Mechanism of Serum Cholesterol Reduction by Oat Bran

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Nine normolipidemic young men consumed a constant diet for 2 mo into which oat bran was incorporated during the second month so that we might test the hypotheses that oats lower serum cholesterol concentrations by decreasing bile acid and fat absorption and increasing bile acid synthesis. Bile acid kinetics were determined by measuring the ^{13}C enrichment of serum cholic and chenodeoxycholic acids. Oat bran consumption decreased serum cholesterol levels ($p < 0.01$) and cholic acid pool size ($p < 0.05$). Deoxycholic acid pool size ($p < 0.01$) and the synthesis and fractional turnover rates of both primary bile acids ($p < 0.05$) increased. Total bile acid pool size did not change. Fecal excretion of total bile acids, the two secondary bile acids and fat increased significantly. The results demonstrate that oat bran lowers serum cholesterol levels in part by altering bile acid metabolism. In addition, the substantial increase in the proportion of the total bile acid pool that was deoxycholic acid is consistent with the hypothesis that oat bran also decreases cholesterol synthesis. (HEPATOLOGY 1994;20:1450-1457.)

Most studies demonstrate a reduction in serum cholesterol levels when oats are consumed, although the magnitude of the change varies with the extent of dietary control, the amount and kind of dietary lipid and the initial serum cholesterol concentrations of the study population (1). Even when controlled diets have been used, responses in fecal bile acid and fat excretion have been variable when oatmeal or oat bran is consumed. Consumption of oatmeal increased fecal fat and bile acid excretion but did not significantly change serum cholesterol levels in normocholesterolemic individuals (2). In contrast, whereas oat bran decreased serum cholesterol concentrations in hypercholesterolemic men (3, 4), the increase in daily fecal bile acid excretion was significant only in one of the studies (3).

Two general mechanisms have been proposed to explain the serum cholesterol decrease observed with soluble dietary fiber sources (5, 6). One hypothesis is that soluble fiber acts in the gastrointestinal tract to decrease absorption of cholesterol or fatty acids (5) or decrease absorption of biliary cholesterol or bile acids (5, 6). It has also been proposed that soluble fibers reduce cholesterol synthesis by altering serum concentrations of hormones or short-chain fatty acids that affect lipid metabolism (5). Physiological concentrations of one short-chain fatty acid, proprionate, significantly decreased *de novo* cholesterol synthesis in isolated rat hepatocytes (5). Our objective was to evaluate aspects of the first hypothesis. Stable isotope–labeled bile acids were used to determine the effect of oat bran on bile acid metabolism in normocholesterolemic men consuming constant diets and to compare the results to fecal bile acid and fat excretion.

SUBJECTS AND METHODS

Subjects and Diets. Subjects were recruited locally to participate in an outpatient, 2-mo, constant diet study intended to evaluate the effect of oat bran on small- and large-bowel function. A low-fiber control diet was consumed during the first 28 days. Oat bran was incorporated into the same diet to form the high-fiber diet that was consumed for days 29 through 56 of the study. A single stable-isotope technique using CA and CDCA labeled with ^{13}C was employed for determination of bile acid kinetics. The study was approved by the College of Agricultural and Life Sciences Committee on Research Involving Human Subjects, University of Wisconsin–Madison. Nine healthy, normocholesterolemic young men volunteered for the study and gave informed consent. The mean (±S.D.) age and height were 23.8 ± 2.2 yr and 179 ± 5 cm. The men were at normal weight for height (body mass index, 22.7 ± 1.5). None of the subjects had any history of gastrointestinal disease or food allergy. No medication, except for an occasional nonprescription analgesic, was used during the study.

Two-day cycles of daily menus containing 2,700, 3,000, 3,300 and 3,600 kcal were developed, using typically consumed foods, to contain 15% of the kilocalories as protein, 35% as fat

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Other abbreviations used in the text: amu, atomic mass unit; CA, cholic acid; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid, GC, gas chromatograph; LCA, lithocholic acid; MSD, mass selective detector.

