose (MAL+GLU; *n*=7), maltodextrin plus fructose (MAL+FRU; *n*=9), or maltodextrin plus fructose with pectin and sodium alginate (MAL+FRU+PEC+ALG; *n*=9). Data are means (error bars: 95%CI).

A close up of a map

Description automatically generated

**Figure 4**. Plasma glucose (**A**), lactate (**B**), insulin (**C**), and non-esterified fatty acid (NEFA; **D**) concentrations during 120 min of running at 60% peak with the ingestion of 1.5 g⋅min-1 of carbohydrate in the form of, maltodextrin plus fructose (MAL+FRU; *n*=9), or maltodextrin plus fructose with pectin and sodium alginate (MAL+FRU+PEC+ALG; *n*=9). Data are means (error bars: 95%CI). \**p*<0.05 for MAL+FRU *versus* MAL+FRU+PEC+ALG.

A close up of a map

Description automatically generated

**Figure 5**. Ratings of perceived exertion (**A**), upper (**B**), central (**C**), and lower (**D**) gastrointestinal (GI) symptoms during 120 min of running at 60% peak with the ingestion of 1.5 g⋅min-1 of carbohydrate in the form of, maltodextrin plus fructose (MAL+FRU; *n*=9), or maltodextrin plus fructose with pectin and sodium alginate (MAL+FRU+PEC+ALG; *n*=9). Data are medians (error bars: 95%CI).

A close up of a map

Description automatically generated

**Table 1. Participant characteristics.**

|  |  |
| --- | --- |
|  | **Characteristics** |
| Age | 22 (18-30) years |
| Body mass | 69 (61-74) kg |
| Height | 1.82 (1.74-1.88) m |
| peak | 63 (56-72) mL⋅min-1⋅kg-1 |
| Running speed to elicit 60% peak | 10.7 (9.3-11.8) km⋅h-1 |

Data are means (ranges). peak, peak oxygen consumption.