Effect of soy isoflavone protein and soy lecithin on endothelial function in healthy postmenopausal women

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ABSTRACT

Objective: To assess the effects of soy isoflavone protein concentrate and soy lecithin on endothelial function, measured as flow-mediated dilation (FMD) of the brachial artery in healthy postmenopausal women.

Design: This was a randomized, double-blind, placebo-controlled crossover trial with 25 participants (mean age, 61 years; body mass index, 25.46 kg/m²). The women underwent endothelial function testing at baseline and after 4 weeks of randomly assigned treatment with intervening 4-week washout periods. Treatment assignments included soy isoflavone protein (25 g/day) and soy lecithin (20 g/day), soy isoflavone protein (25 g/day) and placebo lecithin, placebo protein and soy lecithin (20 g/day), and double placebo. FMD and serum lipid levels were assessed at baseline and the end of each 4-week treatment phase.

Results: Twenty-two women completed the trial. No statistically significant (P > 0.05) difference was seen in FMD between treatment groups. A trend was suggested with FMD highest after treatment with soy protein plus lecithin (7.50 ± 9.85), followed by soy protein (5.51 ± 10.11), soy lecithin (5.35 ± 6.13), and lowest after placebo (4.53 ± 7.84). Soy isoflavone protein and soy lecithin significantly increased the high-density lipoprotein/low-density lipoprotein ratio (soy isoflavone protein plus soy lecithin, 0.64 ± 0.19, P < 0.0001; soy isoflavone protein plus placebo lecithin, 0.58 ± 0.17, P = 0.0058; placebo protein plus soy lecithin, 0.65 ± 0.18, P < 0.0001) relative to the baseline value (0.49 ± 0.15).

Conclusions: In this sample of healthy postmenopausal women, soy isoflavone protein and soy lecithin significantly improved the lipid profile. A favorable influence on endothelial function could not be confirmed.


Cardiovascular disease is the leading cause of morbidity and mortality among postmenopausal women in westernized societies. Women are largely protected from coronary disease before menopause, but their risk increases rapidly after the cessation of ovarian function and the resultant decline of endogenous estrogens. Basic research findings suggest a favorable effect of estrogens on cardiovascular parameters such as lipid profile, endothelial function, and antioxidant activity, yet the clinical cardioprotective role of hormone therapy (HT) in postmenopausal women remains controversial. Recent results of the Women’s Health Initiative and long-term follow-up of the Heart and Estrogen/progestin Replacement Study demonstrate no cardiovascular benefit among postmenopausal...
women using HT. Even before these results were obtained, only 18% to 20% of postmenopausal women in the United States were prescribed HT, and of those, more than 70% were noncompliant, with a mean duration of use of approximately 1 year.29-31 This pattern of HT use is attributable in large part to patients’ and physicians’ concerns about the adverse effects and possible long-term risks of therapy.10-12 Women are increasingly seeking alternatives to traditional HT, including nutritional supplements, vitamins and minerals, and herbal remedies.13

Phytoestrogens, nonsteroidal, plant-derived compounds with estrogenic activity,14,15 are currently the most popular alternative to HT.16 Isoflavones, including genistein and daidzein, are the most common types of phytoestrogens and are found most abundantly in legumes and beans, particularly soy.17 Soy protein (SP) has been shown to improve the lipid profile18 and to improve both lipids19 and metabolic control in diabetes.20

Endothelial function refers to arterial vasomotor responses mediated by the release of chemicals, including nitric oxide (vasodilating) and endothelin (vasoconstricting), from the vascular endothelium.21 Impaired release of nitric oxide results in endothelial dysfunction, in which vessels tend to constrict and impede flow in response to stimuli that should lead to dilatation and flow augmentation.22 Endothelial function can be assessed noninvasively through the induction of hyperemic flow and shear stress to stimulate nitric oxide release.23 Because of the strong correspondence between peripheral and coronary endothelial responses,24,25 measurement of endothelium-dependent flow-mediated dilation (FMD) of the brachial artery using high-resolution ultrasonography has become a standard research assessment method.26

Menopause is associated with impaired endothelial function,27 which is widely viewed as an indicator of coronary risk.24,28 Estrogen administration in postmenopausal women induces positive effects on endothelial function and blood flow in normal and atherosclerotic arteries.29-32 Estrogen receptors in the vascular endothelium play an important role in the vasodilatory effect of estrogens, especially in the synthesis of nitric oxide.33