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TABLE 1. Range of nutrient and energy contents in 2-day cycle menus

Parameters	Control	Oat bran
Kilocalories	2,667-3,607	2,661-3,629
Protein (gm)	100-133	100-134
% of kcal	15	15
Fat (gm)	105-139	105-139
% of kcal	34-35	34-35
Carbohydrate (gm)	336-468	338-468
% of kcal	50-51	50-51
Cholesterol, mg/1,000 kcal	112-124	110-119
% of total fat		
Saturated fat	24-28	24-26
Oleic acid	35-38	32-36
Linoleic acid	26-27	24-26
% of total carbohydrate		
Starch	49-59	48-56
Endogenous sugar	21-28	20-27
Sucrose	15-24	16-28

Calculated from published data (7-9), except for selected values for which food label data were used. Data are the ranges of the means for the 2 days of menus for each energy level (2,700, 3,000, 3,300, and 3,600 kcal).

and 50% as carbohydrate (7-9) (Table 1). The menus contained amounts of micronutrients that were equal to or greater than the recommended dietary allowances (10), and ~5 gm/1,000 kcal of dietary fiber (11) (analyzed range, 4.6 to 5.7 gm fiber/1,000 kcal). The ratio of polyunsaturated to saturated fatty acid ranged among the 16 menus from 0.92 to 1.07 (mean ± S.D., 1.00 ± 0.06); cholesterol content ranged from 110 to 124 mg/1,000 kcal (Table 1). Energy needs for maintenance of body weight during the study were estimated from 5-day food intake records completed by each subject before the study, initial body weights and the typical exercise and activity patterns of each subject. Daily energy intakes were changed for two subjects, one in wk 2 and one in wk 7. Initial mean body weight of 72.6 ± 6.4 kg during wk 1 was maintained throughout the study (wk 4, 72.1 ± 6.4 kg; wk 8, 72.0 ± 6.3 kg).

All foods, except for milk and fresh produce, were purchased as single lots. To form the high-fiber diet, we incorporated 100 gm of oat bran—forms used as hot or cold cereals (Quaker Oats, Co., Barrington, IL)—into foods in each menu. Carbohydrate and fat from other sources were adjusted to compensate for those amounts provided by oat bran. Wheat gluten was included in the low-fiber diet so that the proportion of vegetable protein was similar for both experimental periods. Meals were weighed, prepared (if needed) and consumed in an outpatient metabolic unit.

The content and composition of dietary fiber in the two 2,700-kcal control and two 2,700-kcal oat bran daily menus and in the oat bran were determined by means of a modification (12) of a chemical method of fiber analysis (13). (1→3)(1→4) β-glucans were determined enzymatically (14). The oat bran was 16.1% total dietary fiber, of which 38% was (1→3)(1→4) β-glucans and 46% was soluble fiber.

Bile Acid Administration and Blood Analyses. On days 21 and 49 of the study, subjects ingested 60 mg of each isotopically labeled bile acid after an 11-hr fast under experimental new drug permit 33,222. No food was consumed for 2 hr after ingestion of the dose. The bile acids were dissolved in 100 ml of deionized, distilled water containing 1.5% (wt/vol) sodium bicarbonate. [24-^{13}C]CA and [24-^{13}C]CDCA were obtained from MSD Isotopes (Montreal, Quebec, Canada). Isotopic enrichment was measured to be 96.94% ^{13}C for both bile acids.

Blood samples (~5 ml) for total serum cholesterol and triglyceride analyses were drawn on days 7 and 1 before study for the baseline determination and on days 27 and 28 and days 55 and 56 for the low-fiber and high-fiber measurements, respectively. Serum cholesterol and triglyceride concentrations were determined in duplicate with colorimetric/enzymatic assays (catalog numbers 352 and 3391, respectively; Sigma Chemical Co., St. Louis, MO). Data from each 2-day set of blood samples were averaged to yield values for each subject. Blood samples (~14 ml) for measurement of the labeled bile acids were drawn 1.5 to 2.5 hr after subjects began eating lunch on days 19 and 47 for determination of the basal isotope ratio and at the same time after lunch on days 22 through 25 and 51 through 54 for determination of the isotopically enriched bile acid ratios. All serum was prepared by means of centrifugation and stored frozen (−15° C) until it could be analyzed.

Serum bile acids from duplicate aliquots (2 ml) were prepared for analysis according to the procedure described by Everson (15), with the following slight modifications. After hydrolysis of conjugated bile acids, all reactions were carried out in glassware treated with dimethylchlorosilane. Reaction conditions for formation of the trimethylsilyl ethers from the methyl esters of the extracted bile acids were 60° C, 12 to 16 hr in a heating block. Derivatized bile acids were stored in 20 μl of a 98:1:1 solvent mixture of iso-octane, hexamethyldisilazine and pyridine until analyzed. Duplicate samples of pooled control serum (2 ml) containing 10 μCi of sodium [24-^{14}C]taurocholate (catalog number CFA 501; Amersham Corp., Arlington Heights, IL) were analyzed with each set of three to five experimental serum samples. Twenty sets of samples were analyzed; the mean (±S.D.) recovery of the labeled taurocholate was 81% ± 7%.

