Soy Protein Reduces Serum LDL Cholesterol and the LDL Cholesterol:HDL Cholesterol and Apolipoprotein B:Apolipoprotein A-I Ratios in Adults with Type 2 Diabetes1–3

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Abstract

Type 2 diabetes is highly prevalent in North America and is associated with increased risk of cardiovascular disease (CVD). Evidence supports a role for soy protein in the reduction of serum lipids related to CVD risk; however, few studies have focused on adults with type 2 diabetes who are not on lipid-lowering medications and/or do not have diabetic complications. The purpose of this study was to determine the effect of soy protein isolate (SPI) consumption on serum lipids in adults with diet-controlled type 2 diabetes. Using a double-blind, randomized, crossover, placebo-controlled intervention study design, adults with diet-controlled type 2 diabetes (n = 29) consumed SPI (80 mg/d aglycone isoflavones) or milk protein isolate (MPI) for 57 d each separated by a 28-d washout period. Twenty-four–hour urine samples were collected on d 54–56 of each treatment for analysis of isoflavones and blood was collected on d 1 and 57 of each treatment and analyzed for serum lipids and apolipoproteins. SPI consumption increased urinary isoflavones compared with MPI. SPI consumption reduced serum LDL cholesterol (P = 0.04), LDL cholesterol:HDL cholesterol (P = 0.02), and apolipoprotein B:apolipoprotein A-I (P = 0.05) compared with MPI. SPI did not affect serum total cholesterol, HDL cholesterol, triacylglycerol, apolipoprotein B, or apolipoprotein A-I. These data demonstrate that consumption of soy protein can modulate some serum lipids in a direction beneficial for CVD risk in adults with type 2 diabetes. J. Nutr. 139: 1700–1706, 2009.

Introduction

Prevalence of type 2 diabetes is increasing, as evident by projections of the total number of people with diabetes increasing from 171 million in 2000 to 366 million in 2030 (1) and the knowledge that up to 90% of diabetes cases are type 2 diabetes (2). Cardiovascular disease (CVD), particularly coronary heart disease, is a major diabetic complication, as its risk is significantly greater than in those without diabetes (3) and it is the main cause of death in adults with type 2 diabetes (4,5). Serum lipids are established CVD biomarkers for type 2 diabetes (6) and are therefore practical endpoints to examine when exploring intervention strategies to reduce CVD risk in type 2 diabetes.

Dietary intervention has been proven successful at improving serum lipids in adults with type 2 diabetes (7) and soy is a dietary component of recent interest (8). Epidemiological studies document that consumption of soy protein isolate (SPI) is associated with improved serum lipids in individuals without diabetes (9–11) and this has been substantiated in meta-analyses of intervention studies that summarize favorable effects of soy protein consumption on serum lipids, primarily in adults without diabetes (12–15).

The documented lipid-lowering effect of soy protein has prompted investigation into a similar effect in individuals at higher risk of CVD such as adults with type 2 diabetes. The majority of soy intervention studies in adults with type 2 diabetes have included those on glucose- and/or lipid-lowering medications (16–22), those who are obese (20), and those who have diabetic complications such as nephropathy (16,19,22,23), microalbuminuria (18), or retinopathy (24). Other studies of adults with type 2 diabetes have examined isoflavones extracted...
from soy protein (24,25) or red clover (26), which removes the natural matrix with which the isoflavones are associated. Finally, other studies of adults with type 2 diabetes have investigated SPI but used controls such as fiber (17) or cellulose (27), which make the treatment and control imbalanced in nutrient content. Results of these studies have shown inconsistent effects on circulating lipids, including some favorable (16–23,27) or none at all (24–26), and, together, have not produced a consensus regarding the effect of soy on circulating lipids in adults with type 2 diabetes.