Isoflavones also act through an estrogen receptor-mediated mechanism.34 Soy isoflavones have been shown to influence endothelial function positively in primates,35 but studies in postmenopausal women have produced conflicting results. Three studies reported a significant increase in flow-mediated vasodilation of the brachial artery with isoflavone treatment36-38 whereas four studies reported no effect on endothelial function.39-42

Lecithin, a phosphatidylcholine-containing compound, has been shown to lower cholesterol in hyperlipidemic animals43-46 and humans,47 but not in normolipidemic animals and humans.47,48 Choline is a component of lecithin and is a precursor to acetylcholine, which leads to vasodilation in healthy endothelium and vasoconstriction in unhealthy endothelium.49 To our knowledge, soy lecithin’s effect on endothelial function has not been studied.

We therefore conducted a randomized, double-blind, placebo-controlled, crossover trial of SP containing isoflavones and soy lecithin (SL) products on endothelial function in healthy postmenopausal women.

METHODS

Participants

Healthy postmenopausal women were recruited from the general population of southwestern Connecticut, primarily through mass media (newspaper advertisements, press releases) and posters. Women (N = 89) who responded to recruitment efforts were prescreened using a semistructured telephone interview. Inclusion criteria were healthy postmenopausal women (defined as absence of menses for at least 1 year, follicle-stimulating hormone level >40 mIU/mL, and estradiol <25 pg/mL) not currently using HT who were normotensive (<140/90 mmHg) and normolipidemic by laboratory assay (total cholesterol <240 mg/dL).

Exclusion criteria were smoking; history of cardiovascular disease; breast or endometrial cancer; vasoactive medication use; daily prescription drug use; regular use of high-dose vitamin C of more than 250 mg, vitamin E more than 400 IU, or fiber supplements; and failure to meet inclusion criteria or anticipated inability to complete the study protocol.

Women who met initial prescreening criteria (n = 33) underwent a clinical screening examination (height, weight, body mass index, and blood pressure measurements) and laboratory testing (fasting cholesterol, high-density lipoprotein [HDL], low-density lipoprotein [LDL], triglyceride levels, estradiol, follicle-stimulating hormone, choline/phosphatidylcholine, and isoflavone). Participants provided written informed consent before undergoing screening and study procedures. The study was approved by the Institutional Review Board of Griffin Hospital, Derby, CT.

Study protocol

Participant management

After meeting eligibility criteria, 25 women underwent a baseline ultrasound scan and were randomly
assigned to treatment groups by the data manager using block randomization. They were randomly assigned to a sequence of four sustained treatment phases, each 28 days (4 weeks) in duration with a 28-day (4-week) washout in between. Treatment products were consumed twice daily (in the form of packets of powder and packets of granules) and included SP containing isoflavones (25 g/day) and SL (20 g/day); SP containing isoflavones (25 g/day) and placebo lecithin; placebo protein (50:50 calcium/sodium caseinate) and SL (20 g/day); and double placebo. All products were analyzed before administration. The results of the analysis are presented in Appendix A.

Participants were instructed throughout the study to consume one package of powder (mixed with water to create a beverage shake, chocolate and vanilla flavored) and one package of granules twice a day. Treatments were taken in the morning and then later in the day. They were instructed to consume any missed treatments as soon as they remembered, unless it was time for the next treatment, in which case they were instructed to return the unused doses at the next scan.

On the last day of each treatment period, after an overnight fast (nothing to eat or drink after midnight) and timed to precede the scheduled scan time by 2 hours, participants ingested (at home) the final morning treatment dose with water only, and then reported to the Prevention Research Center for a morning treatment dose with water only, and then 2 hours, participants ingested (at home) the final morning treatment dose with water only, and then reported to the Prevention Research Center for a compliance adherence review, endothelial function testing, and phlebotomy.

Compliance/adherence review

All participants were contacted by telephone every 2 to 4 weeks and 2 days before the end of each treatment phase to monitor compliance, inquire about any study-related issues, significant side effects, reinforce compliance, serve as a reminder for morning previsit testing instructions, and answer potential questions. At each visit, adherence to morning pretesting instructions was verified with the women before each scan. The women returned any unused treatment product, which was used to corroborate self-reported compliance. Compliance was defined as more than 80% use of treatment. Compliance records were maintained for each phase of the study, and the women reported an overall compliance rate above 85%.

