

# Effects of Different Cereal Fibers on Cholesterol and Bile Acid Metabolism in the Syrian Golden Hamster<sup>1</sup>

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## ABSTRACT

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This study examined the effects of various cereal fibers and various amounts of  $\beta$ -glucan on cholesterol and bile acid metabolism. Hamsters were fed semisynthetic diets containing 0.12% cholesterol, 20% fat, and either 16% total dietary fiber (TDF) from wheat bran (control) or 10% TDF from oat bran, 13% TDF from oat bran concentrate or barley grains, 16% TDF from oat fiber concentrate, barley flakes, or rye bran. After five weeks, plasma total cholesterol and liver cholesterol concentrations were significantly lower (20 and 50%, respectively) only in hamsters fed rye bran. Diets containing any of the oat ingredients or barley had no effect on total cholesterol. Changes in the pattern of biliary bile acids occurred in hamsters fed 16% TDF from barley flakes or 10% TDF from

oat bran. Hamsters fed rye bran had a significantly higher fecal bile acid excretion when compared with controls fed wheat bran. Because rye bran caused the most pronounced lowering effect of total cholesterol despite the lowest content of  $\beta$ -glucan and soluble fibers, components other than  $\beta$ -glucan and soluble fibers seem to be involved in its hypocholesterolemic action. Since the effects of the oat and barley ingredients were not solely correlated to the  $\beta$ -glucan content, structural changes occurring during processing and concentrating of the products may have impaired the hypocholesterolemic potential of the  $\beta$ -glucans, and other factors such as solubility and viscosity of the fiber components seem to be involved.

The cholesterol-lowering potential of cereal fibers like oat, barley, and rye bran has been shown in many animal and human studies (Kahlon and Chow 1997, Kritchevsky 1997). However, the underlying mechanisms and the components responsible for the cholesterol-lowering effects are still not completely defined (Kritchevsky 1997).

In the study of Swain et al (1990), the hypocholesterolemic effect of oat fiber was, as concluded by these authors, only a result of the exchange of dietary fat and cholesterol for complex carbohydrates and fiber, but their experimental design does not justify this as a general mechanism for oat  $\beta$ -glucan. On the other hand, Ripsin et al (1992) evaluated 20 human studies examining the cholesterol-lowering effects of oat fibers in a meta-analysis and found a potential dose-response relationship between the amount of soluble fiber and the degree of lipid reduction. Moreover, the cholesterol-lowering potential of oat products is well documented in many animal studies with rats (Shinnick et al 1990, Mälkki et al 1992) and hamsters (Kahlon et al 1993, Zhang et al 1994a). Numerous studies concerning the cholesterol-lowering effects of various barley fibers in chicks (Newman et al 1991, Martinez 1992, Wang et al 1992) and hamsters (Wang et al 1997) have been published, and they report significant reductions in plasma cholesterol, but there are also less conclusive results (German et al 1996).

Many studies have focused on  $\beta$ -glucan as the component mainly responsible for the cholesterol-lowering effect of cereal fibers like oat and barley bran.  $\beta$ -glucans are endospermic cell-wall polysaccharides consisting of (1 $\rightarrow$ 3)(1 $\rightarrow$ 4) linked glucopyranosyl-monomers that cannot be degraded by the intestinal digestion enzymes. It is thought that, upon ingestion,  $\beta$ -glucan increases the intestinal viscosity and thus decreases the absorption of cholesterol and the reabsorption of bile acids. Newman et al (1991) investigated the effects of supplementation with  $\beta$ -glucanase to barley diets and found the  $\beta$ -glucanase diets were less effective in lowering cholesterol. Fadel et al (1987) found even stronger results when adding  $\beta$ -glucanase to a barley diet fed to chicks resulted in the complete loss of the hypocholesterolemic effect.

In the present study, in addition to oat and barley fibers, rye bran was included because little is known about its cholesterol effects. Rye bran showed hypocholesterolemic and gallstone-preventing properties in hamsters (Zhang et al 1994a) but was less effective in a human study (Zhang et al 1994b). Rye bran contains less  $\beta$ -glucan but more fiber as highly viscous arabinoxylans (Åman et al 1997).

The Syrian golden hamster was used as an animal model because of similarities with the human cholesterol and bile acid metabolism (Kris-Etherton and Dietschy 1997). The objectives of this study were to examine the effects of various cereal fibers on cholesterol and bile acid metabolism, to further investigate the role of the soluble fiber and  $\beta$ -glucan contents in the cholesterol-lowering action, and to elucidate mechanisms by which cereal fibers (and  $\beta$ -glucans) elicit hypocholesterolemic effects.

## MATERIALS AND METHODS

### Animals, Diets, and Feeding Procedures

Male golden Syrian hamsters (SASCO, Omaha, NE) weighing  $65.3 \pm 5.0$  g were randomly assigned to one of seven dietary groups ( $n = 10$  per group). Hamsters were housed in groups of three to four per cage in a temperature-controlled environment under a 12-hr light-dark cycle (lights on at 18:00). Hamsters were given free access to semipurified diets and water. The actual food consumption was recorded daily. Body weights were monitored on a weekly basis. All experimental protocols and procedures were approved by the Animal Care and Use Committee at the University of Kiel, Germany.

