

Physiological Responses of Men and Women to Barley and Oat Extracts (Nu-trimX). I. Breath Hydrogen, Methane, and Gastrointestinal Symptoms

Judith Hallfrisch^{1,2} and Kay M. Behall¹

ABSTRACT

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While consumption of diets high in fiber is perceived to result in undesirable gastrointestinal symptoms, the fermentation of undigested carbohydrate in the large intestine may, in fact, have beneficial health effects. In this study, we compared the effects of oats, barley, and their extracts with a glucose control for 24 hr on breath hydrogen and methane production as a marker of colonic fermentation and also assessed gastrointestinal symptoms. Nine men and 11 women (35–57 yr) consumed 1 g/kg of body weight of carbohydrate as glucose or 0.66 g/kg of body weight sugar and 0.33 g/kg of body weight as oat bran, barley flour, oat extract, or barley extract (Nu-trimX) in a Latin square design. Expired alveolar

breath samples were collected after instruction at fasting, 2, 4, 5, 6, 7, 8, 9, 10, and 24 hr after consumption of the test meals. All test meals increased breath hydrogen and methane (both $P < 0.0001$). Hydrogen, but not methane, responses to barley, oats, and extracts of each were higher (barley > oats, $P < 0.05$) than responses to glucose ($P < 0.0001$). Reported gastrointestinal symptoms were not related to specific test meals. Oats and barley, as well as their extracts, can be consumed in greater amounts by Americans to increase soluble fiber and lower fat intake, and thus lower risk factors for chronic disease.

Research examining the dietary habits of Paleolithic man suggests that his fiber intake exceeded 100 g/day (Eaton et al 1996). Present day consumption in the United States is approximately one-fifth of this amount. Most health organizations and government agencies involved in the health of various populations recommend an increase in dietary fiber (Gallaher and Schneeman 1996; USDA and Health and Human Services 1996; FAO/WHO 1998). Recent National Cholesterol Education Program guidelines (US Department of Health and Human Services et al 2001) specifically recommend increase of viscous fibers as one of the lifestyle strategies to reduce low-density lipoprotein (LDL) cholesterol. Health claims for oats suggest that oats are effective in lowering blood cholesterol levels. (FDA 2001). However, the recommended effective level of consumption is four servings per day each containing at least 0.75 g of soluble fiber. Oats and barley are both high in soluble fibers (Lee et al 1992) and are effective in lowering blood cholesterol in humans (McIntosh et al 1995).

Regardless of the beneficial health effects of a high fiber diet, the perception is that consumption results in undesirable gastrointestinal side effects (Rosado et al 1991). Diarrhea and flatulence may occur (Pittler and Ernst 2001). Expiration of breath hydrogen is a measure of the fermentation in the large intestine of carbohydrate that has escaped digestion in the small intestine (Perman 1991; Olesen et al 1994). Hydrogen production has been positively associated with reduced risk for colon cancer (Neale 1988). One mechanism proposed for lowering cholesterol by foods containing high levels of soluble fiber is that fermentation in the large intestine, indicated by increases in breath hydrogen, results in production of short chain fatty acids, specifically propionate, which is inversely related to serum cholesterol (Wolever et al 1996). This property of fiber-containing foods has also been suggested as a protective mechanism against development of colorectal cancer (McIntosh 1993; Ahmed et al 2000).

A new procedure to produce fat substitutes from a variety of grains was developed by Inglett (2000). Nu-trimX is an acronym for NUtrient Technical Research Involving Metabolism-bran eXtracted.

This process extracts solubilized β -glucans from oats or barley endosperm while reducing the cellulose components (Inglett 2001). This wet-extraction process removed the bran fiber components from cooked grains and processed flours and resulted in hydrocolloids that can be used as substitutes for cream and other high fat components, resulting in substantial reductions of fat, saturated fat, and energy intake, as well as substantial increases in soluble fiber intake. The barley cultivar Prowashonupana has a high level of soluble fiber; it contains $\approx 2\times$ the amount of soluble fiber found in the oat bran used.