Brachial artery reactivity studies methodology

The brachial artery reactivity studies (BARS) methodology is comparable to methods of other leading laboratories and as described by Corretti et al, enhanced by the use of software (Brachial Analysis Tools, Medical Imaging Applications 2001, Iowa City, IA) to automate the brachial artery diameter measures. The BARS procedure is designed to measure FMD in the brachial artery as a percentage of resting vessel diameter. Our methods have been published previously. In brief, brachial artery reactivity was evaluated at baseline (week 0) and after each treatment (weeks 4, 12, 20, 28). Endothelial function was measured noninvasively in the right brachial artery by means of a high-frequency ultrasound machine (Philips Medical Systems, Sonos 4500, Andover, MA) in accordance with published guidelines. Participants were required to lie at rest in a quiet, temperature-controlled, softly lit room for at least 15 minutes before scanning was initiated. Participant comfort was enhanced with the addition of an angled knee cushion, which relieved back strain.

To create a flow stimulus in the brachial artery, a sphygmomanometer cuff was placed on the upper arm proximal to the transducer. The reference diameter of the brachial artery was measured from two-dimensional ultrasound images using a high-frequency, 10- to 15-MHz, vascular ultrasound transducer (Philips Medical Systems, 15-6L L7540 linear array transducer). The brachial artery was imaged at a location 3 to 7 cm above the antecubital fossa in the longitudinal plane. A segment with clear anterior and posterior intimal interfaces between the lumen and vessel wall was selected for continuous two-dimensional gray-scale imaging. The transmit (focus) zone was set to the depth of the near wall because of difficulty in differentiating the near from the far wall “m” line (the interface between media and adventitia). Diameter measurements were taken from the anterior to the posterior m line, over a consistent segment of vessel at least 10 to 15 mm in length in diastole. Arterial flow velocity was measured by means of a pulsed Doppler signal at a 70-degree angle to the vessel, with the range gate in the center of the artery. Flow was determined automatically by multiplying the arterial cross-sectional area (πr²) by the Doppler flow velocity. A reference blood flow and diameter are recorded. Arterial occlusion is created by cuff inflation to 50 mm Hg above the systolic blood pressure. The cuff is inflated for 5 minutes. This causes ischemia and consequent dilation of downstream resistance vessels via autoregulatory mechanisms. Cuff deflation induces a brief high-flow state through the brachial artery (reactive hyperemia) to accommodate the dilated resistance vessels. The resulting increase in shear stress causes the brachial artery to dilate. A pulsed Doppler signal is...
obtained within 15 seconds of cuff release to assess hyperemic velocity, and a longitudinal image of the artery is recorded continuously from 20 seconds to 2 minutes after cuff deflation.

The timing of each image frame with respect to the cardiac cycle was determined with simultaneous electrocardiographic gating during image acquisition via the high-quality mainframe ultrasound system. Images were acquired on videotape and magnetic optical disk for evaluation and analysis. All BARS were completed before noon.

Handling of BARS images and data

Measures of vessel diameter and flow velocity were generated after each scanning session. Velocity measures were generated automatically using the pulsed-wave Doppler. Diameter measurements were obtained by automatic identification using edge-detection software (Brachial Analysis Tools, Medical Imaging Applications 2001), an automated method for near and far wall detection and vessel diameter measurements in brachial ultrasound image sequences. The method automatically learns properties for the analyzed vessel in one frame of a sequence that is analyzed under training parameters. The vessel properties were reflected in the cost function used in a graph search–based border detection process. This automated method decreased variability by generating an average diameter measurement derived from multiple measures obtained along a segment of the vessel. Several automated quality control steps are incorporated to improve accuracy and reproducibility. These computerized readings are charted on a standardized scan form and scanned into the database for analysis. Measurement of vessel diameter and flow velocity was conducted by a dedicated vascular research specialist who was blinded to treatment assignment. A random sample of 30 BARS was provided to the clinical research specialist for a blinded second reading. The resultant coefficient of intraobserver reliability was 0.98 (P < 0.0001).

Serum assays and analyses

Venous whole blood was drawn from each woman for serum assays for lipids, choline/phosphatidylcholine, and isoflavones (equol, daidzein, dihydrodaidzein, O-desmethylandolensin, genistein), which were assessed at baseline and after each treatment period. Serum for choline and phosphatidylcholine analysis was sent to the University of North Carolina, and serum for isoflavone analysis was sent to the University of Alabama (Dr. S. Barnes).

Adverse effects

An adverse effects questionnaire was administered at the end of each treatment assignment to compare side effects of SL, SP-containing isoflavones, and placebo.

