

The use of a wireless motility device (SmartPill®) for the measurement of gastrointestinal transit time after a dietary fibre intervention

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Abstract

Historically, measurement of gastrointestinal transit time has required collection and X-raying of faecal samples for up to 7 d after swallowing radio-opaque markers; a tedious, labour-intensive technique for both subjects and investigators. Recently, a wireless motility capsule (SmartPill®), which uses gut pH, pressure and temperature to measure transit time, has been developed. This device, however, has not been validated with dietary interventions. Therefore, we conducted a controlled cross-over trial to determine whether the device could detect a significant difference in transit time after ten healthy subjects (five men and five women) consumed 9 g of wheat bran (WB) or an equal volume, low-fibre control for 3 d. A paired *t* test was used to determine differences in transit times. Colonic transit time decreased by 10.8 (SD 6.6) h ($P=0.006$) on the WB treatment. Whole-gut transit time also decreased by 8.9 (SD 5.4) h ($P=0.02$) after the consumption of WB. Gastric emptying time and small-bowel transit time did not differ between treatments. Despite encouraging results, the present study had several limitations including short duration, lack of randomisation and unusable data due to delayed gastric emptying of the capsule. With minimal participant burden, the SmartPill technology appears to be a potentially useful tool for assessing transit time after a dietary intervention. This technology could be considered for digestive studies with novel fibres and other ingredients that are promoted for gut health.

Key words: Dietary fibre: Wheat bran: Colonic transit time: Wireless motility device

Traditional methods for determining gastrointestinal transit time are cumbersome and labour-intensive both for subjects and investigators. The two most commonly used methods are radio-opaque markers (ROM) and scintigraphy. ROM can be used to determine gastric emptying time (GET), colonic transit time (CTT) or whole-gut transit time (WGTT). Measurement of GET or CTT is achieved through the use of abdominal X-rays, whereas WGTT is measured by collecting and X-raying faecal samples for 5–7 d^(1,2). The ROM WGTT methodology involves a large amount of participant burden and requires exceptional compliance because missing stool samples affect results.

Measurement of GET or CTT by scintigraphy requires consumption of radioactive isotopes followed by frequent X-rays of the participant's abdomen⁽³⁾. Scintigraphy has been used in a number of studies, but results of these studies have been mired by no universally accepted method⁽³⁾. Recently, a multi-centre study designed to standardise the

GET scintigraphic method has been able to find similar gastric retention between each centre⁽⁴⁾. Whole-gut scintigraphy can be used to determine GET, small-bowel transit time (SBTT), CTT and WGTT; however, this method requires the subject to undergo frequent abdominal scans and requires a 3 d stay in an inpatient facility⁽⁵⁾. Another disadvantage of scintigraphic methods is that the results must be examined by a gastroenterologist and are subject to interpretation errors⁽³⁾. Nonetheless, these methodologies are acceptable measures of gastrointestinal transit time.

Recently, a wireless motility device called the SmartPill was developed that simplifies the measurement of GET, SBTT, CTT and WGTT. It measures pH, pressure and temperature in real time and transmits this information wirelessly to a receiver worn on the participant's clothing. These data can be used to determine GET, SBTT, CTT and WGTT. Previous studies have compared gastrointestinal transit time using the SmartPill technology with ROM and scintigraphy^(6–10). These studies

Abbreviations: CTT, colonic transit time; GET, gastric emptying time; ROM, radio-opaque marker; SBTT, small-bowel transit time; WB, wheat bran; WGTT, whole-gut transit time.

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have shown favourable correlations between scintigraphy gastric retention and SmartPill GET at 120 min (r 0.95; $P < 0.01$) and 240 min (r 0.70; $P = 0.024$)^(9,10). Also, WGTT was found to be similar between scintigraphy and SmartPill⁽⁹⁾. Furthermore, favourable correlations between ROM and SmartPill were found for CTT and WGTT in healthy and constipated individuals⁽⁷⁾. Overall, this series of studies shows favourable comparisons between SmartPill and traditional methodologies for measuring gastrointestinal transit time.