Derivatized bile acids were analyzed for ^{13}C isotopic enrichment with a Hewlett-Packard 5890 Series II Gas Chromatograph attached to a Hewlett-Packard 5970 Mass Selective Detector (Hewlett Packard Co., Naperville, IL). Both the GC and the MSD were controlled by a Pascal version Hewlett-Packard Chemstation. Derivatized bile acids were separated on a 30 m × 0.25 mm fused silica capillary column with a 0.25-μm methylsilicone coating (J&W Scientific, Folsom, CA) (15). Samples (1.8 μl) were injected by means of a splitless technique onto a 1 m × 0.32 mm deactivated fused silica retention gap

TABLE 2. Content and composition of insoluble and soluble dietary fiber fractions from the 2,700-kcal low- and high-fiber menus

Fiber component	Low fiber (gm/day)		High fiber (gm/day)	
	Insoluble	Soluble	Insoluble	Soluble
Cellulose	4.3	0	6.5	0
Hemicelluloses	2.9	2.5	6.4	3.1
β-glucan	0	0	1.5	5.4
Pectins	1.0	1.0	1.9	1.3
Klason lignin	2.1	0	5.7	0
TOTAL	10.2	3.5	21.8	9.8

Composites of all food in each menu were prepared by blending to yield a homogeneous slurry and lyophilized. Dietary fiber composition was determined by means of a chemical method of analysis (12-14). Data are the means of the analyses of each of the 2 days of menus consumed during each study period.

(16) at an oven temperature of 70° C and an injector temperature of 300° C. After 0.5 min, the oven temperature was increased at 15° C/min to 230° C, then at 10° C/min to 295° C, and held for 10 min. The temperature of the capillary direct interface between the GC and the MSD was 295° C. We identified the gas chromatography peaks using mass spectra obtained by operating the MSD in the scan mode and comparing the spectra with published spectra (17).

We measured isotope ratios from the relative sizes of peaks for ions at 458 and 459 amu for CA and 370 and 371 amu for CDCA while operating the MSD in the selected ion monitoring mode (15, 18). Because the MSD produces ion peaks with widths of about 0.5 amu at half height, and the exact positions of the maxima for these peaks drift, we developed a routine in the data-collection program to integrate the peaks. Twenty-measurements (the most that Chemstation can monitor) in 0.1-amu increments were monitored; during elution of CDCA, from 369.6 to 371.5 amu; and during elution of CA, from 457.6 to 459.5 amu. Data from each atomic mass unit increment were averaged for the 10 most abundant sets of measurements. Isotope ratios were calculated as the ratio of the sums of the five most abundant atomic mass unit increments under each of the two ion peaks being monitored. Isotopic enrichment was expressed as atom percent excess and was calculated from isotope ratios as described previously (18). We maintained day-to-day reproducibility by injecting a standard sample at the beginning and end of each day. The MSD was retuned if the isotope ratios for the standards were not within 5% of the expected values.

Fecal Analyses. Complete stool collections from days 22 through 26 and 50 through 54 were individually weighed, homogenized with water and lyophilized. We prepared a proportional 5-day fecal composite for each diet period by combining 75% of the dry weight of each stool excreted during the collection period. Acidic steroids were extracted from duplicate aliquots and analyzed by means of gas chromatography as previously described (19-21). Fecal fat was measured in duplicate with Association of Official Analytical Chemists Method 14.019 as modified for analysis of body tissues (22). The coefficients of variation for duplicate acidic sterol analyses of each sample were less than 10%; for duplicate fat determinations, less than 5%.

Calculations and Statistics. Kinetic parameters for CDCA and CA were obtained from linear-regression plots of the natural logarithms of atom percent excess vs. time (18); the slopes of these lines are the fractional turnover rates. Pool sizes were calculated with the equation of Stellaard (18). Synthesis rates were calculated as the products of fractional turnover rates and pool sizes. Pool sizes for deoxycholic acid were calculated from the ratios of the DCA peak to the CDCA peak (15). Fat digestibility was calculated as the difference between the 5-day intake calculated from food composition tables (7-9) and the 5-day fecal excretion and expressed as a percentage. All data are expressed as mean ± S.D. Statistical significance was determined with Student's two-tailed paired t test in all instances except for the CA pool size, for which Student's one-sided t test was used (23).

RESULTS

The dietary fiber composition of the 2,700-kcal control and oat bran menus illustrate the heterogeneity of the fiber in mixed-food diets (Table 2). Hemicelluloses were the fiber component present in the highest concentration in all menus. Oat bran added (1→3)(1→4) β-glucans to the fiber. Mean total dietary fiber intake among the nine subjects during the low-fiber control diet was 16.0 ± 1.5 gm/day, of which 4.0 ± 0.3 gm/day was analyzed as soluble fiber. Dietary fiber intake during the diet containing oat bran was 33.9 ± 1.5 gm/day, of which 10.3 ± 0.4 gm/day was soluble fiber.