Statistical analysis

The sample size was determined to allow for approximately 10% attrition and noncompliance rate and provide at least 80% power to detect a minimal difference of 3.5% in FMD between isoflavone and placebo.

Data were analyzed using SAS software (version 8.2 of the SAS System for Windows, SAS Institute Inc, Cary, NC). Endothelial function was assessed as FMD, calculated as the percentage of change in diameter after occlusion of the brachial artery at 60 seconds relative to the measurement at baseline (before cuff inflation). To account for variability in the strength of the stimulus that triggered endothelial reactivity (ie, hyperemic flow), FMD was divided by flow at 15 seconds after cuff deflation to create a stimulus-adjusted response measure (SARM). Other measures include plasma analytes.

Paired t testing was performed to assess change in FMD, SARM, serum measures, and blood pressure from baseline. The paired t test was also used to compare baseline measures of FMD, SARM, and serum measures to the values obtained at the end of each washout period to demonstrate complete washout. To adjust for any potential carryover effect after washout, treatment sequence (timing of each treatment) was entered as a control variable in multivariable analyses. The change in FMD, SARM, and serum measures between the treatment groups was assessed using repeated-measures analysis of variance. The combined effects of independent variables and treatment assignment on endothelial function were assessed with multivariable models using analysis of covariance. A two-tailed α of less than 0.05 was considered statistically significant.

RESULTS

Participants

Participants ranged in age from 46 to 76. Mean age was 61.5 years, body mass index was 26.34 kg/m², and the mean time from menopause was 118.91 months. Demographic data for the study population are provided in Table 1. Twenty-two of 25 eligible, recruited, and randomized participants completed the study. Two women withdrew from the study because...
of incompatibility with treatment (dietary preferences and menopausal symptoms); one woman withdrew for reasons unrelated to the study.

**Brachial artery FMD**

Table 2 provides a summary of the results of the vascular reactivity studies. The mean baseline (pre-treatment) FMD was 8.60 ± 7.20%. FMD did not change significantly (P > 0.05) from baseline with any of the four treatments. No statistically significant difference was seen in FMD between treatment assignments. A trend was suggested, however, with FMD highest after treatment with both SP and lecithin (7.50 ± 9.85%), followed by SP (5.51 ± 10.11%), SL (5.35 ± 6.13%), and lowest after placebo (4.53 ± 7.84%). Our results persist after controlling for respondent characteristics. A similar trend was observed with SARM.

**Lipid panel**

Total cholesterol and LDL decreased significantly (P < 0.001) from baseline after all four treatments (Table 2). The between-treatment cholesterol reductions did not differ significantly (P > 0.05). Treatment with both SP containing isoflavones plus SL significantly (P < 0.05) increased HDL relative to double placebo. SP containing isoflavones and SL significantly increased the HDL/LDL ratio (SP containing isoflavones plus SL, 0.64 ± 0.19, P < 0.0001; SP containing isoflavones plus placebo lecithin, 0.58 ± 0.17, P = 0.0058; placebo protein plus SL, 0.65 ± 0.18, P < 0.0001) relative to the baseline value (0.49 ± 0.15).

**Serum choline**

Betaine levels increased significantly after treatment with SP containing isoflavones plus SL and SL (98.94 ± 29.63 nmol/mL, P < 0.0001; 92.06 ± 28.00 nmol/mL,

### Table 1. Baseline demographic characteristics (N = 25)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
</tr>
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<tbody>
<tr>
<td>Age, y</td>
<td>61.50 ± 8.20</td>
</tr>
<tr>
<td>Time from menopause, mo</td>
<td>118 ± 107.97</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>70.96 ± 10.10</td>
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<tr>
<td>Height, cm</td>
<td>164.07 ± 4.75</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.34 ± 3.86</td>
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<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>135.27 ± 17.00</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>77.27 ± 9.43</td>
</tr>
<tr>
<td>Pulse rate, per min</td>
<td>76.89 ± 9.72</td>
</tr>
<tr>
<td>Room temperature, °F</td>
<td>72.71 ± 1.49</td>
</tr>
</tbody>
</table>

