Effects of rye bran, oat bran and soya-bean fibre on bile composition, gallstone formation, gall-bladder morphology and serum cholesterol in Syrian golden hamsters (*Mesocricetus auratus*)*

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The effects of rye bran, oat bran and soya-bean fibre on serum lipids, bile composition and gallstone formation were studied in male Syrian golden hamsters (*Mesocricetus auratus*). The control groups received fibre-free stone-provoking (O1 diet) or non-stone-provoking (O2 diet) diets. The serum cholesterol levels were lower for all groups fed on the diets supplemented with the dietary fibre sources compared with the control groups. The total content of bile acids in bile was higher in groups given rye-bran diets compared with the corresponding controls. The proportion of cholic acid was higher and that of chenodeoxycholic and lithocholic acid lower in the groups given rye-bran-, oat-bran- or soya-bean-fibre-supplemented diets, compared with the corresponding controls. The secondary:primary bile acid ratio was lower in the group given the rye-bran-supplemented O1 diet. The lithocholic:deoxycholic acid ratio was lower in the groups given rye-bran-, oat-bran- or soya-bean-fibre-supplemented diets than in the corresponding controls. A lower frequency of gallstones was observed only for the group receiving the rye-bran-supplemented O1 diet while the lithogenic index was lower in the groups given the rye-bran-supplemented O2 diet. A decreased epithelial volume density of the gall-bladder and an increased smooth muscular volume density were observed in animals given oat-bran- and rye-bran-supplemented O1 diets, whereas for the soya-bean-fibre-supplemented O1 diet, only the smooth muscular volume density was increased.

Rye bran: Oat bran: Soya-bean fibre: Bile: Serum lipids: Hamsters

It is well known that the physiological effects of dietary fibres (DF) vary with their sources. Oat bran, which is rich in water-soluble fibre, has hypocholesterolaemic effects (Chen *et al.* 1981; van Horn *et al.* 1986). Soya-bean fibre, although containing less water-soluble fibre than oats, also has cholesterol-lowering effects (Lo *et al.* 1986). Rye bran contains considerable amounts of water-soluble, highly viscous fibre (Petterson & Åman, 1987), but little is known about its physiological effects. Some purified fibre components such as cellulose and pectin prevent cholelithiasis in animals by an influence on bile metabolism (Kritchevsky *et al.* 1984), but little information is available on such effects from natural dietary fibre sources. Bile acids and their derivatives occurring after bacterial action have been considered to be associated with carcinogenesis of the colon (Hill *et al.* 1971; Nair,

* Part of this work has been reported in the proceedings of Fibre 90 meeting, Norwich, England, 1990.
† For reprints.

1988). A higher lithocholic acid:deoxycholic acid (LCA:DCA) ratio in the faeces is suggested to be an aetiological factor in colorectal cancer in humans (Owen *et al.* 1986). It is of interest to investigate how the fibre source affects bile acid metabolism. A lithogenic diet causes changes in the morphology of the gall-bladder in mice (Wahlin, 1976), but whether dietary fibre sources have an effect on the morphology of the gall-bladder is still obscure.

The purpose of the present study was to investigate the effects of rye bran, oat bran and soya-bean fibre on serum cholesterol level, bile composition, gallstone formation, and morphology of the gall-bladder in hamsters.

MATERIALS AND METHODS

Fibre sources and diets

Oat bran was obtained from the Technical Research Centre of Finland, soya-bean fibre from Ralston Purina Ltd, USA, and rye bran from Wasabröd AB, Sweden. The DF content (soluble and insoluble fractions) was analysed by the method of Asp *et al.* (1983). The contents of protein, fat, ash and moisture in the fibre sources were analysed by methods approved by the Association of Official Analytical Chemists (1975). The nutrients and DF contents are listed in Table 1.

Two basal fibre-free diets were used as controls: a stone-provoking diet (O1 diet), based on glucose and casein (Dam & Christensen, 1952) and a non-stone-provoking diet (O2 diet) based on starch, milk protein and maize oil. The experimental diets, O-O1, S-O1 and R-O1, were prepared by supplementation of the O1 diet with oat bran (O), soya-bean fibre (S) and rye bran (R). The S-O2 and R-O2 diets were the O2 diet supplemented with soya-bean fibre (S) and rye bran (R) respectively. Diet composition and calculated nutrient content are listed in Table 2.

