Effects of high- and low-isoflavone soyfoods on blood lipids, oxidized LDL, homocysteine, and blood pressure in hyperlipidemic men and women1–3

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ABSTRACT

Background: Many of the benefits of soy have been attributed to soy isoflavones.

Objective: The objective was to determine the effects of high- and low-isoflavone soy-protein foods on both lipid and nonlipid risk factors for coronary artery disease (CAD).

Methods: Forty-one hyperlipidemic men and postmenopausal women participated in a study with three 1-mo diets: a low-fat dairy control diet and high- (50 g soy protein and 73 mg isoflavones daily) and low- (52 g soy protein and 10 mg isoflavones daily) isoflavone soyfood diets. All 3 diets were very low in saturated fat (<5% of energy) and cholesterol (<50 mg/d). Fasting blood samples were drawn and blood pressure was measured at the start and end of each diet.

Results: No significant differences were seen between the high- and low-isoflavone soy diets. Compared with the control diet, however, both soy diets resulted in significantly lower total cholesterol, estimated CAD risk, and ratios of total to HDL cholesterol, LDL to HDL cholesterol, and apolipoprotein B to A-I. No significant sex differences were observed, except for systolic blood pressure, which in men was significantly lower after the soy diets than after the control diet. On the basis of blood lipid and blood pressure changes, the calculated CAD risk was significantly lower with the soy diets, by 10.1 ± 2.7%.

Conclusion: Substitution of soyfoods for animal products, regardless of isoflavone concentration, reduces the CAD risk because of both modest reductions in blood lipids and reductions in oxidized LDL, homocysteine, and blood pressure. Am J Clin Nutr 2002;76:365–72.

KEY WORDS Soy protein, isoflavones, diet, cardiovascular disease risk, blood lipids, oxidized LDL, homocysteine, blood pressure

INTRODUCTION

The scope of the benefits that soy may confer in preventing coronary artery disease (CAD) and also the question of which components of soy are responsible are the focus of much discussion. Studies over the past 30 y have strongly supported the view that soyfood consumption will reduce the risk of heart disease (1–11). Much of the emphasis has been on soy protein and a reduction in LDL cholesterol. However, as with other naturally occurring hypocholesterolemic food components (eg, viscous fibers and plant sterols), there is debate over ways in which to maximize effectiveness. For soy protein, the interest has focused on the amino acid composition (12) and particular peptides and soy-protein fractions (13). Recently, considerable attention has been paid to the isoflavones associated with soy protein. These isoflavones are classified as phytoestrogens because of their weak estrogenic activity (14). Not only have they been implicated in cholesterol lowering through LDL receptor up-regulation (6), but they also possess antioxidant activity (15–18) and are associated with improved vascular reactivity (19). However, it is not known whether, in addition to improvements in blood lipids and vascular reactivity, isoflavones contribute to other soy-related improvements in cardiovascular risk, such as blood pressure reduction (20, 21) and lower homocysteine concentrations (22). Both of these improvements have been shown to be associated with soy consumption (20–22). Nevertheless, it must be emphasized that isoflavones by themselves (without soy protein) have not been shown to lower serum lipids.

Mammalian estrogens are also thought to confer a range of cardiovascular benefits, including favorable effects on the blood lipid profile (23), improved antioxidant status (24), improved vascular...
reactivity (25), and possibly lower blood pressure (26). Most recently, elevated homocysteine concentrations, unrelated to significant changes in vitamin status, were reported in postmenopausal women (27), suggesting that estrogens may play a role in homocysteine metabolism.

We therefore assessed the effect of feeding soyfoods either high or low in isoflavones, as weak plant-derived estrogenic compounds (14), on a range of cardiovascular risk factors in hyperlipidemic men and postmenopausal women. Our research has focused on feeding soyfoods that are available in the supermarket and health food store (18, 28, 29). Our present study involved a range of different types of soy products made from tofu and soy-protein isolate that were consumed as part of the diet, not as an experimental beverage containing soy-protein isolate to be taken as a supplement, as was the case in many other studies. Furthermore, the soyfoods we used were components of diets that were very low in saturated fat.

