

# High-fiber oat cereal compared with wheat cereal consumption favorably alters LDL-cholesterol subclass and particle numbers in middle-aged and older men<sup>1-3</sup>

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## ABSTRACT

**Background:** No studies have examined whether increased consumption of oat cereal, rich in soluble fiber, favorably alters lipoprotein particle size and number.

**Objective:** We examined the effects of large servings of either oat or wheat cereal on plasma lipids, lipoprotein subclasses, lipoprotein particle diameters, and LDL particle number.

**Design:** Thirty-six overweight men aged 50–75 y were randomly assigned to consume daily for 12 wk either oat or wheat cereal providing 14 g dietary fiber/d. Before and after the intervention, plasma lipid and lipoprotein subclasses were measured with proton nuclear magnetic resonance spectroscopy, and whole-body insulin sensitivity was estimated with the frequently sampled intravenous-glucose-tolerance test.

**Results:** Time-by-treatment interactions ( $P < 0.05$ ) for LDL cholesterol (oat:  $-2.5\%$ ; wheat:  $8.0\%$ ), small LDL cholesterol (oat:  $-17.3\%$ ; wheat:  $60.4\%$ ), LDL particle number (oat:  $-5.0\%$ ; wheat:  $14.2\%$ ), and LDL:HDL cholesterol (oat:  $-6.3\%$ ; wheat:  $14.2\%$ ) were observed. Time-by-treatment interactions were nearly significant for total cholesterol (oat:  $-2.5\%$ ; wheat:  $6.3\%$ ;  $P = 0.08$ ), triacylglycerol (oat:  $-6.6\%$ ; wheat:  $22.0\%$ ;  $P = 0.07$ ), and VLDL triacylglycerol (oat:  $-7.6\%$ ; wheat:  $2.7\%$ ;  $P = 0.08$ ). No significant time-by-treatment interactions were observed for HDL cholesterol, HDL-cholesterol subclasses, or LDL, HDL, and VLDL particle diameters. Insulin sensitivity did not change significantly with either intervention.

**Conclusions:** The oat compared with the wheat cereal produced lower concentrations of small, dense LDL cholesterol and LDL particle number without producing adverse changes in blood triacylglycerol or HDL-cholesterol concentrations. These beneficial alterations may contribute to the cardioprotective effect of oat fiber. *Am J Clin Nutr* 2002;76:351–8.

**KEY WORDS** Lipoproteins, triacylglycerol, LDL subclass, LDL particle number, oat fiber, wheat fiber, men, high-fiber diet

## INTRODUCTION

A diet high in fiber has been linked to a decreased risk of mortality from cardiovascular disease (CVD), independent of energy intake, dietary fat intake, and other dietary factors (1, 2). Meta-analyses have shown that the consumption of soluble fiber, such as  $\beta$ -glucan in oat products, reduces blood total cholesterol and LDL-cholesterol concentrations (3, 4). Thus, the ability of soluble fiber to reduce CVD risk is in part related to its ability to favorably modify blood lipids and lipoproteins.

Many persons with apparently normal blood lipid profiles will develop CVD (5, 6). Examination of blood lipid indexes that are not traditionally measured (eg, lipoprotein subclasses and particle size, diameter, and number) may provide greater insight into a person's actual CVD risk and into the effectiveness of an intervention to modify this risk. For example, small, dense LDL particles appear to be more atherogenic than do larger, less-dense LDL particles (7–10), and persons with a predominance of small, dense LDL particles (pattern B lipoprotein profile) have a greater risk of coronary artery disease (CAD) than do those with a predominance of large LDL particles (pattern A) (7, 8, 10, 11). Small, dense HDL particles, more commonly referred to as HDL<sub>3</sub> cholesterol, appear to be less cardioprotective than the larger, less-dense HDL<sub>2</sub> cholesterol (12). An elevated LDL particle number, often indicated by high apolipoprotein B concentrations, has also been linked to an increased CAD risk (8, 13).

The adoption of a high-carbohydrate, low-fat diet sometimes produces unfavorable changes in blood lipids and lipoproteins, specifically an increase in plasma triacylglycerol and a decrease in HDL-cholesterol concentrations (14). This phenomenon was recently reviewed by Parks and Hellerstein (15). Elevated triacylglycerol concentrations may, in turn, contribute to increased concentrations of both small, dense LDL and HDL particles (16). Because of this phenomenon, some have suggested that the replacement of carbohydrate for fat is inappropriate (17). Evidence indicates that changes in lipoprotein profiles in response to a high-carbohydrate, low-fat diet may be dependent on the LDL subclass phenotype (18).

No studies have examined the effects of fiber-rich oat and wheat cereal consumption on lipoprotein subclasses, particle size, and particle number. It is also not clear whether adverse lipid and lipoprotein changes induced by an increase in carbohydrate consumption are differentially altered by cereals rich in soluble (eg, oat) or insoluble (eg, wheat) fiber. Thus, the purpose of this investigation was to determine the effects of adding 2 large servings

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per day of either oat or wheat cereal on plasma lipid indexes that have not previously been studied, including lipoprotein subclasses, lipoprotein particle diameters, and LDL particle number.

