Combined Effect of Vegetable Protein (soy) and Soluble Fiber Added to a Standard Cholesterol-Lowering Diet

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Dietary treatment of hyperlipidemia focuses on reducing saturated fat and dietary cholesterol. Other aspects of diet are not emphasized at present, despite growing evidence that a number of plant components decrease serum cholesterol. We therefore determined whether a combination of two plant components, vegetable protein and soluble fiber, further reduce serum lipids when incorporated into the currently advocated low–saturated-fat diet. Thirty-one hyperlipidemic men and women ate two 1-month low-fat (<7% of total energy from saturated fat), low-cholesterol (<80 mg cholesterol/d) metabolic diets in a randomized crossover study. The major differences between test and control diets were an increased amount of vegetable protein (93% *v* 23% of total protein), of which 33 g/d was soy, and a doubling of soluble fiber. Fasting blood samples were obtained at the start and end of each phase. On the last 3 days of each phase, fecal collections were obtained. Compared with the low-fat control diet, the test diet decreased total cholesterol (6.2% ± 1.2%, $P < .001$), low-density lipoprotein (LDL) cholesterol (6.7% ± 1.7%, $P < .001$), apolipoprotein B (8.2% ± 1.2%, $P < .001$), and the ratios of LDL to high-density lipoprotein (HDL) cholesterol (6.3% ± 2.0%, $P = .004$) and apolipoprotein B to A-I (5.4% ± 1.5%, $P = .001$). A combination of vegetable protein and soluble fiber significantly improved the lipid-lowering effect of a low–saturated-fat diet. The results support expanding the current dietary advice to include increased vegetable protein and soluble fiber intake so that the gap in effectiveness between a good diet and drug therapy is reduced.

THE NATIONAL CHOLESTEROL Education Program (NCEP) guidelines have formed the basis internationally for the treatment of hyperlipidemia.[1] Dietary advice has emphasized the need to reduce saturated fat, cholesterol, and body weight. Additional advice has included exercise, and this appears to play a key role in reducing serum lipids.[2] Nevertheless, other potentially effective dietary strategies have not yet received official support. At the same time, by current treatment criteria,[1] as many as one quarter of all middle-aged men in some Western nations will require cholesterol reduction by drug therapy.[3] The standard drug therapy using 10 to 20 mg of a hepatic hydroxymethyl glutaryl coenzyme A reductase inhibitor can reduce low-density lipoprotein (LDL) cholesterol by as much as 21% to 44%[4] or more. However, due to the possible undesirable effects and expense of chronic drug therapy, there is also concern that cholesterol-lowering medications should be used only where diet proves inadequate.[1] By comparison, the most effective application of the current NCEP step 2 diet (less than 7% of calories as saturated fat and less than 200 mg dietary cholesterol per day) has been reported to decrease LDL cholesterol by 19% compared with a typical North American diet.[5]

An important question is therefore what dietary additions to the current lipid-lowering strategy can be used to enhance the effectiveness of low–saturated-fat diets. The more effective the diet, the greater the section of the population for whom the need for medications may be reduced or eliminated. Soluble fiber and vegetable protein have both been shown independently to decrease serum cholesterol.[6-9] We have therefore assessed whether a further lipid reduction could be obtained by adding a combination of soluble fibers and vegetable proteins to a diet already low in saturated fat and dietary cholesterol.