To date, very few studies have focused on the effects of SPI in adults with diet-controlled type 2 diabetes. Most relevant to the current study is a study of 32 postmenopausal women with diet-controlled type 2 diabetes in which 12 wk of soy protein (30 g soy protein; 132 mg isoflavones) significantly reduced total cholesterol, LDL cholesterol, and total cholesterol: HDL cholesterol compared with cellulose (27); however, the cellulose control lacked protein, causing a mismatch in protein content with the treatment. More research is needed on the effect of SPI on serum lipids in adults with type 2 diabetes and this would be of particular value in individuals who are taking glucose- or lipid-lowering medications and do not have any diabetic complications, because it would explore a scenario that represents a prevention opportunity. Therefore, the purpose of the current study was to determine the effect of isoflavone-rich soy protein consumption on serum lipids in adults with diet-controlled type 2 diabetes compared with a protein-matched control.

Methods

Study design. This study used a randomized, crossover, double-blind design that consisted of 2 57-d treatment periods separated by a 28-d washout period. The study protocol was approved by the Human Research Ethics Board of the University of Guelph and all participants provided written informed consent.

Participant recruitment and screening. Participant inclusionary criteria included adult (>19 y old) males and postmenopausal females (no menstrual bleeding for at least 12 mo or >50 y old with a hysterectomy), diagnosis of type 2 diabetes [fasting plasma glucose ≥7.0 mmol/L (28)], stable glycemic control [hemoglobin A1C (HbA1c) <8% (28)], management of their diabetes with a stable diet, and medication-stable for at least 3 mo. Participant exclusionary criteria included premenopausal females; BMI >35 kg/m²; use of oral hypoglycemic agents, insulin therapy, or lipid-lowering medications; presence of diabetic complications; use of hormone replacement therapy; alcohol consumption >2 drinks/d or >7 drinks/wk (1 drink = 10 g alcohol); antibiotic use within 3 mo; allergy to soybeans or milk; soy consumption >3 servings/wk; vegans and elite athletes.

Potential participants were screened using a brief phone or email eligibility questionnaire followed by an in-person meeting where they completed a more in-depth eligibility questionnaire, had their body weight measured, provided their most recent HbA1c value, and sampled the study treatment protein powders. Eligible and interested participants then attended a study orientation where they were provided with a study handbook that outlined all aspects of the study. A total of 34 participants started the study.

Study treatments and diet. The study treatments included SPI and milk protein isolate (MPI) beverage powders (Solae) that were provided in 2 29-g packets/d in a 14-d supply on d 1, 15, 29, and 43 of each treatment period. The treatment protein powders were comparable in energy and nutrient content and contributed a daily total of 837 kJ, 8–9 g carbohydrate, 40 g protein from soy (SPI) or milk (MPI), 88 mg (SPI) or 0 mg (MPI) isoflavones (expressed as aglycone equivalents with an isoflavone distribution of 65% genistein, 31% daidzein, and 4% glycitein), 1 g fat, 0–10 mg cholesterol, and 1400–1600 mg calcium. The SPI product was made with SUPRO/RISOY isolated soy protein with isoflavones. The SPI was water-washed to preserve isoflavone content. The MPI product was made with MPI (TMP 1240, manufactured by New Zealand Milk Products) in which casein and whey proteins were isolated together from milk (information provided by Solae).

Participants supplemented their habitual diets with the treatment protein powders and were instructed to avoid specific foods to minimize background phytoestrogen intake, including soy products (soy lecithin and soy oil were permitted), flaxseed, beans and legumes (green beans were permitted), and whole grains. Participants were also instructed to avoid natural health products, protein bars, green tea, and limit alcohol consumption to <7 drinks/wk (1 drink = 10 g alcohol). Finally, because the study treatment powders were fortified with calcium, participants were instructed to avoid fluid milk and calcium-fortified beverages.

To create a more consistent exposure to the isoflavones within the SPI, participants were instructed to consume their 2 treatment protein powder packets at separate times each day at least 4 h apart. Participants were counseled by a registered dietitian to consume their treatment protein powders in place of other high-protein foods (e.g. milk, cheese, deli meats) and were encouraged to reconstitute their treatment powders with water with the option of using Nestle flavor packets.

Data collection. All study visits occurred on d 1, 15, 29, 43, and 57 of each treatment period at the Human Nutriceutical Research Unit at the University of Guelph.