Dietary fibre has long been noted for its laxative effect. Wheat bran (WB) is widely regarded as the gold standard for laxation, with many studies supporting its effects^(11–15). WB is partially fermented in the large intestine by the intestinal microflora, which decreases gastrointestinal transit time and increases both faecal wet and dry weight in a dose-dependent fashion^(14,16–18). In addition, coarse WB is more effective than fine-ground WB; therefore, it was chosen for the present study^(19–21). The present study is the first to examine the SmartPill technology in combination with a dietary intervention, and the purpose was to determine whether it is able to detect a significant difference in gastrointestinal transit time when feeding healthy subjects a dose of WB previously shown to decrease WGTT using ROM^(11,21,22).

Methods

Ten healthy subjects (five men and five women) aged 18–65 years (mean 24 years) were recruited from the University of Minnesota community by flyers posted on campus to participate in a controlled cross-over trial. The subjects were screened via telephone to determine eligibility. Exclusion criteria included contraindicated conditions for the SmartPill: dysphasia, gastric bezoars, strictures, fistulas, bowel obstructions, diverticulitis, previous gastrointestinal surgery, implanted electromechanical medical devices and medications shown to influence gastrointestinal transit time. Exclusion criteria also included diagnosis of CVD, diabetes, cancer, Crohn's disease, ulcerative colitis, irritable bowel disease, BMI of < 18.5 or > 30 kg/m², pregnant or lactating, irregular menstrual cycle, smoke or chew tobacco, high dietary fibre intake, consumption of probiotics or fibre supplements, vegetarian diet, taken antibiotics less than 3 months earlier and food allergies to the test products.

Participants consumed one serving of either the control or WB cereal for 3 d before each study visit. During this time, the subjects also completed one 24 h food diary before each treatment; this was done in order to quantify usual dietary habits, specifically dietary fibre intake. Participants were not blinded to the treatment due to the obvious appearance and texture of WB in the test cereal. Gastrointestinal transit time was measured on two separate occasions, with participants completing the control treatment first followed by the WB treatment. Women participated in the study during the follicular phase of their menstrual cycles. The subjects were normal weight with an average BMI of 26 (range 22–29.5) kg/m².

On the morning of each study visit, the subjects arrived at the University of Minnesota campus after fasting for 12 h. The subjects consumed a modified breakfast of earlier

SmartPill studies, which included 120 g of Egg Beaters[®] (ConAgra Foods, Inc., Omaha, NE, USA), and either a low-fibre (control) hot cereal or a high-fibre (test) hot cereal with 250 ml of water^(6–10). The control cereal consisted of 52 g of Cream of Wheat[®] (B&G Foods, Inc., Parsippany, NJ, USA) providing 2 g of dietary fibre. The test cereal consisted of 30 g of Cream of Wheat[®] and 22 g of coarse-ground red WB (SunOpta, Inc., Brampton, ON, Canada) that provided an additional 9 g of dietary fibre, a dose previously shown to significantly decrease WGTT using ROM^(11–13). Additional details on the nutrient composition of the breakfast components can be found in Table 1. The subjects were given 10 min to consume the breakfast and immediately afterwards swallowed the SmartPill capsule. The SmartPill was calibrated before swallowing as described elsewhere⁽⁹⁾. After swallowing the capsule, the subjects were asked to refrain from eating for 6 h in order to determine GET. After 6 h, the subjects were allowed to resume their usual diets.

In addition, the subjects were instructed to complete a gastrointestinal tolerance survey. Tolerance was assessed by the subjects by recording flatulence, bloating, abdominal cramps, stomach noises, nausea, diarrhoea and constipation on a ten-point scale with 0 being no symptom and 10 being the worst imaginable symptom, which was adapted from a previous study⁽²³⁾. Also, the cereals were consumed once a day in the morning until the capsule had passed. When the subjects had bowel movements, they were instructed to let the stool remain in the toilet for 5 min; this time allowed the SmartPill receiver to detect a temperature decrease and to indicate whether or not the capsule had passed. If the indicator light appeared after the bowel movement, the subjects knew the capsule had passed; if it did not appear, they knew to continue wearing the receiver. The subjects were also asked to visually confirm whether the SmartPill had passed. The subjects were allowed to participate in their normal activities with the exception of strenuous physical activity.

