# Contrasting effects of viscous and particulate fibers on colonic fermentation in vitro and in vivo, and their impact on intestinal water studied by MRI in a randomized trial

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## ABSTRACT

**Background:** Wheat bran, nopal, and psyllium are examples of particulate, viscous and particulate, and viscous fibers, respectively, with laxative properties yet contrasting fermentability.

**Objectives:** We assessed the fermentability of these fibers in vitro and their effects on intestinal function relevant to laxation in vivo using MRI.

**Methods:** Each fiber was predigested prior to measuring gas production in vitro during 48-h anaerobic incubation with healthy fecal samples. We performed a randomized, 3-way crossover trial in 14 healthy volunteers who ingested 7.5 g fiber twice on the day prior to study initiation and once with the study test meal. Serial MRI scans obtained after fasting and hourly for 4 h following meal ingestion were used to assess small bowel water content (SBWC), colonic volumes, and T1 of the ascending colon (T1AC) as measures of colonic water. Breath samples for hydrogen analysis were obtained while patients were in the fasted state and every 30 min for 4 h following meal ingestion

**Results:** In vitro, the onset of gas production was significantly delayed with psyllium (mean ± SD: 14 ± 5 h) compared with wheat bran (6 ± 2 h, $P = 0.003$) and was associated with a smaller total gas volume ($P = 0.01$). Prefeeding all 3 fibers for 24 h was associated with an increased fasting T1AC (>75% of values >90th centile of the normal range). There was a further rise during the 4 h after psyllium (0.3 ± 0.3 s $P = 0.009$), a fall with wheat bran (−0.2 ± 0.2 s; $P = 0.02$), but no change with nopal (0.0 ± 0.1 s, $P = 0.2$). SBWC increased for all fibers; nopal stimulated more water than wheat bran [AUC mean (95% CI) difference: 7.1 (0.6, 13.8) L/min, $P = 0.03$]. Breath hydrogen rose significantly after wheat bran and nopal but not after psyllium ($P < 0.0001$).

**Conclusion:** Both viscous and particulate fibers are equally effective at increasing colonic T1 over a period of 24 h. Mechanisms include water trapping in the small bowel by viscous fibers and delivery of substrates to the colonic microbiota by more fermentable particulate fiber. This trial was registered at clinicaltrials.gov as NCT03263065. *Am J Clin Nutr* 2020;112:595–602.

**Keywords:** fiber, bran, nopal, psyllium, MRI, intestine, colon, water

## Introduction

The underlying physicochemical and functional properties of dietary fibers vary widely. Gel forming fibers such as psyllium have evolved as mucilage plant polymers with extremely high water-holding capacity which despite their large molecular weight (in excess of 1 MDa) are easily able to hydrate. Such fibers form highly viscous solutions and gels when dissolved in water. In contrast, some fibers such as wheat bran, which has a large particle size (>100 μM), have very limited solubility and do not form a gel nor contribute significantly to viscosity in the bowel (1).

Clinical evidence shows that some viscous, gel-forming fibers (e.g., psyllium) benefit patients with irritable bowel syndrome whereas fiber from different sources (e.g., bran) may worsen symptoms (2), suggesting that the differing physicochemical

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Supplemental Table 1 and Supplemental Figure 1 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: FODMAP, fermentable oligo-, di-, mono-saccharides and polyols; SBWC, small bowel water content; SCFA, short chain fatty acids; T1AC, T1 of the ascending colon; 5-HT, 5-hydroxytryptamine.

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properties have an impact on the mode of action in the gut, although this has to date not been studied in detail.

Psyllium fiber is a hemicellulose-rich mucilage comprising highly branched arabinoxylan, composed of a xylan polymer densely decorated with arabinose and xylose sidechains (3). Although this is poorly fermented it facilitates water holding in the small bowel, causing an increase in both small bowel and colonic water content as well as colonic volume, as assessed by MRI (4). Constipated patients have lower colonic water content which can be normalized by therapeutic doses of psyllium (7 g 3 times daily) (4), which are widely used to treat constipation.

The main fiber component of wheat bran is also an arabinoxylan, which comprises the majority of the cell wall in wheat but unlike the arabinoxylan in psyllium is highly fermentable (5). Wheat bran acts as a substrate for the colonic microbiota and is fermented to produce significant amounts of short-chain fatty acids (SCFA) (6, 7). Several studies have shown that wheat bran also accelerates orocecal transit (8) and increases small bowel water content (SBWC) (9).

Nopal fiber is an extract from the nopal cactus *Opuntia ficus-indica*. In contrast with psyllium, nopal fiber is primarily a pectic mucilage comprising a complex mixture of galacturonan, rhamnogalactans, and rhamnogalacturonans as well as arabinoxylans, which are gel forming (10–12) but readily fermentable. Nopal has been traditionally used as a laxative in North Africa and Mexico (13) but its effects on human gut microbiota and function have yet to be examined.