SUBJECTS AND METHODS

Study protocol

The study followed a randomized crossover design in which 41 subjects participated in three 1-mo phases; each phase was separated by a minimum 2-wk washout period. The 3 phases consisted of a dairy- and egg-protein phase (control) and 2 soy-protein phases, one high and the other low in isoflavones. During all 3 study phases, subjects followed their own self-selected National Cholesterol Education Program Step II diets (< 7% of energy from saturated fat and < 200 mg dietary cholesterol/d) (30) but substituted dairy foods or soyfoods very low in fat, with which they were provided, for the major sources of protein in their customary diets. Subjects were blinded to the amount of isoflavones in the soyfoods.

Subjects

Healthy hyperlipidemic men (n = 37) and postmenopausal women (n = 36) were recruited by newspaper advertisement and from patients attending the Risk Factor Modification Center, St Michael’s Hospital (Toronto). Eighteen subjects withdrew either before or after randomization but before starting the first phase, and 14 withdrew during or after completing 1–2 study phases. Five subjects quit for reasons directly related to the study: dislike of dairy foods (n = 1), dislike of soyfoods (n = 1), tired of eating soy (n = 1), belief that the soy flavoring caused bladder irritation (n = 1), and constipation (n = 1). Of the subjects that withdrew, most (n = 9) did so for reasons unrelated to the study: dislike of dairy foods (n = 1), dislike of soyfoods (n = 1), tired of eating soy (n = 1), belief that the soy flavoring caused bladder irritation (n = 1), and constipation (n = 1). Of the subjects that withdrew, most (n = 9) did so for reasons unrelated to the study: work-related reasons (n = 4), personal or family-health reasons (n = 4), and loss of interest (n = 1). Forty-one subjects (23 men and 18 women) completed all 3 phases of the study. The subjects had a mean ± SE age of 62 ± 2 y and a body mass index (in kg/m²) of 25.3 ± 0.5. All subjects had elevated LDL-cholesterol concentrations (> 4.1 mmol/L) on initial assessment. Before the start of the study, 8 subjects had elevated triacylglycerol concentrations (> 2.3 mmol/L; range: 2.76–4.77 mmol/L). None of the subjects had clinical or biochemical evidence of diabetes or liver or renal disease, and none were taking hypolipidemic agents. Five women were receiving hormone replacement therapy and 3 were taking levothyroxine. Five men were taking 1 or 2 of the following medications: β-blocking agents (n = 2), angiotensin-converting-enzyme (EC 3.4.15.1) inhibitors (n = 1), an angiotensin II receptor blocker with a calcium channel blocker (n = 1), and a calcium channel blocker alone (n = 1). Four women were taking these drugs: an angiotensin II receptor blocker (n = 1), a calcium channel blocker (n = 2), and a calcium channel blocker with an angiotensin-converting-enzyme inhibitor (n = 1). The dosages of all medications were held constant throughout the study. Subjects were also asked to maintain their habitual level of physical activity throughout all 3 study phases. The study was approved by the Ethics Committee of the University of Toronto and St Michael’s Hospital, and informed consent was obtained from all subjects.

Diets

During the study phases, the subjects consumed self-selected National Cholesterol Education Program Step II diets in which the main protein-containing foods [meats, fish, dairy foods, eggs, nuts (eg, peanut butter), and legumes] were replaced during the control phase with low-fat dairy products: skim milk, yogurt, cottage cheese, very low-fat Hoop cheese (Western Creamery, Toronto), cheese made with skim milk (NutriSpring Farms, Dundas, Canada), and egg substitute (Egg Beaters; Lipton’s, Toronto). During the high- and low-isoflavone soy phases, the main protein-containing foods were replaced with low-fat soymilk (0.1% fat; Sanitarium Pt, Sydney, Australia); soy hot dogs, breakfast links, soy burgers, and cold cuts (Yves Veggie Cuisine, Vancouver, Canada); tofu nuggets (Soy City Foods, Toronto); and tofu burgers (La Soyerarie, Hull, Canada). These products were made from either alcohol-washed or nonalcohol-washed-soy-protein isolate (Protein Technologies International, St Louis) or from tofu that was made from soybeans selected for their very high or very low isoflavone content (First Line Seeds, Guelph, Canada; Advantage Seed Growers and Processors, Lucknow, Canada). The nutrient profiles of the dairy and soyfood substitutions were balanced for fatty acid composition and dietary cholesterol intake by adding butter (group mean: 11 g/wk) and one egg (53 g/wk) per 8.4-MJ (2000-kcal) soy diet. For the control diet, fatty acid balance was achieved with the use of an 8-g/d oil mixture providing 0.3 g soy oil/d, 1.9 g safflower oil/d, 4.0 g corn oil/d, and 1.7 g canola oil/d. The foods provided were designed to represent 20% of the subjects’ estimated daily total energy intake (31) and contributed ~13.5% of energy as protein, expressed as a percentage of the daily recorded energy intake (Table 1). Analyses of isoflavones as aglycones in the soyfoods indicated that the mean daily intake of isoflavones for the 41 subjects was 10 ± 0 mg/d during the low-isoflavone soy phase and 73 ± 3 mg/d during the high-isoflavone soy phase.

