Effects of Cereal and Vegetable Fiber Feeding on Potential Risk Factors for Colon Cancer[1]

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Abstract

The effects of two doses of cereal fiber and vegetable fiber on mean transit time, stool weight, fecal pH and fecal bile acids were examined in 34 healthy volunteers. Subjects consumed five diets in random order for 23 days each, consisting of a fiber-free liquid diet and quick breads containing 0 g added dietary fiber, 10 g fiber as wheat bran (WB), 30 g fiber as WB, 10 g fiber as vegetable fiber (VF), and 30 g fiber as VF. Fecal wet and dry weights were 43% and 19% higher, respectively, on WB as compared to VF ($P < 0.0001$). Fecal pH was lower on WB than on VF ($P < 0.0001$) and decreased with increased fiber intake ($P < 0.005$). Transit time was 36% faster with WB than with VF ($P < 0.0001$). There was no VF dose effect on transit time, but transit time was 23% faster on 30 g WB than on 10 g WB ($P = 0.04$). Total bile acid concentrations decreased with increased fiber dose ($P < 0.0001$) but were not significantly different between WB and VF. Daily total bile acid excretion was 14% lower on VF compared to WB ($P = 0.01$). There was no VF dose effect on total bile acid excretion, but excretion was 13% lower on 30 g WB than on 10 g WB ($P = 0.04$). These findings are consistent with the capacity of fiber to alter potential risk factors for colon cancer but do not explain differences in epidemiological data between vegetable and cereal intake.

Introduction

Ecologic studies describe a negative relationship between apparent national fiber consumption and a risk of colon cancer (1–3). However, case-control studies produce mixed results. Some show fiber and fiber-containing foods to be protective (4, 5); some indicate that they may increase risk (6, 7); and others indicate no relationship (8–9). Many more studies support a lower risk of colon cancer with vegetable fiber than with cereal fiber, and the most consistent association is between vegetable consumption and a reduced risk of colon cancer (10–12).

Certain aspects of bowel function have been associated with an increased risk of colon cancer, including increased (*i.e.*, more alkaline) fecal pH (13), increased fecal bile acid concentrations (14), and decreased fecal bulk (15). Dietary fibers tend to increase fecal bulk and lower fecal pH, thus potentially reducing the risk of colon carcinogenesis (16). It is unclear whether the association between a reduced risk of colon cancer and vegetable consumption as compared to cereal consumption is due to fiber differences, other compositional differences between vegetables and cereals, or other risk factors that associate differently with vegetable fiber *versus* cereal intake. Cereal fiber is generally not as fermentable as vegetable fiber and therefore does not lower colonic pH to the same extent as vegetable fiber (17). Although both fiber sources may cause fecal bulking, thereby diluting bile acids, vegetable fibers may impede the production of secondary bile acids because of the fermentation-induced lowering of colonic pH (17). Specific anticarcinogens in vegetables may contribute further to the capacity of vegetables to lower risk (12, 18).

The purpose of this study was to examine the effects of vegetable and cereal fiber at two doses on potential risk factors for colon cancer. Transit time, fecal bulk and hydration, fecal pH, and fecal bile acid excretion were measured in healthy subjects consuming well-controlled, defined diets.

Materials and Methods

Subjects. Healthy nonsmokers with no antibiotic use within 6 months prior to the start of the study were screened for their ability to complete a rigorous schedule of defined diet ingestion and extensive biological sample collection. The design of the study was approved by the Committee on Use of Human Subjects in Research at the University of Minnesota, and informed written consent was obtained from all subjects prior to the start of the study.

Thirty-four subjects (16 women, 18 men) finished all aspects of the study. The subjects were between the ages of 19 and 50 years (mean ± SE, 27.1 ± 2.1 years). Forty-six subjects were initially randomized into the study, but due to the commitment required, nine people dropped out during the first week on the defined diet, and three more dropped out after two diet periods.

