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Dietary Fiber and Lipid Metabolism[1] (42201)

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Dietary fiber appears to be involved in regulating lipid metabolism in several ways. This involvement has been extensively reviewed (1–8). The interaction of dietary fiber with bile acids and the resultant effects on lipid metabolism have been a major part of this relationship and will be the subject of this review.

The relationship between the ability of some sources of dietary fiber to prevent cholesterolemia in rabbits and steroid excretion was reported some time ago. Among these early reports, Cookson *et al.* (9) observed a reduction in serum cholesterol in cholesterol-fed rabbits when alfalfa was added to their ration and reported a concomitant increase in fecal steroid excretion (10). This suggested that alfalfa was preventing or reversing the effects of dietary cholesterol in rabbits by increasing steroid excretion. Earlier, Portman and Murphy (11) had observed increases in cholic acid pool size and excretion of digitonin precipitable material in rats fed a commercial ration when compared to rats fed a fiber-free, semipurified diet, again suggesting an involvement of sources of dietary fiber in bile acid excretion.

More direct evidence of the interaction between dietary fiber and bile acids appeared at about this same time. Eastwood and Hamilton (12) observed a significant *in vitro* adsorption of bile acids by dry grain, a by-product of the brewing industry. They suggested that the adsorption was hydrophobic in nature since the dihydroxy bile acids were adsorbed to a greater extent than trihydroxy. Later we observed a similar *in vitro* adsorption of bile acids by a variety of dietary fiber sources, including wheat straw, wheat bran, oat hulls, and a high level of adsorption by alfalfa (13, 14). We also measured adsorption by some components of dietary fiber and found cellulose bound very little bile acid while lignin bound more than any of the dietary fiber sources.

In an effort to examine the correlation of this *in vitro* adsorption with the ability of these materials to alter cholesterol accumulation in cholesterol-fed rats, we fed rats a semipurified diet containing 0.5% cholesterol and added several sources or components of dietary fiber (15). In control animals this diet resulted in about a threefold increase in liver cholesterol. Lignin and pectin prevented this increase in liver cholesterol while cellulose did not. Others had also shown the ability of lignin and pectin to prevent increases in cholesterol levels in rats (16, 17).

These observations led to the hypothesis that adsorption of bile acids by dietary fiber resulted in reduced absorption of bile acids, increasing their excretion and increasing the amount of cholesterol needed for bile acid synthesis. In addition, adsorption of bile salts in the small intestine would reduce cholesterol absorption, increasing neutral steroid excretion and reducing dietary input to cholesterol pools. Data suggested that sources of dietary fiber which reduced cholesterol levels also increased steroid excretion and adsorbed bile acids *in vitro*.

This hypothesis relates the intake of dietary fiber to two human diseases of major concern. Hypercholesterolemia is a risk factor for coronary heart disease and the use of dietary fiber as a part of a diet designed to reduce blood cholesterol levels could reduce this risk. Increased concentrations of bile acids in the colon as indicated by fecal concentrations have been related epidemiologically in man and experimentally in rats to an increased susceptibility to colon cancer. Dietary fiber can play two roles in determining fecal bile acid concentration since it both adsorbs bile acids, potentially increasing concentration, and absorbs water, tending to dilute bile acids and reduce their concentration. In examining the effects of dietary fiber sources on bile acid excretion we must evaluate both total daily excretion and concentration of fecal bile acids in order to obtain a complete picture of their usefulness in a variety of situations and avoid reducing

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risk of one disease at the expense of increased risk for a second disease.

In an effort to evaluate the role played by dietary fiber in bile acid metabolism in light of the above discussion of its relation to human disease, we have investigated two issues which we hope will help determine the usefulness of dietary fiber in human nutrition. The first is an investigation of the component of dietary fiber responsible for the observed *in vitro* adsorption of bile acids and the second, an evaluation of the relationship between changes in bile acid and neutral steroid excretion and cholesterol accumulation in response to sources of dietary fiber in rats.