Hamsters were fed semipurified diets for five weeks. Diets contained 20% fat, 3.2% nitrogen (20% protein), and 0.12% cholesterol. The dietary fiber sources were: wheat bran (WB, control), oat bran (OB), oat bran concentrate (OBC), oat fiber concentrate (OFC), barley grains (BG), Prowashonupana barley flakes (PBF), and rye bran (RB). WB was purchased from a local grocery store; OB was obtained from Peter Kölln Köllnflockenwerke, Elmshorn, Germany; OBC and OFC were provided by Cerefi Ltd, Espoo, Finland. BG were a crossbreeding of Arena (*Hordeum vulgare*) and uncultivated barley (*H. spontaneum*) and were kindly provided by the Institute of Crop Science and Plant Breeding from the University of Kiel, Germany. PBF were provided by ConAgra Grain Products Company, Omaha, NE, and the RB was provided by Wasabröd AB, Filipstad, Sweden. All cereal components were analyzed for total dietary fiber (TDF), soluble fiber,  $\beta$ -glucan, carbohydrates, protein, and fat (Table I), and the contents were considered when

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diets were prepared. To exclude any influence of the fatty acid composition on the lipid-lowering effects, the ratio of polyunsaturated to saturated fatty acids (P/S ratio 0.33) and the fatty acid composition (saturated fatty acids 42.9–44.0%, monounsaturated fatty acids 38.6–40.4%, polyunsaturated fatty acids 14.0–14.4%) were kept constant in all diets by mixing various types of fats (butter, palm oil, olive oil, sunflower oil) at different ratios. The composition of the diets is given in Table II.

After five weeks, hamsters were fasted for 15 hr individually in wire-bottomed cages and then exsanguinated under anesthesia using a gaseous mixture of CO<sub>2</sub> and O<sub>2</sub> (50:50). The liver, small intestine, and cecum were excised, blotted, and weighed. A portion of the liver of the same lobe and a similar size was removed and frozen for hepatic cholesterol analysis. Immediately after removal of the cecum, the pH of the cecal contents was measured using a spear-tip pH electrode. The total contents were then removed and the cecal wall was rinsed with 0.15M NaCl, dried, and weighed. Gallbladder bile was aspirated, weighed, and analyzed for biliary lipids and bile acid composition.

### Methods and Analyses

Blood samples were drawn into an ethylenediaminetetraacetic acid (EDTA)-wetted syringe by cardiac puncture, and plasma was separated immediately by centrifugation at 2,600 × g for 10 min. Plasma total cholesterol (TC) and triacylglycerol (TG) concentrations were determined by enzymatic assays (kits 352 and 336,

respectively, Sigma Chemicals, Deisenhofen, Germany). For lipoprotein isolation, plasma was taken from a single hamster or was pooled from two hamsters with similar plasma TC concentrations. Plasma lipoproteins were isolated by sequential ultracentrifugation (Havel et al 1955) using an L7-65 ultracentrifuge and a 50.4 Ti rotor (Beckman Instruments, Munich, Germany). A preservative solution (final concentration in plasma: 1 mM benzamidine, 0.04% EDTA, 0.005% gentamycinulphate, 0.05% NaN<sub>3</sub>) was added to protect lipoproteins from enzymatic degradation. Three lipoprotein fractions were isolated based on the following densities: VLDL (d < 1.006 kg/L), LDL (1.006 < d < 1.055 kg/L), HDL (1.055 < d < 1.21 kg/L). LDL and HDL fractions were dialyzed against 0.15M NaCl containing 0.04% EDTA and 0.05% NaN<sub>3</sub> at 4°C for 24–36 hr. Total cholesterol (TC), free cholesterol (FC), triacylglycerol (TG), and phospholipid (PL) concentrations were determined using enzymatic assays (Sigma kit 352 for TC and kit 336 for TG; Wako Free Cholesterol C kit for FC, and Wako Phospholipid B kit for PL, Wako Chemicals, Düsseldorf, Germany). Protein concentration was determined by a modification of the Lowry procedure (Markwell et al 1978). To verify the density cut-points and to check for cross-contaminations, LDL and HDL apolipoproteins were separated by gradient SDS-PAGE (4–20%), and stained with Coomassie Brilliant Blue dye. No traces of apoB<sub>100</sub> could be detected in the HDL fractions (data not shown).

Cholesterol concentrations were analyzed after a modified Folch extraction (Folch et al 1957) with chloroform and methanol follow-

**TABLE I**  
Nutrient and Fiber Content of the Cereal Sources (g/100 g)<sup>a</sup>

Content <sup>b</sup>	WB	OB	OBC	OFC	BG	PBF	RB
Dry matter	86.5	91.5	90.4	90.7	88.8	91.7	86.5
Nitrogen	2.0	3.2	3.6	3.1	2.3	2.6	2.1
Fat	4.4	9.5	4.5	4.1	3.6	4.7	2.8
Carbohydrates	21.5	33.4	18.1	12.9	46.2	38.4	39.8
Total dietary fiber	42.3	24.3	40.7	49.3	22.6	30.9	26.8
Soluble dietary fiber	3.4	11.1	18.9	23.8	4.4	18.5	3.8
β-Glucan	2.1	12.9	20.7	24.6	5.6	17.9	2.9

<sup>a</sup> WB = wheat bran, OB = oat bran, OBC = oat bran concentrate, OFC = oat fiber concentrate, BG = barley grains, PBF = Prowashonupana barley flakes, RB = rye bran.

<sup>b</sup> Total and soluble dietary fiber were analyzed according to the AOAC method 991.43, protein by the Kjeldahl method, fat by the method of Amtliche Sammlung von Untersuchungsverfahren nach 35 LMBG, 1982 (L17.00-4), β-glucan by AOAC method 995.16. Total carbohydrates were calculated as the difference.

**TABLE II**  
Composition of Diets (g/kg, dwb)<sup>a</sup>

Content <sup>b</sup>	WB (control)	OB	OBC	OFC	BG	PBF	RB
Protein							
Casein/wheat gluten	120/33	117/—	120/8	120/18	119/—	117/—	120/—
Carbohydrates							
Wheat starch/dextrose	157/140	161/140	210/140	196/140	2/140	38/140	—/140
Fat							
Butter/palm oil	37/101	39/87	37/95	37/94	36/89	41/88	40/94
Olive oil/sunflower oil	40/6	35/—	41/13	41/15	54/—	47/—	40/9
Fiber sources							
WB	378	...	...	...	...	...	...
OB	...	411	...	...	...	...	...
OBC	...	...	320	...	...	...	...
OFC	...	...	...	325	...	...	...
BG	...	...	...	...	575	...	...
PBF	...	...	...	...	...	518	...
RB	...	...	...	...	...	...	597
Fiber components							
β-Glucans	8	53	66	80	32	93	17
Soluble fibers	13	46	60	77	25	96	23
Insoluble fiber	147	54	70	83	105	64	137
Total dietary fiber	160	100	130	160	130	160	160

<sup>a</sup> WB = wheat bran, OB = oat bran, OBC = oat bran concentrate, OFC = oat fiber concentrate, BG = barley grains, PBF = Prowashonupana barley flakes, RB = rye bran.

