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Changes in serum cholesterol and sterol metabolites after intake of products enriched with an oat bran concentrate within a controlled diet

Ågot Lia Amundsen[1,2], Brita Haugum[1,3] and Henrik Andersson[1]

[1]Department of Clinical Nutrition, Annedalsklinikerna, Göteborg University, Göteborg, Sweden; [2]Institute for Nutrition Research, University of Oslo, Norway; [3]Central Hospital of Akershus, Lørenskog, Norway

Abstract

Background: The serum (S) cholesterol-lowering capacity of oat fibre has been confirmed in several earlier studies. Food products containing oat bran concentrate (OBC) may become a useful tool in the dietary treatment of hypercholesterolaemia when incorporated in the daily diet, but possible adverse effects of processing have to be investigated.

Objective: To investigate the S-cholesterol-lowering effect of food products containing OBC in hypercholesterolaemic subjects. Furthermore, to study the effects of the OBC on serum markers of cholesterol (lathosterol) and bile acid (7α-hydroxy-4-cholesten-3-one) synthesis.

Design: The study was a single-blind, randomized cross-over study, for 2 × 3 weeks. Sixteen hypercholesterolaemic subjects aged 57 ± 7.9 years (mean ± SD), with mean S-cholesterol 7.47 ± 0.65 mmol l^{-1}, were randomized to eat a premade diet containing 5 g oat β-glucan daily (OBC diet) or a control diet (CTRL diet) without β-glucan. Mean β-glucan solubility in the OBC food products was 50%.

Results: Serum cholesterol and low-density lipoprotein decreased by 6.0% ($p = 0.021$) and 9.0% ($p = 0.03$), respectively, in the OBC compared with the CTRL diet period. There was no significant differences in lathosterol or 7α-hydroxy-4-cholesten-3-one responses between the diet periods, but the short-term (day 0–3; $r = 0.64$, $p < 0.01$) and long-term changes (day 0–22; $r = 0.55$, $p < 0.05$) correlated well with each other.

Conclusions: 5 g of β-glucan daily (2.7 g soluble) induced a significant reduction in S-cholesterol when incorporated into food products as OBC. An immediate response in the sterol metabolism was shown shortly after the introduction of the OBC diet. Oat β-glucan-enriched products could be a useful tool in the prevention and treatment of hypercholesterolaemia.

Keywords: *oat bran concentrate*; *oat fibre*; *oat β-glucan*; *β-glucan solubility*; *7α-hydroxy-4-cholesten-3-one*; *hypercholesterolaemia*; *lathosterol*; *serum cholesterol*

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Introduction

In 1997, the Food and Drug Administration (FDA) in the USA decided to authorize the use of health claims on the association between soluble fibre from whole oats and reduced risk of coronary heart disease (CHD). The soluble fibre found in oats, i.e. the mixed-linked (1-3),(1-4)β-D-glucan (β-glucan), is primarily responsible for the serum cholesterol (S-cholesterol)-lowering effect of whole oats, including oat bran, rolled oats and whole oat flour. According to the health claims, a total daily intake of 3 g of soluble β-glucan fibre may reduce S-cholesterol concentration and the risk of CHD if it is a part of a diet low in saturated fat and cholesterol. The reduction in S-cholesterol seems to increase with increasing baseline S-cholesterol concentrations (1, 2) and also with increasing dose of soluble fibre (1).

The mechanism behind the S-cholesterol-lowering effect is mainly an increased bile acid excretion mediated by the viscous β-glucan fraction (3–6). Increased bile acid excretion stimulates bile acid synthesis as well as cholesterol synthesis (7). The concentration of 7α-hydroxy-4-cholesten-3-one and

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the ratio of lathosterol to cholesterol in serum reflect the rates of bile acid and cholesterol synthesis, respectively (8, 9). Changes in the sterol metabolism due to oat β-glucan intake are therefore expected to be reflected by changes in these markers.

The aim of this study was to investigate the S-cholesterol-lowering effect of food products containing oat bran concentrate (OBC) when incorporated into a diet low in saturated fat and cholesterol in a group of hypercholesterolaemic subjects. Furthermore, the effects of the OBC diet on serum markers of cholesterol and bile acid synthesis were investigated.