Serum cholesterol levels decreased in all subjects (Fig. 1). The mean serum cholesterol concentration at the end of the low-fiber period, 3.93 ± 0.68 mmol/L (152 ± 28 mg/dl), was significantly lower than the wk 0 mean of 4.58 ± 1.00 mmol/L (177 ± 40 mg/dl) ($p < 0.01$); the high-fiber mean serum cholesterol level, a 3.57 ± 0.73 mmol/L (138 ± 30 mg/dl), was significantly lower than the low-fiber mean ($p < 0.01$). Consumption of the control diet significantly lowered serum triglyceride concentrations ($p < 0.05$), but addition of oat bran resulted in no further change. Mean wk 0 serum triglyceride concentration was 1.04 ± 0.32 mmol/L (92 ± 30 mg/dl), the control value was 0.79 ± 0.27 mmol/L (70 ± 25 mg/dl) and the high-fiber value was 0.73 ± 0.22 mmol/L (65 ± 21 mg/dl).

Incorporation of oat bran into the constant diet substantially altered the kinetics of both primary bile acids (Fig. 2). The synthesis and fractional turnover rates of both of the two primary bile acids increased significantly when oat bran was consumed. The pool size of CA decreased (Fig. 2), whereas the pool size of its secondary bile acid, DCA, doubled (Fig. 3). Total bile acid pool size was unaffected by oat bran (Fig. 4).

Total daily fecal bile acid excretion more than doubled

when the oat bran was incorporated into the metabolic diet (Table 3). Daily excretion of the two secondary bile acids increased significantly during the oat bran period. Excretion of CDCA and CA also increased, but the changes were not statistically significant. Mean daily fecal fat excretion among the nine subjects increased significantly, from 3.8 ± 1.2 gm/day during the control diet to 6.8 ± 1.1 gm/day during the oat bran diet ($p < 0.002$). Fat digestibility decreased from 96.9% ± 0.8% to 94.4% ± 1.0% with oat bran ($p < 0.002$). Mean daily stool output increased from 110.5 ± 21.3 gm/day during days 22 through 26 to 159.3 ± 28.3 gm/day during days 50 through 54 ($p < 0.05$).

DISCUSSION

Bile acid synthesis accounts for 40% to 50% of the daily elimination of cholesterol (24, 25), and quantitatively, the most important substrate for bile acid synthesis is plasma lipoprotein cholesterol (26). Our study is the first to demonstrate that increased bile acid synthesis and decreased bile acid absorption are two mechanisms by which oat bran lowers serum cholesterol levels in healthy individuals. Everson et al. (27) used similar methodology to study the effects of psyllium hydrophilic mucilloid on bile acid metabolism in 20 hypercholesterolemic men. Psyllium, compared with usual diet alone or that supplemented with placebo (cellulose), increased the pool size of CDCA and the fractional turnover rates and synthesis of both primary bile acids. However, these investigators observed no changes in CA or DCA pool sizes.

It is well established that some dietary fibers (i.e., cellulose and wheat bran) do not affect serum cholesterol levels (6, 28). However, these fiber sources increase stool weight (28, 29), as did the oat bran we studied. The mean daily stool output with oat bran ingestion (159 gm/day) was greater than the 141 gm/day we measured when wheat bran was added to a low-fiber diet similar to the one used in the oat bran study (30). By using a low-fiber control diet, we demonstrated in this study that stool weight was increased and serum cholesterol decreased with oat bran fiber, in contrast to other stool-bulking fibers (29) that have no effect on serum cholesterol levels (6, 28). Stool bulking reflects an increase in bacterial mass, as well as the presence of unfermented dietary fiber (29). Even though oat bran is referred to as a soluble dietary fiber, it is more than half insoluble fiber (31). The insoluble fiber fraction has a neutral sugar composition similar to that in wheat bran (31), suggesting that it contains arabinoxylans and cellulose, both of which are only partially fermented (32). Contrasting results when a diet containing oat bran vs. one containing wheat bran is consumed suggests that an increase in bacterial mass (and the implied accompanying increase in bacterial metabolic activity) is not a major effector of hypercholesterolemia.