<sup>b</sup> All diets contained 0.12% dietary cholesterol, 0.3% choline chloride, 1.2% Hayes-Cathcart vitamin mix, and 4.6% Ausman-Hayes mineral mix (Hayes et al 1989). Diets were equal in fat (20%), P/S ratio (0.33), and nitrogen (3.2%).

ing the procedure described previously (Trautwein et al 1993a). TC was determined enzymatically (using Sigma kit 352) and FC was analyzed using HPLC (Kim and Chung 1984). The concentrations of esterified cholesterol (EC) were calculated as the difference between TC and FC.

Gallbladder bile lipids were isolated using a modified Folch extraction (Folch et al 1957), which results in an almost complete recovery of the biliary lipids. Biliary cholesterol and PL were determined enzymatically in an aliquot of the chloroform phase (Wako Free Cholesterol C kit and Wako Phospholipid B kit). Biliary bile acids were analyzed in an aliquot of the methanol-KCl phase as taurine and glycine conjugated bile acids using an isocratic HPLC method adapted from Rossi et al (1987) as previously described (Trautwein et al 1993a). Total bile acid concentration was calculated as the sum of individual bile acids using taurine and glycine conjugates of cholate, chenodeoxycholate, deoxycholate, and lithocholate as external standards.

Fecal samples were collected over a three-day period during week four from six randomly selected hamsters per diet group housed individually in wire-bottomed cages to measure fecal bile acid and neutral sterol excretion. The distribution of the individual fecal bile acids was determined according to the micro method of Czubayko et al (1991) with some modifications (Trautwein et al 1998b). Bile acid standard mixture consisted of 5 $\beta$ -cholanic acid (ursocholanic acid) as internal standard, ursodeoxycholic acid, lithocholic acid, deoxycholic acid, cholic acid, chenodeoxycholic acid, hyodeoxycholic acid (all from Sigma Chemicals), 5 $\beta$ -cholanic acid-3 $\beta$ -ol, 5 $\beta$ -cholanic acid-3 $\alpha$ -ol-12-one (12-ketolithocholic acid) and 5 $\beta$ -cholanic acid-3 $\alpha$ -7 $\alpha$ -diol-12-one (Steraloids, Wilton, NH). To determine the total bile acid and neutral sterol concentration, the oven-dried fecal samples were analyzed using a modification of

the method of Suckling et al (1991) as described previously (Trautwein et al 1993b). Total bile acid concentration was determined enzymatically (Sigma bile acid kit 450). Neutral sterols were analyzed by gas chromatography as free sterols according to the method of Ausman et al (1993) as reported previously (Trautwein et al 1997).

### Statistical Analysis

Statistical differences were calculated using one-way analysis of variance (ANOVA). When significant *F* ratios were found, individual means were further compared by the Bonferroni-Dunn post-hoc test utilizing the SuperANOVA statistical software package (version 1.11, Abacus Concepts Inc., Berkeley, CA). Differences were considered significant at *P* < 0.05. Results were expressed as means and standard deviation (SD).

## RESULTS

No significant differences in food intake, final body weight (160  $\pm$  15 g for all animals), and daily body weight gain were observed among the seven diet groups (data not shown). Cecal weights were significantly greater for the OBC diet group when compared with the other diets, except for the RB and PBF groups. Small intestine weights differed significantly only between the animals fed RB and BG, but were not significantly different compared with the WB control. The pH of the cecal contents did not differ among diet groups (Table III). No differences were observed for the liver weights (6.5  $\pm$  0.9 g for all animals) when expressed as absolute values or as g of liver/kg of body weight (data not shown).

Plasma total cholesterol (TC) was slightly (not significantly) decreased in hamsters fed the BG, PBF, OB, and OBC diets; unchanged with the OFC diet; and significantly lowered by 20%

**TABLE III**  
Small Intestine and Cecal Weights and pH Values of the Cecal Contents of Hamsters Fed Diets Containing 0.12% Cholesterol, 20% Fat, and Different Cereal Fiber Products for Five Weeks<sup>a</sup>

Content	WB (control)	OB	OBC	OFC	BG	PBF	RB
Small intestine, g	1.96 $\pm$ 0.41ab <sup>b</sup>	1.63 $\pm$ 0.13ab	1.87 $\pm$ 0.25ab	1.70 $\pm$ 0.16ab	1.58 $\pm$ 0.48a	1.68 $\pm$ 0.24ab	2.08 $\pm$ 0.40b
Cecum, g	1.57 $\pm$ 0.46a	1.36 $\pm$ 0.16a	2.28 $\pm$ 0.88b	1.58 $\pm$ 0.39a	1.51 $\pm$ 0.39a	1.78 $\pm$ 0.28ab	1.94 $\pm$ 0.30ab
Cecal content, g	1.05 $\pm$ 0.44a	0.83 $\pm$ 0.17a	1.71 $\pm$ 0.87b	1.02 $\pm$ 0.41a	1.00 $\pm$ 0.36a	1.18 $\pm$ 0.33ab	1.31 $\pm$ 0.32ab
pH	7.42 $\pm$ 0.11	7.39 $\pm$ 0.17	7.41 $\pm$ 0.07	7.44 $\pm$ 0.19	7.32 $\pm$ 0.15	7.26 $\pm$ 0.14	7.38 $\pm$ 0.15

<sup>a</sup> WB = wheat bran, OB = oat bran, OBC = oat bran concentrate, OFC = oat fiber concentrate, BG = barley grains, PBF = Prowashonupana barley flakes, RB = rye bran. Mean values  $\pm$  standard deviation, *n* = 10 per diet.

