The Effect of Combining Plant Sterols, Soy Protein, Viscous Fibers, and Almonds in Treating Hypercholesterolemia

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Reductions in low-density lipoprotein-cholesterol (LDL-C) result from diets containing almonds, or diets that are either low in saturated fat or high in viscous fibers, soy proteins, or plant sterols. We have therefore combined all of these interventions in a single diet (portfolio diet) to determine whether cholesterol reductions could be achieved of similar magnitude to those reported in recent statin trials which reduced cardiovascular events. Twenty-five hyperlipidemic subjects consumed either a portfolio diet (n = 13), very low in saturated fat and high in plant sterols (1.2 g/1,000 kcal), soy protein (16.2 g/1,000 kcal), viscous fibers (8.3 g/1,000 kcal), and almonds (16.6 g/1,000 kcal), or a low-saturated fat diet (n=12) based on whole-wheat cereals and low-fat dairy foods. Fasting blood, blood pressure, and body weight were obtained at weeks 0, 2, and 4 of each phase. LDL-C was reduced by 12.1% ± 2.4% ($P < .001$) on the low-fat diet and by 35.0% ± 3.1% ($P < .001$) on the portfolio diet, which also reduced the ratio of LDL-C to high-density lipoprotein-cholesterol (HDL-C) significantly (30.0% ± 3.5%; $P < .001$). The reductions in LDL-C and the LDL:HDL-C ratio were both significantly lower on the portfolio diet than on the control diet ($P < .001$ and $P < .001$, respectively). Mean weight loss was similar on test and control diets (1.0 kg and 0.9 kg, respectively). No difference was seen in blood pressure, HDL-C, serum triglycerides, lipoprotein(a) [Lp(a)], or homocysteine concentrations between diets. Combining a number of foods and food components in a single dietary portfolio may lower LDL-C similarly to statins and so increase the potential effectiveness of dietary therapy.

RECENTLY, to boost effectiveness of diet, the Expert Panel on the Detection and Treatment of High Blood Cholesterol in Adults (ATP III) of the National Cholesterol Education Program (NCEP) has recommended plant sterols (2 g/d) and viscous fibers (10 to 25 g/d) as additional dietary options.[1] The American Heart Association (AHA) has also drawn attention to the possible benefits of soy proteins[2] and the potential value of nuts.[2] In turn, the Food and Drug Administration (FDA) now permits health claims for coronary heart disease (CHD) risk reduction on foods delivering adequate amounts of plant sterols,[3] viscous fibers (oat β-glucan and psyllium),[4,5] and soy protein,[6] and a health claim for nuts has recently been granted. These 4 categories of food were therefore chosen for study. At present, the effect of combining these dietary factors is not known. Their combination may result in synergy, addition, or even quenching of their individual cholesterol-lowering effects. However, based on their differing mechanisms of action, it is likely that at least an additive effect can be expected. In a preliminary study that lacked a control arm, a mean 29% reduction in low-density lipoprotein-cholesterol (LDL-C) was seen after 4 weeks on a low–saturated fat diet containing soy protein foods, viscous fibers, plant sterols, and almonds.[7] However, although historical controls were used in this preliminary study, it did not permit assessment of the degree to which the very-low–saturated fat and cholesterol intake on the portfolio diet contributed to the large LDL-C reductions observed. We have therefore randomized subjects to 1 of 2 diets, the portfolio diet or an equally low–saturated fat, low-cholesterol diet that lacked the active ingredients of the portfolio diet. The aim was to assess the contribution of reduced saturated fat and cholesterol to the lipid-lowering seen with the portfolio diet.

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Submitted February 10, 2003; accepted April 1, 2003.

Supported by the Canada Research Chair Endowment of the Federal Government of Canada, Loblaw Brands Ltd, and the Almond Board of California.