In studies of the cholesterol-lowering effects of fiber in which diet intake is recorded but not constant, a pretest period consisting of the American Heart Association Step I diet is frequently used (1, 6). The reduction in dietary fat precipitates decreases in serum cholesterol and triglyceride levels. Although the control diet we used was not as low in fat content as the American Heart Association Step I (30% of kilocalories), it represented a substantial decrease in fat intake for the subjects (prestudy fat intake of 40% to 45% of kilocalories). Diet-induced reductions in serum lipid levels are fully expressed within 4 wk of the diet change (33). Thus the reductions in serum triglyceride and cholesterol levels we observed during the control diet were a response to this fat intake lower than what the subjects typically consumed, whereas the lack of change in serum triglyceride and the decrease in cholesterol concentrations during the test period are the responses to oat bran consumption, as previously shown (5).

Enterohepatically circulating primary bile acids and DCA (24, 34) inhibit primary bile acid synthesis (25) by affecting hepatic cholesterol 7α-hydroxylase activity.

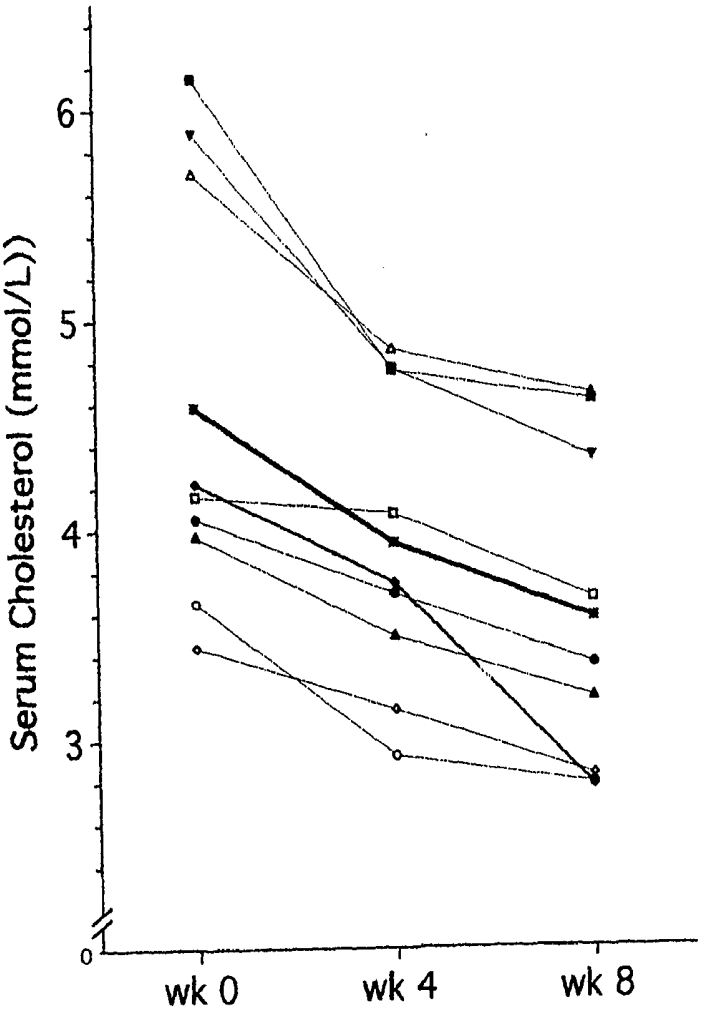

FIG. 1. Reduction in serum cholesterol levels of nine normocholesterolemic young men after 4 wk of a constant low-fiber diet containing 35% of kilocalories as lipid and 4 wk of the same diet into which 100 gm of oat bran was incorporated. The heavy line represents the group means. Each data point is the mean of the analysis of two separate blood samples. Samples for basal values were drawn on days 7 and 1 before commencement of the low-fiber diet, for the low-fiber values on days 27 and 28 and for the high-fiber values on days 55 and 56 of the study. The mean of wk 4 data was significantly different from that of wk 0 ($p < 0.01$), and the mean of wk 8 data was significantly different from that of wk 4 ($p < 0.01$).