### Table 2. Flow-mediated dilation and plasma analyte values at baseline and after treatment assignment (n = 22)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Soy protein plus soy lecithin</th>
<th>Soy protein plus placebo lecithin</th>
<th>Placebo protein plus soy lecithin</th>
<th>Double placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial artery response</td>
<td></td>
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</tr>
<tr>
<td>FMD, %</td>
<td>7.50 ± 9.85</td>
<td>5.51 ± 10.11</td>
<td>5.35 ± 6.13</td>
<td>4.53 ± 7.84</td>
</tr>
<tr>
<td>SARM</td>
<td>0.039 ± 0.05</td>
<td>0.028 ± 0.046±</td>
<td>0.028 ± 0.032±</td>
<td>0.017 ± 0.056±</td>
</tr>
<tr>
<td>Lipid panel</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>188.55 ± 21.83</td>
<td>184.32 ± 26.5±</td>
<td>179.73 ± 19.16±</td>
<td>181.83 ± 31.37±</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>98.41 ± 44.82</td>
<td>86.91 ± 35.88±</td>
<td>94.45 ± 42.65±</td>
<td>89.96 ± 39.52 ±</td>
</tr>
<tr>
<td>LDL, mg/dL</td>
<td>104.55 ± 20.50±</td>
<td>107.77 ± 23.78±</td>
<td>99.36 ± 18.26±</td>
<td>107.43 ± 25.4±</td>
</tr>
<tr>
<td>HDL, mg/dL</td>
<td>64.73 ± 14.45±</td>
<td>59.59 ± 14.13±</td>
<td>62.00 ± 11.13±</td>
<td>56.70 ± 13.25±</td>
</tr>
<tr>
<td>HDL/LDL</td>
<td>0.64 ± 0.19±</td>
<td>0.58 ± 0.17±</td>
<td>0.65 ± 0.18±</td>
<td>0.55 ± 0.15±</td>
</tr>
<tr>
<td>Choline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betaine, nmol/mL</td>
<td>98.94 ± 29.63±</td>
<td>36.50 ± 8.90±</td>
<td>92.06 ± 28.00±</td>
<td>33.27 ± 11.19±</td>
</tr>
<tr>
<td>Choline, nmol/mL</td>
<td>24.31 ± 8.92</td>
<td>8.49 ± 2.59</td>
<td>23.84 ± 6.32</td>
<td>6.89 ± 1.92</td>
</tr>
<tr>
<td>Phosphatidylcholine, nmol/mL</td>
<td>2095.51 ± 2232.22</td>
<td>2029.35 ± 263.76</td>
<td>2080.56 ± 220.38</td>
<td>2058.33 ± 250.68</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Systolic, mm Hg</td>
<td>124.95 ± 15.97±</td>
<td>125.33 ± 12.45±</td>
<td>128.35 ± 17.02±</td>
<td>121.61 ± 13.69±</td>
</tr>
<tr>
<td>Diastolic, mm Hg</td>
<td>70.50 ± 9.26±</td>
<td>71.24 ± 9.67±</td>
<td>71.96 ± 9.18±</td>
<td>66.87 ± 7.97±</td>
</tr>
<tr>
<td>Isoflavone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equol, μmol/L</td>
<td>59.74 ± 101.89±</td>
<td>58.96 ± 103.66±</td>
<td>0.31 ± 1.46</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Daidzein, μmol/L</td>
<td>409.91 ± 256.96±</td>
<td>413.77 ± 214.20±</td>
<td>28.32 ± 27.07</td>
<td>26.24 ± 59.81</td>
</tr>
<tr>
<td>Dihydrodaidzein, μmol/L</td>
<td>119.10 ± 11.10±</td>
<td>86.35 ± 92.64±</td>
<td>15.77 ± 33.87</td>
<td>11.41 ± 38.63</td>
</tr>
<tr>
<td>O-desmethylangolensin, μmol/L</td>
<td>166.77 ± 181.85±</td>
<td>119.31 ± 118.88±</td>
<td>26.70 ± 72.19</td>
<td>10.91 ± 28.23</td>
</tr>
<tr>
<td>Genistein, μmol/L</td>
<td>831.31 ± 747.64±</td>
<td>926.18 ± 694.50±</td>
<td>47.78 ± 39.54</td>
<td>60.54 ± 139.98</td>
</tr>
<tr>
<td>Total isoflavones, μmol/L</td>
<td>1586.83 ± 1045.9±</td>
<td>1604.58 ± 887.3±</td>
<td>118.88 ± 157.62</td>
<td>109.10 ± 244.18</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

FMD, flow-mediated dilation; SARM, stimulus-adjusted response measure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

*P < 0.05 in paired t test.

*P < 0.05 versus soy lecithin plus placebo.