SUBJECTS AND METHODS

Thirty-one hyperlipidemic men (n = 19) and postmenopausal women (n = 12) completed two 1-month metabolic diets separated by at least a 2-week washout period in a randomized crossover study. The mean age was 56.5 ± 9.0 years (range, 31 to 70) and the body mass index was 24.6 ± 2.3 kg/m^2 (range, 20.8 to 29.1). All subjects had elevated serum LDL cholesterol concentrations (>4.1 mmol/L)[1] and triglyceride levels less than 4.0 mmol/L at recruitment. None had clinical or biochemical evidence of diabetes or liver or renal disease, and none were taking hypolipidemic agents, with the exception of one man who took 20 mg/d lovastatin throughout the study. One woman was taking hormone replacement therapy. Two women were taking levothyroxine, and one man and one woman were taking β-blocking agents. Dosage levels of medications were held constant for both study periods. Subjects were also asked to maintain their habitual level of physical activity throughout. Blood samples were obtained and blood pressure was measured seated after 12 to 14 hours of overnight fasting prior to the study and at the end of weeks 2 and 4 of each metabolic phase. Serum was stored at −70°C prior to analysis. Body weight was measured at the start and at weekly intervals on both metabolic phases. Twenty-four-hour urine collections and 3-day fecal collections were made on an outpatient basis at the end of both metabolic periods. For fecal collections, subjects were provided with underseat lavatory frames lined with plastic bags that were removed after use. A 5- to 10-mL fecal sample was then aspirated with a modified syringe and expelled into a screw-top plastic tube. Both

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the plastic bag and tube were labeled, placed on frozen carbon dioxide in a polystyrene container, and returned by courier to the laboratory. Feces were then weighed and stored at −20°C before freeze-drying. Tubes were stored at −70°C for short-chain fatty acid analysis. On completing each metabolic diet, subjects were asked to rate their feelings of satiety using a seven-point scale, with −4 representing extremely hungry, 0 neutral, and +4 completely satiated.[10]

The study was approved by the Ethics Committee of the University of Toronto. Informed consent was obtained from all subjects.

Diets

The metabolic diets were designed to conform to NCEP step 2 dietary principles, but the dietary intake of cholesterol was further reduced. The macronutrient profile of the metabolic diets eaten by the subjects on each phase is listed in Table 1.

The test and control metabolic diets followed a 7-day rotating menu plan. The control diet was a lacto-ovo vegetarian diet, but the milk products were low-fat, consisting of skim milk, 1% dairy fat yogurt, skim milk cheese, and low-fat cottage cheese. Eggbeaters (Lipton's, Toronto, Ontario, Canada) were used rather than whole eggs to further reduce cholesterol intake.

Table 1. Calculated Macronutrient Intake (mean ± SE) on the Test and Control Metabolic Diets (N = 31)

Intake	Control	Test
Energy		
kcal/d	2,519 ± 86	2,341 ± 88
MJ/d	603 ± 21	560 ± 21
Total protein		
g/d	121 ± 4	118 ± 4
%	19.2 ± 0.2	20.2 ± 0.1
Vegetable protein		
g/d	27 ± 1	110 ± 4
%	4.3 ± 0.1	18.8 ± 0.1
Available carbohydrate		
g/d	343 ± 12	318 ± 12
%	54.6 ± 0.3	54.3 ± 0.3
Total dietary fiber		
g/d	36 ± 1	62 ± 3
g/1,000 kcal	14.3 ± 0.2	26.3 ± 0.2
Soluble fiber		
g/d	9 ± 0	18 ± 1
g/1,000 kcal	3.4 ± 0.0	7.6 ± 0.1
Total fat		
g/d	71 ± 3	66 ± 2
%	25.5 ± 0.2	25.5 ± 0.2
SFA		
g/d	18 ± 1	16 ± 1
%	6.5 ± 0.0	6.0 ± 0.1
MUFA		
g/d	24 ± 1	22 ± 1
%	8.4 ± 0.1	8.4 ± 0.1
PUFA		
g/d	24 ± 1	25 ± 1
%	8.7 ± 0.1	9.6 ± 0.1
Dietary cholesterol		
mg/d	76 ± 3	77 ± 4
mg/1,000 kcal	30.2 ± 0.4	33.0 ± 1.4
Alcohol		
g/d	0 ± 0	0 ± 0
%	0.1 ± 0.1	0.1 ± 0.1

Abbreviations: SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

In the test diet, 93% of the animal protein was replaced with vegetable protein from soy, other legumes, and cereal foods provided as easy-to-prepare meals or frozen dishes, meat substitutes, and vegetarian "cold cuts." Soluble fiber was increased by inclusion of oats, barley, and legume dishes as breakfast cereals, soups, and main dishes. The fatty acid profile and dietary cholesterol intake on both diets were balanced by inclusion of butter and whole eggs on the test diet (eg, one egg per week on a 2,000-kcal/d diet). Test food items used in this study were all readily available and were obtained from either supermarkets (Too Good To Be True Products, Loblaw Supermarkets, Toronto, Ontario, Canada) or health food stores (Yves Veggie Cuisine, Vancouver, British Columbia, Canada; MGM Products, Cedar Lake, MI; and Fantastic Foods, Petaluma, CA).