The 3 fibers used in this study, with the contrasting physicochemical properties described above, can be expected to be associated with different physiological behavior in the gastrointestinal tract but these have not previously been directly compared in humans.

Our aim was to compare equal doses of wheat bran, nopal, and psyllium fibers on gas production by microbial fermentation in vitro; and their dynamic effects on SBWC, colonic volume, and water content of the chyme in the ascending colon in vivo using MRI in healthy human volunteers.

## Methods

Two studies were performed; the first examined the effects of the 3 fibers in a laboratory model of colonic fermentation (in vitro fermentation study) and the second examined in healthy subjects the effects of ingesting the 3 fibers for 2 d on SBWC, colonic volume, and colonic water content using MRI and breath hydrogen (human MRI study).

The fibers used for both the in vitro fermentation study and the human MRI study were the following: coarse wheat bran (Holland and Barrett), nopal provided as dehydrated cactus leaf (OroVerde Nopal Cactus Green Leaf Powder), and psyllium husk (98%, Supernutrients). Their composition, shown in **Table 1,** analyzed at Medallion Labs by use of standard AOAC methods and at Quadram Institute Biosciences by use of a Megazyme Fructan HK enzymatic assay kit (Megazyme) according to manufacture recommendations (14); see **Supplementary Methods** for details.

**TABLE 1** Composition of the 3 test fibers (1)

| Test | Wheat bran | Nopal | Psyllium |
|---|---|---|---|
| Resistant starch | <2% | <2% | <2% |
| Total dietary fiber | 41.3% | 50.8% | 88.9% |
| Soluble fiber | 6.2% | 13.2% | 23.5% |
| Total fructans[1] | 1.2% | 0.1% | — |
| Total sugars | 4.4% | 4.9% | — |
| Mannitol | trace | 0.1% | — |
| Glucose | 2.0% | 1.4% | — |
| Fructose | 0.7% | 2.2% | — |
| Sucrose | ND | 1.2% | — |
| Raffinose | 0.1% | trace | — |
| 1-Kestose | 0.1% | trace | — |
| Maltose | 1.42% | 0.1% | — |
| Nystose | ND | trace | — |
| Kestopentose | ND | ND | — |

[1]Quantified using high-performance anion exchange chromatography with pulsed amperometric detection. ND, not detectable.

### In vitro fermentation study

In vitro fermentations for the 3 test fibers were carried out using a well-established model of the human colon seeded with microbiota obtained from healthy human volunteers (15–18). Prior to the fermentation, wheat bran and nopal underwent in vitro digestion using the INFOGEST, a validated international consensus method (19) that mimics small intestinal digestion and absorption of nonfiber carbohydrates that would otherwise be fermented in the in vitro fermentation model. Digestions were performed using the INFOGEST digestion method (19) with the addition of amyloglucosidase (final concentration 3 U/mL) at the intestinal phase. On completion, predigested fiber samples were frozen and lyophilized for 6 d. Once dry, samples were washed with absolute ethanol to release unbound sugars. Ethanol was added at the concentration of 20 mL ethanol/g dried substrate, and the sample was mixed and incubated at room temperature for approximately 90 min. Samples were centrifuged to allow excess ethanol to be removed, and the remainder was evaporated through for 3 d. Once this process was complete, the final mass of substrate was recorded. Psyllium did not undergo digestion as it is 98% dietary fiber.

Gas production from the 3 fibers was measured using single-stage anaerobic colon models (20). In brief, per 125 mL vessel, 0.5 g predigested wheat bran, predigested nopal, or psyllium were mixed with 76 mL of media, as described by Williams et al. (20), and kept anaerobic under a constant stream of $CO_2$. Once sealed, bottles were injected with 5 mL of a vitamin and buffer solution and 1 mL of the reducing solution (20) and prewarmed overnight at 37°C.

Fecal samples were obtained from 5 healthy individuals who had no history of gastrointestinal disease or antibiotic use in the previous 3 months and who were nonsmokers. Ethical approval for collection of stool samples from healthy people was obtained from the London–Westminster Research Ethics Committee (15/LO/2169). Individual fecal samples were diluted in prereduced PBS (10% wt/vol) and strained to remove particulates. Each fiber substrate was fermented in triplicate per volunteer fecal sample. Each vessel was inoculated with 3 mL of slurry by injection and incubated at 37°C for 10 d. Gas production was measured at regular intervals using a pressure transducer (Omega USB-H transducer, Omega Engineering) and syringe. At each time point, the pressure in the bottle was recorded with the transducer and the volume was measured by removing gas with a syringe to bring the pressure in the bottle to atmospheric pressure. Data are reported as cumulative gas volume produced

during fermentation, averaged from 5 volunteers and measured in triplicate per fiber type, a total of 15 fermentation studies per fiber.