Subjects and methods

Subjects

The participants were selected from a group of men and women responding to an announcement in the local newspaper. Altogether, 27 subjects were screened for the study. Twenty subjects met the inclusion criteria (age 35–70 years for men and 50–70 years for women, total S-cholesterol concentration >6 mmol l^{-1}) and volunteered for participation. Exclusion criteria were secondary hyperlipidaemia, diabetes mellitus and thyroid, kidney or liver diseases, body mass index (BMI) >30 kg m^{-2}, S-triacylglycerol (TG) >4 mmol l^{-1}, and the use of cyclic postmenopausal hormone therapy. None of the subjects was using cholesterol-lowering medication or other drugs that could affect the serum lipid concentration. Of the 20 subjects, four subjects were excluded from the final analyses. Two men dropped out during the study for personal reasons, one man had an allergic reaction in the washout period and one woman had a very low compliance (58%). Sixteen subjects were included in the analyses of the results, nine men and seven women aged 57.0 ± 7.9 years (mean $\pm$ SD), BMI 25.4 ± 1.9 kg m^{-2} and S-cholesterol 7.47 ± 0.65 mmol l^{-1}. One subject was on omeprazol therapy (Losec®), two were on medication for elevated blood pressure (Cozaar comp®, Salures-K®) and two women were receiving postmenopausal hormone therapy (Ovestrin). The medication was kept constant throughout the study.

The subjects gave their written consent to the study, which was approved by the ethics committee at Sahlgrenska University Hospital in Gothenburg.

Study design

The study was a single-blind, randomized cross-over study lasting for 2×3 weeks separated by a washout period of 2.5 weeks. The experimental diet included test products containing oat bran concentrate (OBC), while the control (CTRL) diet period was based on the same diet and included the corresponding products without OBC. The subjects were randomly assigned to start with the OBC diet or the CTRL diet. All food was prepared in advance and administered to the subjects during both diet periods. Routine laboratory measurements were taken at the screening visit to ensure normal health status. Fasting blood samples were taken on days 0, 3, 20 and 22 in each diet period. Body weight was recorded in the morning at the start and end of each diet period. The treatments were blinded to the participants, and the blood lipid analyses were blinded until the study was completed.

Diets

A diet composed according to the AHA step I recommendations was prepared and served in both diet periods. Diets containing 8.4, 10 or 11.7 MJ were used, according to the subjects' requirement calculated from body weight. The menu planning and calculations were done using the computer program MATS (Rudans Lättdata, Västerås, Sweden).

In the OBC diet period, an oat bran concentrate (Swedish Oat Fiber, Väröbacka, Sweden) containing 15% of oat β-glucan was included in eight of the food products. The OBC was produced from ground and sifted oat bran extracted by ethanol. The test products were muesli, extruded breakfast flakes, bread, teacakes (bread buns), muffins, fresh tagliatelle pasta, macaroni and an apple drink. In addition, rolled oats and oat bran were included in some of the products but supplied less than 20% of the oat β-glucan. All products were supplied by Kungsörnen (Järna, Sweden). The amounts of total and soluble oat β-glucan in the products and servings are presented in Table 1. The amount of oat β-glucan served in the OBC diet period was 5.1 g day^{-1}. The mean solubility of the β-glucan in the products was about 50%. Thus, the content of soluble β-glucan in the OBC diet was 2.7 g day^{-1}. For each OBC product, there was a corresponding control product (Kungsörnen) without oat β-glucan but including insoluble dietary fibre from wheat or rye.

Table 1. Content of β-glucan in the oat bran concentrate (OBC) products and servings

Food items (g per serving)	Total β-glucan 100 g^{-1} (g)	Total β-glucan per serving (g)	Soluble β-glucan (%)	Soluble β-glucan per serving (g)
OBC bread (34 g)	1.2	0.4	50	0.2
OBC teacake (105 g)	1.0	1.1	57	0.6
OBC muesli (60 g)	2.4	1.4	45	0.6
OBC breakfast flakes 60 g[a]	2.0	1.2	48	0.6
Oatmeal (35 g)	4.2	1.5	40	0.6
OBC muffins (40 g)	1.4	0.6	40	0.2
OBC macaroni (70 g)	0.5	0.8	22	0.2
OBC fresh pasta (130 g)	0.4	0.8	59	0.5
OBC apple drink (200 g)	0.3	0.6	70	0.4

[a]Including 30% raisins.