Soymilks for the study were delivered by courier to the subjects’ homes at the beginning of each of the 3 phases. All other foods were provided biweekly and were refrigerated or frozen by the subjects until consumed. The subjects were provided with self-taring digital electronic scales on which to weigh all soy and dairy foods before consumption and were instructed to check off these items on the weekly lists provided as each item was eaten. All food eaten was expected to be weighed during the weeks when the diet histories were recorded. Individual 7-d diet histories recorded during week 4 of the first phase were photocopied and given to each subject at the beginning of the 2 subsequent phases to serve as a template from which to model their dietary intakes. Subjects were also instructed to eat no additional soy or dairy foods, legumes, nuts, or viscous fiber sources such as psyllium during the study.

Compliance was assessed on the basis of the 7-d diet histories, the completed weekly checklists of foods eaten, and the amount of
The palatability of the foods provided was assessed at the conclusion of the study by asking subjects to rate the foods on a semantic scale of 0–10, where 0 was very distasteful, 5 was neutral, and 10 was very appetizing.

### Analyses

Serum, stored at −70 °C, was analyzed according to the Lipid Research Clinics protocol (32) for total cholesterol, triacylglycerol, and HDL cholesterol after dextran sulfate–magnesium chloride precipitation (33). All samples from a given subject were analyzed in the same batch. LDL cholesterol was calculated with the use of the Friedewald equation (34). Serum apolipoprotein A-I and B were measured by nephelometry (35), and lipoprotein(a) was measured with a commercial enzyme-linked immunosorbent assay (Macra Lp(a) Kit; Trinity Biotech USA, Jamesmont, NY).

Total t-homocysteine was measured in citrated plasma, stored at −70 °C, that had been refrigerated at 4 °C for 1.5 h before separation with the use of fluorescence polarization immunoassay (IMX homocysteine assay; Axis-Shield, Oslo).

Oxidized LDL was measured in serum stored at −70 °C as conjugated dienes in the LDL fraction after isolation of LDL particles by precipitation with buffered heparin at their isoelectric point (36). The results were expressed as total serum conjugated dienes in the LDL fraction (37).

Dietary isoflavone concentrations were measured as 3 aglycones (genistein, daidzein, and glycitein) in foods, which had been freeze-dried. After acid hydrolysis of the endogenous isoflavones, aglycones in alcoholic extracts were identified and quantitated by HPLC (38, 39) with the use of a 600E multisolvant delivery system with a photodiode array detector monitoring at 200–350 nm (Waters, Marlborough, MA) and with a Nova Pak C18 column (diameter 5 μm, 150 mm × 3.9 mm internal diameter; Waters) equipped with a C18 guard column. Appropriate isoflavone standards were analyzed. Biochanin A was used as an internal standard, with recovery values ranging from 80% to 100%. Urinary metabolites of isoflavones (genistein, daidzein, glycitein, equol, and o-desmethylangolensin) were measured by HPLC after enzymatic hydrolysis in the first group of subjects to complete the study (n = 24) (39). Chromatographs were obtained from the 3-dimensional array by using a photodiode array detector at 258 nm to allow assessment of common regions of relatively high absorbance for daidzein, genistein, and flavone—the added recovery standard.

Freeze-dried soy and dairy foods were analyzed in the laboratory by using methods of the Association of Official Analytical Chemists for fat and protein (40) and fiber (41) with available carbohydrate calculated as the difference between the sample weight and the weight of moisture, ash, fiber, fat, and protein. The fatty acid composition was determined by gas chromatography (42). Diet histories were assessed by using a computer program based on US Department of Agriculture data (43), data from food labels, and data from the results of foods analyzed in the laboratory. The percentages of soluble and insoluble fiber were derived from published data (44).