Adsorption. As was discussed above, our earlier adsorption experiments had found that isolated lignin bound significant levels of bile acids and salts (14). Others had also suggested that lignin was an important component of dietary fiber in imparting adsorption capacity (12, 18). In an effort to investigate the importance of several components of two sources of dietary fiber which have very different adsorption capacities and different effects on cholesterol levels, alfalfa and wheat bran (19), we used a sequence of extraction procedures which removed various dietary fiber components (and other materials) and measured bile acid adsorption after each extraction, assuming that a change in adsorption resulted from removal of that component. As can be seen in Table I, removal of lipids, saponins, and other fat-soluble components from alfalfa or wheat bran did not significantly reduce adsorption of cholic or deoxycholic acid. Extraction of pectins and other water-soluble components of dietary fiber also failed to reduce adsorption. Delignification did reduce adsorption significantly for both alfalfa and wheat bran confirming earlier speculation as to its importance. Interestingly the remaining holocellulose (cellulose plus hemicellulose) retained a significant level of adsorption. These results suggested that saponins were not required for the adsorption phenomenon as had been suggested by others (20), that lignin appeared to be an important component in this phenomenon, and that holocellulose retained a significant amount of adsorption which we suggested was due to the presence of hemicellulose since isolated cellulose has never been shown to adsorb bile acids.

In order to examine the adsorption capacity of hemicellulose, we needed to modify our methodology. The previous data were derived using a method in which the dietary fiber source was incubated with a radioactive bile acid solution, the mixture centrifuged, the supernatant assayed for radioactivity, and adsorption calculated as the disappearance of radioactivity from the solution. Adsorption to water-soluble components would thus not be measured since these complexes would remain in the supernatant. In order to avoid this problem we filtered the supernatant using a 50,000 MW cutoff filter to capture the large molecular weight polysaccharides and assayed the filtrate for radioactivity, calculating adsorption as before. Table II contains data derived in this manner for a variety of water-soluble components of dietary fiber. Hemicellulose A (insoluble) and B (soluble) derived from corn bran both exhibit bile acid adsorption capacity as does intact corn bran. Pectin and other gums also have adsorption capacity for cholic and deoxycholic acid when measured in this manner.

These data would suggest that lignin and hemicellulose are the components of dietary fiber which are largely responsible for bile acid adsorption. However, it must be noted that these conclusions are based on data derived using materials chemically isolated from the original dietary fiber. We know little concerning the effects of these isolation procedures on

TABLE I. BILE ACID ABSORPTION BY ALFALFA, WHEAT BRAN, AND THEIR FRACTIONS[a]

Alfalfa extraction	Wheat bran		
	Cholate[b]	Deoxy-cholate[b]	Deoxy-cholate[b]
None	100[c]	266	232
Petroleum ether			
Acetone	99	263	246
95% Ethanol			
50% Ethanol	99	311	348
Hot water	80	274	269
Sodium chlorite	31	88	79

[a] Story *et al.* (19).

[b] Bile acid concentration, 5 m*M*; 100 mg dietary fiber in 35 ml solution.

[c] Given as a percentage of cholate adsorption for whole alfalfa.

TABLE II. ABSORPTION OF BILE ACIDS BY WATER-SOLUBLE COMPONENTS OF DIETARY FIBER

	Adsorption of	
	Cholate	Deoxycholate
Corn bran	100[a]	172
Corn bran hemicellulose A	70	179
Corn bran hemicellulose B	84	206
Guar gum	100	268
Pectin	12	97

[a] Given relative to adsorption by corn bran.

adsorption capacity but one can assume they would be significant since breaking down of the matrix of the cell wall would expose new surfaces with altered physical properties. In order to substantiate the importance of the components thought to be responsible for adsorption, another approach which would have fewer confounding factors is needed.

Steroid Excretion. Our goal for some time has been to simultaneously measure changes in cholesterol accumulation and fecal steroid excretion in rats fed various sources of dietary fiber in an effort to test the hypothesis discussed earlier. In our first attempt we compared the effects of cellulose, alfalfa, and whole oats in a semipurified diet with and without 0.25% added cholesterol fed to rats (21). As suggested by the data in Table III, all three sources of dietary fiber resulted in reduced liver cholesterol levels in the rats fed cholesterol-free diets. Cholesterol accumulation was higher in all the cholesterol-fed groups and this change was reversed only by alfalfa. Fecal concentrations of bile acids and total steroids were reduced by alfalfa and cellulose in comparison to no fiber and were higher in oat-fed groups. Daily excretion of bile acids and total steroids did not correlate with reduced liver accumulation as our hypothesis would have predicted. All three sources of fiber resulted in increased excretion of steroids when compared to the no-fiber group, regardless of the change in liver cholesterol level. Oats and cellulose feeding resulted in the highest level of steroid excretion and no reduction in liver cholesterol level when cholesterol was added to the diet while alfalfa feeding resulted in lower excretion and lower liver cholesterol level.