The SmartPill is a cylindrical capsule with dimensions of 26.8 mm long by 11.7 mm in diameter, which measures pH, pressure and temperature in real time; the data are wirelessly transmitted to a data receiver that is attached to the participant's clothing. The pH sensor has a range of 0.5–9 units with an accuracy of ± 0.5 units. The temperature sensor has a range of 25–49°C with an accuracy of $\pm 1^\circ\text{C}$. MotiliGI software (SmartPill, Inc., Buffalo, NY, USA) uses changes in pH

Table 1. Composition of the breakfast components

	Control cereal (Cream of Wheat [®])	Test cereal (30 g Cream of Wheat [®] + 22 g red WB)	Egg Beaters [®]
Serving (g)	52	52	120
Energy (kJ)	795	645	251
Carbohydrate (g)	40	39	2
Dietary fibre (g)	2	11	0
Protein (g)	4	6	12
Fat (g)	0	1	0

WB, wheat bran.

and temperature to determine GET, SBTT, CTT and WGTT. GET is defined as the time between capsule ingestion and an abrupt rise in pH above gastric baseline pH. This rise in pH corresponds with the transition from the acidic stomach to the alkaline duodenum⁽²⁴⁾. SBTT is the time between duodenum entry and caecum entry⁽⁷⁻⁹⁾. Caecal entry is defined as the first sustained drop in pH of more than 1 unit that occurs at least 30 min after entry into the small bowel⁽⁷⁾. The decrease in pH is thought to be the result of fermentation of the digestive residue by the large intestine^(7,24,25). CTT is the difference between entry into the caecum and exit from the body, which is indicated by an abrupt decrease in temperature⁽⁷⁾. WGTT is the time between the SmartPill ingestion and exit from the body.

The 24 h food diaries were analysed using the dietary analysis program, Nutrition Data System for Research (version 2007; Nutrition Coordinating Center, Minneapolis, MN, USA). Nutrition Data System for Research provided detailed nutrient information including total energy, carbohydrate, fat, protein and fibre intake.

Data were analysed using the Statistical Analysis Systems statistical software package version 9.1 (SAS Institute, Cary, NC, USA). A two-sided paired *t* test procedure was used to determine differences in transit times, dietary intake and tolerance. Tolerance scores were analysed individually and as a sum of all categories. Statistical significance was achieved at $P < 0.05$. Two subjects had extremely long GET between 18.5 and 20.4 h. These GET are not physiologically plausible since such a delayed GET would probably result in tolerance issues, which were not reported in the tolerance questionnaire. The reason for the delayed GET is consumption of a meal while the SmartPill is still in the stomach. The meal will return the body to the fed state, which inhibits the migrating motor complex that expels the SmartPill out of the stomach⁽⁶⁾. For this reason, any extreme GET value is not accurate and should not be used in statistical analysis⁽¹⁰⁾. Additionally, extremely delayed GET would skew WGTT, since WGTT is the sum of GET, SBTT and CTT; therefore, these observations were omitted from statistical analysis as well.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the University of Minnesota Institutional Review Board Human Subjects Committee. Written informed consent was obtained from all subjects.

Results

All ten subjects completed both treatments and successfully passed the SmartPill. Transit times are shown in Table 2. The WB treatment significantly decreased CTT ($P = 0.006$) and WGTT ($P = 0.02$) compared with the control; however, it had no effect on GET ($P = 0.2$) or SBTT ($P = 0.8$). Men and women had similar GET ($P = 0.08$), SBTT ($P = 0.5$), CTT ($P = 0.09$) and WGTT ($P = 0.09$).