## SUBJECTS AND METHODS

### Subjects

Men aged 50–75 y with a body mass index (in kg/m<sup>2</sup>) between 25 and 35 were recruited from the surrounding community of Fort Collins, CO. Only subjects who were sedentary or minimally physically active (fewer than two 30-min aerobic exercise sessions per week) were included. Individuals were excluded if they reported or were observed to have CVD, to have self-reported diabetes or a fasting blood glucose concentration >7.0 mmol/L, to have a systolic blood pressure >160 mm Hg or a diastolic blood pressure >99 mm Hg, to have asthma, to have tobacco use, to have a history of eating disorders or of thyroid gland disorders, or to use any medications known to affect any of the dependent variables in the study. Subjects were excluded if they reported a high habitual intake of dietary fiber (eg, >30g/d), as determined with Block's questionnaires (19): the Fat Screener and the Fruit, Vegetable, and Fiber Screener (19). The subjects tasted the cereal products before enrollment to ensure that they found the cereal palatable. About 150 men were screened for the study, 39 of whom were enrolled. Two men were excluded after enrollment, because they were found to have fasting blood glucose concentrations >7.0 mmol/L, and another man dropped out after enrollment because of a broken limb, which necessitated the use of medications. A total of 36 men completed the protocol: 18 per intervention group. This study was approved by the Human Research Committee at Colorado State University. All subjects provided written, informed consent before participation.

### Experimental design

After the screening, subjects were randomly assigned to consume whole-grain oat or wheat cereals providing 14 g dietary fiber/d for 12 wk. The oat group consumed 60 g Quaker Oatmeal and 76 g Quaker Oat Bran ready-to-eat cold cereal (Quaker Oats Co, Barrington, IL), and the wheat group consumed 60 g Mother's Whole Wheat Hot Natural Cereal (Quaker Oats Co) and 81 g Frosted Mini-Wheats (Kellogg Co, Battle Creek, MI). The combination of oat cereals provided 5.5 g  $\beta$ -glucan, as determined by the manufacturer. The amount of cereal provided was matched between groups to achieve similar intakes of energy, macronutrients, and dietary fiber according to information provided by the manufacturer and the USDA Nutrient Database for Standard Reference (release 12; Washington, DC). Daily, the cereal provided 513 kcal (8 g fat, 95 g carbohydrate, 13.5 g simple sugar, 21 g protein, and 14 g dietary fiber) in the oat group and 480 kcal (3 g fat, 112 g carbohydrate, 20.6 g simple sugar, 14 g protein, and 14 g dietary fiber) in the wheat group. The subjects were instructed to not alter their dietary habits, other than the daily inclusion of the cereals for breakfast and a snack.

The cereal increased the mean total carbohydrate intake in both grams and as a percentage of energy from carbohydrate by  $\approx$ 5% (oat group: 47–52%; wheat group: 50–55%) and significantly decreased the absolute and relative fat content by  $\approx$ 5% (oat group: 35–30%; wheat group: 33–28%). These dietary changes resulted in a mean fat intake  $\leq$ 30% of total energy.

Subjects returned uneaten cereal packets to the investigators on a biweekly (eg, every other week) basis so that compliance could be determined. Compliance with the intervention was not significantly different between the groups. The oat and wheat groups consumed a mean ( $\pm$ SEM) of  $96 \pm 4\%$  and  $95 \pm 5\%$  of the required cereal servings, respectively. Only one individual reported <88% compliance; exclusion of this subject from the data analysis did not change any of the findings significantly.

### Anthropometric measurements

Body weight was measured to the nearest 0.1 kg with a balance scale while the subjects were wearing only light indoor clothing (Detecto, Webb City, MO), and height (cm) was measured with a wall-mounted stadiometer while the subjects were barefooted. Body weight was reassessed biweekly throughout the study. Skinfold-thickness measurements (mm) were obtained at 8 sites (chest, abdomen, triceps, suprailiac, midaxillary, subscapular, thigh, and medial calf) with calipers (Lange; Cambridge Scientific Industries, Cambridge, MD). Waist circumference was measured (cm) at the level of the umbilicus with a nonstretchable tape (Gulick II Measuring Tape; Country Technology, Gays Mills, WI). Anthropometric measurements were repeated during the last week of the intervention.

### Dietary assessment

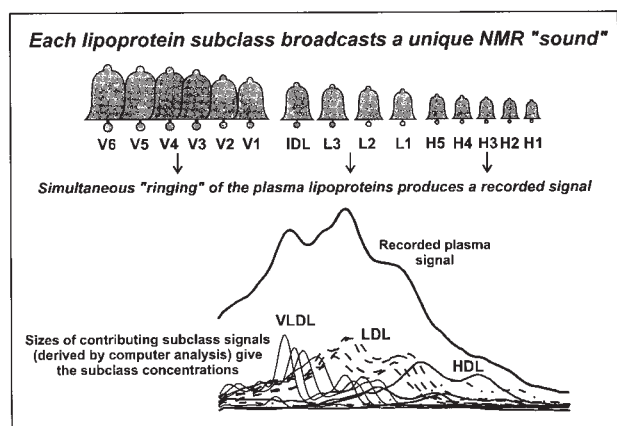
Each subject kept a 4-d food intake record at baseline and during the final week of the study to assess dietary intake. The subjects were instructed by a research dietitian (BD) to accurately record their food intakes (eg, portion sizes, food preparation methods, and brand names of products) with the use of 2-dimensional food models. The dietitian reviewed all records with the subjects on completion for accuracy and sufficiency of detail. The subjects were asked to provide food labels for products used to determine appropriate substitutions when actual items consumed were not in the software database. Food intake records were analyzed by using the Food Intake Analysis System (FIAS 3.98 nutrient analysis program; University of Texas School of Public Health, 1998). The FIAS database consists of the Primary Data Set and the Survey Nutrient Database of the National Nutrient Data Bank, developed and maintained by the US Department of Agriculture.