An unexpected change was observed in this experiment regarding the spectrum of bile acids excreted. In response to dietary cholesterol, rats change the spectrum of bile acids synthesized in favor of derivatives of chenodeoxycholic acid, because they are less readily absorbed (22, 23). This seems to be an important mechanism by which rats regulate their cholesterol levels in the face of high dietary input. In these cholesterol-fed animals we observed a similar change in all groups. The ratio went from about 50:50 (cholic:chenodeoxycholic) in the no-fiber, cholesterol-free group to about 30:70 in all the cholesterol-fed groups regardless of source of dietary fiber. Unexpectedly we also observed a change in favor of chenodeoxycholic derivatives in response to alfalfa and oats in the groups not fed cholesterol (alfalfa = 28:72, cellulose = 51:49, oats = 37:

TABLE III. LIVER CHOLESTEROL LEVELS AND FECAL STEROID EXCRETION IN RESPONSE TO ALFALFA, CELLULOSE, AND WHOLE OATS IN RATS[a]

Dietary fiber	Dietary cholesterol	Liver cholesterol	Fecal		Total fecal steroids	
			Bile (mg/g)	Acids (mg/day)	(mg/g)	(mg/day)
None	−	100[b]	100	100	100	100
	+	227	115	134	181	210
Alfalfa	−	83	75	224	34	101
	+	131	73	250	38	134
Cellulose	−	77	124	329	110	297
	+	202	175	450	174	447

[a] Kelley *et al.* (21).
[b] Given relative to no-fiber, no-cholesterol control.

63). These changes were not translated into increased excretion as we might have expected considering their role in cholesterol-fed rats, but we know chenodeoxycholic acid also alters cholesterol synthesis and little is known concerning the effects of its metabolites (lithocholic, hyodeoxycholic, and muricholic acids).

In an effort to better characterize these changes in bile acid excretion in a variety of sources of dietary fiber and test our original hypothesis more thoroughly, we fed rats similar diets with or without added cholesterol and with no fiber, cellulose, alfalfa, oat bran, or corn bran (15%) added (Table IV). Results similar to those reported earlier were observed, in that all sources of dietary fiber reduced liver cholesterol in the cholesterol-free diet groups. In the cholesterol-fed groups, alfalfa again reduced accumulation while cellulose did not. Oat bran, unlike whole oats, reduced accumulation substantially and corn bran did not. Steroid concentrations in feces were reduced by all sources of dietary fiber when compared to the no-fiber control groups. In rats oat bran causes little change in fecal weight in comparison to fiber-free diet groups and, thus, with increased excretion of steroid, concentrations are higher than those in the other dietary fiber-fed groups. Daily excretion of bile acids was increased in response to all dietary fiber sources as was total steroid excretion. The magnitude of these changes again did not agree in every case with the observed change in liver cholesterol accumulation. Although the reductions in accumulation in response to alfalfa and oat bran are accompanied by increases in fecal steroid excretion in comparison to the no-fiber control, the steroid excretion in cellulose- and corn bran-fed groups was also higher and they caused no change in liver cholesterol accumulation. The spectrum of bile acids excreted was altered by these sources of dietary fiber, although the changes were not as dramatic as in the first experiment. Consistent increases of approximately 5% were observed in chenodeoxycholic acid derivatives in response to oat bran, corn bran, and alfalfa in comparison to cellulose.

Several human studies have explored the effects of some of these same sources of dietary fiber on serum lipids and steroid excretion. Kirby *et al.* (24) reported a reduction in serum cholesterol levels and an increase in fecal bile acid excretion in hypercholesterolemic men given 94 g of oat bran for 10 days as part of an otherwise normal diet. More recently, Anderson *et al.* (25) compared the effects of oat bran and beans under similar conditions. After 2 weeks of treatment, both dietary fiber supplements caused an approximate 20% reduction in serum cholesterol (Table V). As had been reported earlier, oat bran resulted in an increase in fecal bile acids excreted daily (65%) and increased total steroid excretion (22%) while bile acid concentration increased only slightly (6%) and total steroid concentration

TABLE IV. EFFECTS OF CELLULOSE, ALFALFA, OAT BRAN, AND CORN BRAN ON LIVER CHOLESTEROL AND FECAL STEROID EXCRETION IN RATS

Dietary fiber	Dietary cholesterol	Liver cholesterol	Fecal			
			Bile	Acids	Total fecal steroids	
None	–	100[a]	100	100	100	100
	+	327	158	152	153	139
Alfalfa	–	76	63	201	37	118
	+	271	104	392	61	229
Cellulose	–	66	36	195	21	112
	+	398	56	341	36	218
Oat bran	–	75	82	120	65	95
	+	210	169	237	130	183
Corn bran	–	83	43	200	27	122
	+	400	85	403	54	252

[a] Given relative to no-fiber, no-cholesterol control.