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0026-0495/03/5211-0049$30.00/0

doi:10.1016/S0026-0495(03)00260-9

MATERIALS AND METHODS

Subjects

Twenty-five healthy hyperlipidemic subjects completed the study: 16 men and 9 postmenopausal women; (mean ± SD) age, 60 ± 9.9 years (range, 36 to 85); body mass index (BMI), 26.6 ± 2.9 kg/m^2 (range, 20.2 to 33.2). Twenty-six subjects were recruited from patients attending the Risk Factor Modification Center at St. Michael's Hospital and from newspaper advertisements. One subject withdrew during the first week of the portfolio diet due to taste preferences and inconvenience of the metabolic diet. All subjects had previously raised LDL-C levels (>4.1 mmol/L)[1] and were either reluctant to take medication to lower serum cholesterol or if taking medications (n = 6) wished to know whether more intensive dietary strategies might eliminate the need for drug therapy. Those patients taking cholesterol-lowering drugs at recruitment were asked to discontinue them at least 2 weeks prior to starting the study. No subjects had a history of cardiovascular disease, diabetes, or renal or liver disease, and none were taking medications known to influence serum lipids apart from 2 women who were on stable doses of thyroxine. No other subjects had thyroid disfunction. None had evidence of left ventricular hypertrophy and only 1 subject smoked.

Study Protocol

Subjects were following their own low–saturated fat therapeutic diets for 1 month prior to the start of the study. They were then randomized to either a control very-low–saturated fat dairy and whole-grain cereal diet or the portfolio diet containing soy foods, viscous fibers, plant sterols, and almonds. Both diets were vegetarian: the control diet was lacto-ovovegetarian and the portfolio diet was vegan with its emphasis on soy protein and almonds and oats. The duration of both diet phases was 1 month. All foods were provided except for fresh fruit and vegetables. Subjects were instructed to take no source of calories other than those provided or included on the menu plan and to maintain their habitual level of exercise throughout the study. Exercise undertaken during the previous week was documented and discussed at each clinic attendance to ensure consistency. Body weights were checked weekly and blood samples were obtained after 12-hour overnight fasts at 2-week intervals. On each clinic visit, blood pressure was measured in the nondominant arm using a mercury sphygmomanometer by the same 2 observers. Seven-day diet histories were obtained for the week prior to the 1-month diet periods. Completed menu checklists were returned at weekly intervals during the 4-week diet periods.

At weekly intervals subjects recorded their overall feeling of satiety on the diet using a 9-point bipolar semantic scale where −4 was excessively hungry, 0 was neutral, and +4 was discomfort due to excess food intake. At the end of the study, subjects were also asked if the portfolio diet, possibly with minor modifications, would be acceptable for routine use. Responses were recorded on an 11-point semantic scale where 0 was totally unacceptable, 5 was acceptable with minor modifications to form the regular diet (ie, sustainable), and 10 was highly desirable without modification.

The study was approved by the Ethics Committees of the University of Toronto and St. Michael's Hospital. Informed consent was obtained from the subjects.

Diets

The diets eaten before the 4-week test diets were the subjects' routine therapeutic low-fat diets, which approximated to NCEP Step 2 guidelines (≤7% energy from saturated fat and <200 mg/d dietary cholesterol).[1] Subjects were provided with self-tarring electronic scales and asked to weigh all food items consumed prior to and during the study period. During the study periods all foods to be consumed by the subjects were provided at weekly clinic visits with the exception of fruit and most low-calorie vegetables ie, non–starch-containing vegetables, including broccoli, carrots, red peppers, tomato, onions, cauliflower, and eggplant. Okra was provided on the portfolio diet. Subjects were instructed to obtain specific fruit and vegetables from their local stores and were reimbursed on presentation of receipts. Subjects were provided with a 7-day rotating menu plan on which they checked off each item as eaten and confirmed the weight of the foods. The same menu plan was used for all subjects but was modified to suit individual preferences providing the goals for viscous fiber, soy protein, plant sterol, and almond consumption were met. Viscous fiber in this diet was taken as 50% of the total fiber or the β-glucan component of the oat and barley fiber ("soluble fiber"), 85% of the psyllium fiber, and 50% of the okra and eggplant fiber. The nutrient profile is given in Table 1. For ease of consumption, items were prescribed, where possible, in whole units (eg, cup of instant soup, or 1 frozen dinner, 1 soy deli slice, soy burger, soy hot dog, etc).