Diets. The subjects consumed a fiber-free liquid nutrition supplement (Resource, Sandoz Nutrition, Minneapolis, MN) and deionized water as the basal diet. During all test diet periods, a quick bread, prepared in our laboratory, was the vehicle used to deliver the fibers. Five test

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Table 1 Nutrient content of fiber-containing quick breads

	0 g fiber	10 g WB	30 g WB	10 g VF	30 g VF
Total dietary fiber (g)	2.1 ± 0.2[a]	11.0 ± 0.5	29.9 ± 1.5	14.3 ± 0.4	36.5 ± 0.3
Insoluble fiber (g)	1.4 ± 0.1	9.8 ± 0.6	27.1 ± 1.0	11.7 ± 0.1	31.4 ± 0.4
Soluble fiber (g)	0.7 ± 0.2	1.2 ± 0.2	2.8 ± 0.6	2.6 ± 0.5	5.1 ± 0.3

[a] Mean ± SD of five bread samples, one from each feeding period.

diets were consumed in assigned random order: (*a*) 0 g added fiber; (*b*) 10 g dietary fiber as WB[3]; (c) 30 g dietary fiber as WB; (*d*) 10 g dietary fiber as mixed VF; (e) 30 g dietary fiber as mixed VF. Fiber sources included white wheat bran (American Association of Cereal Chemists, St. Paul, MN), pea fiber (Fiberich Food Products, Inc., Minneapolis, MN), soy polysaccharide (Protein Technologies International, St. Louis, MO), and orange pectin (Hercules, Wilmington, DE). The vegetable fiber in the 10-g VF and 30-g VF breads was a mixture of pea fiber, soy polysaccharide, and pectin, added at levels of 62, 33, and 5% by weight of total fiber, respectively. The quick breads were formulated based on the total dietary fiber content of the products as reported by the companies. A quick bread without added fiber, which was isocaloric compared to the fiber-containing breads, was provided during the 0-g fiber treatment. Total dietary fiber and soluble and insoluble fiber content (Table 1) were determined in our laboratory by a modification of the current Association of Official Analytical Chemists method, which allows determination of the soluble and insoluble fiber fractions (19).

Sample Collection and Analysis. Prior to the start of the feeding study, baseline data were collected for 9 days while subjects consumed their habitual, SS diets. Radiopaque pellets were swallowed on days 1 and 7 to measure transit time, and all stools were individually collected and frozen at −20°C. Five-day diet records were analyzed for nutrient and dietary fiber content using a computerized nutrient analysis program (Nutritionist III; N-Squared Computing, Silverton, OR).

Each test diet was consumed for 3 weeks. There was a washout period of at least 10 days between each diet period, during which subjects resumed their habitual diets. Subjects consumed the test diets for 1 week before any samples were collected. Radiopaque pellets were swallowed on days 7, 13, and 19 of each period, and all stools were individually collected and frozen as during the baseline period. A 5-point scale was used to rate stool consistency; 1, watery, liquid that can be poured; 2, soft, pudding-like; 3, moist, soft stool that retains shape; 4, dry, stool remains firm; 5, dry pellets, small hard discrete boli. Stool consistency ratings were assigned to all fecal samples by the subjects and confirmed by the investigators.

All fecal samples were weighed, and mean stool weight and mean daily fecal weight were determined. The samples were X-rayed for pellet content, and the time needed to pass each pellet was averaged to calculate mean transit time (20). The appearance of the first pellets swallowed on days 13 and 19 was used as the marker for fecal composites. Starting with stools containing pellets swallowed on day 13, all stools up to the appearance of pellets swallowed on day 19 were included in the composite. Composites were homogenized, and fecal pH was measured. Duplicate aliquots of the homogenates were freeze-dried to determine fecal dry weight and moisture content. Bile acid content of dry fecal samples was determined as described by Subbiah (21). Bile acid results have been previously presented in an article on serum lipids and fecal bile acid changes (22), which also included sugar beet fiber feeding.

Statistical Analysis. Statistical evaluation of results was done by two-way analysis of variance using the factors of subject and diet. Orthogonal contrasts were used to determine treatment differences of interest. [Orthogonal contrasts are a method of evaluating the contribution of specific diet comparisons contained in the treatment sum of squares of the analysis of variance (23).] Due to the large number of diets and the inappropriateness of making all possible comparisons the following diet comparisons were decided upon *a priori*: (*a*) 0 g fiber *versus* the mean of 10 g WB, 30 g WB, 10 g VF, and 30 g VF; (*b*) 10 g WB *versus* 30 g WB; (c) 10 g VF *versus* 30 g VF; (*d*) the mean of 10 g WB and 30 g WB *versus* the mean of 10 g VF and 30 g VF. When data were available from the self-selected period, the comparison of the SS *versus* the mean of 0 g fiber, 10 g and 30 g WB, and 10 g and 30 g VF was included. These specific contrasts were chosen to compare the effects of fiber type and dose and to compare the effect of fiber to that of a fiber-free control. Unless otherwise indicated, data are presented as least squares means ± least squares SE, a procedure allowing comparison of means when observations are missing (23).