### Statistical analysis

The results are expressed as means ± SEs. The isoflavone effect was assessed by comparing the 3 treatments with the use of analysis of covariance with a Tukey adjustment to determine the significance of differences between treatments (45). The statistical model included week 4 values as the response variable, treatment and sequence as the main effects, treatment × sex as the interaction term, a random subject effect nested within sex by sequence,
TABLE 2
Body weight, blood lipids, and blood pressure measured during the control and low- and high-isoflavone soy phases.

<table>
<thead>
<tr>
<th></th>
<th>Control phase</th>
<th>Low-isoflavone phase</th>
<th>High-isoflavone soy phase</th>
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<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 4</td>
<td>Week 0</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>71.4 ± 1.8</td>
<td>71.0 ± 1.8</td>
<td>71.1 ± 1.9</td>
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<tr>
<td>Cholesterol (mmol/L)</td>
<td></td>
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<tr>
<td>Total</td>
<td>6.84 ± 0.10</td>
<td>6.64 ± 0.12</td>
<td>6.68 ± 0.13</td>
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<tr>
<td>LDL</td>
<td>4.62 ± 0.10</td>
<td>4.47 ± 0.11</td>
<td>4.52 ± 0.12</td>
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<tr>
<td>HDL</td>
<td>1.33 ± 0.05</td>
<td>1.23 ± 0.05</td>
<td>1.32 ± 0.05</td>
</tr>
<tr>
<td>Triacylglycerol (mmol/L)</td>
<td>1.96 ± 0.17</td>
<td>2.07 ± 0.22</td>
<td>1.84 ± 0.18</td>
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<tr>
<td>Apolipoproteins (g/L)</td>
<td></td>
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<tr>
<td>A-I</td>
<td>1.69 ± 0.04</td>
<td>1.60 ± 0.04</td>
<td>1.66 ± 0.04</td>
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<tr>
<td>B</td>
<td>1.48 ± 0.03</td>
<td>1.46 ± 0.03</td>
<td>1.45 ± 0.03</td>
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<tr>
<td>Homocysteine (μmol/L)</td>
<td>7.6 ± 0.3</td>
<td>8.0 ± 0.4</td>
<td>8.2 ± 0.3</td>
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<tr>
<td>Lipoprotein(a) (mg/dL)</td>
<td>19.6 ± 3.1</td>
<td>21.6 ± 3.4</td>
<td>20.2 ± 3.1</td>
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<tr>
<td>Ratios</td>
<td></td>
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<tr>
<td>Total:HDL cholesterol</td>
<td>5.39 ± 0.19</td>
<td>5.69 ± 0.21</td>
<td>5.30 ± 0.19</td>
</tr>
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<td>LDL:HDL cholesterol</td>
<td>3.63 ± 0.14</td>
<td>3.85 ± 0.17</td>
<td>3.62 ± 0.16</td>
</tr>
<tr>
<td>Apolipoprotein B:A-I</td>
<td>0.89 ± 0.03</td>
<td>0.94 ± 0.03</td>
<td>0.90 ± 0.03</td>
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<td>Oxidized LDL</td>
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<tr>
<td>LDL conjugated dienes</td>
<td>71.3 ± 4.8</td>
<td>78.0 ± 12.2</td>
<td>82.2 ± 7.1</td>
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<tr>
<td>Blood pressure (mm Hg)</td>
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<tr>
<td>Systolic</td>
<td>125 ± 3</td>
<td>123 ± 3</td>
<td>124 ± 3</td>
</tr>
<tr>
<td>Diastolic</td>
<td>78 ± 2</td>
<td>78 ± 1</td>
<td>78 ± 1</td>
</tr>
<tr>
<td>Coronary artery disease risk, 10 y (%)</td>
<td>0.12 ± 0.01</td>
<td>0.13 ± 0.01</td>
<td>0.12 ± 0.01</td>
</tr>
</tbody>
</table>

1 ± SE; n = 41. To convert cholesterol and triacylglycerol values to mg/dL, multiply by 38.67 and 88.57, respectively. To convert apolipoprotein A-I and B values to mg/dL, multiply by 100. There were no significant differences between the high- and low-isoflavone soy phases and no significant difference in the response to treatment between the sexes, except for blood pressure.