### Lipid and lipoprotein analysis

Blood samples were obtained at baseline and after the 12-wk intervention. After the subjects had fasted overnight, blood was obtained from an indwelling intravenous catheter into tubes containing EDTA. Samples were inverted and then centrifuged at 4 °C for 20 min at  $2500 \times g$  to obtain plasma, which was then stored at  $-70$  °C until analyzed.

Plasma lipid and lipoprotein concentrations and lipoprotein particle size were measured by using nuclear magnetic resonance (NMR) spectroscopy (LipoMed, Inc, Raleigh, NC). This method is based on the principle that when plasma is exposed to the NMR magnet, the methyl group protons of each of the 4 types of lipids (phospholipid, cholesterol, cholesterol ester, and triacylglycerol) in the lipoproteins together emit a bulk NMR signal. The unique signal produced by the various lipoprotein particles of differing diameters (based on the phospholipid shell) contribute to this bulk signal, analogous to the sound produced by simultaneously ringing numerous bells of differing size and shape (**Figure 1**). This composite signal then undergoes deconvolution by using linear least squares regression analysis to separate the lipoprotein subclasses based on prior knowledge of the methyl signal frequency





**FIGURE 1.** Lipoprotein subclasses behave like bells in the nuclear magnetic resonance analyzer. Reprinted with permission from reference 20.

and shape emitted by individual lipoprotein subclasses. The plasma concentration of each lipoprotein subclass is then calculated based on knowledge about the known relations between signal amplitude and subclass concentration (20, 21). To perform these calculations, software is used that contains a reference library of subclass spectra obtained by isolating lipoprotein particle size ranges from fasting plasma of normolipidemic and dyslipidemic subjects by using ultracentrifugation and agarose gel filtration chromatography (20). This process allows the simultaneous measurement of 15 lipoprotein subclasses, including VLDL triacylglycerol (V1–V6), LDL cholesterol (IDL, L1–L3), HDL cholesterol (H1–H5), and chylomicrons (**Table 1**). HDL<sub>2</sub> corresponds to the sum of H4 and H5, HDL<sub>3</sub> is the sum of H1, H2, and H3. On the basis of comparisons with the lipoproteins separated by flotation ultracentrifugation, small LDLs correspond to L1 and large LDLs refer to the sum of L2 and L3 (20, 21). Individual lipoprotein lipid concentrations are then calculated based on the average measured lipid values for each of the lipoproteins, based on values previously determined from

**TABLE 1**

Lipoprotein subclasses determined by nuclear magnetic resonance spectroscopy<sup>1</sup>

Lipoprotein and subclass	Diameter range (nm)
VLDL	
V6	150 ± 70
V5	70 ± 10
V4	50 ± 10
V3	38 ± 3
V2	33 ± 2
V1	29 ± 2
LDL	
IDL	25 ± 2
L3	22 ± 0.7
L2	20.5 ± 0.7
L1	19 ± 0.7
HDL	
H5	11.5 ± 1.5
H4	9.4 ± 0.6
H3	8.5 ± 0.3
H2	8.0 ± 0.2
H1	7.5 ± 0.2

<sup>1</sup> $\bar{x} \pm \text{SEM}$ .

spectrophotometric analysis of lipids from reference samples (21). Total plasma cholesterol, triacylglycerol, LDL-cholesterol, and HDL-cholesterol concentrations are then determined by summing the lipid concentrations of the various subclasses. Cholesterol (LDL and HDL cholesterol) and triacylglycerol (VLDL triacylglycerol) concentrations are expressed in mmol/L. Strong correlations between NMR and chemical analysis for VLDL-triacylglycerol, LDL-cholesterol, and HDL-cholesterol concentrations have been reported ( $r = 0.98, 0.91, \text{ and } 0.93$ , respectively) (21). LDL and HDL subclass distributions between NMR and gradient gel electrophoresis (GGE) also correlated well (21).

Average particle sizes (diameter, nm) of VLDL, LDL, and HDL and concentrations (particle number) of the LDL particles (nmol/L) were also determined. Reference standards for VLDL and LDL subclass diameters for the NMR method are based on electron microscopy and for HDL by polyacrylamide GGE (20). Correlations between NMR and GGE for LDL and HDL particle size have been reported to be 0.70–0.90 and 0.88 (21), respectively. LDL subclass diameters obtained with the NMR method are  $\approx 5$  nm smaller than those obtained by using GGE, but agree with electron microscopy data and calculations based on LDL chemical composition (21). Individuals were classified as having LDL subclass phenotype pattern A if their mean particle size was  $> 20.5$  nm and as having pattern B if they had a mean baseline LDL particle size  $\leq 20.5$  nm (12), and lipoprotein responses to the intervention were analyzed by LDL subclass phenotype and cereal group.

CVs obtained by NMR have been reported to be 1.5–2.9% for standard lipid panel variables, 1.8% for LDL-particle concentrations, and  $\approx 0.5\%$  for average LDL and HDL particle sizes (20). A more detailed treatment of the use of NMR for measuring plasma lipid and lipoprotein concentrations and lipoprotein particle size was described previously (20–22).