Results

The effects of the fiber diets on bowel function are presented in Table 2. WB and VF feeding significantly lowered transit time ($P < 0.0001$), increased fecal bulk ($P < 0.0001$), and altered stool consistency ($P < 0.0001$) and fecal pH ($P = 0.001$) compared to the fiber-free diet. Only fecal moisture content, measured as percentage of water, did not differ between the fiber-free diet and the four fiber diets ($P = 0.26$). Similarly, baseline data on bowel function obtained during the SS period was significantly different from that for the controlled diets ($P < 0.005$), with transit times and fecal weights for the SS period similar to those for the 30-g WB diets.

The 30-g WB diet had the most pronounced effect on fecal bulk and transit time of all the diets, and for all bowel function parameters measured, 30 g WB was significantly different from 10 g WB ($P < 0.05$). A less pronounced dose effect was observed for VF. Although 30 g VF resulted in significantly greater fecal weights ($P < 0.0001$) and lower pH ($P = 0.001$) compared to 10

[3] The abbreviations used are: WB, wheat bran; VF, vegetable fiber; SS diet, self-selected diet.

Table 2 Bowel function parameters for 34 subjects[a] on SS fiber-free, WB-containing and VF-containing diets

	SS	0 g fiber	10 g WB	30 g WB	10 g VF	30 g VF	P^b
Mean transit time (h)	51 ± 4[c]	81 ± 4	54 ± 4	44 ± 4	68 ± 4	65 ± 4	0.0001
Fecal wet weight (g/day)	149 ± 5	64 ± 5	94 ± 5	170 ± 5	76 ± 5	109 ± 5	0.0001
Fecal dry weight (g/day)	42 ± 1	18 ± 1	26 ± 1	43 ± 1	23 ± 1	35 ± 1	0.0001
Fecal moisture (% water)	70.1 ± 0.5	71.3 ± 0.5	71.2 ± 0.5	74.7 ± 0.5	68.5 ± 0.5	68.0 ± 0.5	0.0001
Stool consistency[d]	3.2 ± 0.1	3.4 ± 0.1	3.1 ± 0.1	2.6 ± 0.1	3.2 ± 0.1	3.0 ± 0.1	0.0001
Stool weight (g/stool)	152 ± 6	118 ± 6	128 ± 6	165 ± 6	125 ± 6	163 ± 6	0.0001
Fecal pH	6.6 ± 0.04	7.9 ± 0.04	7.5 ± 0.04	7.2 ± 0.04	7.7 ± 0.04	7.5 ± 0.04	0.0001

[a] n = 33 for 10 g VF.
[b] P for diet effect.
[c] Least squares mean ± least squares SE.
[d] Based on 5-point subjective rating scale (1 = liquid to 5 = hard boli).

g VF, there was no difference in mean transit time (P = 0.52), fecal moisture content (P = 0.50), or consistency (P = 0.16) between the two doses of VF.

The type of fiber consumed had a significant effect on all parameters except individual stool weight. Transit time was faster, and fecal wet weight and dry weight were higher for WB than for VF ($P < 0.0001$). While consuming WB, subjects produced softer stools (P = 0.008) with a higher fecal water content ($P < 0.0001$) than VF, and fecal pH was lower for the WB diets than for the VF diets ($P < 0.0001$).

Fecal bile acid concentrations (Table 3) and daily fecal bile acid excretion (Table 4) were significantly altered by fiber consumption. Concentrations of all fecal bile acids measured were greater for the 0-g fiber diet than for the four fiber-containing diets ($P < 0.05$). Daily excretion of deoxycholic acid was highest on the 0-g fiber diet (P = 0.002), contributing to greater total bile acid excretion compared to the mean of the four fiber diets (P = 0.03).

Higher doses of WB and VF significantly lowered total bile acid concentrations due to decreased concentrations of the secondary bile acids, lithocholic acid and deoxycholic acid, and the primary bile acid, chenodeoxycholic acid ($P < 0.005$). Although the effects of fiber doses on bile acid concentration were similar for WB and VF, daily bile acid excretion in response to dose varied with fiber type. The two levels of VF (10 g and 30 g) were similarly potent for the daily excretion of all bile acids ($P > 0.1$). However, with WB, deoxycholic acid (P = 0.005) and the miscellaneous bile acids (P = 0.04) were present in significantly lower amounts for 30 g WB as compared to 10 g WB, contributing to a lower total daily bile acid excretion for 30 g WB than for 10 g WB (P = 0.04). Interestingly, 10 g WB but not 10 g VF resulted in a daily bile acid excretion similar to that of the 0-g fiber diet.

