Cholesterol Reduction by Glucomannan and Chitosan Is Mediated by Changes in Cholesterol Absorption and Bile Acid and Fat Excretion in Rats\(^1,2,3\)

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ABSTRACT Glucomannan, a viscous polysaccharide, and chitosan, a derivative of chitin, have both been demonstrated to lower cholesterol in animals. However, the mechanism of cholesterol lowering has not been established for either material. This study was conducted to determine the effect of glucomannan (G), chitosan (CH), or an equal mixture of the two (G + CH) on cholesterol absorption and fat and bile acid excretion. Rats were fed a modified AIN-93G diet for 18 d containing 0.125 g/100 g cholesterol and initially 10 g/100 g of the test materials or cellulose (C) as the control. However, the concentration of test materials and cellulose was reduced to 7.5 g/100 g after 1 wk due to lower weight gain compared with controls. Total liver cholesterol was significantly reduced in G, CH and G + CH groups compared with the C group. The intestinal contents supernatant viscosity of the C and the CH groups was negligible, whereas both G and G + CH produced high viscosities. Cholesterol absorption, measured by the fecal isotope ratio method, was significantly reduced from 37.5% in the C group to 20.2% in G, 18.2% in G + CH and 9.4% in CH. Daily fecal fat excretion did not differ between the C and G groups, but was significantly greater in G + CH and CH compared with the C and G groups. Daily bile acid excretion was significantly greater in the CH and G + CH groups compared with the C and G groups. These results suggest that G lowered liver cholesterol by a viscosity-mediated interference of cholesterol absorption. In contrast, CH appears to lower cholesterol through a different mechanism. J. Nutr. 130: 2753–2759, 2000.

KEY WORDS: • glucomannan • chitosan • cholesterol • bile acids • fecal fat • rats

Chitosan is the deacetylated form of chitin, an aminopolysaccharide found in the exoskeleton of arthropods and certain fungi (Furda 1983). Although it is not derived from plants, it shares the characteristic with dietary fiber of being a polysaccharide that is indigestible by mammalian digestive enzymes. Several studies have shown chitosan to be hypocholesterolemic in animal models (LeHoux and Grondin 1993, Razdan and Pettersson 1994, Sugano et al. 1978 and 1980). How chitosan reduces cholesterol, however, remains uncertain.

Chitosan acts as a weak anion exchange resin and exhibits a substantial viscosity in vitro. Either of these properties of chitosan could mediate its hypocholesterolemic effect. Cholestyramine, a commercial anion exchange resin used as a hypocholesterolemic agent, decreases cholesterol absorption (McNamara et al. 1980) and increases bile acid excretion (Gallaher and Franz 1990, Stanley et al. 1973). Increased bile acid excretion could reduce cholesterol concentrations because plasma or liver cholesterol would be utilized to maintain the bile acid pool. Alternatively, bile acid binding within the small intestine could disrupt micelle formation, leading to a reduced ability to solubilize cholesterol (as well as monoglycerides and fatty acids) and consequently, reduced cholesterol absorption. In this regard, it is interesting that chitosan has been shown to reduce ileal fat digestibility in broiler chickens (Razdan and Pettersson 1994 and 1996). Alternatively, it is possible that the cholesterol-lowering effect of chitosan is due to an increase in the viscosity of intestinal contents. Increased intestinal contents supernatant viscosity is highly correlated with reduced plasma and liver cholesterol (Gallaher et al. 1993a and 1993b) and reductions in cholesterol absorption (Carr et al. 1996) in hamsters. However, Sugano et al. (1988) found that chitosan preparations of different in vitro viscosities all demonstrated equivalent hypocholesterolemic effects, arguing against a role for viscosity. Further, the viscosities of ileal digesta supernatants of broiler chickens fed chitosan were equal to those of birds fed a chitosan-free diet (Razdan and Pettersson 1996). Thus, the anion exchange property of chitosan would seem to be favored as an explanation for its hypocholesterolemic properties.
Konjac mannan, a viscous glucomannan, is a highly branched polysaccharide derived from the tuber Amorphophallus konjac. Konjac mannan has also demonstrated hypcholesterolemic effects (Shimizu et al. 1991, Yun-Hua et al. 1990), but again the mechanism by which this effect is mediated is not established. Konjac mannan has no anion exchange property, but it is highly fermentable within the large intestine. Fermentation of dietary fiber leads to the production of several short-chain fatty acids, primarily acetate, propionate and butyrate. Propionate, in particular, has been proposed to mediate the hypcholesterolemic effect of fermentable fibers such as guar gum and oat bran (Chen et al. 1984). The finding that propionate reduced cholesterol synthesis rates in cultured hepatocytes (Wright et al. 1990) supports this possibility. However, human studies in which propionate was infused rectally found no decrease in serum cholesterol (Wolever et al. 1989 and 1991). Further, rats fed dietary propionate showed no reduction in cholesterol synthesis (Illman et al. 1988).