We assessed caloric requirements using standard tables, with adjustment for each subject's physical activity and 7-day dietary record.[7] Diets were devised using a database in which the majority of foods were previously analyzed in the laboratory with the Association of Official Analytical Chemists methods for fat, protein,[11] and fiber[12] and available carbohydrate by difference. The fatty acid composition was determined by gas chromatography.[13] The food composition tables of the US Department of Agriculture[14] and food labels were used for foods that were not previously analyzed directly. The similarity of the macronutrient profile of both the test and control diets was assessed by direct analysis of 24-hour composites of all 7 days of each metabolic diet.[11,12] Expressed as a percent of the control value, the analyzed macronutrients for test and control diets agreed within 6% (total fat 1.2%, protein 5.8%, and available carbohydrate 1.4%). The percentage figures for soluble and insoluble fiber were derived from tables[15] and applied to our database values for total dietary fiber. Soluble fiber was also measured on composites of day 7 test and control diets as soluble nonstarch polysaccharides.[16] A comparison of calculated and analyzed dietary fiber values indicated that the values calculated from the database were 110% of the analyzed values for soluble fiber but only 78% for total dietary fiber. The analyzed fatty acid profiles were similar for test and control diets, as were the plant sterol and β-carotene intake (Table 2). At each clinic visit, the dietitian assessed compliance using the subjects' menus, on which each food was checked when eaten. Additional items were noted in a blank column opposite the prescribed diet. These data were used to calculate dietary intake (Table 1). Body weight was measured at each clinic visit, and the results were used to adjust total caloric intake. Complete diets were packed at a central location and delivered weekly by courier to the subjects' homes at a time convenient to them.

Analysis

Serum was analyzed according to the Lipid Research Clinics protocol[17] for total cholesterol, triglyceride, and high-density lipoprotein (HDL) cholesterol, after dextran sulfate–magnesium chloride precipitation, in a single batch.[18] LDL cholesterol was calculated. Serum apolipoprotein A-I and B levels were measured by nephelometry,[19] and the lipoprotein(a) [Lp(a)] level was measured with a commercial enzyme-linked immunosorbent assay (Terumo, Elkton, MD).

Twenty-four-hour urine collections were analyzed for C-peptide[20] and creatinine (29 subjects).[21]

Fecal bile acids were determined for 30 subjects in finely ground freeze-dried feces by gas-liquid chromatography with a DB-1 column (J&W Scientific, Folson, CA) and 5β-cholanic acid as an internal standard.[22] Fecal short-chain fatty acid levels were measured after vacuum distillation by high-performance liquid chromatography (HPLC) (29 subjects).[23,24]

Freeze-dried 24-hour composites of the 7-day test and control diets were used for measurement of plant sterols by HPLC.[25] Serum was also used to measure β-carotene by reverse-phase analytical HPLC.[26] Measurements of lipid and protein oxidative stress as thiobarbituric-

Table 2. Mean Percentage Fatty Acid Composition and Daily Intake of Beta-Carotene and Phytosterols From Analysis of the Seven-Day Composites of Test and Control Metabolic Diets