Deoxycholic acid (P = 0.02) and chenodeoxycholic acid (P = 0.01) concentrations were significantly lower for the WB diets than for the VF diets. Lower daily excretion of lithocholic acid ($P < 0.0001$) and the miscellaneous bile acids (P = 0.005) contributed to significantly lower daily total bile acid excretion (P = 0.03) for the VF diets than for the WB diets, with total excretion being lowest for the 30-g VF diet.

Discussion

With both WB and VF diets, stools were heavier, transit time was faster, and fecal pH was lower than with the fiber-free control diet. These effects were more marked with the higher fiber doses of both WB and VF, and with the WB as compared to VF. Numerous other studies have reported a significant bulking effect of wheat bran (24–26). Fibers that are more readily fermented by colonic microflora, generally the more soluble fibers, do not contribute as much to water-holding capacity and fecal bulk (27, 28). In our study soluble fiber contents of the WB and VF were similar, with VF providing approximately 16% of total dietary fiber as soluble fiber and WB providing 10% (Table 1). However, WB and the components of the mixed vegetable fiber diet are known to differ in fermentability, with pectin, soy, and pea fibers being more rapidly degraded than WB in an *in vitro* fermentation system (29, 30). This may account, in part, for the differences in fecal weight and transit time between WB and VF. In addition, fiber sources were used in the form provided by the manufacturers, with particle size being larger for the WB than for the VF diets. The white wheat bran was ground to a coarse particle size,

Table 3 Fecal bile acid concentrations for subjects on fiber-free and fiber-containing diets

	0 g fiber (n = 34)	10 g WB (n = 34)	30 g WB (n = 34)	10 g VF (n = 33)[a]	30 g VF (n = 34)	P^b
Lithocholic acid	14.2 ± 0.3[c]	10.0 ± 0.3	5.5 ± 0.3	9.3 ± 0.4	5.7 ± 0.3	0.0001
Deoxycholic acid	14.3 ± 0.4	8.8 ± 0.4	4.4 ± 0.4	9.6 ± 0.5	5.7 ± 0.4	0.0001
Chenodeoxycholic acid	1.4 ± 0.1	0.8 ± 0.1	0.5 ± 0.1	1.0 ± 0.1	0.6 ± 0.1	0.0001
Cholic acid	0.3 ± 0.1	0.2 ± 0.1	0.1 ± 0.1	0.2 ± 0.1	0.1 ± 0.1	0.09
Miscellaneous bile acids	1.8 ± 0.1	1.3 ± 0.1	1.0 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	0.0001
Total bile acids	32.0 ± 0.8	21.1 ± 0.8	11.4 ± 0.8	21.2 ± 0.8	13.0 ± 0.8	0.0001

[a] One subject did not complete the 10-g VF diet.
[b] P for diet effect.
[c] μmol/g dry feces, least squares means ± least squares SE.

Table 4 Daily fecal bile acid excretion for subjects on fiber-free and fiber-containing diets

	0 g fiber (n = 33)[a]	10 g WB (n = 33)	30 g WB (n = 33)	10 g VF (n = 33)	30 g VF (n = 34)	P^b
Lithocholic acid	245 ± 11[c]	269 ± 11	241 ± 11	212 ± 11	198 ± 11	0.0001
Deoxycholic acid	247 ± 11	237 ± 11	190 ± 11	218 ± 11	197 ± 11	0.001
Chenodeoxycholic acid	23 ± 2	20 ± 2	20 ± 2	22 ± 2	21 ± 2	0.59
Cholic acid	5 ± 2	6 ± 2	5 ± 2	4 ± 2	4 ± 2	0.82
Miscellaneous bile acids	30 ± 3	32 ± 3	41 ± 3	24 ± 3	32 ± 3	0.006
Total bile acids	551 ± 23	564 ± 23	497 ± 23	481 ± 23	450 ± 23	0.002

[a] Fecal composites were incomplete for one subject on the 0-g fiber diet, another on 10 g WB, and another on 30 g WB; one subject did not complete the 10-g VF diet.
[b] P for diet effect.
[c] μmol/day, least squares means ± least squares SE.

and the pea fiber, soy polysaccharide, and pectin were provided in powdered form. Fine grinding of fibers has been shown to reduce fecal bulk, lower fecal moisture, and slow intestinal transit (31, 32). Thus, particle size may also account in part for differences between the WB and VF diets.