The aim of the portfolio diet was to provide 1.2 g plant sterols per 1,000 kcal of diet as an enriched margarine; 8.3 g viscous fibers per 1,000 kcal of diet from oats, barley, and psyllium; 16.2 g soy protein per 1,000 kcal; and 16.6 g unblanched whole almonds per 1,000 kcal of diet. Emphasis was placed on eggplant and okra as additional sources of viscous fiber (0.2 g/1,000 kcal and 0.4 g/1,000 kcal, respectively). Thus, 200 g eggplant and 100 g okra were prescribed to be eaten on a 2,000-kcal diet on alternate days.

The low–saturated fat, whole-grain cereal and dairy diet achieved a similar protein intake to the portfolio diet by the use of skim milk, skim milk cheese and yogurt, egg substitute, and liquid egg white. High fiber intake was achieved by the use of whole-grain breakfast cereals (2.7 g fiber/1,000 kcal), bread (2.2 g fiber/1,000 kcal), and wheat bran added to the breakfast cereal (5.4 g fiber/1,000 kcal of diet). The low–saturated fat diet therefore lacked sources of viscous fibers and plant sterols, while the skim milk products replaced the soy and vegetable protein foods in the portfolio diet. Weight-maintaining diets were provided based on estimated caloric requirements.[8]

Compliance was assessed from the completed weekly checklists and from the return of uneaten food items.

Analyses

All samples from a given individual were analyzed in the same batch. Serum was analyzed according to the Lipid Research Clinics protocol[8] for total cholesterol, triglyceride, and high-density lipoprotein-cholesterol (HDL-C), after dextran sulfate-magnesium chloride precipitation.[9] LDL-C was calculated.[10] Serum apolipoprotein (apo) A-l and B were measured by nephelometry (intra-assay coefficient of variation [CV], 2.2% and 1.9%, respectively).[11] Lipoprotein(a) [Lp(a)] was measured with a commercial enzyme-linked immunosorbant assay (CV, <2.0%) (Macra, Lp(a) Kit, Trinity Biotech USA, Jamestown,

Table 1. Nutritional Profiles of Prescribed NCEP Step 2 (control) and Portfolio (test) Diets

	NCEP Step 2 (control) Diet (n = 12)	Portfolio (test) Diet (n = 13)
Energy (kcal/d)	2422 ± 121	2426 ± 110
Total protein (% of energy)	19.6 ± 0.2	20.0 ± 0.1
Vegetable protein (% of energy)	5.9 ± 0.1	19.8 ± 0.1*
Available carbohydrate (% of energy)	58.8 ± 0.2	56.6 ± 0.3*
Total dietary fiber (g/1,000 kcal)	26.6 ± 0.4	37.2 ± 0.3*
Total fat (% of energy)	21.6 ± 0.2	23.2 ± 0.3*
SFA (% of energy)	4.4 ± 0.0	4.9 ± 0.0*
MUFA (% of energy)	8.5 ± 0.1	9.5 ± 0.2*
PUFA (% of energy)	7.5 ± 0.1	7.9 ± 0.2*
Dietary cholesterol (mg/1,000 kcal)	34 ± 2	48 ± 1*
Satiety (−3 to +3)	2.63 ± 0.31	2.69 ± 0.17
Acceptability (0 to +10)	7.3 ± 0.6	7.1 ± 0.6

NOTE. Values are means ± SE.

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

*$P \leq .001$, treatment difference represents the % difference of control v test using the general linear model in SAS.

NY). Total L-homocysteine was measured in citrated plasma, which had been stored in the refrigerator at 4°C for approximately 1.5 hours prior to separation, using a fluorescence polarization immunoassay (Imx, Abbott Laboratories, Mississauga, Canada). Serum samples, stored at −70°C, were analyzed for C-reactive protein by end-point nephelometry (Behring BN-100, N high-sensitivity C-reactive protein reagent, Dade-Behring, Mississauga, Canada).