All food dishes were prepared and frozen before the start of the study. Rapeseed oil, olive oil, liquid margarine and a low-fat margarine of rapeseed oil (Van den Bergh Foods, Helsingborg, Sweden) were used in the cooking, as salad dressings and as spread. A 1 week circulating menu was used, including two hot meals per day. Pasta was used frequently since both macaroni and fresh pasta were among the test products. Two ready-to-eat fish dishes and one meat dish were supplied by Nestlé Sweden. An example of a 1 day food intake is presented in Table 2.

Table 2. Example of food items included in a 1 day menu

	Intake (g)		
	8.4 MJ diet	10 MJ diet	11.7 MJ diet
Muesli[a]	60	60	60
Low-fat milk (0.5%)	200	240	280
Bread[a]	68	102	136
Teacake[a]	55	55	105
Rye crispbread	0	24	68
Low-fat margarine	8	12	22
Cheese (28% fat)	10	10	10
Soft cheese (16% fat)	0	20	40
Apple drink[a]	400	400	400
Rice	0	50	80
Fish and macaroni[a]			
Gratin	1 port.	1.4 port.	1.8 port.
Casserole with beef	1 port	1.4 port.	1.8 port
Green salad, tomato	50	60	70
Olive oil, vinegar dressing	8	10	12
Muffin[a]	40	40	40
Orange	0	125	145
Coffee and tea in free amounts (without cream)			

[a]Test product with or without oat bran concentrate.
port.: portion.

Adherence to the diets was monitored from food records, where food was checked off as eaten or not eaten. The subjects were allowed to eat one extra piece of fruit per day and small amounts of specified sweets, yoghurts or drinks containing negligible amounts of fat. Two glasses of wine (375 g) or two bottles of beer (660 ml) were allowed each week. Any food eaten outside the diet was recorded in a food diary. A copy of the food records in the first diet period was returned to the subjects and they were instructed to eat in the similar way during the second diet period.

Before the start of the study, the subjects made a 7 day food record. A food diary booklet with photographs of portion sizes (Menyboken, Livsmedelsverket, Sweden) was used, and the subjects recorded their food intake during 7 consecutive days. The mean dietary intakes in the group before and during the intervention periods are presented in Table 3.

Laboratory measurements

Fasting blood samples were drawn in the morning, between 07.00 and 10.00 h, at baseline (day 0) and on days 3, 20 and 22. Analyses of S-cholesterol, high-density lipoprotein (HDL)-cholesterol and TG were performed using enzymic methods (Boehringer Mannheim). Low-density lipoprotein (LDL)-cholesterol was calculated using Friedewald's equation: $\text{LDL} = \text{total}\quad \text{S-cholesterol} - (\text{HDL} + 0.45 \times \text{TG})$ (10). The body weight of the subjects, wearing light clothing, was measured at baseline and at the end of the study. Non-fasting body weight was also checked once a week to follow weight changes. Serum lathosterol was quantified by gas chromatography according to Miettinen and Koivisto (11) and the serum concentration of 7α-hydroxy-4-cho-

lesten-3-one was analysed by the method of Axelsson et al. (8). Total and soluble β-glucan were analysed by the method of Åman and Graham (12).

Statistical analysis

Statistical analyses were performed using Excel software (Microsoft Office 95) and the SYSTAT statistical package (SPSS, Evanston, IL, USA). Data are presented as mean ± SD or SEM. Student's *t*-test was used for paired comparisons and Pearson's correlation test was applied for correlation analyses. A statistical significance level of $p < 0.05$ was chosen. The mean of days 20 and 22 was used for the statistical analyses of lipids. To estimate the number of subjects needed in the study, a power calculation was performed using the data from a pilot study, in which the same OBC was consumed by nine free-living subjects. With a power of 90%, a change of 10% in S-cholesterol could be detected in 15 subjects. Owing to the strictly controlled diet in the present study, 20 subjects were assumed to be enough.

Results

Dietary adherence and serum lipid changes

The intake of β-glucan in the OBC period in the 16 subjects was 5.05 ± 0.12 g (mean ± SD), which corresponds to a compliance of 98.7% (range 90.5–100%).