Finally, germfree rats fed guar gum had significant reductions in plasma and liver cholesterol, demonstrating that fermentation is unnecessary to produce the hypcholesterolemic effect associated with this fiber (Alvarez-Leite et al. 1994). At present, there is no strong support for a role for cholesterol lowering by propionate. However, fermentation could reduce cholesterol levels by another means. Increased fermentation could alter the bile acid profile by increasing bacterial numbers and/or activity in the large intestine, thus increasing the proportion of bacterially modified bile acids, the secondary bile acids. Increasing the proportion of deoxycholic acid in the bile acid pool by feeding this secondary bile acid reduced choles-
terol synthesis in rats (Heuman et al. 1988). Thus, the hypo-
cholesterolemic effect of Konjac mannan could be mediated by its viscosity, fermentability or, indeed, both because these two effects are not mutually exclusive.

The objective of this study was to examine the effect of chitosan, glucomannan and a combination of the two, on cholesterol absorption and bile acid and fat excretion to un-
derstand how these materials lower cholesterol. The effect of these materials on fat excretion was also of interest as a possible explanation for the observation in several studies that chitosan supplements accelerated weight loss in subjects con-
suming hypocaloric diets (Sciutto and Colombo 1995, Ven-
eroni et al. 1996).

MATERIALS AND METHODS

Animals and diets. Male Wistar rats (initial body weight 50–75 g) (Harlan Sprague Dawley, Indianapolis, IN) were housed individual-

ly in stainless steel mesh cages and were allowed free access to a commercial rat diet (Rodent Laboratory Chow 5001, Purina Labora-
tories, St. Louis, MO) and water for 2 dt o allow adaptation to the commercial rat diet (Rodent Laboratory Chow 5001, Purina Labora-
tories) (Harlan Sprague Dawley, Indianapolis, IN) were housed individ-
ually from Harlan Teklad (Madison, WI). The test materials were chitosan, glucomannan (G; Propol, from Amorphophallus konjac) (both provided by Natural Alternatives, San Mateo, CA), an equal mixture of chitosan and glucomannan (CH + G) or cellulose (C) as the control. However, because of the slower rate of growth in rats fed CH and/or G, after 7 d, the dietary concentration of the test substances was reduced to 7.5 g/100 g by dilution with food devoid of test materials.