Red blood cell fragility was assessed on fresh red blood cells collected in vacutainer tubes containing EDTA (Becton Dickinson, Mississauga, Canada). A 0.2-mL quantity of packed red blood cells was added to 2 mL unbuffered saline, covering the range of sodium chloride concentrations from 0.20 to 0.60 g/L in 0.05 increments. A distilled water tube was also included to achieve maximum hemolysis. After 3 hours, the cells were centrifuged at 1,000 × *g* at room temperature for 5 minutes and the absorbance of the supernatant read by spectrophotometry at 520 nm.[12] Red blood cell fragility was measured since studies in spontaneously hypertensive stroke prone rats had suggested that plant sterols increased the risk of stroke associated with increased red blood cell fragility and cell membrane stiffness.[13]

Diets were analyzed using a program based on US Department of Agriculture (USDA) data[14] with additional data on foods analyzed in the laboratory for protein, total fat, and dietary fiber using Association of Official Analytical Chemists (AOAC) methods[15] and fatty acids by gas chromatography.[16] Additional dietary fiber values were obtained from the tables of Anderson and Bridges.[17]

Statistical Analysis

The results were expressed as means ± SE. No significant difference in blood lipids was seen between values at weeks 2 and 4 using paired *t* test (2-tailed) and the week 4 value has therefore used throughout as the response variable. The significance of the differences between treatments was assessed by analysis of covariance (ANCOVA) and 2-sample Student's *t* test (PROC GLM, PROC TTEST/SAS).[18] The ANCOVA model used had the week 4 treatment value as the response variable and treatment, sex, and sex by treatment interaction as main effects, with baseline and body weight as covariates. Student's paired *t* test (2-tailed) was used to assess the significance of the percentage change from pretreatment. The Framingham 10-year cardiovascular disease risk equation was applied to the data using systolic blood pressure, age, sex, and total:HDL-C values to calculate cardiovascular disease risk.[19] The concentration of saline required to obtain 50% hemolysis of red blood cells was determined as the index of red blood cell fragility, assuming a linear response between consecutive observations. For each subject the optical density of the distilled water hemolysate represented the 100% hemolysis value for that treatment for that subject.

RESULTS

For the majority of subjects, compliance in terms of caloric intake was good at 92% ± 3% for the low–saturated fat diet and 86% ± 4% for the portfolio diet estimated from daily menu checklists, completed by each subject and returned on a weekly basis. Compliance did not differ between the 2 diets ($P = .143$). The overall acceptability rating of the diet was 7.3 ± 0.6 (scale of 0 to 10) for the low-fat and 7.1% ± 0.6% for the portfolio diet, both of which were significantly above 5.0 ($P = .003$ and $P = .004$, respectively), the level at which diet was acceptable for long-term use, with minor modifications. All subjects felt they were eating as much food as they were capable without experiencing discomfort (satiety rating of 3.0) on both the low-fat and portfolio diets (satiety rating 2.6 ± 0.3 and 2.7 ± 0.2 at week 4, respectively). Subjects lost a similar amount of weight on the low–saturated fat diet (0.9 ± 0.3 kg/mo, $P = .016$) and on the portfolio diet (1.0 ± 0.4 kg/mo, $P = .029$).

Blood Lipids

No differences were seen between the 2 subject groups in baseline blood lipid measurements (Table 2). On the low–saturated fat diet, the percentage reduction at week 4 was 12.1% ± 2.4% ($P < .001$) for LDL-C and 5.1% ± 3.0% ($P = .120$) for the LDL:HDL-C ratio. On the portfolio diet, the respective figures were 35.0% ± 3.1% ($P < .001$) for LDL-C and 30.0% ± 3.5% ($P < .001$) for the LDL:HDL-C ratio, with no differences between week 2 and 4 values (Fig 1). The reductions in blood lipids at week 4 on the portfolio diet were significantly greater ($P < .001$) than the respective figures for the low–saturated fat diet for total cholesterol, LDL-C, apo B, and the ratios total:HDL-C, LDL:HDL-C, and apo B:A-I (Table 2). No differences in response were seen between the sexes. The study was well powered to detect the lipid differences observed. Only 6 subjects on each treatment are required to detect the 22.9% treatment difference in LDL-C with a SD of effect of 11.24% ($\alpha = 0.05$, $\beta = 0.8$).

Blood Pressure, Lp(a), and Homocysteine

No significant treatment differences were seen in blood pressure, Lp(a), or homocysteine (Table 2).