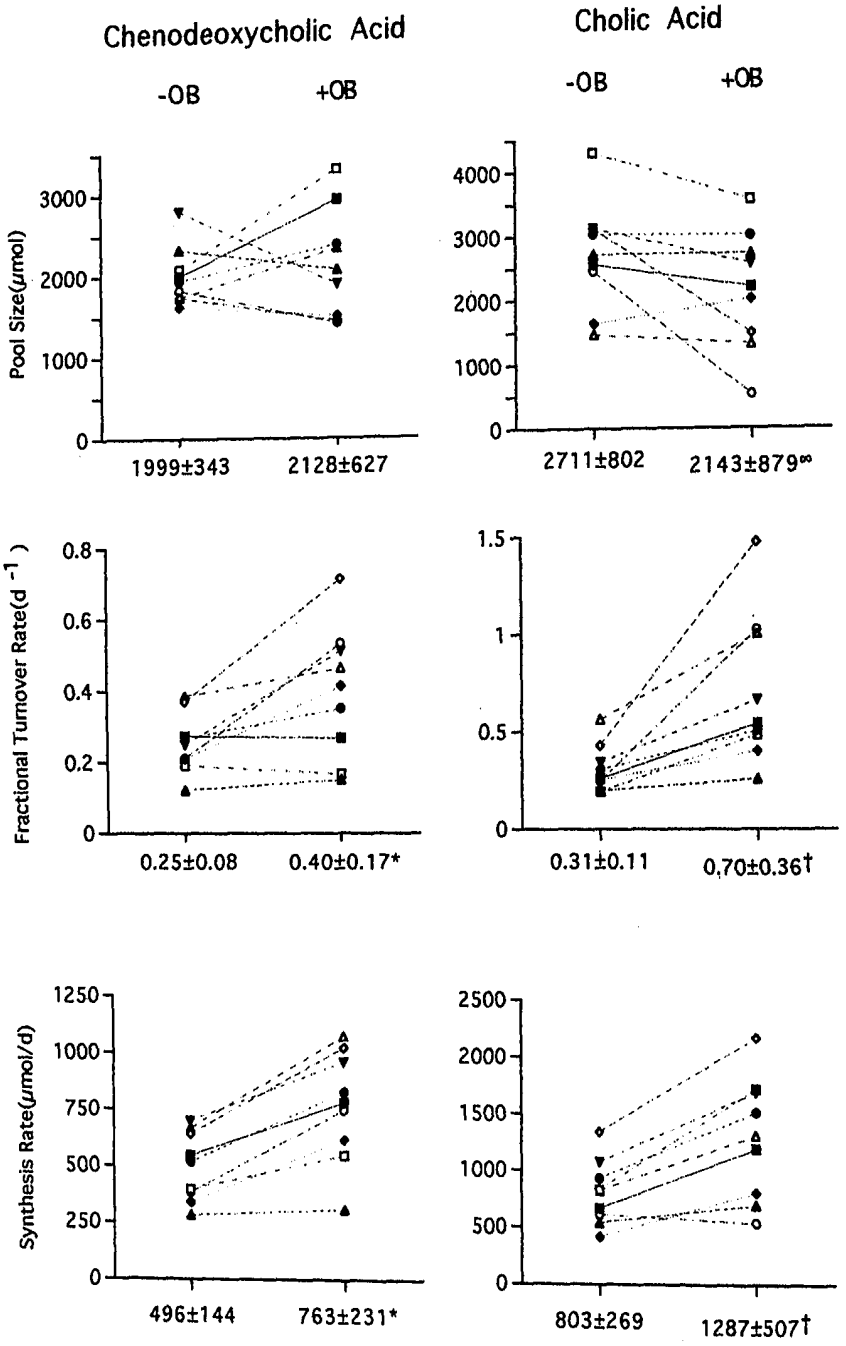

FIG. 2. Changes in kinetic parameters for primary bile acids in nine normocholesterolemic young men after 4 wk of a constant low-fiber diet containing 35% of kilocalories as lipid vs. 4 wk of the same diet into which 100 gm of oat bran was incorporated. Bile acid kinetics were determined by measurement of the stable isotopes [24 – ^{13}C]CA and [24 – ^{13}C]CDCA in serum samples. The natural abundance of the ^{13}C-labeled bile acids was measured in serum collected on days 19 and 47 before ingestion of the labeled bile acids (60 mg each) and enrichment daily for 4 days after ingestion on days 21 and 49. Mean ± S.D. values are below each set of individually plotted data points. Significantly different than value for low-fiber period by two-sided paired Student's t test: *$p < 0.05$; †$p < 0.01$; ∞Significantly less than value for low-fiber period by one-sided paired Student's t test ($p < 0.05$). *OB*, oat bran.

The reduction in the flux of bile acid returning to the liver when oat bran was consumed may have been the stimulus for the increased synthesis of both primary bile acids. However, the increased proportion of total bile acids that was DCA may have limited the increase in synthesis. This stimulus dampening may have been responsible for the failure of synthesis to maintain the size of the CA pool during the oat bran diet. In other dietary fiber studies, increases in biliary DCA have been accompanied by a decreased proportion of the total biliary bile acid pool that was CA when the diet was supplemented with pectin (35) but not psyllium (27).