### Human MRI study

The human MRI study was a single-center, randomized, 3-treatment crossover study of the effects of wheat bran, nopal, and psyllium on SBWC, colonic volume, and water content of the chyme in the ascending colon assessed by MRI and on exhaled breath hydrogen concentration. The study followed the principles of Good Clinical Practice in accordance with the Declaration of Helsinki and was approved by the University of Nottingham Medical School Ethics Committee (51-1707). The study was completed between September 2017 and March 2018 and prospectively registered on www.clinicaltrials.gov as NCT03263065. There were no changes to the protocol or endpoints throughout the study.

### Participants

Healthy volunteers were recruited by poster advertisement on University of Nottingham campuses and gave written informed consent. Participants were eligible for inclusion if they were ≥18 y old and were able to give informed consent. The exclusion criteria were pregnancy, history of pre-existing gastrointestinal disorder including irritable bowel syndrome, previous intestinal resection, any serious medical condition, contraindications to MRI scanning, and inability to stop medications known to alter intestinal motility. All assessed subjects completed the study protocol (see **Supplementary Figure 1**).

### Test fibers and controlled diet

The wheat bran, nopal, and psyllium consumed in the study were identical to those used in the in vitro fermentation, except that the wheat bran and nopal did not undergo predigestion. All fibers were stored in a sealed container in a cool, dry, and dark environment. Doses were standardized to provide approximately 7.5 g of total fiber per dose, so participants received 20.6 g wheat bran, 14.8 g nopal, and 8.4 g psyllium per dose (see Table 1 for nutritional composition). The preweighed test fiber was mixed with 300 mL of water and taken with breakfast and lunch the day before the study visit and then again at the research center on the day of the study visit (therefore 3 doses in total over a 24-h period). Participants consumed the 3 fibers in random order, with study days separated by at least 6 d to ensure adequate washout.

The order of fiber consumption was determined by random sequence generated using the online program www.randomization.com. The researchers were not blinded to the order of fiber allocation as they prepared the supplement and water mix on the day. Although participants were not informed about the order of fiber allocation, the differing appearance, taste, and texture of the fiber supplement meant that the participants could not be formally blinded to the fiber consumed that day. However, all study MRI and other data were link-anonymized via a study identifier, and MRI analysis was done blinded to the intervention.

While consuming the fiber supplements (i.e., the day before and the day of the study visit), participants were instructed to avoid caffeine, alcohol, and strenuous exercise and were provided with a standardized controlled diet (see **Supplementary Table 1**) that was low in fermentable carbohydrates [low FODMAP diet, known to reduce the symptoms of bloating (21)] and otherwise low in fiber. This aimed to reduce the intra- and inter-individual variability in colonic fermentation due to background diet and effects on gastrointestinal motility.

### Protocol

On the day prior to the study day, the allocated test fiber was provided at 2 meals (breakfast and lunch). All food was provided as low-fiber, low-FODMAP meals (see Supplementary Methods), including a supervised and standardized breakfast and lunch, and a standardized dinner was provided for participants to consume in the evening at home. Participants arrived the following morning at the Sir Peter Mansfield Imaging Centre at the University of Nottingham after an overnight fast and verbally confirmed compliance with dietary restrictions. MRI safety questionnaires were completed with the radiographer. Participants underwent a fasted MRI scan (see Supplementary Methods for details) and measurement of breath hydrogen by exhaling into a gas analyzer (GastroCH4eck). Participants then consumed the same meal and fiber supplement as was taken for lunch the previous day. MRI scans were performed immediately after the meal and then hourly for 4 h with hydrogen breath tests every half hour (see **Figure 1** for study schematic).

Abdominal MRI was performed on a 3.0 T Philips Achieva scanner (Best) using a parallel imaging SENSE 16-element torso coil. Images were acquired with an expiration breath-hold between 13 and 24 seconds, with participants spending approximately 15 min inside the magnet at any one time. MRI parameters included SBWC, colonic volume, and T1 of the chyme in the ascending colon (T1AC). T1 is the time constant for the water hydrogen protons to return to their equilibrium state following radiofrequency excitation. More watery chyme has a longer T1 relaxation time, and the T1 of the descending colon has been recently shown to correlate with stool water content (4).

The primary outcome was the T1AC 4-h postmeal ingestion, measured by MRI. Secondary outcomes included the fasting T1AC and change in small bowel water content, colonic volume, and breath hydrogen over the same time period (0–4 h). We also compared fasting values to our normal range for T1AC and colonic volumes. There were no changes to the prespecified endpoints during the course of the study.