2–4 Significantly different from the control phase at week 4 (Tukey’s test): 2 P < 0.05, 3 P ≤ 0.001, 4 P ≤ 0.01.

5 n = 37.

6 Analysis of the sexes separately showed that for men only, the high- and low-isoflavone soy diets tended to result in lower blood pressure than did the control diet: P = 0.065 and P = 0.007, respectively.

FIGURE 1. Mean (±SEM) percentage change from week 0 in total cholesterol (TC), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), apolipoprotein (apo) B, apo A-I, and homocysteine in the control (□), low-isoflavone soy (■), and high-isoflavone soy (■) groups. **Significantly different from the control group: 7 P < 0.05, **P < 0.01. n = 41.
and baseline as a covariate. For the urinary excretion data, because pretreatment samples were not collected, analysis of variance was used with week 4 values as the response variable, treatment and sequence as the main effects, and a subject effect nested within sex by sequence. Sex was not included because none of the women whose urine was analyzed took high-isoflavone soy in the first phase followed by low-isoflavone soy in the second phase. It was therefore not possible to use both sex and sequence in the same model. Nevertheless, similar results were obtained when the sex × diet interaction term was substituted for sequence in the model. To assess the effect of soy protein, the high- and low-isoflavone data were combined, because the 2 soy treatments produced similar results, and compared with the control data by using the CONTRAST test in SAS (45). Weights of −0.5 were assigned to each of the combined soy treatments and weights of 1.0 to the single control treatment. Student’s t test for paired data (two tailed) was used to assess the significance of the percentage changes from baseline to week 4 for individual treatments. CAD risk was calculated by using the ratio of total to HDL cholesterol and systolic blood pressure in the Framingham cardiovascular disease risk assessment equation (46). SAS version 8 software was used for all statistical analyses (45).

RESULTS

Compliance was good. Intakes of the prescribed foods during the 3 diet phases, expressed as a percentage of energy, were as follows: 97.2 ± 0.7% during the control phase, 96.9 ± 0.8% during the low-isoflavone soy phase, and 97.8 ± 0.5% during the high-isoflavone soy phase. No significant differences were observed between treatments. The subjects perceived the high- and low-isoflavone foods to be identical, and no significant differences in palatability (control diet: 6.6 ± 0.4 out of 10; both soy diets: 7.3 ± 0.3 out of 10) or in body weight change (control diet: −0.3 ± 0.1 kg; low-isoflavone soy diet: −0.3 ± 0.1 kg; and high-isoflavone soy diet: −0.4 ± 0.1 kg) were observed (Table 2).

Blood lipids, blood pressure, oxidized LDL, and homocysteine

In general, values for the blood lipid risk factors for CAD decreased equally during both soy phases and to a greater extent than during the control phase (Figure 1). No significant differences in blood lipid responses were seen between the low- and high-isoflavone soy phases, but both were lower than values during the control phase for total cholesterol (P = 0.016 and P = 0.045, respectively), total:HDL cholesterol (P = 0.001 and P = 0.018), LDL:HDL cholesterol (P = 0.001 and P = 0.004), apolipoprotein B:A-1 (P = 0.010 and P = 0.002), and estimated CAD risk (P < 0.001 and P = 0.033) (Table 2). In addition, LDL cholesterol (P = 0.024) and apolipoprotein B (P = 0.020) were also lower during the high-isoflavone soy phase than during the control phase. LDL cholesterol and apolipoprotein B were also lower during the low-isoflavone soy phase than during the control phase, but not significantly so (P = 0.077 and P = 0.076, respectively).

Only for systolic blood pressure was there a significant difference between the sexes in response to dietary treatment. Assessment of men and women separately indicated a tendency to lower systolic blood pressure for men during the high-isoflavone soy phase (P = 0.065), which was significant during the low-isoflavone soy phase (P = 0.007) compared with the control phase. Because of the lack of significant differences in results between the high- and low-isoflavone soy phases and to assess the effect of soy protein, the combined results for the high- and low-isoflavone soy phases were compared directly with the control data by using the CONTRAST test (Table 2). LDL cholesterol (P = 0.006), apolipoprotein B (P = 0.005), homocysteine (P = 0.044), and oxidized LDL (P = 0.030) assessed as conjugated dienes in the LDL fraction in the whole group and systolic blood pressure in the men only (P = 0.002) were lower during the soy phases than during the control phase. In addition, the reductions in total cholesterol (P = 0.003), in the lipid and lipoprotein ratios (P < 0.001), and in the estimated CAD risk (P < 0.001) were in line with what was reported above for the comparisons between the 3 phases individually. The percentage change in conjugated dienes from baseline in men and women during each phase is shown in Figure 2.