Mean dietary intake, from a 24 h food diary before each treatment and not including the test cereals, is shown in

Table 2. Transit times
(Mean values and standard deviations)

	<i>n</i>	Control		WB		Difference	
		Mean	SD	Mean	SD	Mean	<i>P</i>
GET (h)	8*	3.2	0.8	3.8	1.6	0.6	0.23
SBTT (h)	10	4.9	1.8	4.8	1.6	-0.1	0.83
CTT (h)	10	23.1	12.2	12.7	13.8	-10.8	0.006
WGTT (h)	8*	31.4	5.8	22.5	14.6	-8.9	0.02

WB, wheat bran; GET, gastric emptying time; SBTT, small-bowel transit time; CTT, colonic transit time; WGTT, whole-gut transit time.

* Two subjects were excluded from the analysis of GET and WGTT due to extremely long GET.

Table 3. There was no difference in background total fibre intake between the control and WB treatments ($P = 0.6$). In contrast, women had a significantly higher total fibre intake ($P = 0.03$), but did not have different transit times compared with men when averaged across treatments. Total energy and the percentage of energy from carbohydrate and fat were similar between treatments; however, protein intake was higher ($P = 0.009$) on the WB treatment.

Adherence to the cereal supplement was excellent with no adverse events after consuming the cereals or swallowing the SmartPill. No differences in gastrointestinal tolerance between the control and WB treatments were observed, with the exception of a significantly higher mean flatulence score with the WB treatment ($P = 0.03$).

Discussion

Recent SmartPill studies have been conducted primarily for the purposes of comparing gastrointestinal transit times between the wireless device and other methods such as ROM or scintigraphy^(6,7,9,10). Additional studies have used the SmartPill for evaluating transit times in individuals with various motility disorders including gastroparesis and constipation^(7,8,26,27). Our study was the first to use the SmartPill technology for the determination of gastrointestinal transit time with a dietary fibre intervention.

Our results show that the SmartPill technology is able to detect a significant decrease in CTT and WGTT after a 9 g WB intervention. We conclude that the decrease in WGTT

Table 3. Dietary intake from a 24 h food diary before each treatment
(Mean values and standard deviations)

	Control		WB		<i>P</i>
	Mean	SD	Mean	SD	
Total energy (kJ)	7967	715	6979	450	0.13
Soluble fibre (g)	5	1.4	4	1.3	0.3
Insoluble fibre (g)	11	6.1	9	6.2	0.4
Total fibre (g)	15	7	14	7.5	0.4
Carbohydrate (%)	43.4	11.8	42.4	7.9	0.7
Protein (%)	15.2	3.8	19.2	5	0.009
Fat (%)	38.6	14.5	36.0	8.8	0.4

WB, wheat bran.

(−8.9 h) is due to decreased CTT (−10.8 h) since GET (+0.6 h) and SBTT (−0.1 h) did not change. A previous study using the SmartPill found a strong significant correlation (r 0.92; P < 0.0001) between WGTT and CTT, thus supporting our conclusion⁽⁸⁾. The results of the present study compare favourably with previous studies that examined WGTT with a WB intervention using ROM^(11–15). These results were not confounded by usual dietary fibre intake since it was not different between treatments. The ability to detect significant decreases in CTT and WGTT suggests that the SmartPill technology may be useful in dietary intervention studies.

The SmartPill did not detect differences in GET or SBTT after 9 g of a coarse-ground WB fibre intervention in the present study. Our results are inconsistent with an earlier study showing that 15 g of WB fibre with a particle size of 2–5 mm significantly delays GET and reduces SBTT⁽²⁸⁾. However, this study had an older population than our study (60 *v.* 25 years), higher WB dose (15 *v.* 9 g), and used scintigraphy. In this study, GET was defined as 50% gastric retention of the radio-labelled meal, while SBTT was defined as the difference between GET and 50% colonic arrival of the radio-labelled meal; therefore, due to different definitions of GET and SBTT, direct comparisons may not be appropriate. Furthermore, scintigraphic meals may exit the stomach before the non-digestible SmartPill capsule because such foreign body objects empty from the stomach with the phase III migrating motor complex, which is initiated in the fasting state⁽⁶⁾. The standard SmartPill protocol allows subjects to resume eating 6 h after swallowing the capsule; therefore, if the capsule had not passed before the subsequent meal, it would skew GET by returning the subject to the fed state. Delayed GET was observed in 26% of subjects in previous studies; therefore, the 20% extremely delayed GET (between 18.5 and 20.4 h) observed in the present study is consistent with previous findings using the SmartPill technology^(8,10). In an effort to reduce the chance of experiencing this problem, future studies should consider increasing the length of time between breakfast and a subsequent meal, or should require subjects to monitor the pH readings on the data receiver before eating is resumed. As a result, direct comparisons of GET between the scintigraphy and the SmartPill may not be appropriate. Nonetheless, our results suggest that WB does not affect GET or SBTT; however, fibres with different physiochemical properties such as highly viscous fibre may have an influence on GET or SBTT.