Animals and experimental procedures

Male Syrian golden hamsters (*Mesocricetus auratus*) aged 4–6 weeks were randomized into seven dietary groups, with eight to fourteen animals in each group. The animals were kept at 20° with a 12 h light–12 h dark cycle, and had free access to the experimental or control diets and tap water for 6 weeks before killing. The individual body weight was registered weekly until killing. No significant difference in mean body weight between the dietary groups was observed in 6 weeks. The methods for sampling and analysis of bile acids and bile cholesterol and the evaluation of the gallstone formation were performed as previously described (Zhang *et al.* 1990). The bile phospholipids were determined by an enzymic–colorimetric procedure involving the release of choline by phospholipase D (*EC* 3.1.4.4), oxidation of choline with choline oxidase (*EC* 1.1.3.17) and the subsequent reaction of hydrogen peroxide formed with a chromogen (Qureshi *et al.* 1980; Gurantz *et al.* 1981). The serum high-density-lipoprotein (HDL)- and total cholesterol contents were analysed by an enzymic–colorimetric assay using commercial kits (Diagnostica; Boehringer Mannheim GmbH, Germany). The lithogenic index (LI) was calculated according to Thomas & Hofmann (1973):

$$\mathrm{LI} = \frac{\text{actual molar percentage of cholesterol in the sample}}{\text{molar percentage of cholesterol present at saturation}}.$$

The actual molar percentage of cholesterol in the sample is calculated as:

$$100 \times [\mathrm{CH}]/([\mathrm{CH}]+[\mathrm{PL}]+[\mathrm{BA}]),$$

Table 1. *Nutrient and fibre content of oat bran, soya-bean fibre and rye bran (g/kg)*

	Oat bran	Soya-bean fibre	Rye bran
Protein	172	100	151
Fat	80	7	35
Carbohydrate*	386	4	184
Moisture	122	35	98
Ash	27	41	54
Dietary fibre	213	813	478
Soluble	153	88	98
Insoluble	60	725	380

* Dietary fibre excluded.

Table 2. *Composition and nutrient content (g/kg) of stone-provoking (O1) or non-stone-provoking (O2) fibre-free diets, and these diets supplemented with oat bran (O), soya-bean fibre (S) or rye bran (R)*

Diet...	O-O1	S-O1	R-O1	O1	S-O2	R-O2	O2
Component							
Glucose	315	619	544	727	0	0	0
Casein	86	171	151	202	0	0	0
Wheat starch	0	0	0	0	326	262	382
Milk protein	0	0	0	0	290	239	376
Maize oil	0	0	0	0	131	119	159
Vitamins*	4	9	7	10	10	10	12
Minerals*	22	43	37	51	51	49	61
Gelatine	10	10	10	10	10	10	10
Oat bran	563	0	0	0	0	0	0
Soya-bean fibre	0	148	0	0	182	0	0
Rye bran	0	0	251	0	0	311	0
Nutrient content							
Protein	179	169	175	180	221	216	261
Fat	46	2	10	2	136	133	164
Carbohydrate†	569	638	620	733	341	331	404
Dietary fibre							
Soluble	34	13	25	0	16	30	0
Insoluble	86	107	95	0	132	119	0

* For composition of vitamin and mineral premixes, see Dam & Christensen (1952).
† Dietary fibre excluded.

where [CH] is the molar concentration of cholesterol, [PL] is the molar concentration of phospholipids and [BA] is the molar concentration of bile acids.

The molar percentage of cholesterol present at saturation (y) is calculated as:

$$y = 4{\cdot}87 + 39{\cdot}45x - 86{\cdot}9x^2 + 53{\cdot}7x^3 \text{ (when } x < 0{\cdot}320\text{) and}$$
$$y = 117{\cdot}4 - 755{\cdot}0x + 1756x^2 - 1377x^3 \text{ (when } x > 0{\cdot}320\text{),}$$

where $x = [PL]/([PL]+[BA])$.