Cholesterol absorption and synthesis also appear to be affected by changes in the relative composition of the bile acid pool. DCA, compared with CA and CDCA, has been shown to be a substantially more effective inhibitor of hydroxymethylglutaryl–CoA reductase, the rate-limiting enzyme in the cholesterol biosynthesis pathway (24). DCA is also a more effective inhibitor of cholesterol absorption than CDCA in healthy human beings (36).

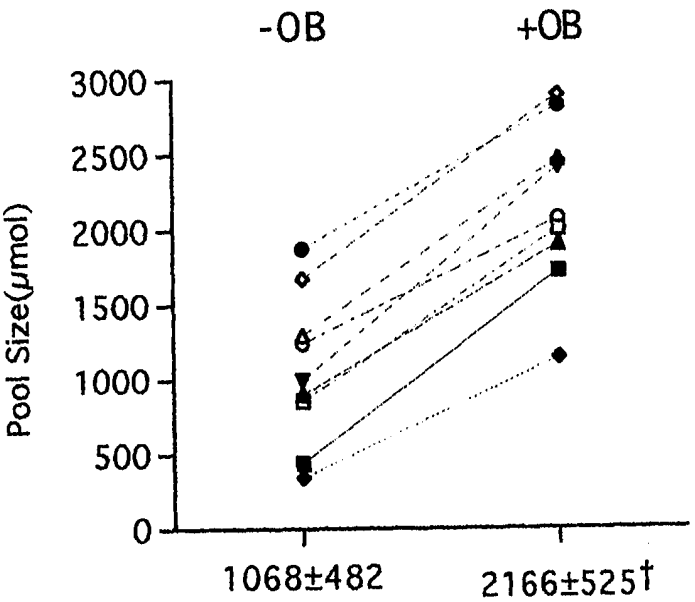

FIG. 3. Changes in DCA pool size in nine normocholesterolemic young men after 4 wk of a constant low-fiber diet containing 35% of kilocalories as lipid vs. 4 wk of the same diet into which 100 gm of oat bran was incorporated. DCA pool size was not measured by means of stable-isotope techniques but by the relative amounts of DCA and CDCA measured in serum by means of gas chromatography and the pool size of chenodeoxycholic acid, which was measured by means of stable-isotope techniques. Mean ± S.D. values are below each set of individually plotted data points. †Significantly different than value for low-fiber period by two-sided paired Student's *t* test; $p < 0.01$. *OB*, oat bran.

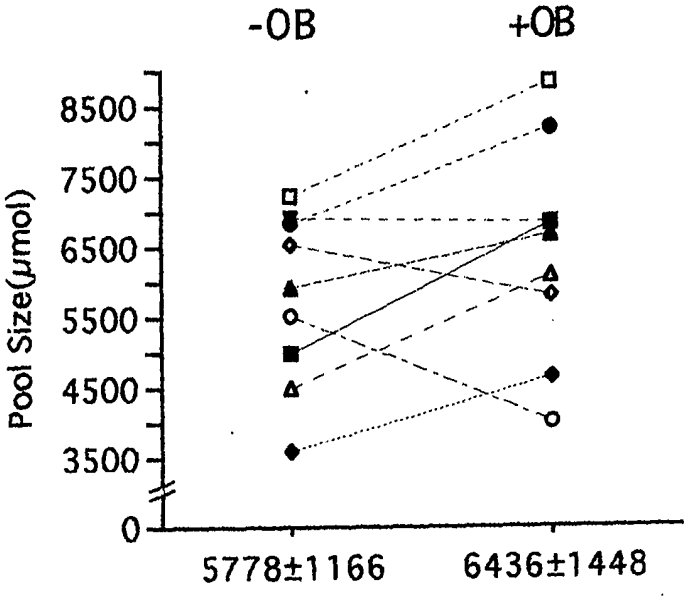

FIG. 4. Total bile acid pool size calculated as the sum of CDCA, CA and DCA pools in nine normocholesterolemic men after 4 wk of a constant low-fiber diet containing 35% of kilocalories as lipid vs. 4 wk of the same diet into which 100 gm of oat bran was incorporated. Primary bile acid pool sizes were measured with stable isotope techniques for ^{13}C-labeled bile acids; DCA pool size was calculated with the ratio of total DCA to CDCA. The natural abundance of ^{13}C was measured in serum collected on days 19 and 47 before ingestion of [24-^{13}C]CA and [24 – ^{13}C]CDCA (60 mg each) and enrichment for 4 days after ingestion on days 21 and 41. Mean ± S.D. values are below each set of individually plotted data points. *OB*, oat bran.