Calculated CAD Risk

On the portfolio diet, the calculated coronary artery disease risk was significantly reduced (31.7% ± 4.7%, $P < .001$). This reduction was also significantly different ($P = .007$) (Table 2) from the reduction (11.2% ± 3.9%, $P = .016$) on the low–saturated fat diet.

Red Blood Cell Fragility

There was a tendency on both diets for the red blood cell fragility to be reduced but the percentage reductions in fragility between diets were not significantly different (test, −1.7% ± 1.0% *v* control −1.9% ± 0.8%, $P = .906$).

DISCUSSION

These data support uncontrolled observations that combining currently recommended cholesterol-lowering dietary components in amounts that were acceptable to the study subjects can produce reductions in LDL-C of 35%, an amount similar to that observed with most doses of some of the currently available statins. These data also indicated that up to 12% of the cholesterol reduction seen on this portfolio diet could be attributed to the reduction in saturated fat and cholesterol. Statin drugs are currently the first choice for cholesterol reduction[1] and in large outcome trials have been shown repeatedly to reduce mean serum LDL-C concentrations by 28% to 35%.[20-23] The corresponding reductions in cardiovascular deaths in both primary and secondary prevention trials using statins have been of the order of 23% to 32%.[21-23] Dietary changes that can reduce LDL-C to the same extent as these statins are therefore promising.

The dietary components selected for this diet are all well recognized for their cholesterol-lowering properties.[3-6,24] Meta-analyses have suggested reductions in serum LDL-C of 12.5%

Table 2. Effect of an NCEP Step 2 (control) Diet and the Portfolio (test) Diet on CHD Risk Factors

	NCEP Step 2 (control) Diet			Portfolio (test) Diet			Treatment Difference[c]
	Week 0	Week 4	% Difference[ab]	Week 0	Week 4	% Difference[ab]	*P* Value
Body weight (kg)	77.1 ± 3.5	76.2 ± 3.4	−1.1 ± 0.4*	74.9 ± 3.4	73.9 ± 3.1	−1.2 ± 0.5*	.828§
Cholesterol							
Total-C (mmol/L)	6.67 ± 0.16	5.99 ± 0.16	−9.9 ± 2.0‡	6.48 ± 0.27	4.72 ± 0.20	−26.6 ± 2.8‡	<.001
LDL-C (mmol/L)	4.64 ± 0.16	4.06 ± 0.15	−12.1 ± 2.4‡	4.40 ± 0.27	2.81 ± 0.14	−35.0 ± 3.1‡	<.001
HDL-C (mmol/L)	1.12 ± 0.05	1.04 ± 0.04	−6.5 ± 3.6	1.16 ± 0.12	1.08 ± 0.10	−6.1 ± 3.4	.362
Triglycerides (mmol/L)	2.00 ± 0.28	1.96 ± 0.28	4.9 ± 11.2	2.03 ± 0.24	1.84 ± 0.23	−6.3 ± 7.8	.254
Apolipoproteins							
apo A-I (g/L)	1.49 ± 0.02	1.40 ± 0.03	−6.1 ± 1.9†	1.49 ± 0.08	1.38 ± 0.07	−6.8 ± 2.1†	.668
apo B (g/L)	1.40 ± 0.04	1.29 ± 0.04	−8.1 ± 1.9‡	1.37 ± 0.08	0.99 ± 0.05	−26.7 ± 3.3‡	<.001
Ratios							
Total-C:HDL-C	6.06 ± 0.30	5.89 ± 0.34	−2.6 ± 3.1	6.06 ± 0.52	4.68 ± 0.36	−20.8 ± 3.6‡	<.001
LDL-C:HDL-C	4.20 ± 0.20	3.98 ± 0.22	−5.1 ± 3.0	4.15 ± 0.42	2.78 ± 0.23	−30.0 ± 3.5‡	<.001
Apo B:Apo A-I	0.94 ± 0.02	0.93 ± 0.04	−1.8 ± 2.0	0.96 ± 0.09	0.74 ± 0.06	−21.5 ± 3.0‡	<.001
Homocysteine (μmol/L)	7.2 ± 0.5	7.3 ± 0.5	2.6 ± 2.5	7.3 ± 0.4	7.2 ± 0.5	−0.7 ± 4.1	.764
Lp(a) (mg/dL)	9.7 ± 3.2	9.8 ± 3.1	1.6 ± 2.6	13.1 ± 3.4	12.3 ± 3.4	−5.0 ± 5.8	.414
Blood pressure (mm Hg)							
Systolic	122 ± 4	114 ± 4	−6.2 ± 1.7†	116 ± 5	109 ± 3	−4.9 ± 2.7	.820
Diastolic	72 ± 3	69 ± 3	−3.6 ± 1.7	73 ± 3	75 ± 3	4.0 ± 5.4	.223
CHD risk (10-yr %)¶	14 ± 1	12 ± 1	−11.2 ± 3.9*	12 ± 2	8 ± 1	−31.7 ± 4.7‡	.007