Parameter	Control	Test
SFA (%)		
10:0	0.4	0.3
12:0	0.1	0.0
14:0	2.9	2.6
16:0	15.7	16.2
18:0	5.4	5.6
20:0	0.5	0.5
22:0	0.3	0.7
24:0	0.2	0.3
Total	25.5	26.2
MUFA (%)		
14:1n5	0.2	0.2
16:1n7	0.5	0.6
18:1n9	35.2	32.4
18:1n7	1.6	1.5
20:1n9	0.7	0.6
22:1n9	0.3	0.1
Total	38.6	35.5
PUFA (%)		
18:2n6	32.0	33.5
18:3n6	0.1	0.1
18:3n3	3.8	4.7
Total	35.9	38.3
Beta-carotene (μg/d)	1,484	1,359
Phytosterols (mg/d)		
Campesterol	87	67
Stigmasterol	14	31
Sitosterol	208	224
Total	310	322
Animal sterols (mg/d)		
Coprostane	14	19
Cholesterol	50	64
Total	64	83

Abbreviations: SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

reactive substances (TBARS) and protein thiol groups, respectively, were also performed in serum.[27,28]

Statistical Analysis

The results are expressed as the mean ± SE. Weight change was expressed as kilograms per month. The cholic acid synthesis rate was calculated, assuming steady-state excretion, as the sum of the daily fecal output of cholate and deoxycholate,[29] and the chenodeoxycholate synthesis rate was the sum of the remaining three bile acids.[29] The percentage difference between the endpoint values for both diets was assessed by Student's *t* test (two-tailed) for paired data. The absolute difference between treatments was assessed using the General Linear Model procedure and SAS software[30] with the end of treatment value as the response variable and the main effects of diet, sex, treatment order (sequence), diet by sex, sex by sequence, and a random term representing subject nesting within the sex by sequence interaction, and the baseline value as a covariate.

RESULTS

Of 31 subjects, 16 received the test diet first. The diets were well accepted and compliance was good. On the test diet, subjects consumed 95% ± 7% of the calories provided. The respective control figure was 96% ± 6%. Both diets had high satiety scores (2.5 ± 0.2 for the test diet and 2.3 ± 0.2 for the control diet; satiety scale, −4 to +4). There was a significant weight gain on the control diet (0.2 ± 0.1 kg, $P = .043$) and a nonsignificant weight loss on the test diet (0.1 ± 0.2 kg, $P = .484$). The treatment difference approached significance (0.3 ± 0.2 kg, $P = .069$).

Fasting Blood Lipids and Apolipoproteins

There were no significant differences in pretreatment values between the test and control diets (Table 3). Blood lipid concentrations were generally lower on the test diet compared with the control diet for weeks 2 and 4 (Fig 1). Using the mean of weeks 2 and 4, the percentage difference assessed by paired *t* test between the two dietary treatments demonstrated significantly lower mean test values for total cholesterol (6.2% ± 1.2%, $P < .001$), LDL cholesterol (6.7% ± 1.7%, $P < .001$), apolipoprotein B (8.2% ± 1.2%, $P < .001$), and the ratios LDL:HDL cholesterol (6.3% ± 2.0%, $P = .004$) and apolipoprotein B:A-I