### Statistical considerations

#### *Sample size determination.*

Our previous studies of psyllium showed a mean ± SD increase in T1AC of 0.35 ± 0.42 s (unpublished data on file) after therapeutic doses of psyllium, which is a mild laxative, and this increase represents a minimal clinically significant difference. Using the PS Power and Sample Size Calculations program, version 3.0.43 with a false discovery rate of 0.05 and power of

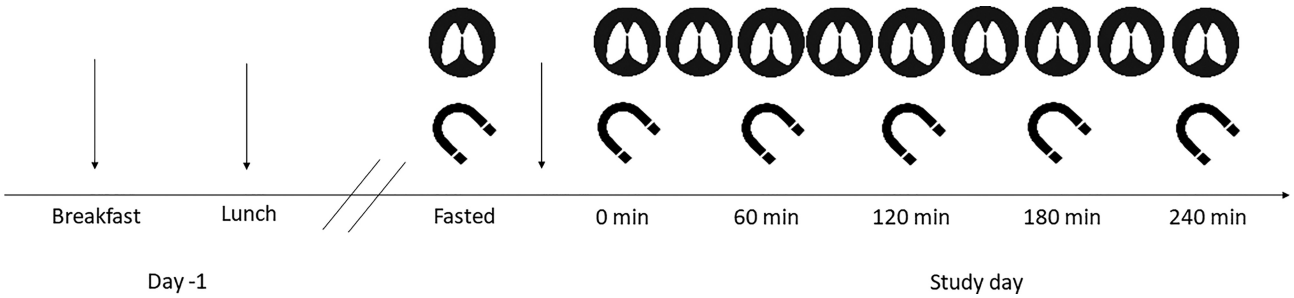


**FIGURE 1** Schematic of events during the human MRI study. MRI scans are represented by , hydrogen breath tests by and test meal ingestion by ↓. Test meals comprised 7.5 g total fiber with a low fiber, low FODMAP meal. Each scan day was separated by a washout period of at least 6 d. FODMAP, fermentable oligo-, di-, mono-saccharides and polyols.

80% we calculated that we would need 13 subjects in order to demonstrate such a difference.

### *Statistical analysis.*

Symmetrical data are presented as means ± SDs and nonsymmetrical data as median (IQR). Differences are represented as mean (95% confidence intervals)All statistical analyses were performed using Graphpad Prism version 8.2.1 for Windows (GraphPad Software). Repeated measures 1-way ANOVA followed by Tukey's multiple comparisons test was performed for AUC volume over time for in vitro gas production of and comparison of time to onset of T1AC, SBWC, and total colonic volumes. Equal variance was not assumed, the Geisser-Greenhouse correction was used, and normality of the distributions was assessed with the D'Agostino–Pearson test. Friedman's test followed by Dunn's multiple comparisons test was used to assess nonsymmetrical breath hydrogen data at 4 h. We have assessed multiple MRI endpoints but have not corrected the *P* values for this. While we can be confident that our primary outcome result is not due to chance, the secondary endpoints must be confirmed in further studies. The onset of fermentation was assessed from the inflection point of the volume versus time plot.

## Results

### In vitro fermentation study

AUC total gas production over 48 h was significantly different between fibers (1-way ANOVA $F = 9.07$, $P = 0.01$), with a significantly greater AUC for wheat bran than psyllium [mean (95% CI) difference: 370.4 (76.8, 664.0) mL/h, $P = 0.02$] but not nopal [mean (95% CI) difference: 164 (−117.6, 446.4) mL/h, $P = 0.2$; see **Figure 2**]. The time to gas production onset was significantly longer for psyllium than wheat bran and nopal [mean (95% CI) differences: 8.4 (2.9, 13.9), $P = 0.004$, and 10.1 (4.6, 15.6) h, $P = 0.001$, respectively].