Baseline measurements obtained on d 1 of treatment period 1 included height, blood pressure, and heart rate. Height was measured without shoes using a stadiometer (SECA Portable Stadiometer 214). Systolic and diastolic blood pressures were measured in duplicate on the left arm after 5 min of rest using an automatic blood pressure monitor (UA-767PC Blood Pressure Monitor, A&D Medical). Body weight was measured in fasting participants on d 1, 15, 29, 43, and 57 of each treatment period using a calibrated digital scale (SV 100, Acculab North America) with participants wearing light clothes without socks. BMI was calculated as body weight (kg)/height (m²). Waist and hip circumferences were measured on d 1 and 57 of each treatment period using a metric tape measure; waist circumference was measured at the midpoint between the iliac crest and the lowest rib, and hip circumference was measured around the widest part of the buttocks next to light clothing. Body composition was measured on d 1 and 57 of each treatment period using bioelectrical impedance analysis (BodyStat 1500). Participants were instructed to consume at least 500 mL of water the night before their bioelectrical impedance analysis measurement to ensure hydration for a more accurate measurement.

Three-day food records were completed once during the week before the first treatment period and on d 2–4, 26–28, and 50–52 of each treatment period. Participants were provided with predated food record forms labeled with the dates on which they were to be completed, spaces to record the type of food consumed, and the time of consumption and information such as cooking method and brand name. Participants were also asked to provide as much detail as possible in the food records and were encouraged to submit nutritional labels of packaged foods consumed. Food samples were collected on d 1 and 57 of each treatment period at a consistent time for each participant. Participants were instructed to avoid all food and beverages (except water, which was encouraged) for 12 h prior to their blood sample and to avoid alcohol, strenuous activity, and over-the-counter medications for 72 h prior to their blood sample. Blood was collected into red-top vacutainers with no anticoagulant and left at room temperature for 30 min prior to centrifugation at 5℃ for 15 min at 1500 × g. Serum was then aliquoted into cryovials and frozen at −80℃ until analysis for lipids and apolipoproteins. A blood sample from fasting participants was also collected on d 1 of the first treatment period into a tube containing EDTA and frozen at −20℃ until analysis for HbA1c.

Twenty-four-hour urine collections were completed on d 54–56 of each treatment period. Participants were provided with an opaque 3-L container (VWR International) containing 5 g of ascorbic acid (as a preservative) for each urine collection day. Urine containers displayed a label with space to record the start and end times of the collection and volume of any spills. In addition, participants were provided with a 1-L
Participants completed a daily study diary every day during each treatment period which documented how and when they consumed their treatment powders, treatment powder tolerance issues or adverse effects, medications consumed, physical activity, illnesses, and any other information they thought was relevant. Study diaries were reviewed by a study coordinator at each study visit.

**Analytical methods.** Information from all 3-d food records was entered into a software program (Food Processor SQL edition, version 8.9.1, ESHA Research) that quantified energy, nutrient, and dietary fiber intakes. Three-day mean intakes of energy, protein, carbohydrates, total fat, SFA, monounsaturated fatty acids, PUFA, cholesterol, dietary fiber, and calcium were calculated for each 3-d food record.

Blood samples collected at study entry were analyzed for HBa1c using HPLC at Guelph General Hospital (Guelph, ON) with an interassay variation of 4.02%. All serum samples were analyzed for total cholesterol, HDL cholesterol, and triglycerides (TG) at Guelph General Hospital using an auto-analyzer (Synchron CX Systems, Beckman Coulter). Calculations were completed for LDL cholesterol (29), non-HDL cholesterol, and the ratios of total cholesterol:HDL cholesterol, LDL cholesterol:HDL cholesterol, TG:HDL cholesterol, and non-HDL cholesterol:HDL cholesterol. All serum samples were also analyzed for apolipoprotein B and apolipoprotein A-I by nephelometry (30) using a Behring Nephelometer ProSpec System Assay Loader (Dade Behring) at the Lipid Research Lab at St. Michael's Hospital (Toronto, ON) and the apolipoprotein B:apolipoprotein A-I ratio was calculated. All samples were analyzed in the same batch and included controls to estimate intra-assay variability, which was 0.97% for total cholesterol, 0.61% for HDL cholesterol, 8.90% for TG, 2.53% for apolipoprotein B, and 1.44% for apolipoprotein A-I.