This study constitutes the first controlled human trial using these extracts and it was designed to compare responses of oat and barley extracts with the corresponding parent grain to determine whether the extracts retain the biological effects of the oats or barley.

MATERIALS AND METHODS

The study was approved by the Institutional Review Boards of the United States Department of Agriculture and Johns Hopkins University School of Public Health. Medical evaluation and blood and urine screen were conducted by Karen Herrmann, M.D., Johns Hopkins School of Public Health. Subjects were excluded for abnormal fasting glucose, hyperlipidemia, urinary tract infections, and the use of medications affecting glucose metabolism. Eleven nondiabetic men and 11 nondiabetic women were selected for the study (Table I). Men and women initially were paired for age and body mass index (BMI). Two of the men did not complete the study. One moved out of state and the other had difficulty consuming all of the test meals. The final group of men was slightly older and heavier, but mean age and BMI of the remaining men and the women were similar.

The five experimental periods each consisted of identical three-day menus of controlled feeding containing 30% fat, 15% protein, and 55% carbohydrate (Table II). Subjects consumed breakfast at the Human Study Facility and picked up lunch and dinner each day for home consumption. Subjects were required to consume all foods presented and no others, with the exception of noncaloric beverages, salt, and pepper, the intakes of which were recorded. On the third day of controlled feeding, a tolerance test (1 g of carbohydrate/kg of body weight) as glucose or 0.66 g/kg of body weight pudding (predominantly sucrose) + 0.33 g/kg of body weight oat bran, barley flour, oat extract, or barley extract (Nu-trimX) in a Latin square design (Tables III, IV). Order of treatment was randomly assigned to pairs of age and BMI-matched subjects (one man, one woman). There was an 11-day washout between periods. Water was

¹ Beltsville Human Nutrition Research Center, USDA, ARS, Diet and Human Performance Laboratory, Beltsville, MD 20705.

² Corresponding author. E-mail: hallfrj@ba.ars.usda.gov. Phone: 301-504-9061. Fax: 301-504-9098.

added to the barley and oat treatments to equalize the volume consumed during the glucose tolerance test. Breath samples were collected at fasting, 2, 4, 5, 6, 7, 8, 9, 10, and 24 hr after consumption of the treatment. Breakfast was consumed at 3 hr, lunch was consumed after the breath collection at 6 hr, and dinner was consumed after the collection at 10 hr. Subjects were shown the proper procedure for collection of breath samples, as well as given written directions on each collection day. Alveolar air samples were obtained after subjects exhaled through a mouthpiece connected to a dual-bag system by a three-way valve. The menus contained no known hydrogen producers from lactose in milk products. Subjects were not permitted to exercise during collection. Breath samples were analyzed for hydrogen, methane, and carbon dioxide by gas chromatography (MicroLyzer model SC, Quintron Instrument, Milwaukee, WI). The instrument was calibrated with a reference standard containing measured amounts of hydrogen, methane, and carbon dioxide. Duplicate readings were taken for each sample. Breath hydrogen and methane readings were corrected for carbon dioxide content. Data for breath samples containing carbon dioxide levels below those predicted for alveolar air were excluded from analyses.

Corrected breath hydrogen and methane data were analyzed using the mixed procedure analysis of variance (ANOVA) using SAS v. 6.12. A value of $P < 0.05$ was considered to be statistically significant. Mean separation of significant terms was conducted using least significant difference range test.

RESULTS

Only data from the nine men and 11 women who completed the study are included in the analyses. Breath hydrogen responses were affected by time ($P < 0.0001$), test meal ($P < 0.0001$), and the interactions of test meal \times time ($P = 0.0003$), and sex \times time ($P = 0.02$) (Fig. 1). Time mean levels of breath hydrogen increased significantly over fasting levels and remained so even at 24 hr after

TABLE I
Initial Characteristics of Subjects^a

	Men	Women	Final Men
<i>n</i>	11	11	9
Age	44.6 \pm 5.1	44.2 \pm 6.8	45.8 \pm 4.7
Weight	81.0 \pm 11.2	67.7 \pm 9.9 ^b	83.5 \pm 9.5
Body mass index	25.0 \pm 2.9	25.0 \pm 3.5	25.6 \pm 2.5

^a Values are mean \pm standard deviation.