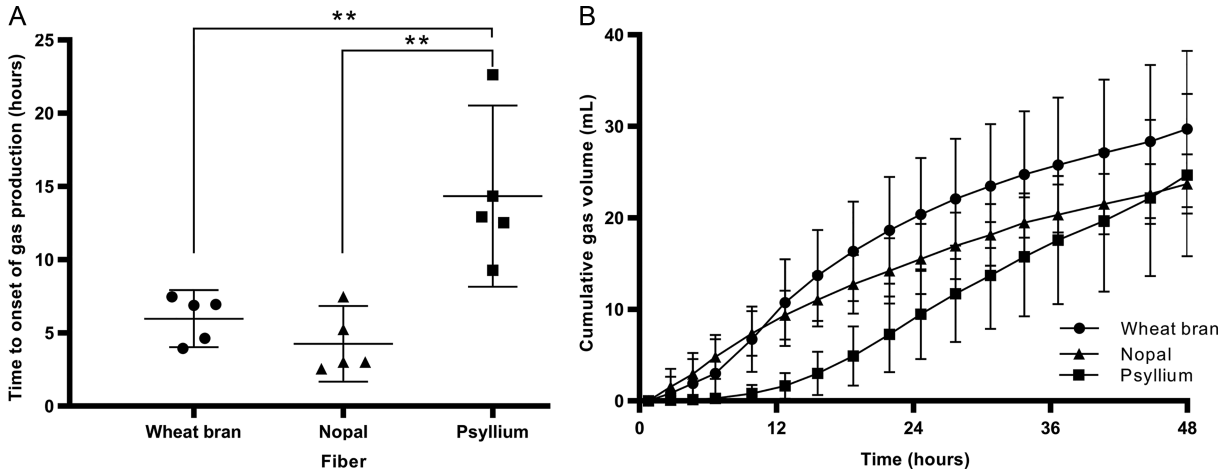


**FIGURE 2** Data are presented as means and 95% CIs, $n = 5$ (in triplicate). In vitro onset of gas production (in hours) when combined with the study fibers, demonstrating significantly longer onset time (defined by the inflection point in the time compared with volume curve) for psyllium than wheat bran, 14 ± 5 h compared with 6 ± 2 h, $P = 0.0031$, and nopal (4 ± 2), $P = 0.0011$ (A). In vitro stool sample gas production when combined with the predigested fibers over 48 h AUCs were significantly different between fibers ($F = 9.07$, $P = 0.0109$), with a significantly greater AUC for wheat bran compared with psyllium, mean (95% CI) difference: 370.4 (76.8, 664.0) mL/h, $P = 0.02$, but not nopal, mean (95% CI) difference: 164 (−117.6, 446.4) mL/h, $P = 0.2$ (B).

**TABLE 2** T1AC of participants, fasted and 4 h postprandially, indicating a more watery colonic chyme for psyllium than nopal and wheat bran after ingestion[1]

| | T1AC (s) | |
|---|---|---|
| Fiber | Fasting | 4 h after meal and fiber |
| Wheat bran | 0.98 ± 0.19 | 0.82 ± 0.18 |
| Nopal | 0.97 ± 0.16 | 0.92 ± 0.16 |
| Psyllium | 0.99 ± 0.17 | 1.26 ± 0.29[2] |

[1]Values are means ± SDs. Repeated-measures 1-way ANOVA shows a significant difference between the fibers 4 h after meal ingestion ($n = 14$, $F = 23.2$), $P < 0.0001$. T1AC, T1 of the ascending colon.

[2]Tukey's multiple comparisons demonstrated a significantly longer T1 for psyllium than wheat bran and nopal, $P < 0.005$.

## Human MRI study

Fourteen participants completed the human MRI study [64% female, median (IQR) age 20 (20–22) y with BMI median (IQR) 22.8 (21.1–25.8)]. All participants consumed the allocated fibers with no adverse effects. Due to equipment failure, 11 complete data sets were available for analysis for SBWC and for breath hydrogen (see Supplementary Figure 1).

## Primary outcome

As **Table 2** and **Figure 3** show, fasting values of T1AC were similar for the 3 fibers, despite participants receiving 2 doses the previous day. However, over the study day T1AC rose significantly with psyllium but not wheat bran or nopal so that the differences were greatest at the end of the study day. T1AC at 4 h showed a significant difference between the fibers (1-way ANOVA $F = 23.2$, $P < 0.0001$) and Tukey's multiple comparisons showed a significant T1 increase for psyllium compared with both wheat bran and nopal [mean (95% CI) difference 0.439 (0.207, 0.672) s, $P = 0.0007$, and 0.338 (0.17, 0.505) s, $P = 0.0004$, respectively.]

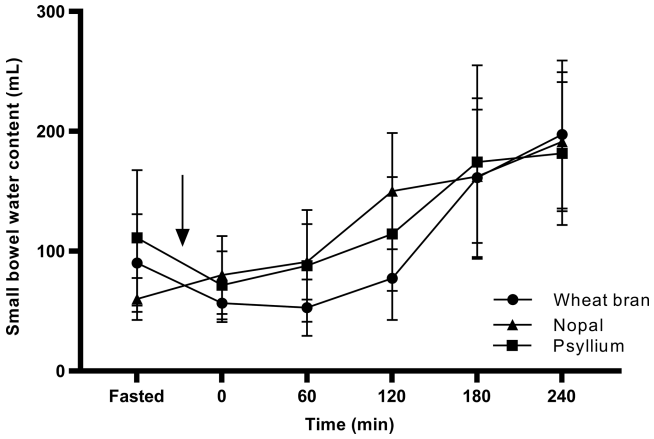


**FIGURE 4** Time course of SBWC (mean, 95% CI) following fiber ingestion on the MR imaging day ($n = 11$). AUC analysis demonstrated a significant difference between fibers, $P = 0.02$; with nopal stimulating significantly more small bowel water than wheat bran, mean (95% CI) difference: 7.1 (0.6, 13.8) L/min, $P = 0.03$. Ingestion of the test meal is designated by ↓. SBWC, small bowel water content.