Aliquots from every 24-h urine collection were analyzed for creatinine by the Animal Health Laboratory of Laboratory Services Division at the University of Guelph using an enzymatic UV method (Randox Laboratories Canada) on a Roche Hitachi 911 auto analyzer, with an interassay variability of 2.85%. Aliquots from each 24-h urine collection of each 3-d urine collection were thawed and combined proportionally to create a pooled sample to represent the entire 3-d urine collection. The pooled samples were analyzed for isoflavones (genisteen and daidzein) and isoflavone metabolites [O-desmethylangolensin (ODMA) and equol] using GC-MS as previously described (31). Interassay variability was 3.1% for genisteen, 4.2% for daidzein, 4.9% for ODMA, and 4.0% for equol.

**Statistical analysis.** SAS, version 9.1 (SAS Institute) was used for all statistical analyses, with \( P \leq 0.05 \) considered significant. Examination of all data using box plots, stem leaf diagrams, and normal probability plots revealed that urinary isoflavones were not normally distributed and required log transformation prior to statistical analysis. Values in the text are presented as mean ± SD for baseline subject characteristic data, as mean ± SE for nutrient intake data, and as geometric mean (95% CI) for urinary isoflavone data.

The effects of treatment on anthropometric, food record, and urinary isoflavone data were determined using repeated-measures ANOVA controlling for participant, treatment period, and treatment. The effect of treatment on serum lipids, apolipoproteins, and their ratios at study d 57 was determined using repeated-measures ANCOVA controlling for participant, treatment period, and treatment, with the inclusion of study d 1 values as a covariate. To ensure the washout period was sufficient, d 1 values for serum lipids and apolipoproteins and their ratios were compared using repeated-measures ANOVA, controlling for participant, treatment, and treatment period. Serum lipid and apolipoprotein data were further analyzed, accounting for variation in urinary equol by inclusion of equol excretor status as a covariate and the interaction between equol excretor status and treatment in the statistical model.

**Results**

**Participant dropouts and exclusions**

A total of 5 participants dropped out or were excluded from the study. Reasons for participant dropout included personal issues \( (n=2) \), dislike of the study treatment powders \( (n=1) \) and cancer diagnosis \( (n=1) \). In addition, 1 participant was excluded due to a baseline HBa1c that was >8%. A total of 29 participants (16 males and 13 females) were included in the statistical analysis. All participants consumed the SPI and MPI treatments every day during each treatment period with no reports of tolerance issues or adverse effects.

**Participant characteristics**

At baseline, participants had good glycemic control (fasting plasma glucose, 6.76 ± 1.30 mmol/L; HBa1c, 5.89 ± 0.62%) (Supplemental Table 1); were not taking any lipid-lowering or glycosicemic medications; were taking 1.80 ± 0.95 medications (Supplemental Table 1), with the top 3 types being ace inhibitors \( (n=8) \), aspirin \( (n=6) \), and beta-blockers \( (n=5) \); and had a mean of 40.8 ± 57.3 mo since diagnosis of their type 2 diabetes (Supplemental Table 1). Baseline age was 60.1 ± 9.64 y, BMI was 29.6 ± 4.07 kg/m², serum total cholesterol was 4.58 ± 0.87 mmol/L, and serum LDL cholesterol was 2.92 ± 0.69 mmol/L (Supplemental Table 1). During the study, body weight, BMI, percent body fat, waist circumference, hip circumference, and the waist:hip ratio did not differ between the treatment periods (data not shown).

**Energy and nutrient intakes.** Energy, protein, carbohydrate, total fat, monounsaturated fatty acids, PUFA, dietary fiber, cholesterol, and calcium intakes did not differ between the SPI and MPI treatments; however, SFA intake was lower during the SPI \( (22.2 ± 1.577) \) compared with the MPI \( (24.4 ± 2.17) \) treatment \( (P = 0.04) \) (Supplemental Table 2). When the 3-d food record completed before the study was compared with the 3-d food records completed during the study, the results indicated that protein \( (P < 0.0001) \) and calcium \( (P < 0.0001) \) were significantly higher during the study, whereas energy, carbohydrate, fat, and dietary fiber intakes did not differ (Supplemental Table 2).