The substantial increase (79%) we observed in the proportion of the total bile acid pool that was DCA is consistent with the hypothesis that the changes that we measured in serum bile acids altered not only hepatic bile acid synthesis but also cholesterol synthesis and absorption. The increase in fecal fat accompanying the oat bran diet also supports our hypothesis that oat bran lowers blood cholesterol levels by interfering with lipid and cholesterol absorption.

Previous studies measuring the effects of dietary fiber on cholesterol absorption and synthesis and concomitant changes in the DCA pool have yielded inconsistent results (27, 37-39). Only when psyllium was added to a very low cholesterol diet (38) or when large amounts of pectin (40 to 50 gm/day) were added to a low cholesterol diet of hyperlipidemic and normolipidemic subjects (39) did cholesterol biosynthesis increase to offset fecal sterol loss. Some of the differences in results among studies of hypocholesterolemic fibers may be due to tocotrienols, compounds found in oats but not in pectin and psyllium. Tocotrienols have been reported to inhibit cholesterol synthesis (40), and a concentrate of these components from palm oil has been shown to lower serum cholesterol levels in some human subjects (41).

Increased excretion of bile acids in response to oat bran, compared with the control diet, is in agreement with the observed increase in bile acid synthesis measured with stable isotopes. However, the magnitude of the fecal losses of CA (as CA plus DCA) and CDCA (as CDCA plus LCA) were less than that measured as the synthesis rate. Daily excretion of CDCA and LCA during the control diet accounted for 43% of the CDCA synthesized; during the oat bran diet it was 33%. Fecal excretion of CA and DCA was 49% of the daily synthesis of CA during both diet periods. This apparent loss likely reflects microbial metabolism of the fecal bile acids to unmeasured derivatives, which have been reported to account for as much as 45% of the total fecal steroids (42, 43). Substantial increases of 40% to 50% in ileal bile acid excretion during oat bran (44) or psyllium seed husk (45) consumption, even though fecal bile acid excretion was not always increased, support the contention that fecal excretion may not fully reflect changes in synthesis or small bowel absorption. It could be argued that subjects were not in a steady state condition at the time of the two assays and that bile acid synthesis was not a measure of their excretion. However, fecal bile acid excretion during the second and third weeks of each diet period were comparable to those reported for the fourth week (data not shown). The loss is probably not due to any atypical methodological error; others have reported daily fecal bile acid excretions comparable to (46) or less than (2-4) what we measured when oat bran (3, 4, 46) or oatmeal (2) was the source of fiber.

Comparison of the bile acid excretion determined by measurement of synthesis using labeled bile acids with fecal steroid excretion suggests that fecal excretion, even under the best of conditions, is an insensitive measure of sterol flux. The implication of the effect that the substantial increase in the contribution of DCA to the

TABLE 3. Fecal bile acid excretion (nmol/day) in young men consuming constant diets without and with oat bran

Bile acids	Control	Oat bran
CDCA	4.7 ± 3.3[a]	20.4 ± 15.6
CA	8.8 ± 3.8	28.4 ± 31.1
LCA	201.8 ± 77.5	350.3 ± 146.5[b]
DCA	253.8 ± 149.9	608.5 ± 369.8[b]
TOTAL	476.4	1026.2[c]

Nine men consumed a constant low fiber diet for 28 days, then the same diet into which oat bran was incorporated for days 29 through 56. Fecal bile acids were measured in duplicate in a lyophilized composite from days 22 through 26 for the low fiber control data and from days 50 through 54 for the oat bran period.

[a]Data expressed as mean ± S.D. for nine men. Bile acid totals include any measured ursodeoxycholic acid.

[b]Significantly different from low-fiber period ($p < 0.006$).

[c]Significantly different from low-fiber period ($p < 0.001$).

unchanged bile acid pool size may have on cholesterol absorption and synthesis also highlights the relative insensitivity of serum cholesterol levels as markers of cholesterol metabolism. Our results suggest that the use of these insensitive measures of sterol flux is likely to be one of the primary reasons diet-induced hypocholesterolemic responses have been variable (1, 5, 6, 28) and significant decreases in serum cholesterol levels are not always accompanied by increased fecal bile acid excretion (45, 47, 48).

Our results indicate that bile acid absorption was reduced and bile acid synthesis increased with oat consumption, but the response in synthesis may have been dampened by the large increase in the proportion of the total bile acid pool that was DCA. Changes that occurred in the bile acid pool are consistent with data that indicate cholesterol absorption and synthesis would be decreased. We conclude that a major route for serum cholesterol depletion is increased bile acid excretion and the concomitant increase in bile acid synthesis. The additional effects of oat bran on the relative composition of the bile acid pool may further modulate bile acid synthesis and alter cholesterol synthesis and absorption.

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