Experimental design. Rats were divided randomly into four treatment groups of approximately equal size (n = 8–9). Body weight was measured weekly. Food intake was determined at d 4, 10 and 14 of the study. A 3-d fecal collection was made in the last week. Three days before they were killed, rats were gavaged with 1H-cholesterol and 14C-sitosterol, and fecal collections were made for determination of cholesterol absorption, as described below. At the end of 17–18 d, rats were deprived of food overnight and presented with 5 g of their respective diets the following morning. Approximately 2 h after presentation of the meal, rats were anesthetized, and livers were excised, rinsed and immediately frozen. The small intestine was removed and contents collected by finger-stripping. Contents were centrifuged at 50,000 × g for 30 min at 37°C. The viscosity of the supernatant was measured using a Wells-Brookfield cone/plate vis-
cometer (Model LVT-CP, Brookfield Engineering, Stoughton, MA) at 37°C using a CP-51 cone. Measurements were taken at a number of shear rates. Viscosity vs. shear rate was plotted on a log-log scale and viscosity estimated by extrapolation of the line to a shear rate of 23.0 s−1. Cecal pH was determined using a combination spear-tip pH electrode (model 81–64, Orion Research, Boston, MA).

Analytical methods. Lipids were extracted from livers by the method of Folch et al. (1957) and cholesterol determined enzymat-
ically (Sigma Diagnostics #352–100, St. Louis, MO) after solubiliza-
tion in Triton X-100 in acetone. Bile acids were extracted from dried feces using organic solvents (Lockert and Gallaher 1989) and total bile acids measured enzymatically as described by Shelatwy and Lowowsky (1975). Fecal fat was determined gravimetrically after extraction with organic solvents.

Cholesterol absorption was measured by a modification of the fecal dual isotope ratio method of Borgstrom (1968). Rats were gavaged on two consecutive days at 0100 h with 5.0 kBq 14C-β-
sitosterol (2.05 GBq/mmol; Amersham Life Science, Arlington Hills, IL) and 34.7 kBq 1H-cholesterol (130 GBq/mmol; Amersham Life Science) using soybean oil as the vehicle. Two consecutive 24-h fecal collections were taken beginning at 1800 h of gavage d 1. Collections were individually lyophilized and stored at −20°C until analysis. Fecal lipids were extracted from each collection by homogenizing ground feces with chloroform/methanol (2:1) according to the method of Folch et al. (1957). The homogenate was filtered, then rinsed twice with normal saline. The filtrate was dried under nitrogen gas and reconstituted with chloroform/methanol (2:1). Radioactivity was determined in aliquots from duplicate samples by liquid scintill-
lation counting. Cholesterol absorption efficiency was determined for each 24-h period and the two values for each rat averaged.

Statistics. One-way ANOVA was used to determine treatment differences (SigmaStat version 1.0, Jandel Scientific, San Rafael, CA). Differences among means were inspected using Student-New-
man-Keuls multiple range test and were considered significant at P < 0.05. Values are reported as means ± SEM, n = 8–9.

RESULTS

Rats fed 10 g/100 g CH, G, or a combination of the two grew at a slower rate than those fed an equivalent level of C (Fig. 1). Consequently, on d 7, the dietary concentration of the test materials and C was reduced to 7.5 g/100 g. Subse-
quently, rats fed G grew at a rate similar to rats fed C. However, rats fed CH or CH + G still had a slightly slower rate of growth. At the termination of the experiment, on d 18–19, the body weights of the rats fed CH, G or the combi-
nation were significantly lower than those fed the C-containing diet. However, body weights of the rats fed CH, G or the combination were not different.

The reduced rate of growth of the G, CH and G + CH groups was undoubtedly due to a reduced food intake (Fig. 2). Daily food intake was lower in each of these groups compared
with the C-fed control group (P < 0.05). Liver weight was also significantly reduced in the G, CH and G + CH groups relative to controls (Table 1; P < 0.05). Cecum weight (with contents), in contrast, was greatest in the G-fed rats (P < 0.05), followed by the G + CH group (P < 0.05), both of which were greater than the C and CH groups. Daily fecal dry weight, however, was lowest in the G group. Fecal dry weight was greatest in the CH group, with an intermediate excretion weight in the C and G + CH groups. Cecal pH did not differ between CH-fed groups, both of which were significantly greater than the C and G groups (Table 1; P < 0.05).