Table 3. Mean dietary intake before the study (Base) and during the control (CTRL) and oat bran concentrate (OBC) diet periods ($n = 16$)

Nutrients	Base diet[a]	CTRL diet[b]	OBC diet[b]
Energy (kJ)	9271	9880	9780
Energy (kcal)	2207	2350	2330
Fat (*E*%)	32.0	24.9	26.3
Sat (*E*%)	13.8	9.1	9.3
Mono (*E*%)	11.5	10.1	10.7
Poly (*E*%)	4.4	4.1	4.3
Carbohydrate (*E*%)	48.3	58.7	57.0
Protein (*E*%)	16.5	16.2	17.2
Alcohol (*E*%)	3.3	1.9	1.3
Cholesterol (mg)	320	229	226
Dietary fibre (g)[c]	20.4	24.3	28.0
Oat β-glucan (g)			5.1

[a]Calculated from 7 day food records; [b]calculated from the 7 day rotating menu, individual compliance lists and food diaries; [c]including oat β-glucan.
E%: energy per cent; Sat: saturated fat; Mono: monounsaturated fat; Poly: polyunsaturated fat.

There was no difference in baseline lipid values between the diet periods. The changes in total S-cholesterol, LDL-cholesterol, HDL-cholesterol and TG in the diet periods are presented in Table 4. Serum cholesterol was 6.0% lower ($p = 0.021$) and LDL-cholesterol 9.0% lower ($p = 0.030$) after the OBC diet period compared with the CTRL diet period. The changes in S-cholesterol correlated with the baseline S-cholesterol in both the CTRL ($r = -0.70$, $p < 0.01$) and OBC ($r = -0.59$, $p < 0.05$) diet period. During the OBC diet period, the S-cholesterol and LDL-cholesterol decreased by 8.8% ($p = 0.002$) and 7.3% ($p = 0.026$), respectively. No significant changes were observed in the CTRL diet period (−3% and −0.8%, respectively). There was no effect of the OBC diet on HDL-cholesterol or TG concentration, but HDL-cholesterol decreased significantly during both the OBC (−11.1%, $p = 0.001$) and CTRL (−8.5%, $p = 0.028$) diet periods.

Body-weight changes

The mean decrease in body weight was 0.8 kg in both diet periods, ranging from −2.3 to +1.9 kg in the OBC diet period and from −2.2 to +1.6 kg in the CTRL diet period. There was no significant difference between the diet periods. The individual body weight changes correlated significantly with S-cholesterol changes within the CTRL ($r = 0.57$, $p < 0.05$) as well as within the OBC ($r = 0.65$, $p < 0.01$) diet period. This correlation was also observed for LDL-cholesterol changes (CTRL diet: $r = 0.65$, $p < 0.01$; OBC diet: $r = 0.56$, $p < 0.05$), but not for changes in body weight, TG or HDL-cholesterol.

Serum sterol metabolites

Fasting serum lathosterol was measured on days 0, 3 and 22. The mean concentrations (± SEM) in the OBC diet period were 162 ± 10.2 μmol/100 mmol, 167 ± 12.1 μmol/100 mmol and 179 ± 11.8 μmol/100 mmol cholesterol, respectively, compared to 164 ± 9.5 μmol/100 mmol, 156 ± 9.6 μmol/100 mmol and 167 ± 11.0 μmol/100 mmol cholesterol, respectively, in the CTRL diet period. There was no statistically significant difference in the serum concentration of lathosterol between the diet periods. There were no significant changes in the serum concentration from day 0 to day 3 or from day 0 to day 22 in any of the diet periods (data not shown). However, the difference between the two periods (OBC – CTRL) in short-term (day 0–3) and long-term (day 0–22) serum lathosterol changes correlated negatively ($r =$

Table 4. Serum lipid changes in the diet periods ($n = 16$)

	CTRL diet period		OBC diet period		Difference[a]		
	Start (mmol l^{-1})	End (mmol l^{-1})	Start (mmol l^{-1})	End (mmol l^{-1})	(mmol l^{-1})	(%)	p
Total cholesterol	7.64 ± 0.24	7.34 ± 0.18	7.66 ± 0.19	6.95 ± 0.16	−0.41 ± 0.19	−6.0 ± 2.5	0.021
LDL-cholesterol[b]	5.12 ± 0.20	5.11 ± 0.15	5.19 ± 0.14	4.79 ± 0.14	−0.39 ± 0.19	−9.0 ± 3.7	0.030
HDL-cholesterol	1.68 ± 0.13	1.53 ± 0.11	1.74 ± 0.13	1.53 ± 0.11	−0.05 ± 0.06	−3.4 ± 3.2	0.392
Triacylglycerol	2.15 ± 0.37	1.68 ± 0.21	1.77 ± 0.25	1.57 ± 0.20	0.27 ± 0.28	1.7 ± 12.7	0.689

Data are shown as mean ± SEM.