The morphological analyses were carried out on 5 μm paraffin sections of the gall-bladder wall stained with haematoxylin and eosin or Van Gieson's method. The point counting method was used for stereological volumetric analysis (Weibel *et al.* 1969). The results were expressed as the volume density of epithelium and smooth muscle of the gall-bladder, i.e. the volume proportion (%) of the epithelium or smooth muscle to whole gall-bladder wall.

Statistics

Data were given as mean and standard error of the mean and subjected to analysis of variance before the evaluations were performed with Student's t test between different dietary groups. Correlations between selected variables were assessed by means of Spearman's rank correlation coefficients (r_s). In evaluating differences in frequency of gallstone formation, Fisher's exact test was used. A comparison was considered to be statistically significant when $P < 0{\cdot}05$.

RESULTS

Serum cholesterol

The serum HDL- and total cholesterol contents in the groups fed on fibre-source-supplemented (oat bran, rye bran and soya-bean fibre) diets (O-O1, S-O1, R-O1, S-O2 and R-O2 diet groups) were significantly lower than in the corresponding control groups (O1 or O2 diet groups) except for serum HDL-cholesterol in the group fed on the soya-bean-fibre-supplemented O1 diet (Table 3). No significant difference in the percentage that HDL-cholesterol formed of the total cholesterol (%HDL-cholesterol) was observed between the groups fed on fibre-source-supplemented diets and the corresponding controls.

Bile acids, secondary:primary bile acids (SBA:PBA) ratio and lithocholic:deoxycholic acid (LCA:DCA) ratio

The concentrations of cholic acid in oat-bran- and rye-bran-supplemented O1 dietary groups (O-O1 and R-O1) and in soya-bean-fibre- and rye-bran-supplemented O2 dietary groups (S-O2 and R-O2) were significantly higher than in the corresponding controls (Table 4). The concentration of chenodeoxycholic acid (CDCA) in oat-bran- and soya-bean-fibre-supplemented O1 diet groups (O-O1 and S-O1), and the concentration of LCA in oat-bran- soya-bean-fibre- and rye-bran-supplemented O1 dietary groups (O-O1, S-O1 and R-O1) were lower than in the control group (O1). The SBA:PBA ratio was significantly lower only in the rye-bran-supplemented O1 dietary group (R-O1) compared with the control (O1). The LCA:DCA ratio was lower in all fibre-source-supplemented dietary groups compared with the corresponding controls (O1 or O2).

The proportion of total bile acids in the bile formed by cholic acid (CA) was higher, and those formed by CDCA and LCA were lower, in all fibre-source-supplemented diet groups than in corresponding controls (Table 5).

Bile composition, lithogenic index and gallstone formation

Total bile acid concentration in the bile of animals fed on rye-bran-supplemented diets (R-O1 and R-O2) was significantly higher than in corresponding controls (O1 or O2; Table 6). No change was observed in the concentration of bile phospholipids between the fibre-supplemented groups and the controls. The concentration of bile cholesterol was lower only in the group fed on the oat-bran-supplemented O1 diet (O-O1) compared with the control (O1). The lithogenic index in the oat-bran-supplemented O1 dietary group (O-O1) and the rye-bran-supplemented O2 dietary groups (R-O2) was significantly lower than in corresponding controls (O1 or O2).

Table 3. *Effect of stone-provoking (O1) and non-stone provoking (O2) fibre-free diets, and these diets supplemented with oat bran (O), soya-bean fibre (S) and rye bran (R) on serum high-density-lipoprotein (HDL)-cholesterol and total cholesterol and HDL-cholesterol as a percentage of total cholesterol in Syrian golden hamsters* (Mesocricetus auratus)†

(Mean values and standard errors of the mean for eight to fourteen hamsters)