<sup>b</sup> Means within a row with different letters are significantly different (*P* < 0.05) using one-way analysis of variance and the Bonferroni-Dunn post-hoc test.

**TABLE IV**  
Plasma Lipids, Lipoprotein Composition, and Liver Lipids of Hamsters Fed Diets Containing 0.12% Cholesterol, 20% Fat, and Different Cereal Fiber Products for Five Weeks<sup>a</sup>

Content <sup>b</sup>	WB (control)	OB	OBC	OFC	BG	PBF	RB
Plasma TC <sup>c</sup> (mmol/L)	5.71 $\pm$ 0.66b <sup>e</sup>	5.38 $\pm$ 0.61ab	5.27 $\pm$ 0.20ab	5.89 $\pm$ 0.56b	5.46 $\pm$ 0.86b	5.38 $\pm$ 0.61ab	4.56 $\pm$ 0.49a
VLDL-C <sup>d</sup>	1.6 $\pm$ 1.1	1.0 $\pm$ 1.0	0.8 $\pm$ 0.4	1.2 $\pm$ 0.7	1.1 $\pm$ 0.4	1.5 $\pm$ 0.7	0.9 $\pm$ 0.3
LDL-C <sup>d</sup>	0.9 $\pm$ 0.4	0.8 $\pm$ 0.5	0.5 $\pm$ 0.1	0.7 $\pm$ 0.2	0.8 $\pm$ 0.3	0.8 $\pm$ 0.2	0.7 $\pm$ 0.2
HDL-C <sup>d</sup>	3.5 $\pm$ 0.3ab	3.7 $\pm$ 0.5ab	4.0 $\pm$ 0.3b	4.0 $\pm$ 0.4b	3.6 $\pm$ 0.2ab	3.3 $\pm$ 0.4a	3.2 $\pm$ 0.3a
HDL-C/(LDL-C+VLDL-C) <sup>d</sup>	1.6 $\pm$ 0.5a	2.5 $\pm$ 1.3ab	3.3 $\pm$ 0.9b	2.4 $\pm$ 0.8ab	2.0 $\pm$ 0.6ab	1.6 $\pm$ 0.6a	2.1 $\pm$ 0.4ab
Plasma TG <sup>c</sup> (mmol/L)	3.14 $\pm$ 1.25	2.14 $\pm$ 0.59	2.17 $\pm$ 0.65	2.44 $\pm$ 1.08	2.39 $\pm$ 0.89	2.89 $\pm$ 0.94	2.43 $\pm$ 0.76
VLDL-TG <sup>d</sup>	4.3 $\pm$ 3.0	3.3 $\pm$ 3.7	2.4 $\pm$ 1.2	3.0 $\pm$ 1.8	2.4 $\pm$ 0.9	3.3 $\pm$ 1.7	2.3 $\pm$ 0.9
LDL-TG <sup>d</sup>	0.14 $\pm$ 0.06b	0.10 $\pm$ 0.04ab	0.07 $\pm$ 0.03a	0.08 $\pm$ 0.02ab	0.08 $\pm$ 0.02ab	0.07 $\pm$ 0.02ab	0.06 $\pm$ 0.02a
Liver lipids <sup>c</sup> ( $\mu$ mol/g of liver)							
TC	73.7 $\pm$ 24.2b	67.5 $\pm$ 11.6b	62.7 $\pm$ 17.0b	76.9 $\pm$ 10.9b	104.9 $\pm$ 11.4c	82.6 $\pm$ 6.2b	37.2 $\pm$ 10.9a
FC	9.4 $\pm$ 0.8	8.6 $\pm$ 1.2	8.4 $\pm$ 0.4	9.3 $\pm$ 0.4	9.4 $\pm$ 0.9	9.2 $\pm$ 0.6	8.5 $\pm$ 0.8
EC	64.3 $\pm$ 23.7b	58.9 $\pm$ 11.9b	54.3 $\pm$ 16.8b	67.6 $\pm$ 11.1b	95.5 $\pm$ 11.7c	73.4 $\pm$ 6.2b	28.7 $\pm$ 10.6a
FC (% of TC)	14.4 $\pm$ 6.6a	13.3 $\pm$ 3.8a	14.1 $\pm$ 3.1a	12.4 $\pm$ 2.1a	9.1 $\pm$ 1.5a	11.2 $\pm$ 1.0a	25.4 $\pm$ 11.1b

<sup>a</sup> WB = wheat bran, OB = oat bran, OBC = oat bran concentrate, OFC = oat fiber concentrate, BG = barley grains, PBF = Prowashonupana barley flakes, RB = rye bran. Mean values  $\pm$  standard deviation.

<sup>b</sup> TC = total cholesterol, TG = triacylglycerol, FC = free cholesterol, EC = esterified cholesterol. VLDL, LDL, HDL = very low, low and high density lipoproteins, respectively. Baseline values in another study (Trautwein et al 1998b) were 3.18  $\pm$  0.36 mmol/L for TC, 1.72  $\pm$  0.24 mmol/L for TG; *n* = 10 from nonfasted animals.

<sup>c</sup> *n* = 9–10 per diet.

<sup>d</sup> *n* = 5–6 per diet (from pooled samples).

<sup>e</sup> Means within a row with different letters are significantly different (*P* < 0.05) using one-way analysis of variance and the Bonferroni-Dunn post-hoc test.

with the RB diet when compared with the WB control (Table IV). The lipoprotein composition of hamsters receiving the test diets was not significantly different from the WB control when expressed as mmol/L (Table IV). The highest ratio of HDL to VLDL+LDL cholesterol was caused by OBC diet, which was more than twice that of control WB diet. Plasma total triglycerides (TG) were not significantly decreased by the test diets due to great inter-individual variations. The concentration of LDL-TG was significantly decreased by RB and OBC when compared with that of the control (Table IV), but the relative distribution of TG among the lipoprotein fractions was not altered (data not shown).