[a]Difference between the changes in the OBC and CTRL diet periods.

[b]$n = 15$.

CTRL: control diet period; OBC: oat bran concentrate diet period; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

−0.77 and $r = -0.89$, respectively, $p < 0.001$) with the S-cholesterol changes (OBC – CTRL).

The fasting serum concentration of 7α-hydroxy-4-cholesten-3-one decreased significantly in the CTRL period between days 0 and 3 ($p = 0.036$) and between days 0 and 22 ($p = 0.015$). In the OBC diet period, there was a tendency towards an increase between days 0 and 3 and a decrease between days 0 and 22 ($p = 0.056$) (Fig. 1). There were no statistical significant differences in serum 7α-hydroxy-4-cholesten-3-one changes between the two diet periods. Significant positive correlations were observed between the differences (OBC – CTRL) in serum lathosterol changes and 7α-hydroxy-4-cholesten-3-one changes, as both short-term changes (day 0–3; $r = 0.64$, $p < 0.01$) and long-term changes (day 0–22; $r = 0.55$, $p < 0.05$).

Discussion

In the present study, a 6% reduction in the S-cholesterol concentration was observed after intake of 5 g β-glucan day^{-1} compared with a control diet without oat β-glucan. The S-cholesterol-lowering

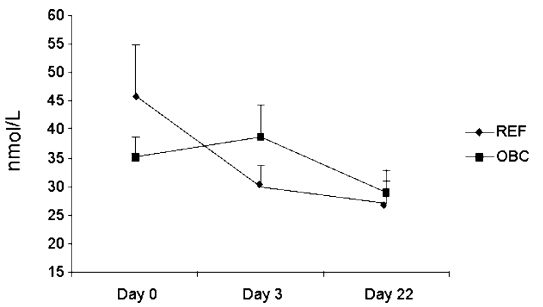

Fig. 1. Serum 7α-hydroxy-4-cholesten-3-one concentration measured on three occasions during two diet periods (mean and SEM, $n = 16$). REF: control diet period; OBC: oat bran concentrate diet period.

effect of oat meal and oat bran has been well investigated and is now well accepted (1). The new aspects of the present study are that a processed oat β-glucan concentrate was used, incorporated into several different food products, and both lipids and sterol metabolites were followed during a strictly dietary controlled study. As also observed earlier (1), there was a significant correlation between baseline S-cholesterol concentration and changes in total S-cholesterol in both diet periods. Parallel changes in serum metabolites reflecting cholesterol synthesis and bile acid excretion were observed.

The S-cholesterol reduction in the present study was induced by an ingredient providing 5.1 g β-glucan day^{-1}, of which 2.7 g was soluble. This is similar to the effective dose stated in the meta-analysis by Ripsin et al. (1). In most studies, however, the solubility was not analysed. The surprisingly low solubility of 50% in the products used here may depend on the processing of the OBC, the preparation of the food products and dishes, and the storage (13). From earlier studies, it was assumed that the β-glucan solubility is about 80%, as this was found in analyses of whole oat groats (12), but this may to a large degree depend on the product. A calculation may therefore give highly unreliable data. The β-glucan solubility of the products in the present study was analysed after extraction of the ground sample in water at 37°C for 2 h. In a previous study (13), hot-water extraction gave a higher solubility than water extraction at 37°C following a simulation of the physiological digestion process. Thus, the method of analysis is of great importance.

Body-weight changes were also observed earlier in studies with large oat fibre intakes (14). The

weight changes observed in the present study may explain some of the S-cholesterol reduction in the subjects with more pronounced weight losses. However, since the weight losses were similar in both diet periods, the extra S-cholesterol reduction in the OBC diet could not be explained by the weight loss.