NOTE. To convert cholesterol and triglycerides to mg/dL, multiply by 38.67 and 88.57, respectively. To convert apo A-I and B values to mg/dL, multiply by 100.

[a]% Difference calculated as (Week 4 - Week 0)/Week 0) × 100.

[b]Superscripts represent the significance of within treatment change (*$P < .05$; †$P < .01$; ‡$P < .001$).

‡*P* value represents the difference of control *v* test by analysis of covariance.

§Body weight was not used in the general linear model for determining significance of treatment difference for body weight.

¶CHD risk was estimated using the Framingham cardiovascular risk equation.[19]

for 45 g/d soy protein;[25] 6% to 7% for 9 to 10 g/d psyllium,[26,27] with smaller reductions for other viscous fibers;[28] 10% for 1 to 2 g plant sterol/d;[29] and 1% for 10 g almonds/d.[24] In no instance have meta-analyses indicated that any of the components used singly in these studies could approach the level of LDL-C reduction observed with their combination in the present study. Moreover the meta-analysis data are derived from studies in which the diets were higher in saturated fat and cholesterol than in the present study. Studies using lower intakes of saturated fat have shown smaller reductions in cholesterol of 4% for 52 g/d of soy protein.[30] Plant sterols also appear to be less effective at lower intakes of saturated fat and cholesterol.[31] The fatty acid

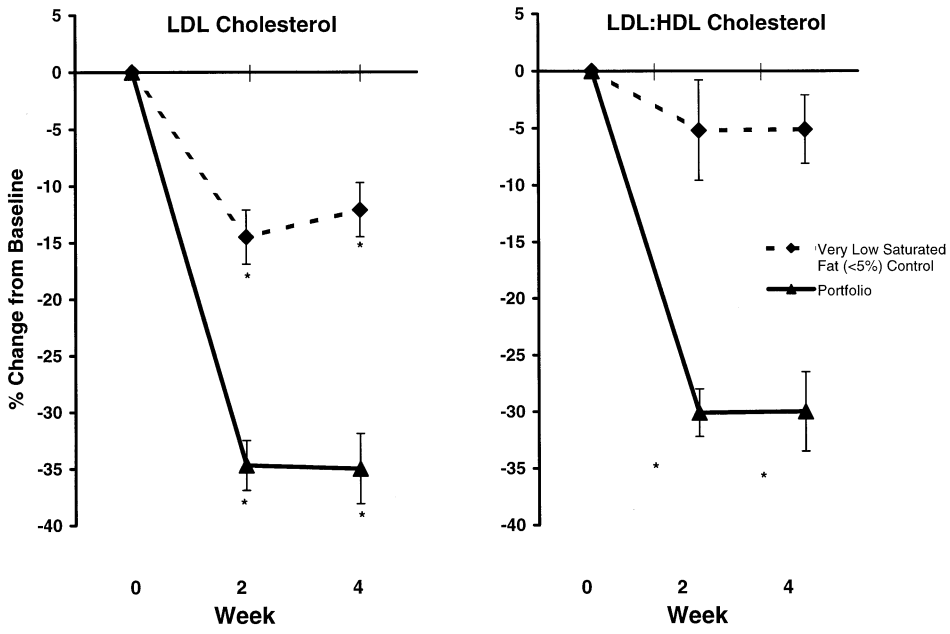

Fig 1. Percent change from baseline in LDL-C and the ratio of LDL:HDL-C on the portfolio (n = 13) (▲) and control (n = 12) (◆) diets. Values are means ± SE. *Significantly different from baseline ($P \leq .001$).

and cholesterol changes on the test diet were similar to the control diet. Assuming an additional 4% to 7% reduction in LDL-C attributable to each of the 4 individual dietary components and a 12% reduction due to low–saturated fat and cholesterol intakes, their combined effect would account for the 35% LDL-C reduction observed on the portfolio diet.