^b Different from corresponding value for men ($P < 0.05$).

TABLE II
Menu for Test Day

Breakfast	Lunch	Dinner
Rice cereal	Turkey breast	Roast beef
Lactose-free milk	Lettuce	Gravy
Orange juice	Tomato	Mashed potato
Blueberry muffin	Mustard	Corn muffin, margarine
Margarine	Roll	Tossed salad
	Celery sticks	French dressing
	Ranch dressing	Canned cherries
	Chocolate chip cookies	Lactose-free milk

TABLE III
Nutrient Value of Test Foods (g/100 g, dry weight)

	Oats		Barley	
	Bran	Nu-trimX	Flour	Nu-trimX
Carbohydrate	66	80	70	74
Crude fiber	3	0	1	0
β -Glucans	9	11	19	14
Protein	18	10	16	12
Fat	7	1	4	5
Moisture	6	7	9	7
Ash	3	2	2	2

the test meal. Test meal breath hydrogen averages for grains and extracts were all higher than hydrogen average for glucose. Averages for barley test meals were significantly higher than averages for corresponding oat test meals. Values at fasting, 2 hr, 10 hr, and 24 hr were similar for all test meals. At 4 hr, breath hydrogen was significantly elevated above glucose response level by barley and by oats and by both extracts. Peak values occurred at 5 hr for barley extract, at 6 hr for oat extract, and at 7 hr for both grains. Mean responses of men and women to the different meals did not differ; their patterns of response were different (sex \times time, $P < 0.02$). Mean time levels of hydrogen were significantly higher at 5 and 6 hr for women than corresponding mean values for men (data not shown).

Breath methane levels were affected only by time. Mean time levels were significantly elevated above fasting level at 6 and 7 hr and methane levels at 24 hr were significantly higher than all other time mean levels. There were no other significant differences in methane response levels (Fig. 2).

The number of subjects that reported gastrointestinal symptoms after consumption of the test meals was not significantly related to the content of the test meal, nor were symptoms more frequent than before the test meals were given (Table V). Subjects were asked if they experienced hunger, satiety, diarrhea, constipation, fla-

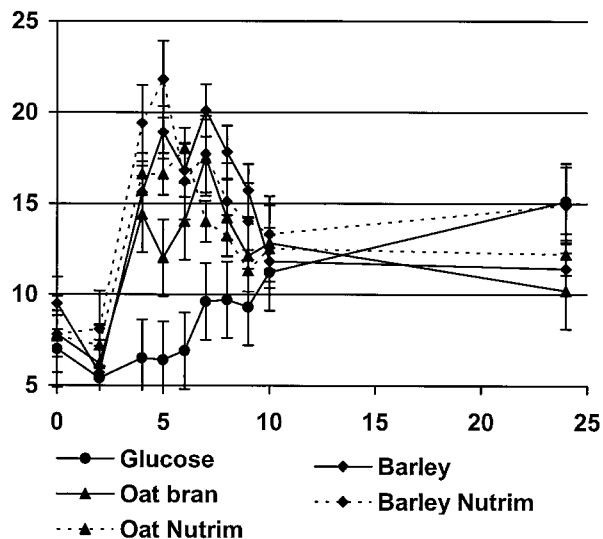


Fig. 1. Corrected breath hydrogen responses of men and women to barley and oats ($n = 20$). Mixed procedure ANOVA: time and test meal ($P < 0.0001$); time \times test meal ($P = 0.0003$); sex \times time ($P = 0.02$). Standard error of the means: test meal (1.5); time (1.7); test meal \times time (2.1); sex \times time (2.3). Breath hydrogen mean values for women were higher at 5 and 6 hr than for corresponding values for men (data not shown).