A significant reduction in the HDL-cholesterol concentration was observed in both diet periods in the present study. A decrease in HDL has previously been observed both in metabolic studies and in ambulatory studies (15). All women in the study had a serum HDL-cholesterol value higher than 1.5 mmol l^{-1}. A reduction in HDL was, however, also seen in men with a lower HDL-cholesterol. One explanation for the observed decrease in HDL-cholesterol is the reduction in fat and the increase in carbohydrate intake in both diet periods compared with the usual intake by the subjects. The exchange of fat with carbohydrate has been observed to induce a decrease in HDL-cholesterol (16).

The serum TG concentration decreased dramatically in some of the subjects during both diet periods, but no overall changes were observed. This is in accordance with earlier studies with oat fibre diets. Two of the subjects had a TG > 4.0 at the start, even though screening values were within the inclusion criteria. When these subjects were excluded from the analysis, the mean decrease in TG was only -0.3% and -0.7% in the control and OBC diet periods, respectively. Thus, the reduction could be explained mainly by a decrease in these two subjects.

The correlation between lathosterol and S-cholesterol changes indicates that there is a stimulation of cholesterol synthesis after oat fibre intake. This is due to an increase in bile acid excretion mediated by the oat β-glucan, which is the main mechanism behind the reduction in S-cholesterol by oat fibre intake (4–6, 17). A reduced reabsorption of bile acids stimulates bile acid synthesis from cholesterol, which has to be synthesized or originate from the plasma pool through hepatic LDL-receptor uptake. It was therefore expected that both lathosterol and 7α-hydroxy-4-cholesten-3-one concentrations would increase during the OBC diet period. No significant increases in either fasting lathosterol or 7α-hydroxy-4-cholesten-3-one were observed, but the strong correlation found between the changes in these serum metabolites shows that parallel changes occur as a response to the increased bile acid excretion from the body. In a recent study, a significant increase in 7α-hydroxy-4-cholesten-3-one was observed at 8 and 12 h after intake of 11 g of oat β-glucan in a test meal (18). However, the fasting concentration 24 h afterwards was not different from the fasting level before the test meal. This indicates that the fasting concentration of 7α-hydroxy-4-cholesten-3-one may not be a good measure of changes in bile acid synthesis after oat β-glucan intake. Rather, the postprandial changes should be measured. However, more knowledge is needed about the intra- and interindividual variation, as well as the changes within the day in this sterol metabolite. Serum lathosterol was measured in an earlier study with β-glucan-rich oat bran, in which no significant changes were found after 4 or 8 weeks (19).

There are some limitations to the present study. The study periods were rather short and no run-in periods included. According to the literature, however, 3 weeks of intervention should be enough to see a S-cholesterol-lowering effect by the oat fibre (1). The subjects had a higher fat intake before the start of the study and were also instructed to eat as normal during the washout period. Thus, it cannot be excluded that a run-in period when the subjects were eating a similar low-fat diet as in the study but without the oat fibre would have influenced the outcome. However, the results did not depend on the whether the subjects received the OBC or the control diet in the first or second period. Another limitation is that the dietary fibre content of the diets was not completely balanced. The oat fibre was added to the control products instead of being balanced with other insoluble fibre in the control diet. This may not be a perfect design, but the results may still reflect what happens when oat fibre is added to a low-fat diet already quite high in dietary fibre.

The present study showed that an OBC with 16% oat β-glucan, incorporated into a variety of food products that could easily be included in a common Swedish diet, lowered total-cholesterol and LDL-cholesterol. The amount of oat β-glucan consumed in this study corresponds to about 63 g common oat bran or 125 g oat meal per day, which are very large amounts for most subjects to consume every day. If, however, a variety of food products with β-glucan were available in the food stores, most subjects would probably find it much easier to increase their oat β-glucan intake.

In conclusion, an intake of food products containing OBC, corresponding to 5 g (2.7 g soluble) oat β-glucan daily, induced an additional S-cholesterol-lowering effect when incorporated into a diet low in fat and cholesterol. Parallel changes in serum metabolites of cholesterol and bile acids occurred shortly after the introduction of oat fibre in the diet, and this confirms that immediate responses in sterol metabolism are induced. The inclusion in the diet of a variety of food products enriched with oat β-glucan could be a useful tool in the prevention and treatment of hypercholesterolaemia.

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Ågot Lia Amundsen
Institute For Ernæringsforskning, Universitetet I Oslo, Postboks 1046, Blindern, NO-0316 Oslo, Norway
E-mail: a.l.amundsen@basalmed.uio.no