#### Intravenous-glucose-tolerance test

An insulin-augmented frequently sampled intravenous-glucose-tolerance test (IVGTT) was administered to these subjects at baseline and after the intervention after they had fasted overnight for 12 h. The test was performed while the subjects were in a supine position, after a 30-min relaxation period. An intravenous catheter was placed in each antecubital vein, one for the administration of insulin and glucose and one for collecting blood samples. Blood samples for the measurement of baseline insulin and glucose concentrations were obtained 10 min and then again 5 min before the infusion of a bolus of glucose (0.3 g/kg in a 50% dextrose solution infused over 90 s). Twenty minutes after the glucose infusion, a bolus of insulin (0.03 U/kg) was infused. Blood samples were obtained 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 18, 22, 25, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, and 180 min after the initial glucose infusion and were then immediately centrifuged at 4 °C for 20 min at  $2500 \times g$  and analyzed for glucose concentrations with the glucose oxidase method by using a glucose autoanalyzer (Yellow Springs Instruments, Yellow Springs, OH). A sample of plasma was stored at  $-20$  °C for later measurement of insulin concentrations by enzyme-linked immunosorbent assay (Diagnostic Systems Laboratories, Inc, Webster, TX). Insulin and glucose values from the IVGTT were entered into the MINMOD program (version 3.0; R. Bergman, University of Southern California) for determination of insulin sensitivity ( $S_I$ ), acute insulin response to glucose ( $\text{AIR}_G$ ), and glucose effectiveness ( $S_G$ ). This model uses measurements of plasma glucose and insulin concentrations over a 3-h period to derive in vivo whole-body  $S_I$  (23).

**TABLE 2**  
Physical characteristics of the subjects before and after 12 wk of the intervention<sup>1</sup>

	Oat group (n = 18)		Wheat group (n = 18)	
	Baseline	Week 12	Baseline	Week 12
Age (y)	57 ± 2	—	61 ± 2	—
Height (cm)	175.9 ± 1.5	—	177.4 ± 1.5	—
Weight (kg) <sup>2</sup>	91.4 ± 3.0	92.1 ± 3.0	92.3 ± 3.0	93.2 ± 3.0
BMI (kg/m <sup>2</sup> ) <sup>2</sup>	29.6 ± 0.8	29.8 ± 0.8	29.2 ± 0.8	29.5 ± 0.8
Sum of skinfold thicknesses (mm) <sup>2</sup>	168.7 ± 7.9	172.4 ± 10.5	175.0 ± 7.9	185.6 ± 10.5
Waist circumference (cm)	104.1 ± 2.2	104.5 ± 2.1	104.8 ± 2.0	105.1 ± 2.1

<sup>1</sup> $\bar{x} \pm$  SEM. There was no significant difference in age or height between the groups. There were no significant group-by-time interactions for weight, BMI, sum of skinfold thicknesses, or waist circumference.

<sup>2</sup>Significant main effect of time,  $P < 0.05$ .

### Statistical analysis

Kolmogorov-Smirnov normality tests were performed on independent and dependent variables before further statistical analysis. Treatment differences were initially assessed by using a 2 (oat compared with wheat)  $\times$  2 (before and after treatment) analysis of variance with a general linear model (SPSS 9.0 for WINDOWS; SPSS Inc, Chicago). A 2  $\times$  2 analysis of covariance was used in which changes in body weight and in dietary macronutrient intakes were used as covariates where appropriate. Lipoprotein responses to the 2 cereals were compared between phenotype patterns (A compared with B) by using analysis of covariance. When there was a significant pattern-by-time interaction, paired  $t$  tests were used to determine differences in lipid and lipoprotein responses to the intervention between pattern A and pattern B. Simple correlational analyses were performed to identify relations among variables that could explain any treatment-related changes.  $\alpha$  was set at  $P < 0.05$ , and all data are expressed as means  $\pm$  SEMs.

### RESULTS

The physical characteristics of the study participants are shown in **Table 2**. No significant differences in subject characteristics between the groups were observed at baseline. Mean body mass index and the sum of skinfold thicknesses increased slightly but significantly in both the oat and wheat groups over time ( $P < 0.05$ ). Body weight increased  $\approx 0.8$  kg ( $P < 0.05$ ).

Despite the slight increase in body weight, no change in energy intake was detected in either cereal group over the 12-wk intervention. However, significant changes in macronutrient intake were noted (**Table 3**), with similar increases in mean intakes of protein (g) and carbohydrate (g and % of total energy) and a decrease in fat intake (g and % of total energy) in both groups. The change was an increase of  $\approx 5\%$  as a percentage of total energy for carbohydrate and a decrease of  $\approx 5\%$  as a percentage of total energy for fat. Intakes of cholesterol and saturated and monounsaturated fatty acids decreased, and the ratio of dietary polyunsaturated to saturated fatty acids (P:S) improved signifi-