Dietary group	n	Cholesterol (mmol/l) HDL Mean	HDL SE	Total Mean	Total SE	%HDL-cholesterol Mean	SE
O-O1	10	2·1**	0·2	2·9***	0·2	71·7	4·0
S-O1	10	2·5	0·2	3·3*	0·2	74·2	2·5
R-O1	10	2·0**	0·1	2·7***	0·2	74·5	1·4
O1	14	3·0	0·2	4·2	0·2	71·9	1·9
S-O2	8	2·2***	0·0	3·1***	0·1	70·1	1·2
R-O2	8	2·1***	0·1	2·9***	0·2	71·5	0·8
O2	9	2·8	0·1	4·0	0·1	68·2	1·3

The mean value was significantly different from that of the corresponding control group: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

† For details of diets and procedures, see Tables 1 and 2 and pp. 862–864.

Table 4. *Effect of stone-provoking (O1) and non-stone-provoking (O2) fibre-free diets and these diets supplemented with oat bran (O), soya-bean fibre (S) and rye bran (R) on biliary bile acid concentration and secondary (SBA):primary bile acids (PBA) and lithocholic (LCA):deoxycholic acid (DCA) ratios in Syrian golden hamsters* (Mesocricetus auratus)†

(Mean values and standard errors of the mean for eight to fourteen hamsters)

Dietary group	n	Biliary bile acid concentration (mmol/l) CA Mean	CA SE	CDCA Mean	CDCA SE	DCA Mean	DCA SE	LCA Mean	LCA SE	SBA:PBA Mean	SBA:PBA SE	LCA:DCA Mean	LCA:DCA SE
O-O1	10	8·4**	0·4	2·0***	0·2	0·9	0·1	0·2*	0·0	0·11	0·01	0·27**	0·05
S-O1	10	6·1	0·5	2·8**	0·2	0·7	0·1	0·2***	0·0	0·10	0·01	0·25**	0·05
R-O1	10	9·4***	0·8	4·2	0·4	0·7	0·1	0·2***	0·0	0·07***	0·01	0·24**	0·05
O1	14	5·4	0·7	4·1	0·3	0·7	0·1	0·4	0·0	0·12	0·01	0·71	0·12
S-O2	8	10·7*	1·4	3·1	0·5	1·7	0·3	0·3	0·0	0·15	0·01	0·17*	0·03
R-O2	8	12·7**	1·0	2·7	0·1	1·4	0·2	0·2	0·0	0·11	0·02	0·16**	0·01
O2	9	7·1	0·6	3·3	0·5	1·1	0·1	0·3	0·0	0·15	0·02	0·35	0·06

CA, cholic acid; CDCA, chenodeoxycholic acid.

Mean value was significantly different from that of the corresponding control group: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

† For details of diets and procedures, see Tables 1 and 2 and pp. 862–864.

The incidence of gallstones in the animals fed on the rye-bran-supplemented O1 diet (R-O1) was significantly lower than in the animals fed on the stone-provoking control diet (O1, Table 7).

Table 5. *Effect of stone-provoking (O1) and non-stone-provoking (O2) fibre-free diets and these diets supplemented with oat bran (O), soya-bean fibre (S) and rye bran (R) on the amounts of individual bile acids as a percentage of total bile acids in the bile of Syrian golden hamsters* (Mesocricetus auratus)†

(Mean values and standard errors of the mean for eight to fourteen hamsters)

		Percentage of individual bile acids							
		CA		CDCA		DCA		LCA	
Dietary group	*n*	Mean	SE	Mean	SE	Mean	SE	Mean	SE
O-O1	10	72·5***	1·9	17·7***	1·4	7·8	0·7	2·0**	0·2
S-O1	10	62·0***	2·1	28·8**	1·8	7·4	0·7	1·7***	0·3
R-O1	10	64·8***	1·8	29·1**	2·0	5·1	0·5	1·1***	0·1
O1	14	49·7	2·2	39·9	2·2	6·4	0·6	4·0	0·4
S-O2	8	67·9***	1·3	19·3**	1·5	11·0	0·9	1·8**	0·2
R-O2	8	74·2***	1·8	16·3***	0·9	8·3	1·4	1·2***	0·1
O2	9	60·2	1·3	27·2	1·4	9·6	1·2	2·9	0·3

CA, cholic acid; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid; LCA, lithocholic acid.
The mean value was significantly different from that of the corresponding control: ** $P < 0·01$, *** $P < 0·001$.
† For details of diets and procedures, see Tables 1 and 2 and pp. 862–864.