The doses of 10 g and 30 g of dietary fiber were chosen to provide subjects with intakes similar to the U.S. average (33) (11 g/day) and to the intake recommended by the National Cancer Institute (34) (25–35 g/day). Mean fiber intake on the SS diet (13 g), however, was well below the 30-g level of the WB and VF diets, but transit times, fecal weights, and fecal pH on the SS diet were similar to those on 30 g WB. Evidently other components of a diet besides dietary fiber contribute to colonic function. The structure of the diet itself (35) and food processing may alter the effects of food products on bowel function (36). In addition, some starch, as part of a mixed diet, escapes digestion in the small intestine and is fermented in the large bowel (37), whereas the rice flour used in the fiber breads is well digested, with little residual carbohydrate reaching the colon (38). Clearly, feeding isolated dietary fiber sources as part of a defined diet has effects that are significantly different from those of the actual consumption of fiber-rich foods.

It is not clear why fecal pH was lower with the WB diets than with the VF diets. Lower fecal pH has been observed with the consumption of more highly fermented fibers (26), but the association between fiber intake and fecal pH is not always clear (39, 40). Analysis of colon lumen contents suggests that pH increases from cecum to descending colon with the absorption of short-chain fatty acids and then decreases in the sigmoid/rectal area as additional fermentation occurs (41). If VF is more readily fermented, increased production and absorption of short-chain fatty acids in the proximal bowel may result in little fermentable substrate reaching the sigmoid/rectal area. Slow but continuing fermentation of the generally less fermentable WB throughout the length of the colon may contribute to the lower fecal pH with WB. Unfortunately, fecal pH provides only the final snapshot of a dynamic process.

WB and VF consumption significantly lowered fecal bile acid concentrations in a dose-dependent manner. The decrease in bile acid concentrations is due to increased fecal bulk, which occurred with increased fiber intake. In the rat, bile acids are colon tumor promoters (42) and cause dysplastic changes in colonic mucosa (43). Higher concentrations of bile acids, particularly secondary bile acids, have been correlated with an increased risk for colon cancer (14). Thus, dilution of fecal bile acids by dietary fiber may be protective against colon cancer. Furthermore, lowered fecal pH as a result of fiber fermentation may inhibit the conversion of primary to secondary bile acids by inhibiting bacterial enzyme activities of modifying bacterial populations (44). Several investigators have reported an increase in the chenodeoxycholic acid pool in the bile of humans consuming WB (45, 46). In our study deoxycholic acid and chenodeoxycholic acid concentrations were significantly lower with WB than with VF. However, the reason for the slightly lower deoxycholic acid concentration without a concomitantly higher cholic acid concentration for WB as compared to VF is not clear.

When the effect of fecal bulk on bile acid excretion is factored out by analyzing for daily bile acid excretion, it is interesting to note that the VF diets, which contained more soluble fiber, resulted in lower bile acid excretion than did the WB diets. This difference is due partly to the negligible effect of the 10-g WB diet, which resulted in excretion similar to that of the 0-g fiber diet, and is due to excretion with 30 g WB similar to that with 10 g VF. Studies have shown that a number of fiber sources adsorb bile acids and may increase daily bile acid excretion (47). Increased bile acid excretion has been observed with soluble fibers such as pectin (27, 28) and oatbran (48) and with gel-forming fibers such as guar (49) and psyllium (50). Wheat bran has not shown a consistent effect on daily bile acid excretion, and there are reports of increased (24) and unaltered excretion with wheat bran (51, 52). It appears that the vegetable fiber in this study does not have the bile acid-binding capacity of other, more soluble fibers, and compared to wheat bran it actually decreases bile acid excretion. If, as suggested by *in vitro* fermentation studies, the vegetable fibers are more fermentable, a more acidic cecal pH may inhibit 7-α-dehydroxylase, the enzyme that catalyzes the conversion of primary to secondary bile acids. This might explain the decreased lithocholic acid excretion with vegetable fiber as compared to wheat bran. However, a lower fecal output of the other secondary bile acid, deoxycholic acid, would also be expected, but this was not observed.

In conclusion, consumption of both wheat bran and vegetable fiber produced a physiological profile associated with a lowered risk for colon cancer, *i.e.*, lower fecal pH, lower fecal bile acid concentrations, and increased fecal bulk. Although case-control studies suggest that vegetables may be protective against colon cancer, there was no indication that the vegetable fiber fed to the participants in this study produced a physiological profile that would be any more protective against colon cancer than fiber from wheat bran.

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