**TABLE 3**  
Dietary intake at baseline and after 12 wk of the intervention<sup>1</sup>

	Oat group		Wheat group	
	Baseline	Week 12	Baseline	Week 12
Energy				
(kJ)	10620 ± 560	10877 ± 536	9398 ± 544	9939 ± 521
(kcal)	2538 ± 134	2599 ± 128	2246 ± 130	2375 ± 125
Protein <sup>2</sup>				
(g)	91.1 ± 5.1	103.3 ± 6.0	82.1 ± 4.9	86.8 ± 5.8
(% of energy)	14.8 ± 0.7	15.9 ± 0.6	14.8 ± 0.7	14.4 ± 0.6
Fat <sup>2</sup>				
(g)	99.8 ± 6.5	89.2 ± 6.0	82.4 ± 6.4	78.3 ± 5.8
(% of energy)	35.3 ± 1.5	29.6 ± 1.2	33.3 ± 1.4	28.0 ± 1.2
Carbohydrate <sup>2</sup>				
(g)	297.2 ± 21.3	336.8 ± 17.3	283.3 ± 20.7	331.6 ± 16.8
(% of energy)	47.0 ± 2.2	51.5 ± 1.6	49.6 ± 2.1	55.0 ± 1.5
Dietary fiber (g) <sup>2</sup>	20.9 ± 1.9	30.2 ± 1.6	18.9 ± 1.9	29.2 ± 1.6
Cholesterol (mg) <sup>2</sup>	406.7 ± 42.2	260.9 ± 31.1	291.4 ± 41.0	232.5 ± 30.2
Fatty acids (g)				
Saturated <sup>2</sup>	35.8 ± 2.4	29.6 ± 2.1	27.6 ± 2.3	24.2 ± 2.0
Lauric acid <sup>2</sup>	1.3 ± 0.3	0.7 ± 0.1	0.6 ± 0.3	0.5 ± 0.1
Myristic acid <sup>2</sup>	3.3 ± 0.3	2.5 ± 0.2	2.4 ± 0.3	2.1 ± 0.2
Palmitic acid <sup>2</sup>	19.2 ± 1.3	16.4 ± 1.1	15.1 ± 1.2	13.5 ± 1.1
Monounsaturated (g) <sup>2</sup>	38.2 ± 2.7	34.3 ± 2.4	32.0 ± 2.6	29.6 ± 2.3
Polyunsaturated (g)	17.9 ± 1.5	18.4 ± 1.8	16.3 ± 1.4	18.5 ± 1.8
P:S <sup>2</sup>	0.5 ± 0.1	0.7 ± 0.1	0.6 ± 0.1	0.8 ± 0.1

<sup>1</sup> $\bar{x} \pm$  SEM. P:S, ratio of polyunsaturated to saturated fatty acids. There were no significant group-by-time interactions.

<sup>2</sup>Significant main effect of time,  $P < 0.05$ .

**TABLE 4**  
Lipid and lipoprotein profiles at baseline and after 12 wk of the intervention

	Oat group		Wheat group		P for interaction
	Baseline	Week 12	Baseline	Week 12	
Cholesterol (mmol/L)					
Total	5.28 ± 0.18 <sup>1</sup>	5.15 ± 0.21	4.91 ± 0.16	5.22 ± 0.18	0.08
LDL	3.58 ± 0.16	3.49 ± 0.14	3.30 ± 0.15	3.57 ± 0.14	0.02 <sup>2</sup>
Small LDL	1.77 ± 0.33	1.47 ± 0.34	1.01 ± 0.33	1.61 ± 0.33	0.01 <sup>2</sup>
Large LDL	1.79 ± 0.31	2.01 ± 0.30	2.28 ± 0.30	1.94 ± 0.29	0.08
HDL	0.87 ± 0.05	0.86 ± 0.05	0.89 ± 0.04	0.85 ± 0.05	0.41
HDL <sub>2</sub>	0.27 ± 0.04	0.24 ± 0.04	0.27 ± 0.04	0.24 ± 0.04	0.92
HDL <sub>3</sub>	0.61 ± 0.03	0.63 ± 0.02	0.62 ± 0.03	0.62 ± 0.02	0.68
Triacylglycerol (mmol/L)	1.83 ± 0.17	1.71 ± 0.18	1.50 ± 0.17	1.83 ± 0.17	0.07
VLDL triacylglycerol (mmol/L)	1.44 ± 0.17	1.33 ± 0.17	1.13 ± 0.16	1.44 ± 0.17	0.08
LDL particle size (nm)	20.08 ± 0.2	20.15 ± 0.2	20.41 ± 0.2	20.16 ± 0.2	0.10
HDL particle size (nm) <sup>3</sup>	8.44 ± 0.1	8.40 ± 0.1	8.56 ± 0.1	8.42 ± 0.1	0.14
VLDL particle size (nm)	50.7 ± 2.0	50.3 ± 1.8	50.1 ± 1.9	50.1 ± 1.8	0.89
LDL particle concentration (nmol/L)	1752 ± 102	1664 ± 101	1503 ± 99	1717 ± 98	0.01 <sup>2</sup>
LDL:HDL cholesterol	4.3 ± 0.3	4.1 ± 0.3	3.8 ± 0.3	4.3 ± 0.3	0.02 <sup>2</sup>
Total:HDL cholesterol	6.4 ± 0.4	6.0 ± 0.5	5.7 ± 0.3	6.4 ± 0.4	0.05

<sup>1</sup> $\bar{x} \pm \text{SEM}$ .