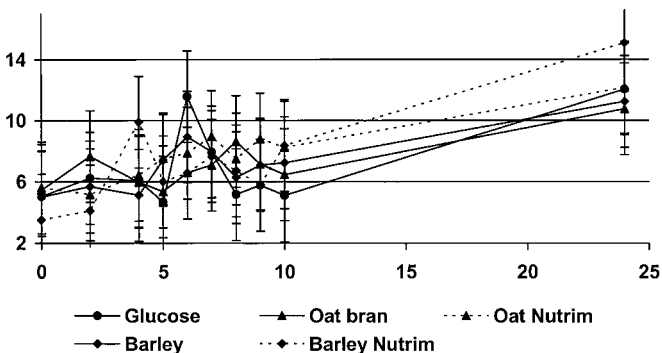


Fig. 2. Corrected breath methane responses to barley and oats ($n = 20$). Mixed procedure ANOVA: time ($P < 0.0001$); test meal, time \times test meal, sex, sex \times time (all not significant). Standard error of the means: time = 1.1. Mean values after 6 and 7 hr significantly higher than value at 0 hr ($P < 0.05$). Mean value at 24 hr higher than all other mean time values.

tulence, or nausea on each of the controlled feeding days, including the test meal day. Only symptoms on the test meal day which differed from symptoms reported on the previous days were considered to be related to the specific test meal. Hunger and feeling too full were reported more frequently before than after consumption of the test meals: hunger was reported before 30 times and after 17 times; too full was reported before 30 times and after 8 times. Diarrhea, constipation, and nausea were reported rarely before or after test meals (0–2 times). Flatulence was the most commonly reported symptom. However, there were more reports of flatulence before consumption of the test meals than after for glucose and oat bran. For oat extract, five subjects reported flatulence both before and after consumption of the test meals; for both barley meals there were two more reports of flatulence after consumption of the test meal than before. There was no relationship between the test meal and the reported symptoms or to the level of hydrogen or methane.

DISCUSSION

Numerous studies have examined the effects of various fiber-containing foods on various physiological responses, but few have studied the effects of barley in humans. Fermentation of undigested carbohydrate to short chain fatty acids has been proposed as the protective mechanism against colon cancer in those who consume diets high in fiber (Ahmed et al 2000), although a recent report questions the role of fiber in colon cancer prevention (Fuchs et al 1999). Due to the previous contention that greater particle size of fiber-containing foods was more beneficial, Jenkins et al (1999) tested wheat particle sizes and found that not only did consumption of the more finely ground wheat bran result in higher fecal butyrate production than the low fiber control, consumption resulted in greater butyrate production than consumption of the larger particle size wheat bran. Our previous study (Hallfrisch and Behall 1999)

comparing breath hydrogen responses to breads made with white or whole wheat flour, found that though breath hydrogen responses to glucose were lower than responses to white or whole wheat bread, neither the amount of fiber nor the particle size of the flour significantly affected the average hydrogen response in middle-aged men and women. However, the range of particle size was not as great in our study as for the study by Jenkins et al. Our study was an acute study, measuring response after only one meal, while the study by Jenkins et al measured chronic effects of consumption.

Neither amount of fiber or hydrogen response correlated with reported gastrointestinal symptoms as reported here. Symptoms were reported more frequently before consumption of the test meals for glucose, oat bran, and barley extract than after the test meals. Menus contained recommended levels of dietary fiber (≈ 25 g/day) which may have exceeded subjects' usual intakes. French and Read (1994) showed that soluble fibers, in combination with a high fat meal, not only slowed gastric emptying but also slowed absorption, prolonging contact of nutrients with intestinal chemoreceptors, which was instrumental in prolonging satiety and intestinal feedback. Wisker et al (1992) suggested that the addition of barley to human diets reduces available energy. Lupton et al (1993) found that barley bran flour decreased intestinal transit time, thus reducing the time available for intestinal absorption. Viscosity of the soluble fibers has also been suggested to be responsible for reductions in the absorption of carbohydrate (Jenkins et al 1978; Wood et al 1989; Braaten et al 1991), and may result in increased amounts of undigested carbohydrate reaching the colon, thus increasing hydrogen and short chain fatty acid production (Botham et al 1997; Danielson et al 1997).