Liver cholesterol contents and concentrations in the C group were approximately twice the values in the G, CH and G + CH groups (P < 0.05), which did not differ from one another (Table 2). Cholesterol absorption efficiency, however, was lowest in the CH group (P < 0.05), intermediate in the G and CH groups, which did not differ and were greater in the C group (P < 0.05).

Fat excretion was greatest in the CH group, more than sevenfold that of the C group (Table 2). Fat excretion in the G + CH group was significantly less than the CH group, but still substantially and significantly (P < 0.05) greater than either the C and G groups, which did not differ. Daily fecal bile acid excretion, in contrast, did not differ between the CH and G + CH groups. Fecal bile acid excretion by the CH and G + CH groups was more than twofold greater than that of the C and G groups.

Intestinal contents supernatant viscosities were very high in both the G and G + CH groups and were not different (Fig. 3). The C and CH groups, in contrast, had negligible supernatant viscosities, thus indicating that only G imparted a substantial viscosity to the intestinal contents.

### DISCUSSION

Glucomannan is considered a dietary fiber. Although CH is not, due to its primarily animal origin, it has dietary fiber-like properties. Like G, CH is a large polysaccharide that is indigestible by mammalian digestive enzymes, but produces significant physiologic effects when ingested. Both G and CH are also highly viscous in vitro (Furda 1983, Rogel and Vohra 1983). However, these two materials differ greatly in their susceptibility to fermentation. Glucomannan is completely fermentable by human fecal bacteria (Matsuura 1998), whereas CH appears to be resistant to fermentation, on the basis of its ability to reduce cecal short-chain fatty acid concentrations (derived from bacterial fermentation) (Razdan and Pettersson 1994) and colonic bacterial populations in mice (Tanigawa et al. 1997). Given these similarities and differences, it was of interest to compare the two for their cholesterol-lowering abilities, and to examine whether a synergy existed between them.

The rat was used as the animal model because its size allows sufficient intestinal contents to be collected to measure their supernatant viscosity without pooling of samples. Although serum cholesterol in rats is relatively unresponsive to dietary intervention at the low dietary cholesterol concentrations used in this experiment (Story et al. 1974), liver cholesterol concentrations are quite responsive. Further, dietary fibers that reduce liver cholesterol in rats have consistently been found to reduce plasma cholesterol in humans (Anderson 1995).

In agreement with other studies (Jennings et al. 1988, Quazi et al. 1983, Sugano et al. 1980), both G and CH
individually reduced liver cholesterol relative to a C control diet (Table 2). On an equal weight basis, the materials seemed to be equipotent. The amount of liver cholesterol in the groups fed the test materials was close to that reported for rats fed a cholesterol-free diet (Overton et al. 1994, Topping et al. 1988). Thus, if the rats had been fed diets containing either a higher concentration of cholesterol or a lower concentration of total test material, differences in the cholesterol-lowering effect of the groups fed the test materials may have become apparent.