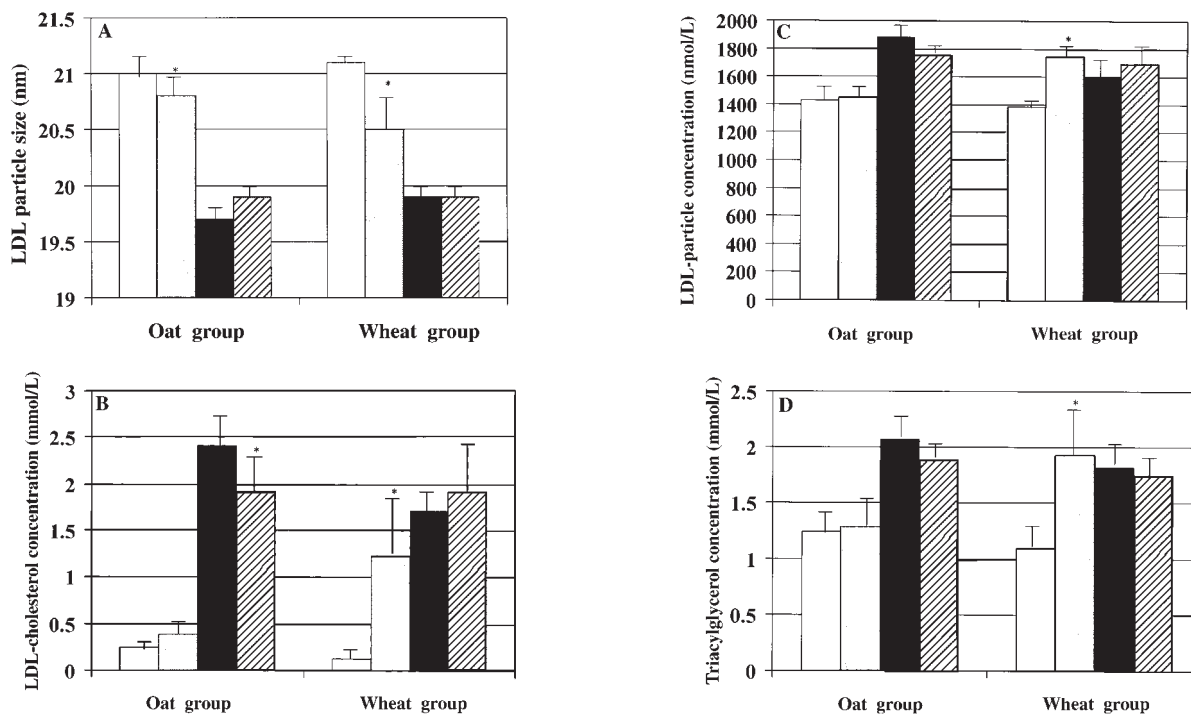
<sup>2</sup>Significant time-by-treatment interaction,  $P < 0.05$ .

<sup>3</sup>Significant main effect of time,  $P = 0.02$ .

cantly in both groups. Unexpected differences in dietary intakes of saturated fat, myristic acid, and palmitic acid were observed at baseline ( $P = 0.02, 0.02, \text{ and } 0.01$ , respectively).

The results of the lipid and lipoprotein analyses are shown in **Table 4**. One subject in the oat group had incomplete lipid data; therefore, the data shown are for 17 subjects in the oat group and 18 in the

wheat group. No significant differences in lipid or lipoprotein concentrations were observed between the 2 groups at baseline. A significant time-by-treatment interaction was observed for LDL cholesterol, the small LDL-cholesterol subclass, LDL particle number, and LDL:HDL cholesterol; the oat group had favorable changes and the wheat group had elevations in these lipid indexes. A significant reduc-



**FIGURE 2.** Mean ( $\pm$ SEM) changes in LDL particle size (A), LDL-cholesterol concentration (B), LDL-particle concentration (C), and triacylglycerol concentration (D) in subjects in the oat and wheat groups with pattern A (predominance of large LDL particles) at baseline ( $\square$ ) and at 12 wk ( $\blacksquare$ ) and with pattern B (predominance of small, dense LDL particles) at baseline ( $\blacksquare$ ) and at 12 wk ( $\boxtimes$ ). \*Significantly different from baseline within same pattern,  $P \leq 0.05$ . Time-by-pattern interaction (repeated-measures ANOVA):  $P = 0.012$  (A),  $P = 0.040$  (B),  $P = 0.055$  (C), and  $P = 0.017$  (D). Oat group: pattern A ( $n = 5$ ), pattern B ( $n = 12$ ); wheat group: pattern A ( $n = 8$ ), pattern B ( $n = 10$ ).

**TABLE 5**  
Insulin and glucose metabolism at baseline and after 12 wk of the intervention<sup>1</sup>

	Oat group		Wheat group		<i>P</i> for interaction
	Baseline	Week 12	Baseline	Week 12	
Fasting glucose (mmol/L)	5.4 ± 0.1	5.6 ± 0.1	5.3 ± 0.1	5.3 ± 0.1	0.17
Fasting insulin (pmol/L)	93.8 ± 15.4	88.4 ± 12.5	55.3 ± 15.4	58.8 ± 12.5	0.34
<i>S</i> <sub>I</sub> (10 <sup>-4</sup> min <sup>-1</sup> · μU <sup>-1</sup> · mL <sup>-1</sup> )	1.8 ± 0.3	1.8 ± 0.3	2.6 ± 0.3	2.2 ± 0.3	0.21
<i>S</i> <sub>G</sub> (min)	0.0198 ± 0.0018	0.0187 ± 0.0017	0.0188 ± 0.0019	0.0224 ± 0.0018	0.03 <sup>2</sup>
AIR <sub>G</sub> (pmol · mL <sup>-1</sup> · min <sup>-1</sup> )	527.6 ± 45.2	471.9 ± 54.5	410.6 ± 47.9	406.1 ± 57.8	0.30

<sup>1</sup> $\bar{x} \pm \text{SEM}$ .