Urinary isoflavones

The urinary output data for genistein, glycitein, daidzein, equol, and ODMA are shown for each phase in Figure 3. Total urinary isoflavone outputs during the control and low- and high-isoflavone soy phases were 2.1 ± 0.7, 11.3 ± 3.1, and 41.3 ± 4.8 mg/d, respectively. The urinary isoflavone output was significantly greater during the high-isoflavone soy phase than during
FIGURE 3. Mean (± SEM) urinary excretion of isoflavones in the control (□), low-isoflavone soy (■), and high-isoflavone soy (■) groups. No significant differences were seen between the control and the low-isoflavone soy groups. * Significantly different from the high-isoflavone soy group; *P = 0.01, **P = 0.037. ***Significantly different from the control diet and the low-isoflavone diet groups, P < 0.001. n = 24, ODMA, α-desmethylangolensin.

the other 2 phases (P < 0.001), which were not significantly different from each other.

DISCUSSION
In terms of CAD risk reduction, the results indicate that a wide range of small but beneficial effects were associated with the substitution of soy-protein for animal-protein foods in diets already very low in saturated fat and dietary cholesterol. No significant differences were observed between the high- and low-isoflavone soy groups, but LDL cholesterol was significantly different only between the high-isoflavone soy and the control groups. Furthermore, no significant differences were observed between men and women, except for the reduction in systolic blood pressure observed after soy consumption in men but not in women.

Many studies have assessed the effects of high- and low-isoflavone intakes either as soy supplements or as isoflavone extracts (5, 6, 8, 10, 19). In general, when the effects of increased isoflavone intakes on blood lipids have been seen in humans, the isoflavones have been associated with soy proteins (5, 6, 8, 10). Lipid-lowering effects have generally not been seen in humans fed isoflavones separated from the soy protein by extraction (19), but other benefits have been shown, including increased vascular compliance of benefit to CAD risk reduction (19). Furthermore, some studies have noted altered endocrine activity with soy feeding (47), whereas others have not (48). Our own study failed to show a benefit of high- compared with low-isoflavone intakes, and it is possible that either a larger number of subjects or a higher soy isoflavone intake would be required to show such differences (8, 10). However, our studies indicated that even low-isoflavone soy-protein foods may have the additional benefits reported for soy, including antioxidant activity (15), lower homocysteine concentrations (22), and blood pressure reduction (20).

Our studies were different from many studies reported in the literature in that we used a wide range of soyfoods to substitute for the sources of animal protein normally eaten in the diet. The proportion of vegetable to animal protein in the soy foods was relatively high, ≈96% of the total protein consumed. This aspect of the diet may be relevant in considering suggestions that the nature of the protein and the amino acid composition of the diet are important for cholesterol lowering and possibly other effects (2, 12, 13). Furthermore, the wide range of soyfoods used, with some made from tofu and the remainder made from soy-protein isolate, supports the generalization that soyfoods are effective regardless of the starting material (11). Very low saturated fat intakes were used because a reduction in dietary saturated fat remains a primary objective of a cholesterol-lowering diet. It was therefore important to show that soy had an effect in improving the blood lipid profile even after dietary saturated fat intakes were reduced maximally. Others have noted greater reductions in LDL cholesterol but the saturated fat intakes in the diets they used were higher (4–8, 10).

We conclude that soy-protein foods, regardless of their isoflavone content, may improve many lipid and nonlipid risk factors for CAD and thus justify the use of soyfoods as part of a dietary strategy to reduce CAD risk. Further studies are required to determine whether all these benefits can be achieved by taking soy as a supplement or whether it is better to substitute soy for animal-protein foods, ie, Is there an optimal ratio of vegetable to animal proteins to maximize the soy effect (1)? Certainly the displacement of saturated fat and cholesterol in the diet with soyfoods may result in the extra dietary advantage of cholesterol lowering, as has been suggested for dietary fiber (49).

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