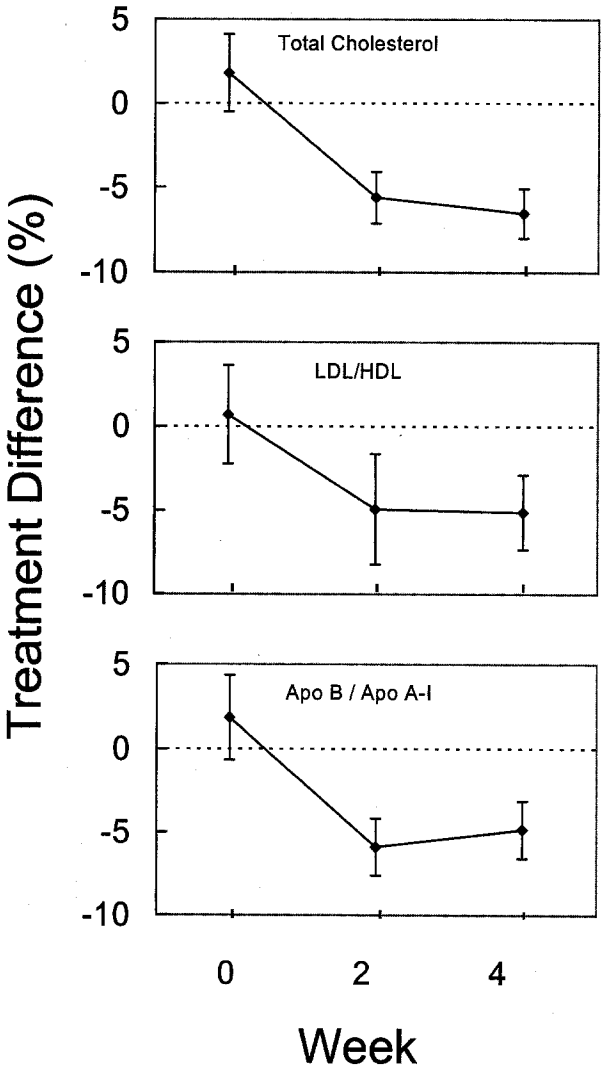

Fig 1. Change in serum cholesterol and lipoprotein and apolipoprotein ratios at weeks 2 and 4 expressed as a percentage of the respective control values (mean ± SE).

(5.4% ± 1.5%, $P = .001$). The percentage treatment differences at week 4 were not significantly different from those at week 2 (Fig 1). The significance of the effect of diet on serum lipids was confirmed by the General Linear Model procedure (total cholesterol, $P < .001$; LDL cholesterol, $P = .001$; apolipoprotein B, $P < .001$; total to HDL cholesterol, $P = .004$; LDL:HDL cholesterol, $P = .006$; and apolipoprotein B:A-I, $P = .002$) (Table 3).

There was a treatment difference between the sexes in the response to diet, with more marked reductions in men versus women for the ratios of total and LDL to HDL cholesterol and apolipoprotein B:A-I ($P < .040$). The one man taking lovastatin and the women taking levothyroxine or hormone replacement therapy were not significantly different from their peers in the blood lipid responses. Controlling for weight change in the General Linear Model procedure did not reduce the significance of the treatment differences despite the nonsignificantly greater weight loss at 4 weeks on the test diet.

β-Carotene and Markers of Oxidative Stress

No difference was found between treatments for week 4 serum concentrations of β-carotene, TBARS, or thiol groups as markers of oxidative stress (Table 3).

Blood Pressure

Systolic and diastolic blood pressure were not different between treatments (Table 3).

Urinary C-Peptide

There were no differences in 24-hour urinary C-peptide excretion either before or after correction for creatinine output (Table 3).

Fecal Weight and Bile Acid Output

Fecal wet and dry weights were significantly increased on the test diet compared with the control diet (wet weight, 281 ± 26 *v* 236 ± 22 g/d, $P = .005$; dry weight, 60 ± 4 *v* 49 ± 3 g/d, $P = .004$), as were the total fecal bile acid output (39% ± 13%, $P = .007$) and the synthesis rates of cholate (52% ± 16%, $P = .003$) and chenodeoxycholate (30% ± 14%, $P = .033$). However, there was no treatment difference in the fecal concentration of total or individual bile acids (Table 4).

Fecal Short-Chain Fatty Acids

The fecal output of short-chain fatty acids was increased on the test diet in comparison to the control diet. The percentage differences between treatments for both the concentration and molar ratio of butyrate were increased on the test diet (24% ± 10%, $P = .017$, and 13% ± 6%, $P = .027$, respectively), but no treatment differences were found for the other two major short-chain fatty acids, acetate and propionate (Table 4).