Liver total cholesterol concentrations were impressively decreased with the RB diet (-50%), while only minor reductions were found with OB and OBC (-8 and -15%, respectively). Unexpectedly, BG significantly (+42%) and PBF slightly (+12%, ns) increased liver cholesterol concentrations when compared with WB. The content ( $\mu\text{mol/g}$  of liver) of free cholesterol (FC) was not different among all diets, but the concentration of esterified cholesterol (EC) was significantly lower in hamsters fed RB and higher in hamsters fed BG when compared with WB controls. Consequently, the percentage of FC was almost doubled with RB compared with WB (Table IV).

No significant differences in the concentration and relative distribution of biliary total bile acids, phospholipids, and cholesterol were found between the control and the test diets (data not shown). However, the biliary bile acid profile showed distinct changes with each cereal fiber (Table V). OB significantly increased the relative proportion of all tauro-conjugated bile acids (tauro-

conjugates of cholic acid, chenodeoxycholic acid, and deoxycholic acid), while the glyco-conjugated bile acids were lowered to various extents. Consequently, the ratio of glycine to taurine-conjugated bile acids significantly decreased (-50%) with OB compared with WB, suggesting a preferred removal of glycine-conjugated bile acids. In contrast, PBF led to a significantly higher glycine-to-aurine ratio. OBC, OFC, BG, and RB produced bile acid patterns that were similar to that of WB. The ratio of primary to secondary bile acids was decreased with the OB and PBF diets, indicating higher concentrations of secondary bile acids when compared with WB.

Hamsters fed the WB and RB diet had significantly higher fecal output than animals consuming the OB, OBC, OFC, BG, and PBF diets (Table VI).

The fecal concentration of cholesterol and its degradation products (neutral sterols,  $\mu\text{mol/g}$ ) was significantly higher with OB and OBC compared with WB (Table VI). The daily excretion of neutral sterols was not significantly changed with the test diets, but RB tended to increase the daily excretion (+26%) when compared with WB. The composition (expressed as a relative percentage of the sum of cholesterol and cholesterol degradation products) was only slightly changed when compared with the WB control. The percentage of coprostanol, cholesterol, and coprostanone was not significantly altered, but all oat and barley test diets revealed a higher percentage of cholestanol.

The concentration of fecal bile acids ( $\mu\text{mol/g}$ ) was significantly higher with all test diets, except the BG diet, when compared with the WB control. However, due to the high feces output of the

**TABLE V**  
Biliary Bile Acid Profile of Hamsters Fed Diets Containing 0.12% Cholesterol, 20% Fat, and Different Cereal Fiber Products for Five Weeks<sup>a</sup>

Content <sup>b</sup> (mol%)	WB (control)	OB	OBC	OFC	BG	PBF	RB
TCA	19 ± 5b <sup>c</sup>	26 ± 7a	17 ± 6b	20 ± 3ab	19 ± 5b	14 ± 3b	18 ± 3b
GCA	45 ± 5ab	32 ± 8c	40 ± 5bc	40 ± 7bc	44 ± 6ab	51 ± 10a	44 ± 2ab
TCDCa	11 ± 2bc	18 ± 5a	14 ± 5ab	13 ± 6ab	12 ± 3abc	7 ± 2c	10 ± 1bc
TDCA	3 ± 2b	6 ± 1a	2 ± 1b	4 ± 2ab	4 ± 1ab	4 ± 2ab	3 ± 1b
GCDCA	18 ± 4ab	13 ± 3b	23 ± 8a	17 ± 4ab	16 ± 4b	16 ± 4b	20 ± 4ab
GDCA	3 ± 1b	4 ± 2b	4 ± 3b	5 ± 2b	5 ± 2b	8 ± 2a	5 ± 1b
Cholate to chenodeoxycholate	2.2 ± 0.2ab	1.9 ± 0.4b	1.7 ± 0.7b	2.1 ± 0.6b	2.4 ± 0.6ab	3.1 ± 1.3a	2.1 ± 0.3b
Glycine to taurine conjugates	2.2 ± 0.7b	1.1 ± 0.5c	2.1 ± 0.5bc	1.8 ± 0.5bc	2.0 ± 0.8bc	3.2 ± 1.2a	2.3 ± 0.4ab
Primary to secondary bile acids	17.6 ± 8.1a	9.0 ± 2.4b	15.3 ± 8.8ab	9.6 ± 4.3ab	11.6 ± 4.6ab	7.6 ± 3.5b	12.5 ± 4.2ab

<sup>a</sup> WB = wheat bran, OB = oat bran, OBC = oat bran concentrate, OFC = oat fiber concentrate, BG = barley grains, PBF = Prowashonupana barley flakes, RB = rye bran. Mean values ± standard deviation, *n* = 8 per diet.

<sup>b</sup> TCA = taurocholic acid, GCA = glycocholic acid, TCDCa = taurochenodeoxycholic acid, TDCA = taurodeoxycholic acid, GCDCA = glycochenodeoxycholic acid, GDCA = glycodeoxycholic acid Tauro- and glycolithocholic acid were either not detectable or found only in trace amounts.

<sup>c</sup> Means within a row with different letters are significantly different (*P* < 0.05) using one-way analysis of variance and the Bonferroni-Dunn post-hoc test.