Earlier research examined the effect of sex on transit time and yielded conflicting results^(29–36). Generally, women have longer transit times compared with men^(29–34). Additional research has examined the influence of the phase of the menstrual cycle on transit time. The majority of research has found no difference between the follicular phase and the luteal phase^(32,36–39); however, some do⁽⁴⁰⁾. A previous study using the SmartPill found that women have significantly longer CTT compared with men; however, that study did not control for the menstrual cycle⁽⁷⁾. Due to the inconsistencies in the literature, we decided to control for the menstrual cycle in the present study by having women complete both study visits during the follicular phase. Since the subjects

consumed the low-fibre control treatment first, there was no need for a washout period before starting the WB treatment. In contrast to the previous findings, we did not observe any differences in transit times between men and women.

Since the present study is the first of its kind, the treatment breakfasts were not provided in a randomised fashion; the subjects always consumed the control treatment before the WB treatment. We wanted to evaluate how the SmartPill would pass through the gastrointestinal tract when the subjects consumed a low-fibre hot cereal before providing the high-fibre cereal because the low-fibre cereal was nutritionally equivalent to the bread and jam breakfast used in all previously described SmartPill studies. The lack of randomisation may be a limitation of the present study; however, laxation is a relatively involuntary measure, so the effects are probably minimal. Another limitation is the relatively small sample size of the present study; however, the ability to detect significant differences in CTT (P = 0.006) with a relatively small sample size demonstrates the sensitivity of this new technology and strength of the treatment effect. WB was chosen due to its well-established laxative effects; however, future studies conducted with less laxative fibres may not yield significant results with a similar sample size. Therefore, careful consideration of sample size must be taken in all subsequent studies using the SmartPill technology.

While the SmartPill is promising for diet intervention studies due to its ease of use and sensitivity, there are certain limitations that may have an impact on future studies. The SmartPill capsule is relatively large at 13 mm × 26 mm, making it not suitable for people with swallowing problems or other gastrointestinal conditions. In addition, the large size of the SmartPill may cause it to get ‘hung up’ in the stomachs of certain individuals; this produces an artificially long GET and WGTT. Also, the data receiver must be kept near the subject at all times and failure to do so results in missing data. The battery life of the data receiver is only 5 d, and after the battery runs low, the data are no longer considered reliable. The data receiver is generally worn on the belt and is therefore sensitive to physical damage. If the data receiver cannot confirm the exit of the SmartPill due to technical problems, an abdominal X-ray is required to confirm the exit of the SmartPill, adding to participant burden and study costs. Lastly, the cost of the capsules is high (approximately \$600.00 per capsule) and may hinder their future use.

Overall, the capacity to non-invasively measure GET, SBTT, CTT and WGTT gives the SmartPill an advantage over both ROM and scintigraphy. Using the SmartPill eliminates the need for the subjects to consume radio-labelled meals, have repeated X-rays and collect faecal samples. This is undeniably less burdensome for both subjects and investigators; however, the technology is costly, and some of the data may not be useable for certain subjects (i.e. the GET may be artificially prolonged if the capsule is retained in the stomach). In conclusion, we were able to detect significant differences in CTT and WGTT after a dietary fibre intervention; this makes the SmartPill technology a potentially useful new tool for measuring gastrointestinal transit in nutrition interventions.

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