Body weight gain in wk 1, when rats were fed 10 g/100 g G and CH, either alone or in combination, was lower than that of the C-fed rats (Fig. 1). To try to normalize weight gain, the concentration of the test materials was subsequently reduced to 7.5 g/100 g. Although weight gain improved by this reduction, it remained lower than that of the C control group; at the end of the experiment, all three groups fed test materials had equivalent but significantly lower body weights than the C group. However, all rats appeared healthy and remained active throughout the experiment. The reduced weight was undoubtedly due to the lower daily food intake of these groups. Sugano et al. (1980) also found a reduced weight gain in rats fed 10 g/100 g CH, but not 5 g/100 g; however, they found no significant reductions in food intake. LeHoux and Grondin (1993) reported that rats fed 7.5 g/100 g CH, the level used in the present experiment after wk 1, had weight gain equivalent to the control diet without CH. Food intake was actually slightly higher in the rats fed CH. A diet containing 10 g/100 g G has also been reported to lower body weight gain and food intake (Yun-Hua et al. 1990), whereas diets containing 5 g/100 g G have either reduced weight gain (Kiriyama et al. 1972) or had no effect (Jie and Shu-Sheng 1997, Quazi et al. 1983). Although the reduced food intake of the rats fed the test materials likely contributed to the lower liver cholesterol in these groups because it resulted in a reduced intake of cholesterol, it does not appear to explain the entire effect. Food intake of the groups fed the test materials varied between 66 and 72% of the control group. However, the liver cholesterol ranged from 33% of the C-fed group and the G + CH group to 42% in the G and CH groups. A reduced rate of body weight gain also does not appear to explain the reduction in liver cholesterol. Rogers and Kris-Etherton (1983) reported that Zucker rats that were restricted in energy to the extent that they lost weight experienced a reduced liver cholesterol concentration. However, when the rats were subsequently fed to maintain their body weight, no further reduction in liver cholesterol was seen. The situation in the present experiment would be most similar to the weight maintenance period because all rats gained weight, although at different rates. In a study more similar to ours, rats that were energy restricted but still gaining weight had microsomal cholesterol concentrations similar to those of freely fed rats (Lemay et al. 1991). Thus, mechanisms other than reduced food intake or weight gain must be in operation.

Reduced cholesterol absorption appears to be one of these mechanisms because cholesterol absorption efficiency was significantly reduced compared with the C group in all three groups fed test materials. This reduction was greatest for the CH group. Reports by others of the effect of CH on cholesterol absorption have been inconsistent. Fecal neutral sterol excretion was greater (Sugano et al. 1980) or not different (Fukada et al. 1991) when diets containing 5 g/100 g CH were fed. Vaheuny et al. (1983) found that intragastric infusion of a lipid emulsion containing CH reduced lymphatic absorption of cholesterol. There appears to be only one report of the effect of G on cholesterol absorption. Shimizu et al. (1991) found no decrease in cholesterol absorption in hamsters fed 3.5 g/100 g Konjac mannan. It should be noted, however, that in their study, cholesterol absorption was evaluated by excretion of radiolabeled cholesterol after gavage, but that a nonabsorbable

### TABLE 2

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>G</th>
<th>Ch</th>
<th>G + CH</th>
<th>Pooled SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver cholesterol, μmol</td>
<td>172.0a</td>
<td>72.4b</td>
<td>71.9b</td>
<td>56.1b</td>
<td>7.2</td>
</tr>
<tr>
<td>Liver cholesterol concentration, μmol/g</td>
<td>17.6a</td>
<td>9.3b</td>
<td>9.7b</td>
<td>7.8b</td>
<td>0.9</td>
</tr>
<tr>
<td>Cholesterol absorption, %</td>
<td>37.5a</td>
<td>20.2b</td>
<td>9.4c</td>
<td>18.2b</td>
<td>1.6</td>
</tr>
<tr>
<td>Fecal fat excretion, mg/d</td>
<td>158c</td>
<td>217c</td>
<td>1192a</td>
<td>830b</td>
<td>25</td>
</tr>
<tr>
<td>mg/d (g food intake)</td>
<td>7.6b</td>
<td>14.6b</td>
<td>69.0a</td>
<td>64.0a</td>
<td>6.6</td>
</tr>
<tr>
<td>Bile acid excretion, μmol/d</td>
<td>20.3b</td>
<td>14.8b</td>
<td>66.7a</td>
<td>58.3a</td>
<td>5.6</td>
</tr>
<tr>
<td>μmol/(d · 100 g body)</td>
<td>9.9b</td>
<td>8.5b</td>
<td>44.9a</td>
<td>45.2a</td>
<td>4.3</td>
</tr>
</tbody>
</table>