DISCUSSION

Our data indicate that the effectiveness of the current dietary advice for serum lipid reduction could be significantly im-

Table 3. Body Weight and Serum, Urinary, and Blood Pressure Data on Test and Control Metabolic Periods (mean ± SE, N = 31)

	Control		Test			
	Baseline (wk 0)	Mean Treatment (mean of wk 2 + 4)	Baseline (wk 0)	Mean Treatment (mean of wk 2 + 4)	Mean Treatment Difference (%)*	*P*
Body weight (kg)†	67.9 ± 2.0	68.1 ± 2.0	68.2 ± 2.0	68.0 ± 1.9	0.1 ± 0.5	.895
Cholesterol (mmol/L)						
Total	6.42 ± 0.17	6.16 ± 0.13	6.48 ± 0.16	5.78 ± 0.14	−6.2 ± 1.2	<.001
LDL	4.37 ± 0.15	4.13 ± 0.10	4.40 ± 0.15	3.85 ± 0.12	−6.7 ± 1.7	<.001
HDL	1.24 ± 0.06	1.17 ± 0.05	1.26 ± 0.06	1.17 ± 0.05	−0.2 ± 1.6	.915
Triglycerides (mmol/L)	1.78 ± 0.14	1.94 ± 0.15	1.79 ± 0.13	1.67 ± 0.12	−8.3 ± 4.4	.068
Apolipoproteins (g/L)						
A-I	1.61 ± 0.04	1.51 ± 0.04	1.60 ± 0.04	1.48 ± 0.04	−2.4 ± 1.3	.078
B	1.73 ± 0.06	1.63 ± 0.05	1.73 ± 0.05	1.49 ± 0.04	−8.2 ± 1.2	<.001
Lp(a) (mg/L)	28.8 ± 4.2	29.6 ± 4.7	31.8 ± 4.7	31.1 ± 4.6	7.2 ± 5.2	.179
Ratios						
Total:HDL cholesterol	5.45 ± 0.26	5.53 ± 0.22	5.38 ± 0.22	5.21 ± 0.21	−5.5 ± 1.7	.002
LDL:HDL cholesterol	3.73 ± 0.20	3.72 ± 0.15	3.66 ± 0.17	3.49 ± 0.16	−6.3 ± 2.0	.004
Apo B:apo A-I	1.10 ± 0.05	1.10 ± 0.04	1.10 ± 0.04	1.04 ± 0.04	−5.4 ± 1.5	.001
Beta-carotene (nmol/L)†	559 ± 81	632 ± 78	611 ± 75	700 ± 85	9.7 ± 7.2	.188
Thiol groups (μmol/L)†	296 ± 6	304 ± 5	302 ± 6	310 ± 5	2.3 ± 1.6	.153
TBARS (μmol/L)†	6.35 ± 0.17	6.22 ± 0.18	6.08 ± 0.21	5.99 ± 0.20	−2.6 ± 3.3	.442
Urine (L/d)†		2.01 ± 0.14		1.84 ± 0.17	−4.0 ± 9.0	.642
C-peptide (nmol/d)†		33 ± 4		34 ± 3	19.0 ± 12.0	.109
Creatinine (mmol/d)†		10 ± 1		10 ± 1	3.3 ± 5.0	.515
C-peptide/creatinine (nmol/mmol)†		3.4 ± 0.4		3.5 ± 0.3	16.0 ± 10.0	.139
Blood pressure (mm Hg)†						
Systolic	120 ± 3	119 ± 2	120 ± 3	121 ± 3	1.3 ± 2.2	.548
Diastolic	80 ± 2	76 ± 1	79 ± 2	77 ± 2	2.1 ± 1.9	.277

NOTE. For Lp(a), beta-carotene, and blood pressure, n = 30. For C-peptide and creatinine, n = 29. To convert cholesterol and triglycerides to mg/dL, multiply by 38.67 and 88.57, respectively. To convert apolipoprotein A-I and B to mg/dL, multiply by 10.

*Treatment difference (%) = [(test − control) × 100]/control.

†Mean treatment data are week 4 values.