**Urinary isoflavone excretion.** Urinary excretion of genisteen, daidzein, and ODMA were higher following consumption of SPI \( [11,849 (9835, 14,247) \text{ for genisteen}; 13,767 (12,175, 15,567) \text{ for daidzein}; 7708 (3842, 15,465) \text{ for ODMA}] \) compared with the MPI \( [90.9 (44.4, 186.2) \text{ for genisteen}; 134.3 (65.6, 275.0) \text{ for daidzein}; 31.8 (17.9, 56.5) \text{ for ODMA}] \ (P < 0.0001 for all comparisons, \( n = 29) \). Variation in urinary equol excretion within the SPI treatment indicated that 6 participants could be classified as equol excretors [urinary equol >1000 nmol/24 h (32)] and the remaining 23 participants could be classified as equol nonexcretors. Among the equol excretors, urinary equol excretion was significantly higher following consumption of the SPI \( [12965 (10,140, 16,577)] \) compared with the MPI \( [21.8 (17.4, 27.3)] \ (P < 0.0001, \ n = 6) \).

**Serum lipids and apolipoproteins.** On d 1, serum lipid and apolipoprotein concentrations did not differ between the 2 treatment periods (Table 1), providing evidence that the washout period was sufficient. Serum LDL cholesterol was significantly reduced following consumption of SPI compared with MPI \( (P = 0.04) \) (Table 1; Fig. 1). SPI consumption did not affect serum total cholesterol, HDL cholesterol, non-HDL cholesterol, TG, apolipoprotein B, or apolipoprotein A-I (Table 1; Fig. 1).
On d 1, serum lipid and apolipoprotein ratios did not differ between the 2 treatment periods (Table 2). The ratios of LDL cholesterol:HDL cholesterol and apolipoprotein B/apolipoprotein A-I were significantly reduced following consumption of SPI compared with MPI (P ≤ 0.05) (Table 2; Fig. 2). SPI consumption did not affect the ratios of total cholesterol:HDL cholesterol, TG:HDL cholesterol, or non-HDL cholesterol:HDL cholesterol (Table 2; Fig. 2).

The effects of SPI consumption on serum lipids and apolipoproteins did not change when equol excretor status was accounted for through inclusion as a covariate in the statistical model; however, there was an interaction identified between equol excretor status and treatment for total cholesterol (P = 0.05) and apolipoprotein B (P = 0.04). Further analysis within equol excretors and equol nonexcretors separately revealed no significant effects of treatment on either total cholesterol or apolipoprotein B.

### Discussion

The purpose of this study was to determine the effect of isoflavone-rich SPI on serum lipids in adults with diet-controlled type 2 diabetes. The study employed a randomized, double-blind, crossover design consisting of 2 57-d treatment periods of SPI and MPI separated by a 4-wk washout period to examine effects on serum lipids, apolipoproteins, and associated ratios. Although previous studies have evaluated the effects of soy isoflavones on serum lipids, apolipoproteins, and associated ratios. The current study detected significant interactions between equol excretor status and treatment for serum total cholesterol and LDL cholesterol.

Urinary isoflavone excretion was significantly higher following consumption of the SPI compared to the MPI in the current study, indicating that participants consumed the SPI and avoided external phytoestrogens during the MPI treatment period. Six of the 29 participants (20.7%) were classified as equol excretors, which is lower than the 28–50% prevalence rates in studies of adults without diabetes (32–36). It is noteworthy that the current study detected significant interactions between equol excretor status and treatment for serum total cholesterol and apolipoprotein B, consistent with the concept that equol may influence the effectiveness of soy interventions on lipids in adults with type 2 diabetes (16–25,27).

Non-HDL cholesterol was calculated by subtracting HDL cholesterol from total cholesterol. This study therefore adds to the literature through its particular emphasis on prevention by studying adults with type 2 diabetes who are free of diabetic complications and not taking glycermic or lipid-lowering medications.