1 Values are means, n = 8–9. Values within a row that do not share a letter differ significantly, P < 0.05.
lipid marker was not used. This can lead to overestimation of cholesterol absorption. The technique used to measure cholesterol absorption in this study, the fecal isotope ratio method, which uses a nonabsorbable lipid marker, is considered a robust method (Gibson 1984). Other studies examining the effect of soluble fibers on cholesterol absorption have been inconsistent. In cholesterol-fed rats, feeding of pectin, psyllium, oat bran (Arjmandi et al. 1992) or guar gum (Favier et al. 1998) led to increased fecal neutral sterol excretion relative to C. Carr et al. (1996) found a decrease in cholesterol absorption in cholesterol-fed hamsters fed hydroxypropyl methylcellulose. However, Turley et al. (1994) found no difference in cholesterol absorption in hamsters fed psyllium compared with those fed a C control diet, and several studies in humans with ileostomies fed oat bran found no increase in cholesterol excretion (Lia et al. 1995, Zhang et al. 1992). Thus, our results suggest that both CH and the soluble fiber G are effective in reducing cholesterol absorption, although CH was the more effective of the two. Interestingly, combining the two materials resulted in a cholesterol absorption efficiency equivalent to that of G alone.

Increased bile acid excretion represents another mechanism by which a reduction in cholesterol can be produced. No increase in total fecal bile acids was found with feeding of G (Table 2). Jie and Shu-Sheng (1997) reported an increase in fecal bile acid excretion in rats fed 5 g/100 g G. However, they quantified bile acids by TLC, an insensitive method, and identified only two bile acids, chenodeoxycholic acid and glycodeoxycholic acid. Neither of these bile acids are present in feces in substantial quantities (Gallaher and Franz 1990). Consequently, their results must be viewed with caution.

Both groups fed CH had a much greater bile acid excretion than the C group, approximately a threefold increase. Chitosan is a weak anion exchanger and consequently would be expected to be able to bind bile acids. This ability has been demonstrated in several studies in vitro. Lee et al. (1999) reported that in vitro CH had approximately half the bile acid binding capacity of cholestyramine, a strong anion exchanger with a high capacity for binding bile acids. Sugano et al. (1980) reported that the in vitro bile acid binding capacity of CH was of a magnitude approximately equivalent to that of cholestyramine. In a more physiologic examination, Ebihara et al. (1989) found that rats fed test meals containing 5 g/100 g CH had greater bile acid concentrations in the intestinal contents solid phase relative to the aqueous phase compared with C-fed rats. Because CH partitions into the solid phase, this suggests binding of bile acids by CH in vivo. Our findings of greatly increased (approximately threefold) fecal bile acid excretion in the groups fed CH, either alone or in combination with G, compared with C-fed animals, are consistent with these studies. It is thus surprising that in several studies in rats, diets containing 5 g/100 g CH did not increase fecal bile acid excretion (Fukada et al. 1991, Sugano et al. 1980). The reason for this discrepancy with the current study is not apparent. However, increased fecal bile acid excretion with CH feeding has been found in rabbits (Hirano and Akiyama 1995) and humans (Maezaki et al. 1993).

Nauss et al. (1983) reported that in vitro, CH could bind micellar lipids in substantial amounts. These authors also indicated that CH could bind the microemulsions of lipids that occur within the small intestine after a fat-containing meal; however, no data were presented to support this conjecture. The results of our study suggest that CH may induce “bind” intestinal lipids in some manner. Feeding CH at 7.5 g/100 g diet led to fecal fat excretion 7.5-fold greater than that of the C-fed group. Indeed, daily fecal fat excretion was equal to 51% of the daily consumption of soybean oil in rats fed 7.5 g/100 g CH. In the group fed the G + CH mixture (equivalent to 3.75 g/100 g CH), fat excretion was more than fivefold greater. Because G feeding produced only a slight insignificant increase in fecal fat, the greater fecal fat in the group fed the mixture may be attributed entirely to the CH present. This indicates that the increase in fecal fat due to CH is nonlinear and that the largest increments in fecal fat excretion come at the lower dietary levels of CH. This effect of CH on fat excretion appears to be specific because Razdan and Pettersson (1994 and 1996) noted that in broiler chickens, CH reduced ileal digestibility of fat but not that of protein and starch. Similarly, Kanauchi et al. (1995) reported that fat digestibility was ~25% in rats fed 5 g/100 g CH relative to a fat digestibility of ~92% in those fed C, whereas protein digestibility was unaffected. In contrast to this effect of CH, no increase in fecal fat was noted with feeding G. There appears to be only one other study in which the effect of G on fecal fat excretion has been examined. In that study, chicks fed diets containing 2 g/100 g G had a more than twofold increase in ether-extractable fat in the excreta compared with chicks fed the control diet (Rogel and Vollra 1983). However, chicks fed G experienced severe growth depression, had a large increase in food consumption and excreta weight, substantial pancreatic enlargement and reduced apparent metabolizable energy. These outcomes indicate a substantial interference in macronutrient digestion and absorption, suggesting that the increase in fecal fat excretion was not a specific effect.