**TABLE VI**  
Fecal Weights and Fecal Excretion of Neutral Sterols of Hamsters Fed Diets Containing 0.12% Cholesterol, 20% Fat and Different Cereal Fiber Products for Five Weeks<sup>a</sup>

Content	WB (control)	OB	OBC	OFC	BG	PBF	RB
Fecal dry weight (g/day)	1.04 ± 0.18b <sup>b</sup>	0.52 ± 0.06a	0.55 ± 0.08a	0.54 ± 0.07a	0.57 ± 0.17a	0.48 ± 0.13a	0.85 ± 0.19b
Neutral sterols <sup>c</sup>							
Total concentration ( $\mu\text{mol/g}$ )	4.7 ± 0.8a	8.5 ± 1.5bc	9.1 ± 2.2c	6.1 ± 1.8a-c	5.4 ± 2.2ab	5.9 ± 1.1a-c	7.3 ± 3.0a-c
Daily total excretion ( $\mu\text{mol/day}$ )	5.0 ± 1.5ab	4.4 ± 0.9ab	5.0 ± 1.4ab	3.2 ± 0.8ab	2.9 ± 1.2ab	2.8 ± 0.6a	6.3 ± 3.9b
Sterol distribution (%)							
Coprostanol	61 ± 6	74 ± 3	56 ± 25	67 ± 2	64 ± 4	58 ± 4	54 ± 12
Cholestanol	7 ± 2a	11 ± 2bc	11 ± 1bc	12 ± 1bc	11 ± 2bc	14 ± 2c	8 ± 2ab
Cholesterol	30 ± 4	15 ± 3	33 ± 25	20 ± 2	24 ± 3	28 ± 5	33 ± 11
Coprostanone	2 ± 2ab	1 ± 1a	1 ± 1a	2 ± 2ab	1 ± 1a	nd <sup>d</sup>	4 ± 1b

<sup>a</sup> WB = wheat bran, OB = oat bran, OBC = oat bran concentrate, OFC = oat fiber concentrate, BG = barley grains, PBF = Prowashonupana barley flakes, RB = rye bran. Mean values ± standard deviation, *n* = 6 per diet.

<sup>b</sup> Means within a row with different letters are significantly different (*P* < 0.05) using one-way analysis of variance and the Bonferroni-Dunn post-hoc test.

<sup>c</sup> Neutral sterols include cholesterol, coprostanol, cholestanol, and coprostanone.

<sup>d</sup> Not detectable.

hamsters receiving 16% TDF from WB, this effect disappeared when the excretion was expressed as  $\mu\text{mol/day}$  (Table VII). Only 16% TDF from RB caused a significantly higher amount of daily excreted bile acids when compared with the WB control. There were distinct changes in the excretion of individual bile acids. RB increased the percentage of deoxycholic acid by 25% when compared with the control, while OB increased the relative percentage of 5 $\beta$ -cholanic acid-3 $\beta$ -ol but decreased 12-ketolithocholic acid. OBC significantly increased the percentage of ursodeoxycholic acid, and PBF caused an increase in the percentage of hyodeoxycholic acid and a decrease in 12-ketolithocholic acid when compared with WB.

## DISCUSSION

This study was designed to compare the cholesterolemic effects of various cereal fibers in the hamster using a moderately cholesterol-enriched diet model. In our study, only RB caused a significant cholesterol-lowering effect when compared with a WB control diet, while the oat and barley fibers failed to produce a significant decrease in plasma total cholesterol.

Soluble fibers have been reported to be good cholesterol-lowering substances (Truswell 1995). The responsible cholesterol-lowering component of cereal fibers like oat and barley bran is thought to be  $\beta$ -glucan (Davidson et al 1991, Braaten et al 1994), which forms viscous gel-like aqueous solutions and increases the viscosity of the intestinal contents. This increased intestinal viscosity leads to an impaired cholesterol and bile acid absorption, which is thought to be one of the major mechanisms of the cholesterol-lowering action of cereal fibers (Lund et al 1989, Anderson and Siesel 1990).

In the oat and barley test diets, various amounts of soluble fiber and  $\beta$ -glucans were realized. However, the use of concentrated (OBC, OFC) or specially bred (PBF) products supplying higher amounts of  $\beta$ -glucan and soluble fiber did not lead to a greater cholesterol-lowering effect, neither generally nor within a cereal type (barley or oat). Nevertheless, reductions of cholesterol (though not significant) were observed in the LDL and VLDL fractions with oat  $\beta$ -glucans, which is in line with results from previous rat studies (Ney et al 1988). On the other hand, as in previous human and animal studies (Anderson and Siesel 1990, Newman et al 1992), HDL cholesterol was slightly increased, especially with the two concentrated oat ingredients. These increases partly compensated for the small decreases in VLDL and LDL cholesterol. As a net effect, the ratio of HDL to VLDL+LDL cholesterol was increased with all test diets, except for PBF.

Differences in the effects of  $\beta$ -glucan of the different cereal ingredients can be due to various factors such as the molecular weight in the native state, the degradation due to endogenous or microbial enzymes, shear forces or heat treatments, and the degree

of solubilization. All of these factors can affect viscosity which develops in the upper intestinal tract. Possibly, small differences in the fine structure such as the frequency of the (1 $\rightarrow$ 3) linkages or the length of the (1 $\rightarrow$ 4) regions of  $\beta$ -glucan influence the solubility and the resistance to hydrolytic degradation (Bamforth 1982, Woodward et al 1988). The molecular weight of  $\beta$ -glucan in barley in the native state is, in general, lower than that of oat. Also, the average length of continuous (1 $\rightarrow$ 4) linked sequences is greater for oat than for barley  $\beta$ -glucan (Wood et al 1994). Furthermore, the molecular weight also varies between different cultivars (Wood et al 1991, Beer et al 1997). Such differences in the physiological effect of cultivars have been published (Fadel et al 1987) from tests of two types of barley that had similar contents of  $\beta$ -glucan. Only one barley type with the higher content of soluble  $\beta$ -glucan effectively lowered serum cholesterol when fed to broiler chicks. In addition, Newman et al (1992) tested two barley cultivars, Prowashonupana and Waxbar, in chicks and found Prowashonupana barley less effective in serum cholesterol-lowering than Waxbar, in spite of the higher soluble fiber content of the Prowashonupana barley. They suggested a loss of  $\beta$ -glucan due to degradation by endogenous  $\beta$ -glucanases. Effects of processing conditions or solubility have also been previously reported. Wood et al (1991) analyzed molecular weights of  $\beta$ -glucan in several commercial oat products and found lower molecular weights in most of the processed oat products. They concluded that besides differences in the oat cultivars, this could be influenced by processing. Kahlon et al (1993) in their experiments with hamsters found a significant reduction of total cholesterol produced by an OB diet containing 4.5%  $\beta$ -glucan when compared with a cellulose control diet, but no significant effects were found in their later experiments (Kahlon et al 1998). This different outcome was linked to the content of soluble fiber. Mälkki et al (1992) prepared various OBC by different extraction techniques and tested the cholesterol-lowering properties. These OBC lowered the serum cholesterol concentration in rats by different degrees, the product with the highest viscosity being the most effective.