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### Table 1

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<th>Total cholesterol, mmol/L</th>
<th>LDL cholesterol, mmol/L</th>
<th>HDL cholesterol, mmol/L</th>
<th>Non-HDL cholesterol, mmol/L</th>
<th>TG, mmol/L</th>
<th>Apolipoprotein B, g/L</th>
<th>Apolipoprotein A-I, g/L</th>
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<tr>
<td></td>
<td>d 1</td>
<td>4.67 ± 0.08</td>
<td>2.98 ± 0.14</td>
<td>1.16 ± 0.05</td>
<td>1.14 ± 0.08</td>
<td>0.95 ± 0.04</td>
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<tr>
<td></td>
<td>d 57</td>
<td>4.53 ± 0.16</td>
<td>2.90 ± 0.12</td>
<td>1.12 ± 0.04</td>
<td>1.13 ± 0.09</td>
<td>0.95 ± 0.04</td>
<td>1.40 ± 0.04</td>
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1 Values are means ± SE, n = 29.
2 P-value is for treatment differences in d 57 values adjusted for variation in d 1 values using repeated-measures ANOVA.
3 LDL cholesterol was calculated (29).
4 Non-HDL cholesterol was calculated by subtracting HDL cholesterol from total cholesterol.

### Table 2

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<tbody>
<tr>
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<td>1.07 ± 0.09</td>
<td>0.67 ± 0.03</td>
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1 Values are means ± SE, n = 29.
2 P-value is for treatment differences in d 57 values adjusted for variation in d 1 values using repeated-measures ANOVA.
3 LDL cholesterol was calculated (29).
4 Non-HDL cholesterol was calculated by subtracting HDL cholesterol from total cholesterol.

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of adults with type 2 diabetes, the issue of equol excretion in diabetes deserves further investigation.

Serum LDL cholesterol was significantly reduced by SPI consumption compared with MPI in the current study, which is consistent with the majority of previous soy intervention studies in adults with type 2 diabetes (17,20–23,27). In contrast, 4 other studies did not find significant changes in serum LDL cholesterol in adults with type 2 diabetes following consumption of extracted soy isoflavones (24,25), SPI (19), or soy protein (16), although with the exception of the Gonzalez et al. (25) study, participants differed from the current study in that they had diabetic nephropathy (16,19) or retinopathy (24) and/or used medications, including insulin (16), oral hypoglycemic agents (19), and lipid-lowering medications (19).

Serum total cholesterol was not significantly affected by SPI consumption in the current study. This result is consistent with 6 previous soy intervention studies in adults with type 2 diabetes that investigated lipid-altering effects of soy protein (17–20) and extracted isoflavones (24–26) for periods of 6 wk to 12 mo. In contrast, 4 previous soy intervention studies in adults with type 2 diabetes did find a significant reduction in total cholesterol following 7–12 wk of consumption of soy protein (16,21,23,27). Participants in these studies differed from those in the current study in that they included groups of men (16,21,23) and postmenopausal (23) or postmenopausal (21) women who were treated with oral hypoglycemic agents (21) or insulin (16) or had diabetic nephropathy (16,23), as well as postmenopausal women who controlled their diabetes with diet (27) (which is comparable to the current study). The fact that these studies did find a significant reduction in circulating total cholesterol justifies further study.

Serum HDL and non-HDL cholesterol concentrations were not significantly affected by SPI consumption in the current study. Although non-HDL cholesterol has not been included in previous soy intervention studies of adults with type 2 diabetes, the HDL cholesterol result is consistent with 9 previous studies that examined SPI (17,20,27), soy protein (in soy food form) (16,18,23), and extracted isoflavones (24–26). In the minority, 2 other studies found that HDL cholesterol significantly increased, 1 of 47 hyperlipidemic adults with type 2 diabetes treated with lipid-lowering medications who consumed a dietary soy supplement for 12 wk (21) and the other of 14 men with diabetic nephropathy treated with oral hypoglycemic agents and lipid-lowering medications who consumed SPI for 7 wk (19). Overall, the majority of soy intervention studies in adults with type 2 diabetes have not demonstrated effects on HDL cholesterol, although maintenance of HDL cholesterol while reducing LDL cholesterol levels can be considered a favorable outcome.