## Secondary outcomes

### *Fasting T1AC.*

Fiber prefeeding for 24 h of resulted in ≥75% of fasting T1AC values lying above the 90th centile of the normal range, with no significant differences between the 3 fibers (repeated measures 1-way ANOVA $F = 0.05$, $P = 0.93$, see Figure 3B).

### *Small bowel water content.*

There was a significant increase in SBWC for all fibers from fasting to 4 h (see **Figure 4**). AUC analysis demonstrated a significant difference between fibers (repeated measures 1-way ANOVA $F = 4.8$, $P = 0.02$), with nopal stimulating significantly more small bowel water than wheat bran [mean (95% CI) difference 7.1 (0.6, 13.8) L/min, $P = 0.03$].

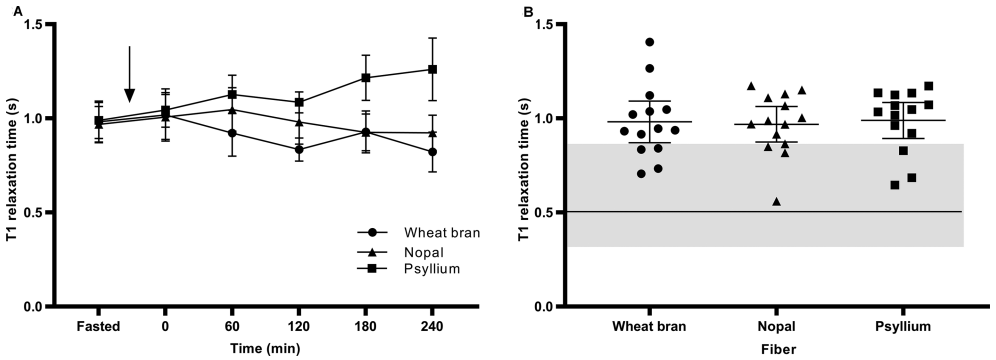


**FIGURE 3** Time course of T1AC (mean, 95% CI) following fiber ingestion on the MR imaging day ($n = 14$); 4 h after ingestion there was a significant difference between the fibers, $P < 0.0001$, and Tukey's multiple comparisons showed a significant T1 increase for psyllium, corresponding to a more watery chyme, compared with both wheat bran and nopal, mean (95% CI) difference 0.439 (0.207, 0.672) s, $P = 0.0007$, and 0.338 (0.17, 0.505) s, $P = 0.0004$, respectively. Ingestion of the test meal is designated by ↓ (A). Fasting T1AC (mean, 95% CI) after 24 h of fiber prefeeding ($n = 14$), demonstrating ≥75% of values lying above the 90th centile of the normal range with no significant differences between the 3 fibers ($P = 0.93$). Normal values for T1AC after an 8-h fasting period have previously been obtained from 29 healthy volunteers from previous studies, published (22) and unpublished, on the same 3.0 T Philips Achieva MRI scanner, and are shown as the median and 10th–90th centiles (B). T1AC, T1 of the ascending colon.

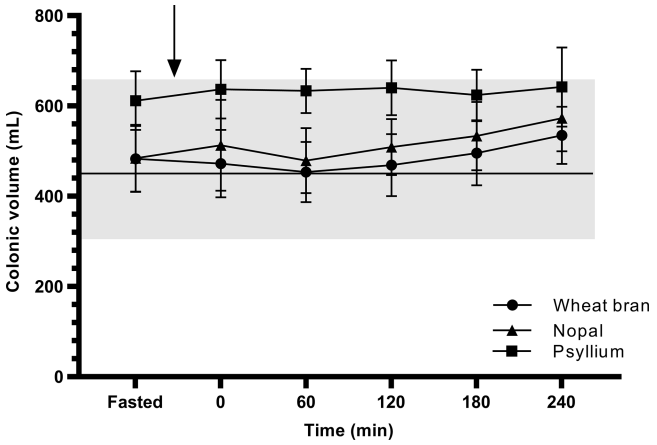


**FIGURE 5** Time course of total colonic volumes (mean, 95% CI) following fiber ingestion on the MR imaging day ($n = 14$). AUC for the study duration was significantly different, $P < 0.0001$; the volumes for psyllium were greater than those for nopal, mean (95% CI) difference: 36.0 (24.1, 47.8) L/min, $P < 0.0001$, and wheat bran, 45.8 (31.1, 60.4) L/min, $P < 0.0001$, with no difference between nopal and wheat bran. Normal colonic volumes after an 8-h fasting period (mean ± SD) have been obtained from 34 healthy volunteers from a previous study (23) on a 1.5T Philips Achieva MRI scanner and are demonstrated in grey. Ingestion of the test meal is designated by ↓.