Table 6. *Effects of stone-provoking (O1) and non-stone-provoking (O2) fibre-free diets, and these diets supplemented with oat bran (O), soya-bean fibre (S) and rye bran (R) on bile composition and lithogenic index in Syrian golden hamsters* (Mesocricetus auratus)†

(Mean values and standard errors of the mean for eight to fourteen hamsters)

		Bile composition (mmol/l)							
		Total bile acids		Phospholipids		Cholesterol		Lithogenic index	
Dietary group	*n*	Mean	SE	Mean	SE	Mean	SE	Mean	SE
O-O1	10	11·6	0·4	5·5	0·4	1·0*	0·1	0·5*	0·1
S-O1	10	9·7	0·7	5·3	0·4	1·3	0·1	0·9	0·1
R-O1	10	14·5*	1·1	6·0	0·5	1·7	0·1	0·8	0·1
O1	14	10·6	1·0	5·6	0·4	1·5	0·2	1·1	0·1
S-O2	8	15·8	2·1	8·3	0·9	1·0	0·1	0·5	0·1
R-O2	8	17·0**	1·1	9·3	0·8	0·8	0·1	0·3***	0·0
O2	9	11·8	1·2	9·6	1·0	1·2	0·1	0·7	0·1

Mean value was significantly different from that of the corresponding control group: * $P < 0·05$, ** $P < 0·01$, *** $P < 0·001$.
† For details of diets and procedures, see Tables 1 and 2 and pp. 862–864.

Morphology of gall-bladder

The epithelial volume density of the gall-bladder was lower in animals given oat-bran- and rye-bran-supplemented O1 diets (O-O1 and R-O1), and volume density of smooth muscle was higher in animals given fibre-source-supplemented O1 diets (O-O1, S-O1 and R-O1) compared with that in animals given the control, O1 diet (Table 8).

Table 7. *Effect of oat bran (O), soya-bean fibre (S) and rye bran (R) on gallstone formation in Syrian golden hamsters* (Mesocricetus auratus) *fed on stone-provoking (O1) and non-stone-provoking (O2) fibre-free diets*†

Dietary group	No. of animals: Total	No. of animals: With stones
O-O1	10	3
S-O1	10	4
R-O1	10	1*
O1	14	8
S-O2	8	1
R-O2	8	0
O2	10	1

The incidence was significantly different from that of the O1 dietary group: * $P < 0.05$.
† For details of diets and procedures, see Tables 1 and 2 and pp. 862–864.

Table 8. *Effects of oat bran (O), soya-bean fibre (S) and rye bran (R) on volume densities of epithelium and smooth muscle of the gall-bladder of Syrian golden hamsters* (Mesocricetus auratus) *fed on stone-provoking (O1) and non-stone-provoking (O2) fibre-free diets*†

(Mean values and standard errors of the mean for eight to thirteen hamsters)

		Volume density to gall-bladder wall (%)			
		Epithelium		Smooth muscle	
Dietary group	*n*	Mean	SE	Mean	SE
O-O1	10	32·4*	1·0	40·8**	2·4
S-O1	9	33·5	1·0	41·3**	2·0
R-O1	10	32·8*	0·8	38·0*	1·2
O1	13	35·9	1·1	33·4	1·2
S-O2	8	33·8	1·0	38·7	2·3
R-O2	8	29·8	1·2	35·6	2·1
O2	8	33·5	1·7	32·7	1·8

Mean value was significantly different from that of the corresponding control group: * $P < 0.05$, ** $P < 0.01$.
† For details of diets and procedures, see Tables 1 and 2 and pp. 862–864.

The epithelial volume density was correlated with the biliary concentration of secondary bile acids only in the rye-bran-supplemented, non-stone-provoking dietary group (R-O2): DCA (r_s 0·88, $P < 0.05$, *n* 8) and LCA (r_s 0·67, $P = 0.05$, *n* 8).