The results of our study confirm that both G and CH have potent cholesterol-lowering effects in cholesterol-fed rats, but suggest that they do so through different mechanisms. Glucomannan feeding results in a high intestinal contents supernatant viscosity, which is strongly and directly associated with cholesterol lowering (Gallaher et al. 1993a) and a reduction in cholesterol absorption (Carr et al. 1996). Consistent with the present results, we have found that contents supernatant viscosity has no effect on bile acid excretion over a wide range of viscosities in rats fed hydroxypropyl methylcellulose (D. Gallaher et al., unpublished observations). Thus, in the case of G, cholesterol lowering appears to be mediated through a viscosity-associated specific reduction in cholesterol absorption.

Chitosan feeding, in contrast, did not increase intestinal contents supernatant viscosity, in agreement with the results of others (Razdan and Pettersson 1996), thereby eliminating viscosity as a mechanism for cholesterol lowering. Unlike G, CH feeding led to greater excretion of both bile acids and fat in addition to decreasing cholesterol absorption. The studies of Nauss et al. (1983), which reported that, in vitro, CH bound bile acid micelles in toto, suggest reduced absorption of all components of a micelle, i.e., bile acids, cholesterol, monoglycerides and fatty acids. This effect would be consistent with the results of the present study in which we found greater excretion of both bile acids and fat. Deuchi et al. (1994), however, proposed a quite different mechanism. They suggested that CH is dissolved in the stomach by gastric acid and subsequently mixes with dietary fat to form a CH-fat complex. This complex was hypothesized to gel in the small intestine, entrapping the fat and thereby preventing lipolysis, with subsequent excretion of the undigested fat, including cholesterol.

Yet another explanation is provided by the recent finding that, in vitro, CH inhibits pancreatic lipase activity (Han et al. 1999). Inhibition of pancreatic lipase within the small intestine would lead to accumulation of a lipid emulsion. In the presence of substantial amounts of unabsorbed lipid within the small intestine, cholesterol will partition into the lipid phase (Jandacek 1982), leading to greater excretion of cholesterol.
This concept is consistent with the finding that administration of the pancreatic lipase inhibitor tetrahydrolipstatin (orlistat) to mice reduced cholesterol absorption (Young and Hui 1999). However, in these two latter mechanisms, both of which postulate interference in triacylglycerol hydrolysis, it is unclear how greater bile acid excretion would occur. Consequently, the results from the current study favor the mechanism of micellar binding (or entrapment) because this would lead to greater excretion of both fecal fat and bile acids.

In conclusion, both G and CH reduce liver cholesterol in cholesterol-fed rats, either alone or as an equal mixture of the two. The mechanism of cholesterol reduction appears to differ between the two. Although both materials decrease cholesterol absorption, CH has the additional effect of greatly increasing bile acid and fat excretions. The greater fat excretion suggests that CH should be explored further as a means to decrease intestinal fat absorption.

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LITERATURE CITED