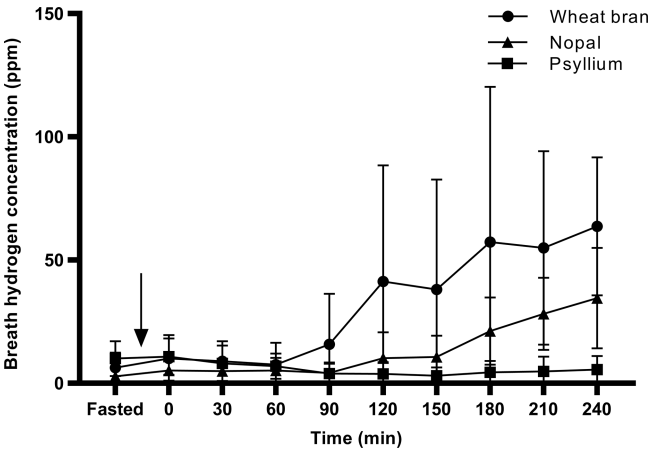


**FIGURE 6** Time course of breath hydrogen concentration (mean, 95% CI) following fiber ingestion on the MR imaging day ($n = 10$). After 4 h there was a significant difference between the fibers ($P < 0.0001$); breath hydrogen concentration was significantly higher for both wheat bran and nopal compared with psyllium, mean ± SD difference: 56.1 ± 42.8 ppm, $P = 0.0003$, and 32.3 ± 32.4 ppm, $P = 0.04$, respectively, with no difference between wheat bran and nopal. Ingestion of the test meal is designated by ↓.

### *Colonic volume.*

There were significant differences in the fasting colonic volume between fibers after 24 h of prefeeding (repeated measures 1-way ANOVA $F = 20.5$, $P < 0.0001$); participants prefed with psyllium for 24 h had larger fasting total colonic volumes than both nopal [mean (95% CI) difference 128 (71, 185) mL, $P = 0.0001$] and wheat bran [mean (95% CI) difference 129 (53, 205) mL, $P = 0.002$], with no significant difference between nopal and wheat bran. The AUC for the study duration was significantly different ($F = 40$, $P < 0.0001$); psyllium was greater than nopal [mean (95% CI) difference 36.0 (24.1, 47.8) L/min, $P < 0.0001$] and wheat bran [mean (95% CI) difference 45.8 (31.1, 60.4) L/min, $P < 0.0001$], with no difference between nopal and wheat bran (**Figure 5**).

### Breath hydrogen

Fasting breath hydrogen concentrations were not different; however, after 4 h there was a significant difference between the fibers (Friedman's test, $P < 0.0001$). Breath hydrogen concentration was significantly higher for both wheat bran and nopal compared with psyllium (mean differences: 56.1 ± 42.8 ppm, $P = 0.0003$; and 32.3 ± 32.4 ppm, $P = 0.04$, respectively), with no difference between wheat bran and nopal (**Figure 6**).

## Discussion

The laxative effects of the many and various dietary fibers is well recognized but the individual underlying mechanisms have until recently been unclear. Our study utilized 3 very different fibers and shows that all 3 increase colonic water but by different mechanisms. We confirmed the results from our previous study (4) by showing that psyllium is highly effective in acutely trapping water in the small bowel, which rose steadily in the hours after meal ingestion. It should be noted that without fiber supplementation postprandial SBWC between 180–240 min has been shown to average <100 mL (9), whereas in our study it was 178 mL. The in vitro fermentation studies, showing more rapid fermentation of wheat bran and nopal fiber compared with psyllium, match the earlier and more substantial rise in breath hydrogen seen in vivo. Psyllium is only very slowly fermented, which ensures a prolonged "trapping" of water in the colon. The larger colonic volume after psyllium may also reflect a lack of stimulation of colonic motility compared with the other more fermentable fibers. Psyllium would be predicted to produce fewer SCFA, which are known to stimulate 5-HT release from colonic enteroendocrine cells (24), a process that is known to have a prokinetic effect.