Table 4. Fecal Output, pH, Bile Acid, and Short-Chain Fatty Acid Data at Week 4 of Test and Control Metabolic Diets (mean ± SE)

Parameter	Control	Test	Treatment Difference (%)*	P*
Fecal output (g/d)				
Wet weight	236 ± 22	281 ± 26	37 ± 12	.005
Dry weight	49 ± 3	60 ± 4	34 ± 11	.004
Fecal pH	7.1 ± 0	6.9 ± 0.1	−2 ± 1	.079
Bile acid output (mg/d)				
Total bile acids	506 ± 53	644 ± 80	39 ± 13	.007
Cholate	47 ± 14	74 ± 30	98 ± 44	.036
Chenodeoxycholate	20 ± 5	29 ± 10	33 ± 26	.225
Deoxycholate	195 ± 20	245 ± 32	52 ± 18	.008
Lithocholate	226 ± 27	268 ± 38	27 ± 14	.060
Ursodeoxycholate	18 ± 2	28 ± 5	67 ± 25	.011
Primary bile acids	67 ± 19	103 ± 39	74 ± 34	.038
Secondary bile acids	421 ± 38	513 ± 59	36 ± 15	.019
Primary:secondary bile acids	0.14 ± 0.03	0.22 ± 0.08	80 ± 51	.122
Bile acid synthesis rate (mg/d)				
Cholate	242 ± 29	319 ± 42	52 ± 16	.003
Chenodeoxycholate	264 ± 31	324 ± 47	30 ± 14	.033
Total bile acid concentration (mg/g wet weight)	2.49 ± 0.26	2.45 ± 0.25	4 ± 8	.562
Short-chain fatty acid output (mmol/d)				
Formate	1.3 ± 0.2	1.6 ± 0.2	44 ± 16	.010
Acetate	16.4 ± 2.3	20.9 ± 3.1	56 ± 16	.002
Propionate	3.8 ± 0.6	4.2 ± 0.6	52 ± 18	.009
Isobutyrate	0.3 ± 0.0	0.3 ± 0.0	29 ± 18	.124
Butyrate	4.6 ± 0.8	6.0 ± 0.8	73 ± 20	.001
Isovalerate	0.5 ± 0.1	0.6 ± 0.1	36 ± 16	.034
Valerate	0.4 ± 0.1	0.4 ± 0.1	33 ± 23	.170
Total	31.4 ± 4.2	38.2 ± 4.4	55 ± 17	.004
Short-chain fatty acid concentration (mmol/L)				
Acetate	60.4 ± 4.6	63.5 ± 4.9	10 ± 7	.142
Propionate	14.4 ± 1.2	13.8 ± 0.9	7 ± 8	.402
Butyrate	17.2 ± 1.9	19.0 ± 1.6	24 ± 10	.017
Short-chain fatty acid molar ratio				
Acetate:total	0.50 ± 0.02	0.50 ± 0.02	2 ± 3	.647
Propionate:total	0.12 ± 0.01	0.11 ± 0.01	0 ± 8	.984
Butyrate:total	0.14 ± 0.01	0.15 ± 0.01	13 ± 6	.027

NOTE. Fecal output and pH, N = 31. Fecal bile acid, n = 30. Fecal short-chain fatty acid, n = 27.
*Significance of percent treatment differences [(test − control) × 100]/control.

proved by also advocating increased consumption of vegetable protein and soluble fiber. The lipid changes we observed included lower levels of serum cholesterol and the ratios of LDL:HDL cholesterol and apolipoprotein B:A-I at both 2 and 4 weeks on the metabolic diet. Lower LDL cholesterol and apolipoprotein B concentrations and their respective ratios with HDL cholesterol and apolipoprotein A-I have been linked to a reduced risk of coronary heart disease.[31-36] Qualitatively, similar lipid effects have been noted in studies where dietary change was associated with regression of human arteriosclerosis.[37,38]

Ninety-three percent of the protein in the test diet was of vegetable origin, compared with 23% in the control diet. Vegetable proteins in general tend to result in lower serum cholesterol levels compared with animal proteins.[8,9] Our test provided a mean intake of 33 g soy protein daily. A recent meta-analysis of human studies indicated a possible 0.23-mmol/L reduction in LDL cholesterol at a mean soy intake of 25 g daily.[9] At the level consumed, soy protein would explain approximately half of the reduction in serum cholesterol we observed. In addition, soy appears to preserve HDL cholesterol[9,39] and may therefore have contributed to the reduction in the LDL:HDL cholesterol ratio in our study.