In the present study, the OFC especially has given an unexpectedly low cholesterol-lowering response. This was most probably due to the greater and more rapid solubility of its  $\beta$ -glucan. The lower weights of the cecum and its contents of this experimental group indicate a weaker microbial activity when compared with the group fed with OBC. This might be due to a breakdown of  $\beta$ -glucan already at an earlier stage in the intestinal tract resulting in less substrate to be fermented and metabolized by bacterial cells in the cecum.

The general lack of significant findings with the oat and barley products in the present study may also be caused by a fermentative breakdown of the fibers in the pregastric pouch of the hamsters. Gallaher et al (1993) found a considerable decrease in intestinal *in vivo* viscosity in hamsters when compared with *in vitro* viscosity

TABLE VII  
Fecal Excretion of Bile Acids of Hamsters Fed Diets Containing 0.12% Cholesterol, 20% Fat, and Different Cereal Fiber Products for Five Weeks<sup>a</sup>

Content	WB (control)	OB	OBC	OFC	BG	PBF	RB
Total concentration ( $\mu\text{mol/g}$ )	3.2 $\pm$ 0.4 <sup>ab</sup>	8.2 $\pm$ 0.8c	6.3 $\pm$ 1.3bc	8.0 $\pm$ 0.6c	5.0 $\pm$ 1.2ab	7.3 $\pm$ 1.1bc	6.4 $\pm$ 2.5bc
Daily total excretion ( $\mu\text{mol/day}$ )	3.4 $\pm$ 0.7ab	4.3 $\pm$ 0.6bc	3.4 $\pm$ 0.7ab	4.3 $\pm$ 0.7bc	2.7 $\pm$ 0.6a	3.5 $\pm$ 1.1ab	5.1 $\pm$ 0.8c
Bile acid distribution (%)							
5 $\beta$ -Cholanic acid-3 $\beta$ -ol	5.9 $\pm$ 0.9a	8.7 $\pm$ 0.8b	5.7 $\pm$ 2.1a	7.0 $\pm$ 0.7ab	6.1 $\pm$ 0.4a	6.5 $\pm$ 0.5a	5.5 $\pm$ 0.3a
Deoxycholic acid	34.4 $\pm$ 3.3a	34.6 $\pm$ 4.3a	37.7 $\pm$ 5.8ab	33.2 $\pm$ 3.7a	31.1 $\pm$ 2.2a	33.7 $\pm$ 3.4a	43.0 $\pm$ 3.1b
Lithocholic acid	37.5 $\pm$ 4.0ab	42.8 $\pm$ 3.3b	32.7 $\pm$ 3.3a	36.3 $\pm$ 3.7ab	36.2 $\pm$ 2.1a	38.1 $\pm$ 3.8ab	34.5 $\pm$ 3.8a
Hyodeoxycholic acid <sup>c</sup>	6.2 $\pm$ 1.6a-c	5.8 $\pm$ 0.7ab	7.9 $\pm$ 1.7b-d	8.3 $\pm$ 0.5cd	7.6 $\pm$ 1.1bc	10.1 $\pm$ 1.8d	5.0 $\pm$ 0.7a
Ursodeoxycholic acid	2.2 $\pm$ 2.5a	2.2 $\pm$ 1.1a	8.0 $\pm$ 4.0b	5.8 $\pm$ 1.5ab	4.5 $\pm$ 1.8ab	5.0 $\pm$ 0.8ab	3.3 $\pm$ 0.7a
12-Keto-LCA <sup>c</sup>	13.9 $\pm$ 4.2bc	6.0 $\pm$ 1.1a	8.0 $\pm$ 5.5ab	9.4 $\pm$ 1.9a-c	14.5 $\pm$ 3.3c	6.6 $\pm$ 3.1a	8.7 $\pm$ 2.0a-c

<sup>a</sup> WB = wheat bran, OB = oat bran, OBC = oat bran concentrate, OFC = oat fiber concentrate, BG = barley grains, PBF = Prowashonupana barley flakes, RB = rye bran. Mean values  $\pm$  standard deviation,  $n = 5-6$  per diet.

<sup>b</sup> Means within a row with different letters are significantly different ( $P < 0.05$ ) using one-way analysis of variance and the Bonferroni-Dunn post-hoc test.

<sup>c</sup> Hyodeoxycholic acid (5 $\beta$ -Cholanic Acid-3 $\alpha$ , 6 $\alpha$ -diol); 12-Keto-LCA, 12-Ketolithocholic acid (5 $\beta$ -Cholanic acid-3 $\alpha$ -ol-12-one). Cholic acid and chenodeoxycholic acid were present only in trace amounts.

after ingestion of guar gum, and this was attributed by the authors to pregastric fermentation. However, fermentation end-products (e.g., short chain fatty acids) were not measured in the pregastric pouch in the present study. This hypothesis seems rather speculative, especially because other soluble and highly fermentable fibers such as psyllium, resistant starch, and inulin (Trautwein et al 1998a,b; 1999) clearly showed a cholesterol-lowering effect.

One could argue that the use of WB as a control fiber may have affected the assessment of the cholesterol-lowering ability of the tested cereal fibers. However, the effect of WB on plasma cholesterol is thought to be small (Truswell and Beynen 1992, Anderson et al 1994) and reported effects of WB on plasma lipids are inconsistent (Kritchevsky 1997). Former studies using 10% cellulose as control fiber in the same diet model (20% fat, 0.12% cholesterol, P/S ratio 0.32) showed similar plasma cholesterol concentrations (5.54 mmol/L) after a five-week feeding period (Trautwein et al 1998b), indicating that WB was a suitable control fiber for the present investigations.