Serum TG was not significantly affected by SPI consumption in the current study, consistent with 6 previous studies that investigated the effects of soy protein (18,19,27) and extracted isoflavones (24–26) on circulating lipids in adults with type 2 diabetes. In contrast, 5 other studies of adults with type 2 diabetes did find significant reductions in TG, including a study of 47 hyperlipidemic adults treated with oral hypoglycemic agents who consumed a soy protein dietary supplement for 12 wk (21), a weight-loss study in which 82 obese adults treated with oral hypoglycemic agents consumed a SPI meal replacement shake for 12 wk (20), a study of 20 adults treated with oral hypoglycemic agents who consumed SPI for 6 wk (17), and 2 studies of adults with diabetic nephropathy who consumed soy protein for 7 wk (23) and 8 (16) wk. The conflicting results among studies, despite the variable study design issues, provide rationale that serum TG deserves inclusion in future soy intervention studies in adults with type 2 diabetes.

The current study included serum apolipoproteins and found that SPI consumption did not significantly affect apolipoprotein B or apolipoprotein A-I, although the apolipoprotein B:apolipoprotein A-I ratio was significantly reduced by consumption of SPI relative to MPI. The only previous study of adults with type 2 diabetes to include apolipoproteins found that 6 wk of a SPI and soy cotyledon fiber supplement significantly reduced plasma apolipoprotein B but did not change apolipoprotein A-I or the apolipoprotein B:apolipoprotein A-I ratio compared with a cellulose control (17). The inclusion of apolipoproteins in future soy intervention studies is highly warranted; their relevance to CVD risk is well established (38) and there is a particular emphasis on the apolipoprotein B:apolipoprotein A-I ratio as highly predictive in the evaluation of cardiac risk (39).

The ratio of LDL cholesterol:HDL cholesterol was also significantly reduced following consumption of SPI relative to MPI in the current study. This result is consistent with 3 previous studies in which adults with type 2 diabetes consumed SPI for 4 wk (participants also had diabetic nephropathy) (19), SPI for 6 wk (17), or a dietary soy protein supplement for 12 wk (participants also had hyperlipidemia) (21) but is inconsistent with 2 other studies in which men with diabetic nephropathy consumed a soy protein diet for 7 wk (23) and postmenopausal women with diabetic retinopathy consumed an extracted isoflavone supplement for 12 wk (24). The other lipid ratios examined in the current study (total cholesterol:HDL cholesterol, TG:HDL cholesterol, and non-HDL cholesterol:HDL cholesterol) were not significantly affected by SPI consumption. Although no previous soy intervention studies of adults with type 2 diabetes to our knowledge included TG:HDL cholesterol and non-HDL cholesterol:HDL cholesterol, 3 studies included total cholesterol:HDL cholesterol and all found a significant decrease following consumption of SPI for 12 wk in 32 postmenopausal women with diet-controlled diabetes (27), a dietary soy supplement for 12 wk in 47 hyperlipidemic men and postmenopausal women (21), and SPI for 7 wk in 14 men with diabetic nephropathy (19). The decrease in total cholesterol: HDL cholesterol in these studies is logical given that there was a decrease in total cholesterol (21,27) and/or an increase in HDL cholesterol (19,21), neither of which occurred in the current study. Inclusion of lipid ratios adds to the literature, because they are not always included in soy intervention studies of adults with type 2 diabetes (16,20,25,26) and they relate to CVD risk (40).

In summary, the current study evaluated the effects of isoflavone-rich SPI in comparison to MPI on serum lipids in
adults with type 2 diabetes. The study utilized a randomized, crossover, double-blind design that included 2, 57-d treatment periods separated by a 28-d washout period. SPI consumption significantly reduced LDL cholesterol and the ratios of LDL cholesterol:HDL cholesterol and apolipoprotein B:apolipoprotein A-I compared with MPI consumption. These results demonstrate a beneficial effect of SPI consumption that relates to CVD risk reduction in adults with type 2 diabetes. This study therefore provides evidence for soy as a dietary preventive strategy for adults with type 2 diabetes to reduce their CVD risk and, in so doing, improve their quality, and possibly length, of life.

Acknowledgments
We thank Erin Balodis, Laura Beaton, Lauren Carde, Stephanie Hass, Mehrnoosh Kashani, Kelly Mascoli, Rachel Masters, and Megan Olson for their help with data collection and data entry and Wendy Thomas for her technical assistance in the urinary isoflavone analyses.

Literature Cited