TABLE V. EFFECTS OF OAT BRAN OR BEANS ON SERUM CHOLESTEROL AND FECAL STEROID EXCRETION IN HYPERCHOLESTEROLEMIC MEN[a]

	% Change	
	Oat bran	Beans
Serum cholesterol	−19.3[b]	−18.8[b]
Fecal bile acids		
mg/g	+6.2	−31.9
mg/day	+65.1	−29.9
Total steroids		
mg/g	−21.8	−6.0
mg/day	+21.9	−2.9

[a] Anderson *et al.* (25).
[b] Change in comparison to control period on diet without dietary fiber source.

was reduced (12%). In spite of the similar nature of the dietary fiber of beans and a like response of serum cholesterol, bile acid and total steroid excretion were decreased in response to the bean treatment. Oat bran resulted in an increase in the absolute amount of chenodeoxycholic acid derivatives excreted on a daily basis while beans resulted in a decrease.

We have also measured fecal steroid excretion in normal subjects given graded levels of hard red wheat bran (HRWB) baked in bread (26). Earlier studies suggested HRWB resulted in a reduction in serum cholesterol (27). Healthy young women on a self-selected diet in a dormitory setting (23 ± 3 g dietary fiber/day) were given HRWB supplements in bread at one of four levels (0, 5.7, 17.1, or 28.5 g dietary fiber/day). As can be seen in Table VI, fecal weight and the speed of transit were both increased with increasing levels of intake of HRWB. All fecal steroid concentrations were reduced by addition of HRWB. Daily bile acid excretion was increased significantly at the higher levels of intake but this change was not of sufficient magnitude to alter daily steroid excretion. Excretion of chenodeoxycholic acid derivatives (mg/day) was increased in response to the increasing levels of intake of HRWB.

Conclusions. The hypothesis that dietary fiber alters cholesterol levels by adsorbing bile acids, which would increase their excretion and alter cholesterol absorption, appears to be too simplistic based on the accumulated data. Some sources of dietary fiber (e.g., oat bran) reduce serum and/or liver cholesterol levels and simultaneously increase steroid excretion. However, these changes do not seem to be of a magnitude sufficient to account for the change in serum cholesterol. In addition, other sources which cause more substantial increases in steroid excretion cause no change in cholesterol accumulation (e.g., corn bran or cellulose) and, in humans, a reduction in serum cholesterol by beans is accompanied by a reduction in steroid excretion. A change in bile acid pool sizes in response to oat bran and the effects this may have on sterol balance may be an additional mechanism for the observed effects. Other situations (i.e., beans) do not fit either of the above mechanisms and will require further investigation.

At this point in time we can make several useful comments concerning the role of dietary fiber in lipid metabolism: (a) We cannot generalize about the effects of dietary fiber on lipid metabolism. We may be able to group sources by composition, to some extent, but the experience with oat bran and beans that, in spite of similar effects, mechanisms may be quite different suggests this must be done with caution. (b) Mechanisms appear to center more on effects on regulatory enzymes of cholesterol and bile acid synthesis than on adsorption and physical effects. We know very little about the effects changes in pool sizes of some of the

TABLE VI. ALTERATION OF FECAL WEIGHT, TRANSIT TIME, AND FECAL STEROIDS IN RESPONSE TO HARD RED WHEAT BRAN[a]

	Hard red wheat bran added[b]			
	0	5.7	17.1	28.5
Fecal weight				
Wet	100[c]	129	194	290
Dry	100	126	175	244
Fecal bile acids				
mg/g	100	102	88	64
mg/day	100	138	165	160
Total steroids				
mg/g	100	79	50	37
mg/day	100	93	92	84

[a] Spiller *et al.* (26).
[b] Basic, self-selected diet contained 23 ± 3 g dietary fiber/day. These amounts (as dietary fiber) were added baked in bread.
[c] Changes given relative to zero added HRWB.

minor bile acids may have in overall sterol balance, considering the key role this may play in explaining the observed effects of some dietary fiber sources. (c) In spite of these shortcomings, we have had experience with several sources of dietary fiber which have been shown to be effective in reducing hypercholesterolemia in men without substantial increases in fecal steroid concentrations. These experimental results should be incorporated into a more complete diet therapy for hypercholesterolemia employing all diet components.

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