Another point to consider is the dietary fat composition of the diets. In this study, we included a total of 20% fat (by weight, equivalent to  $\approx 38\%$  fat as energy) and kept the P/S ratio at a constant level of 0.33. Therefore, the effects observed in this study are mainly a result of differences in dietary fiber content and composition. On the other hand, the total dietary fat content of a diet (high vs. low fat diets) could possibly be an important factor determining whether cereal fibers are effective in cholesterol-lowering or not. In this study, the high fat diet may have at least partly impaired the hypocholesterolemic efficiency of the tested cereal fibers.

Furthermore, the influence of differences in protein and carbohydrate composition of the diets because of matrix differences of the cereals cannot be completely excluded.

Some of the cereal products used may have contained considerable amounts of tocotrienols, which have been shown to inhibit HMG-CoA-reductase activity (Qureshi et al 1986). However, the tocotrienol concentrations were not measured in this study and their influence on plasma cholesterol concentration is not consistent (Peterson and Qureshi 1997), hence their role in this study remains questionable.

The hepatic cholesterol concentrations essentially reflected the changes in the cholesterol concentration in plasma and were again significantly lowered only by RB. The liver cholesterol contents of hamsters fed the various oat brans remained generally unchanged, while the concentration with the PBF diet slightly increased and with the BG diet significantly increased. This unexpected phenomenon is not fully understood. However, Jackson et al (1994) found similar results when investigating the effects of a barley and a malted barley diet compared with WB diet. Although both barley diets were effective in plasma cholesterol-lowering in cholesterol-fed rats, hepatic cholesterol was increased. In contrast, in another study that compared the cholesterol-lowering effects of wheat and barley in chicks, liver cholesterol concentrations of the barley-fed chicks were significantly (up to tenfold) lower than those of the wheat-fed animals (Martinez et al 1992). Possibly, the observed increase in the hepatic cholesterol concentration depends on the type of ingested barley or oat and the already mentioned solubility and structural differences of  $\beta$ -glucan. These disparate findings can, at least in part, also be a result of differences in fecal steroid excretion. In the study of Martinez et al (1992), the crude fat excretion was generally higher with the barley diets. Unfortunately, the fecal sterol excretion was not measured in that study, but it can be assumed that the fecal cholesterol concentration correlates with the fat excretion. In our study, the daily excretion of cholesterol and its metabolic products coprostanol, cholestanol, and coprostanone was highest (though not significant) with the RB diet. Hamsters fed the barley diets had lower daily excretion of neutral sterols than the WB-fed control animals, indicating a possibly higher cholesterol absorption with these diets. The apparently higher cholesterol absorption did not affect plasma cholesterol concentration. There-

fore, it seems reasonable that a larger amount of cholesterol was deposited in the liver.

It is generally accepted that an enhanced synthesis and fecal excretion of bile acids is an important mechanism for the cholesterol-lowering effect of various fibers (Anderson et al 1990). In this study, RB caused a significantly higher daily excretion of bile acids when compared with the WB control and a slightly higher excretion when compared with OB. Zhang et al (1993) and Gallaher et al (1992) found somewhat different results in their studies. Hamsters and rats fed OB had a slightly higher fecal bile acid excretion than animals receiving RB. However, the TDF contents of the RB and OB diets were the same in these studies (12% for OB and RB [Zhang et al 1993], and 8% for OB and RB [Gallaher et al 1992]), whereas in our study, the OB and RB diets contained 10 and 16% fiber, respectively. A concentration of 13% fiber from OBC and 16% fiber from OFC in the diets also resulted in a lower daily fecal bile acid excretion than with RB, indicating, again, an impaired efficacy of  $\beta$ -glucan in both oat concentrates.

In our study, RB induced the most pronounced effect on cholesterol and bile acid metabolism mainly by enhanced bile acid and neutral sterol excretion. The responsible components in RB, however, are still not identified. Most likely, soluble fibers are involved. RB contains only small amounts of  $\beta$ -glucan, but considerable amounts of arabinoxylans, which form highly viscous gels. These gels have been linked to an increase in fecal fat excretion (Pettersson and Åman 1989). Adding xylanase, an enzyme that degrades xylans, and  $\beta$ -glucanase to a rye-based diet significantly increased total serum cholesterol in chicken when compared with a control rye-based diet demonstrating that the cholesterol-lowering ingredients were destroyed (Frigård et al 1994).

Other possible cholesterol-lowering components in RB are lignans. Lignans like those in sesame seeds have been reported to have hypocholesterolemic properties (Ogawa et al 1993). However, the importance of lignans as a cholesterol-lowering ingredient of RB is still not clear. Like other fibers (psyllium) RB could possibly disturb micelle formation, leading to an enhanced cholesterol and fat excretion, and impede bile acid reabsorption, leading to an increased bile acid excretion.

## CONCLUSIONS

In the present study, we have tested the cholesterol-lowering properties of various cereal fibers (barley grains, oat, and rye brans). The tested fibers revealed distinct differences in their impact on cholesterol and bile acid metabolism. The most effective cereal component was RB, which significantly lowered plasma and liver cholesterol concentrations through enhanced cholesterol and bile acid excretion. The various oat and barley fibers failed to show significant effects on total cholesterol when compared with a WB control, although a nonsignificant reduction of VLDL and LDL cholesterol and an elevation of HDL cholesterol was observed. Although  $\beta$ -glucan is thought to be the most important hypocholesterolemic component in oat and barley, increasing amounts of  $\beta$ -glucan (as well as soluble fiber and total dietary fiber) within one cereal type did not show a dose-dependent response. This lack of effect could possibly be related to solubility and structural differences of  $\beta$ -glucans and a reduced resistance of  $\beta$ -glucans to hydrolysis, which may lead to a loss of viscosity and hence of the cholesterol-lowering ability. Since technologically induced influences seem to play an important role, it should be further investigated which physicochemical factors are responsible for the cholesterol-lowering ability of cereal fibers in oats, barleys, and rye.

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