Viscous soluble fibers have been shown to reduce serum cholesterol.[40] These fibers include β-glucans from oats and barley, pectins from vegetables and fruit, certain legume fibers, and psyllium fiber.[41-44] On a low-fat diet similar to the diet provided here and at doses of 5 to 11 g daily, these fibers decreased cholesterol by approximately 5%.[7,41] However, on those low-fat diets, no reduction was found for the ratio of LDL:HDL cholesterol with fiber.[7,44] In the present study, the mean intake of fiber from oats, barley, and legume foods was 8 g/d, which, as with soy, is likely to account for half of the cholesterol reduction observed.[7,44] The combination of soy protein and soluble fiber therefore appears to be additive in reducing LDL cholesterol and has a further benefit in reducing the LDL:HDL cholesterol ratio.

Significant blood lipid reductions were found by 2 weeks. We speculate that the reductions at 2 and 4 weeks are likely to be maintained, as indicated by previous metabolic studies of high-fiber diets.[7]

Dietary components or pharmaceutical agents that decrease serum cholesterol by interfering with micelle formation or bile acid absorption reduce plasma concentrations of fat-soluble vitamins.[45-47] However, the reduction in LDL cholesterol by

vegetable protein and soluble fiber was not associated with a reduction in β-carotene that might have suggested lipid- or fat-soluble vitamin malabsorption.

The test diet also increased fecal bulk and the concentration of butyric acid, but did not increase the fecal concentration of bile acids, as is sometimes found with cholesterol reduction by other dietary and pharmacological means.[48] Fecal butyrate has been suggested to have antineoplastic properties,[49] while high fecal concentrations of secondary bile acids have been associated with an increased risk of colon cancer.[50] The diluting effect of greater fecal bulk and the increased butyrate synthesis may be further advantages of the high-fiber test diet.

The mechanism by which soy decreases serum lipids has not been defined, but may relate to the isoflavonoids associated with soy protein[9] or the amino acid composition of soy.[51,52] Increased fecal bile acid losses have also been proposed as part of the reason for the cholesterol decrease and have been reported in pigs fed soy.[53] No such effects have been noted in human studies, although few have assessed fecal bile acid losses. The 33% increase in total bile acid output in our study was likely a result of increased soluble fiber consumption, which is known to promote fecal bile acid loss[44,54-57] as part of its cholesterol-lowering action.[55-57] The bile acid loss was in proportion to the cholesterol reduction observed.[7] If increased propionate synthesis or reduced insulin secretion had occurred on the test diet, these fiber-related phenomena might also have provided part of the explanation for the lower serum cholesterol observed.[58-60] However, no treatment difference was found for the molar ratio of fecal propionate to the other short-chain fatty acids or for 24-hour urinary C-peptide excretion as a marker of insulin secretion.

Our study was controlled for plant sterols, since these have been shown to decrease serum cholesterol and reduce the LDL:HDL cholesterol ratio.[61-63] One exception was the minor component stigmasterol, which was higher on the test diet. However, unlike β-sitosterol and β-sitostanol,[56-58] we are unaware of any studies of stigmasterol relating to lipid reduction, nor do we know of any significant effects of plant sterols when consumed at the same low levels as stigmasterol (31 mg/d) in the present test study.

In conclusion, the combination of soluble fiber and a moderate intake of soy protein foods reduced both LDL cholesterol and the ratio of LDL:HDL cholesterol. These reductions were achieved on diets that were already low in saturated fat and dietary cholesterol. Such dietary changes may have additional health advantages related to increasing the fecal bulk and the butyrate concentration. We believe our study adds further support for the inclusion of these plant food components as part of the dietary advice to reduce serum lipids. A broadening of the dietary strategy is particularly appropriate now that low–saturated-fat foods that are also high in soluble fiber or soy protein are more generally available. The proposed additions, and others like them in the future, may narrow the gap between a good diet and drug therapy.

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