<sup>2</sup>Significant time-by-treatment interaction, *P* < 0.05.

tion in mean HDL particle size across both groups was noted over time. A paired sample *t* test indicated no significant change in HDL size in the oat group (*P* = 0.32), but a significant reduction in the wheat group (*P* = 0.03). Therefore, this significant time effect was attributed to the greater reduction in HDL particle size in the subjects consuming the high-fiber wheat cereals. Time-by-treatment interactions were nearly significant for total cholesterol (*P* = 0.08), triacylglycerol (*P* = 0.07), VLDL triacylglycerol (*P* = 0.08), and total:HDL cholesterol (*P* = 0.05), the concentrations of which decreased in the oat group and increased in the wheat group. The time-by-treatment interaction for LDL particle size was also nearly significant (*P* = 0.10), because of an increase in particle size in the oat group and a decrease in the wheat group. Few individuals in either group had detectable concentrations of chylomicrons or intermediate-density lipoproteins, with the analyses indicating no significant changes in either group over time (data not shown). Correlational analyses indicated a significant (*P* < 0.05) relation between the change in triacylglycerol concentrations and changes in LDL size (*r* = -0.80), small LDL cholesterol (*r* = 0.76), total cholesterol (*r* = 0.50), LDL cholesterol (*r* = 0.36), and HDL<sub>2</sub> cholesterol (*r* = -0.58).

Because of baseline differences in the dietary intakes of saturated fat, myristic acid, and palmitic acid, additional statistical analyses were performed by using the changes in these dietary variables and the intakes of total fat, polyunsaturated fat, cholesterol, and P:S as covariates. All significant blood lipid and lipoprotein changes remained significant, even after adjustment. Additionally, total cholesterol concentrations were significantly different between the oat and wheat groups over time when changes in the P:S and in polyunsaturated fat intake were used as covariates.

When LDL subclass phenotype (patterns A and B) was used as a covariate, the significant time-by-treatment interactions indicated above remained significant. However, significant differences were noted in response to the intervention according to LDL subclass phenotype (**Figure 2**, A–D). Subjects in the oat group with pattern A (*n* = 5) had a small but significant reduction in LDL size (from 21.0 ± 0.2 to 20.8 ± 0.2 nm; *P* = 0.05), as did subjects in the wheat group with pattern A (*n* = 8) (from 21.1 ± 0.1 to 20.5 ± 0.3 nm; *P* = 0.05). Subjects in the oat group with pattern B (*n* = 12) had a significant reduction in small LDL cholesterol (from 2.41 ± 0.39 to 1.92 ± 0.38 mmol/L; *P* = 0.05), whereas subjects in the wheat group with pattern A had a significant increase in small LDL cholesterol (from 0.13 ± 0.1 to 1.23 ± 0.5 mmol/L; *P* = 0.05) and in LDL-particle concentration (from 1385 ± 89 to 1746 ± 137 nmol/L; *P* = 0.01). Subjects in the wheat group with pattern A had a significant increase in triacylglycerol concentration (from 1.10 ± 0.2 to 1.93 ± 0.4 mmol/L; *P* = 0.05); those with pattern B (*n* = 10) had no significant changes in any of these variables.

Insulin and glucose indexes are shown in **Table 5**. No significant changes in *S*<sub>I</sub>, AIR<sub>G</sub>, or fasting glucose or insulin concentrations were observed. A significant time-by-treatment interaction was observed for *S*<sub>G</sub> (*P* = 0.03); *S*<sub>G</sub> decreased in the oat group and increased in the wheat group. Despite the lack of significant group differences in *S*<sub>I</sub> among individuals in the entire sample, the change in triacylglycerol concentration was significantly associated with the change in *S*<sub>I</sub> (*r* = 0.40, *P* = 0.03), as were the changes in LDL particle number (*r* = 0.46, *P* = 0.01) and LDL cholesterol (*r* = 0.50, *P* = 0.01).

## DISCUSSION

The major finding of this study was that the addition of 2 large servings of oat cereal compared with the addition of wheat cereal to the diet results in lower concentrations of small, dense LDL and LDL particle numbers. Furthermore, despite the increase in carbohydrate intake and the decrease in total and saturated fat intakes, the mean plasma triacylglycerol concentration did not increase in the subjects who consumed high-fiber oat cereals. However, plasma triacylglycerol increased along with other unfavorable changes in lipids and lipoproteins in the subjects who consumed the wheat cereal, as was reported in some studies in which dietary carbohydrate was increased and dietary fat decreased (14). Because a low-fat, high-carbohydrate, high-fiber diet is frequently recommended for the prevention and treatment of CVD, it may be important to distinguish between the type of fiber recommended, eg, soluble compared with insoluble.