DISCUSSION

Oat bran and soya-bean fibre have repeatedly been shown to exert hypocholesterolaemic effects (Chen *et al.* 1981; Anderson *et al.* 1984; Sasaki *et al.* 1985; Lo *et al.* 1986). The results of the present experiment support these former findings (Table 3). The cholesterol-lowering effect was also observed in the animals given diets with rye bran in the present experiment. Concomitantly, the serum HDL-cholesterol levels in these fibre-supplemented groups were also decreased. However, the proportion of cholesterol occurring as HDL-cholesterol was not changed. This indicates that the decreased serum total cholesterol may be due not only to decreased HDL-cholesterol but also to lowered low-density-lipoprotein (LDL)-cholesterol. The water-soluble fraction of oat fibre, containing β-glucans, is thought to be responsible for the hypocholesterolaemic effect (Davidson *et al.* 1991). Diets supplemented with rye bran and soya-bean fibre contain less water-soluble fibre than the oat diet. Some components other than the water-soluble fraction of fibre may also play a role in lowering of serum cholesterol. In rye the DF is predominantly pentosans. The water-soluble part of pentosans is known to produce high viscosity (Petterson & Åman, 1987). Whether this plays a role in lowering serum cholesterol should be further investigated. Several mechanisms have been proposed to explain the hypocholesterolaemic effect of dietary fibre. The influence of dietary fibre on lipid absorption and excretion of bile acids and cholesterol, and the effect of short-chain fatty acids, especially propionate, on cholesterol synthesis are different mechanisms of fibre action which have been reviewed by Furda (1990).

In a previous study (Zhang *et al.* 1992) it was observed that rye bran may reduce the proportion of lithocholic acid, and the SBA:PBA and LCA:DCA ratios in the bile. In the present experiment we found the same results. The observation (Zhang *et al.* 1993) that the LCA:DCA ratio in the bile is well correlated with that in the faeces implies that rye bran may, in some way, affect the metabolism of the microflora in the large intestine. It is also proposed (Brydon *et al.* 1988) that dietary fibre may reduce transit time and thus make less time available for fermentation and reabsorption of secondary bile acids especially lithocholic acid which is poorly absorbed. Low SBA:PBA and LCA:DCA ratios have been suggested to be related to a lower risk of colon cancer in humans (Turjman *et al.* 1984; Owen *et al.* 1986, 1987). Whether rye bran has these effects in humans should be further investigated.

Some purified DF components prevent cholesterol gallstone formation in animal experiments (Bergman & van der Linden, 1975; Rotstein *et al.* 1981; Kritchevsky *et al.* 1984). Although the mechanism for this is still obscure, changes in bile metabolism and a lowered lithogenic index are thought to be the main reasons. In the present work, rye bran supplementation reduced the incidence of gallstone formation significantly (Table 7) compared with the control O1 dietary group. Most gallstones were of the mixed cholesterol and pigment types. Their frequency did not correlate with the lithogenic index. This is inconsistent with previous findings where the stone-provoking diet produced only cholesterol gallstones (Bergman & van der Linden, 1975). The reason for this may be the varying response in different animal strains or some other unknown factors.

When mice are fed on a lithogenic diet, an increase in volume density of the gall-bladder epithelium is observed (Wahlin, 1976). In this experiment the O1 diet seemed to have a similar effect on hamsters. Rye and oat bran supplementation to the lithogenic O1 diet decreased the volume density of the epithelium (Table 8). This effect may be related to the changes in biliary concentration of bile acids induced by fibre supplementation. Whether these changes are associated with the formation of gallstones is not clear.

In conclusion, feeding hamsters with rye bran, oat bran and soya-bean fibre resulted in serum cholesterol-lowering effects. Rye bran was found to increase the total concentration of bile acids in the bile and to prevent gallstone formation in the hamsters. Rye bran, oat bran and soya-bean fibre, when supplemented into a fibre-free, stone-provoking diet, decreased the concentration of lithocholic acid and the LCA:DCA ratio in the bile. These fibre sources also have effects on the morphology of the gall-bladder wall.

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