Previous publications have shown that postprandial SBWC is strongly influenced by nutrient absorption and osmotic factors. Glucose (9), bread, or rice meals (25) lead to rapid falls in SBWC over the next 1–2 h as glucose and sodium are actively absorbed by small-intestinal transporters with accompanying passive water absorption. Psyllium slows nutrient absorption (26), possibly by increasing viscosity and reducing the mixing which is essential to allow access of luminal contents to the mucosa. Psyllium potently retains water within its complex network, making the water unavailable for absorption. We have shown in the current study that repeated doses of psyllium lead to an increase in colonic volumes and water content as assessed by the MRI parameter T1. The rise in colonic volume may be due to the fact that, unlike wheat bran (27), psyllium does not significantly accelerate whole colonic transit (4, 28), a feature that would reduce colonic volumes by increasing the frequency of defecation.

Wheat bran, by contrast, being less viscous, cannot trap water like psyllium but does, however, produce a similar increase in SBWC. Previous studies (8) have shown that 15 g of both wheat bran and plastic particles caused similar acceleration of meal transit, suggesting that this transit is driven by mechanical rather than chemical stimulation of the mucosa. Earlier studies have shown that stroking intestinal mucosa activates neurogenic secretion (29), which could accelerate transit. More recently,

it has been shown that a subpopulation of enterochromaffin cells express mechanosensitive piezo-2 ion channels (30). Enterochromaffin cells are stimulated by shear forces to release serotonin (31), which stimulates crypt secretions. This may be an important mechanism to dilute luminal contents if they become too viscous and threaten to cause intestinal obstruction (9, 32). Another potential mechanism through which particulate fiber can increase postprandial water is inhibiting amylase digestion of starch in a rice meal through adsorption of amylase to the particle surface (33). Wheat bran is also known to increase fecal bacterial mass, a factor that accounts for a substantial proportion of stool mass (34) and may thus exert a laxative effect. Given that both viscous and particulate fiber increase small bowel water content but by different mechanisms, it is perhaps not unexpected that nopal, which contains both mucilage and particulate fiber, had a greater effect on small bowel water than either psyllium or wheat bran alone.

Toward the second half of the 4-h study, small bowel contents would be expected to start entering the ascending colon and hence increase T1AC. At this point, psyllium seemed to be most effective. This finding may reflect the slow breakdown and fermentation rate of psyllium's highly branched structure, demonstrated by the delayed onset in vitro of gas production in our fermentation study and the virtual absence of a rise in breath hydrogen in the MRI study. The undegraded psyllium will continue to trap water, making it unavailable for absorption and hence increasing colonic volumes. Wheat bran, with a particulate structure, a less-branched arabinoxylan, and a small amount of fructans, is more rapidly fermented in vitro and shows a clear rise in breath hydrogen in vivo. This rapid fermentation would increase bacterial mass and produce SCFA that stimulate sodium and water absorption (35). Fermentation products may also stimulate motility and accelerate transit and thereby reducing colonic volumes, though direct evidence of the impact of SCFA on motility is contradictory, with some studies suggesting stimulation (36) and others not (37). More recently it has been shown that SCFA stimulate colonic motility in rats via the release of 5-HT (38) that stimulates colonic peristalsis. Studies using germ-free mice and mice colonized with human microbiota have shown that the presence of colonic microbiota increases serotonin synthesis and release by enteroendocrine cells (39), providing a mechanism whereby dietary fiber modulation of colonic microbiota could accelerate transit.

We assessed fasting values of T1AC after 2 doses of fiber the day before to understand the longer-term effects. Despite the greater rise in T1AC soon (2–4 h) after acute ingestion of psyllium compared with the other fibers, by 24 h, the effects of T1AC were similar, with all 3 fibers increasing T1AC to the upper limit of our normal range. While both wheat bran and nopal increase small bowel water, this does not appear to increase colon volumes in the short term. This may be because, as shown by the greater breath hydrogen response, the more readily fermentable components of both wheat bran and nopal are rapidly fermented and absorbed, thus limiting any increase in colonic volume. Alternatively, this finding may reflect greater stimulation of motility by wheat bran and nopal, which would also reduce colonic volumes, but demonstrating this effect would require further studies. Previous studies have shown a link between increased colonic volumes and the sense of distension and bloating (40) that may limit the use of psyllium in constipated patients.

## Conclusion

In summary, both viscous and particulate fiber stimulate an increase in postprandial small bowel water content and an increase in colonic T1. Possible mechanisms include inhibiting absorption of both water and nutrients or stimulating intestinal secretion. Psyllium appears more effective in trapping small bowel water, and the slow metabolism of psyllium means that colon volumes remain increased over at ≥24 h. Nopal and wheat bran, despite not being viscous, also increase small bowel water but are rapidly fermented in the colon and do not lead to colonic distension. Whether this will translate into greater efficacy and tolerability in the treatment of constipation remains to be seen when clinical trials, currently under way, are completed.

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