We found a trend toward lower triacylglycerol concentrations in the subjects who consumed the oat cereal and elevated triacylglycerol concentrations in the subjects who consumed the wheat cereal (*P* < 0.07). Even modest elevations in blood triacylglycerol concentrations are independently related to increased CVD risk (24), possibly resulting from alterations in the lipid composition of HDL and LDL. The exchange of cholesterol esters for triacylglycerol among these lipoproteins causes them to become relatively cholesterol depleted (22) and triacylglycerol enriched (16). These particles, then, are favorable substrates for hepatic triacylglycerol lipase (EC 3.1.1.3), with triacylglycerol removal resulting in decreases in particle diameter and increases in density. In this investigation, changes in triacylglycerol concentrations were significantly inversely correlated with changes in LDL particle size and HDL<sub>2</sub> and positively correlated with changes in the concentration of small LDL cholesterol. These findings provide support for a relation between a decrease in triacylglycerol concentrations accompanied by an increase in LDL particle size in the subjects who consumed oat but not wheat cereal.

The characteristics of small, dense LDL particles may relate to their increased atherogenic potential. Specifically, these particles

may be more susceptible to oxidation and have a lower clearance rate as the result of a reduced affinity for the LDL receptor (16). LDL particle size is inversely correlated with CAD (7, 10). Studies have suggested that the highest risk for CAD may occur in individuals with a predominance of small LDL (pattern B) and a high LDL-particle concentration (8). The LDL-particle concentration provides some indication of apolipoprotein B concentrations, or the concentration of potentially atherogenic particles in the plasma. Anderson et al (25) found that supplemental oat bran (eg, without an increase in dietary carbohydrate) lowered apolipoprotein B-100 concentrations by 13.7%; however, this could have been attributed to a decrease in body weight. Our data suggest that the type of fiber consumed may be an important factor in determining the concentration and number of small LDL particles.


Our findings also suggest that LDL subclass phenotype may be an important determinant of lipid and lipoprotein responses to an increased intake of dietary carbohydrate and fiber. Among the subjects with pattern B, small LDL-cholesterol concentrations improved in the oat group but failed to improve in the wheat group. Among the subjects with pattern A, small LDL cholesterol, LDL particle number, and triacylglycerol did not change significantly in the oat group but worsened significantly in the wheat group. Thus, the lipid and lipoprotein responses to increased dietary carbohydrate appear to depend on both the LDL subclass phenotype and the type of dietary carbohydrate (eg, soluble or insoluble fiber) consumed.

A positive correlation between habitual dietary fiber intake and  $S_1$  has been reported (26). Increased viscous dietary fiber intake may decrease gastric emptying and increase small intestinal transit time, modify the secretion or action of digestive enzymes, or alter other factors that decrease the rate of glucose absorption (27). This could flatten postprandial glucose and insulin curves and potentially increase  $S_1$ . We found no significant change in  $S_1$  with an increased intake of soluble or insoluble dietary fiber. However, our measurements were made in the fasted state and it is possible that alterations in glucose and insulin metabolism occurred postprandially, which could affect lipoprotein subclasses.

These data indicate that increased carbohydrate consumption resulting from increased intake of high-fiber oat cereals does not reduce HDL-cholesterol concentrations or increase triacylglycerol concentrations. This finding agrees with a recent meta-analysis indicating that soluble fiber does not increase blood triacylglycerol concentrations (3). Wheat-bran supplements (eg, an increase in fiber without an increase in carbohydrate intake) might decrease serum triacylglycerol concentrations (25) but do not generally lower blood total or LDL cholesterol (25, 28–30). However, this has not been a consistent finding (31, 32). We found that high-fiber wheat cereal consumption ( $\approx 500$  kcal) produced increases in total cholesterol, LDL cholesterol, and triacylglycerol in a manner similar to what has been noted in studies substituting dietary carbohydrate for fat (14). The reason for these unfavorable lipoprotein changes in the wheat group is not readily apparent; however, the mechanism by which these alterations are produced does not occur with increased oat consumption. This difference may be related to characteristics of the cereal, eg, its soluble rather than insoluble fiber content. It is also possible that the difference in simple sugar content of the 2 cereal combinations (7.1 g) could have contributed to these differences, although this is unlikely because this amount represents a difference of only 1.4% of total reported energy intake between the 2 groups.

A potential caveat to this study is our use of NMR spectroscopy rather than more conventional methods to determine lipoprotein subclasses. However, there are several observations that support

our use of NMR spectroscopy for this purpose. First, the analyses of the subjects' blood samples before and after the intervention were performed in a single run by observers blind to subject group assignment. Second, the absolute concentrations of plasma lipid and lipoprotein concentrations and the reductions in LDL cholesterol are within a range previously reported with the use of more conventional methods (3). Finally, the fact that the correlation coefficients for change in plasma lipid and lipoprotein concentrations and lipoprotein size with the change in  $S_1$  were significant and in the expected direction also lends support to the use of this technique to quantify plasma lipid and lipoprotein concentrations and lipoprotein particle size. Therefore, we believe that comparisons of these values between groups and within subjects in our sample are meaningful and scientifically valid.

In conclusion, we found that the addition of 2 large servings per day of oat cereal resulted in lower concentrations of small, dense LDL cholesterol and LDL particle number than did the wheat cereal, without producing adverse changes in blood triacylglycerol or HDL-cholesterol concentrations. These data suggest that the type of dietary fiber, such as that found in oat cereal, may be important when recommending a high-fiber, low-fat, high-carbohydrate diet for the improvement of blood lipid and lipoprotein profiles. 

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