Methane is produced as a metabolite of hydrogen in the large intestine in those people who have intestinal bacteria capable of metabolizing hydrogen in a ratio of four hydrogen molecules/molecule of methane produced (Stephen 1994). Although $\approx 50\%$ of adults are reported to be methane producers, in this study seven of the nine men and eight of the 11 women had methane levels 10 ppm

TABLE IV
Macronutrient Content of Test Meals for Men and Women (g)

	Glucose	Oat Bran	Oat Extract	Barley Flour	Barley Extract
Men					
Carbohydrate	83.9 \pm 3.1	83.9 \pm 3.1	83.9 \pm 3.1	83.9 \pm 3.1	83.9 \pm 3.1
Sucrose	0	44.9 \pm 1.7	44.9 \pm 1.7	44.9 \pm 1.7	44.9 \pm 1.7
Soluble fiber	0	3.7 \pm 0.1	3.8 \pm 0.1	7.4 \pm 0.3	5.2 \pm 0.2
Fat	0	3.3 \pm 0.1	0.7 \pm 0.03	2.0 \pm 0.1	2.2 \pm 0.1
Protein	0	7.4 \pm 0.3	3.4 \pm 0.1	6.3 \pm 0.2	4.4 \pm 0.2
Women					
Carbohydrate	67.4 \pm 3.1	67.4 \pm 3.1	67.4 \pm 3.1	67.4 \pm 3.1	67.4 \pm 3.1
Sucrose	0	36.3 \pm 1.7	36.3 \pm 1.7	36.3 \pm 1.7	36.3 \pm 1.7
Soluble fiber	0	3.1 \pm 0.1	3.1 \pm 0.1	6.1 \pm 0.3	4.3 \pm 0.2
Fat	0	2.7 \pm 0.1	0.6 \pm 0.03	1.6 \pm 0.1	1.8 \pm 0.1
Protein	0	6.1 \pm 0.3	2.8 \pm 0.1	5.1 \pm 0.2	3.6 \pm 0.2

TABLE V
Number of Gastrointestinal Symptoms Reported Before and After Consumption of Oats and Barley (men and women combined)^a

Symptom	Test	Glucose	Oat Bran	Oat Extract	Barley	Barley Extract
Hunger	B	9	5	4	6	6
	A	3	4	4	4	2
Too full	B	7	6	7	5	5
	A	1	3	1	2	1
Diarrhea	B	1	0	1	1	1
	A	2	1	1	2	1
Constipation	B	0	0	0	0	1
	A	0	1	0	0	0
Flatulence	B	6	8	5	7	2
	A	3	5	5	9	4
Nausea	B	1	0	0	1	0
	A	0	0	0	0	0

^a Values represent the number of subjects reporting symptoms on either of the two days preceding the test meal (first number B) and the number of subjects reporting symptoms the day of the specific test meal (second number A). There was no consistent effect of any of the test meals on gastrointestinal symptoms reported.

above fasting levels. In our last study only eight of 26 subjects had levels this high (Hallfrisch and Behall 1999).

Reports of gastrointestinal symptoms did not appear to be related to the level of methane production. Van Munster (1994) found as did we (Hallfrisch and Behall 1999), that methane producers also produced higher levels of hydrogen in response to high amylose maize and wheat bread. Because the number of subjects in the present study who did not produce methane was so small, it was not possible to divide the groups in this study as we did in the previous study.

CONCLUSIONS

Our study demonstrates that consumption of oat and barley foods, whether from bran, flour, or extracted components, increases hydrogen production. Consumption of this amount of these extracts of barley and oats did not produce any untoward gastrointestinal symptoms. If hydrogen production is inversely related to risk for colon cancer, then these results indicate that both barley and oats and their extracts increase hydrogen production significantly and would suggest a protective effect. The amount given in these test meals supplied a range of $\approx 2\text{--}5$ g of soluble fiber. This amount of soluble fiber has been reported in numerous studies to have beneficial effects on other physiological variables. These results demonstrate that hydrocolloids extracted from oats and barley are fermentable, like whole grains. The use of oat and barley extracts may be a more manageable means of increasing soluble fiber intake in the American diet with the associated health benefits. Long-term studies are necessary to determine whether these extracts retain the beneficial effects on blood lipids seen with other oat and barley foods.

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