The differing modes of action of the portfolio diet components may have favored an additive effect. Viscous fibers increase bile acid losses,[16] plant sterols reduce cholesterol absorption,[32] and soy proteins reduce hepatic cholesterol synthesis and increase LDL receptor messenger RNA and so potentially increase uptake of cholesterol.[33,34] Almonds contain vegetable proteins, plant sterols, fiber, and monounsaturated fats, and are likely to operate through a range of mechanisms.[35] In addition, the high vitamin E and flavonoid content of almonds may preserve LDL-C from oxidation.[25] No reduced triglyceride or raised HDL-C was associated with increased almond use in this study, as has been reported previously when monounsaturated fat intakes were exchanged for carbohydrate.[36,37] However, in the present study the fatty acid profile was held constant between treatments by the use of high–monounsaturated fatty acid sunflower oil on the control and butter on the portfolio diets.

In the future other plant food components with specific mechanisms of action may be added to this portfolio, including Chinese red rice containing hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors[38] and garlic with allicin,[39] which may also inhibit HMG-CoA reductase activity.[40]

At present statins are advised to be taken by a large proportion of the middle-aged population of Western nations,[1,41] based on the success of recent studies.[21-23,42-44] Although side effects in clinical trials have been relatively insignificant,[23,42,43] the effect of statins on larger sections of the population over very long periods of time remains to be determined. There are also individuals who would prefer to lower cholesterol by means other than drugs. It seems appropriate that emphasis should also be placed on diet to provide an option for individuals with lesser elevations of serum cholesterol and possibly to reduce the dosage required for those controlled with drugs. Other cardiovascular benefits of statins, including improved vascular reactivity and reduced levels of C-reactive protein,[44] must be assessed together with longer-term intervention studies to determine the effectiveness of diet compared with statins in reducing cardiovascular events. The data currently available from clinical trials support a potentially important role for dietary change,[45-47] including angiographic evidence of reversal of cardiovascular disease.[45,46] Furthermore, high fiber intakes have consistently been associated with reduction in CHD risk[47,48] and CHD risk factors,[49] and more recently so has increased nut consumption.[50-52]

In conclusion, very-low–saturated fat diets containing foods high in viscous fibers, soy proteins, plant sterols, and almonds reduce LDL-C levels to the same extent as seen in large randomized controlled trials of statins. The effect of this portfolio of dietary factors on cardiovascular endpoints remains to be determined, but there is hope that these diets may provide a nonpharmacologic treatment option for selected individuals at increased risk for cardiovascular disease.

ACKNOWLEDGMENT

The authors sincerely thank Loblaw Brands Ltd (Toronto, Canada), the Almond Board of California (Modesto, CA), Unilever Canada (Toronto, Canada), The Hain-Celestial Group (Irwindale, CA), Pepsico Foods Canada–Quaker Peterborough Plant (Peterborough, ON), Nestle Canada Inc (Pickering, Canada), Procter and Gamble Canada (Toronto, Canada), and Bartlett Farms, Barwell Food Sales Inc (London, Canada), for the generous donation of foods used in this study. We also wish to thank Robert Chenaux and Larry C Griffin of Loblaw Brands Ltd; Dr Paul Schur of Unilever Canada; Dr Gerry Amantea of The Hain-Celestial Group; Kathy Galbraith of Natural Temptations Bakery, Burlington, Canada; Dr Priscilla Samuel of Quaker, a unit of Pepsico Beverages and Foods (Chicago, IL), and Grant Morrison of Pepsic Foods Canada; and Don Bartlett of Bartlett Farms, Barwell Foods Sales Inc, for their assistance on this project.

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