*P < 0.05 versus double placebo.
with neither high cholesterol nor endothelial dysfunction are also contradictory. Teede et al\(^{42}\) found that in 105 postmenopausal women, 3 months of treatment with 40 g of SP containing 118 mg of isoflavones did not improve vascular function. Hale et al\(^{43}\) reported that 2 weeks of 80 mg of isoflavone in the form of soy tablets failed to affect endothelial function or lipids. Two recent studies showing improvement in endothelial function with isoflavone supplementation used either high doses or long duration of treatment: Steinberg et al\(^{37}\) found that 25 g of SP with 107 mg of isoflavones for 6 weeks favorably affects endothelial function in healthy postmenopausal women, independently of lipid and antioxidant effects. Squadrito et al\(^{46}\) found that 1 year of genistein therapy (54 mg/day) improves endothelium-dependent flow-mediated vasodilation to the same extent as does estrogen-progestin therapy. Contributory factors to the varied outcomes of these studies include the dose and duration of treatment, the type of product used (SP, isoflavone extract, isolated genistein), and the presence of endothelial dysfunction or hypercholesterolemia.

The meta-analysis by Anderson et al\(^{18}\) of 38 controlled clinical trials examining the relationship between SP consumption (averaging 47 g/day) and serum lipid concentrations demonstrated significant reductions, when compared to control diets, in total cholesterol (9.3%), LDL cholesterol (12.9%), and triglycerides (10.5%). HDL cholesterol levels increased by 2.4%, but this increase was not significant. The favorable effects of SP on the lipid profile contributed to US Food and Drug Administration approval of a health claim that “25 g of SP a day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.”\(^{53}\) Whether the hypocholesterolemic effect of soy is attributable to isoflavones has been the subject of much debate. A number of recent studies have failed to confirm the role of isoflavones in the lipid-lowering effects of soy. Several clinical trials have indicated that isoflavones administered as supplements do not reduce cholesterol levels.\(^{31,54-57}\) However, three recent studies in humans do show a link, albeit modest, between isoflavone content and lipid lowering.\(^{58-60}\) A recent meta-analysis by Weggemans and Trautwein\(^{61}\) of the relationship between soy-associated isoflavones and LDL and HDL levels concluded that changes in isoflavones are unrelated to changes in LDL and HDL levels.

Favorable effects of soy supplementation on metabolic control in diabetes were reported by Jayagopal et al\(^{62}\). In a randomized, double-blind, crossover study of 32 postmenopausal women with type 2 diabetes,
fasting insulin and hemoglobin A1C levels improved, along with serum lipids, after 12 weeks of supplementation with SP (30 g/day containing 132 mg/day of isoflavones). Thus, despite the neutral effects of soy observed in the current study, the possibility of cardioprotective effects, at least in certain population subgroups, still exists.

SL has previously been shown to improve the lipid profile in hyperlipidemic patients, but not in normolipidemic patients. In the current study, among normolipidemic women consuming 20 g of SL per day, SL significantly lowered LDL cholesterol relative to baseline and to SP containing isoflavones, but not relative to placebo. The mechanism of lecithin’s lipid-lowering effects remains unknown. In this study, SL also significantly increased levels of choline and betaine. To the best of our knowledge, the effects of lecithin on endothelial function have not been studied. As a source of choline and, therefore, acetylcholine, lecithin could be expected to increase endothelium-dependent vasodilation, but the current study failed to demonstrate a significant effect of lecithin on endothelial function.

This study suggests a favorable trend in FMD with SP containing isoflavones and SL supplementation relative to placebo, but a significant effect on endothelial function could not be confirmed. These findings may be due to study limitations, such as the small sample size, timing of testing, dose, or delivery vehicle.

It is noteworthy that FMD was lower after all treatments, including double placebo, than at baseline (pretreatment). One possible explanation for the decline in FMD from baseline relates to the timing of the testing and the delivery vehicle. The baseline BARS testing was conducted after an overnight fast, but for each of the posttreatment scans, study participants consumed the morning dose of the treatment 2 hours before the scan (after an overnight fast). Furthermore, the shakes provided to women in both the treatment and placebo groups had a high glucose content, and hyperglycemia has been shown to inhibit endothelium-dependent coronary vasodilation through oxidative stress. It is likely that acute glucose loading before the posttreatment scans compromised endothelial function, possibly masking any potential beneficial effects of SP containing isoflavones and SL.

CONCLUSION

In summary, the current study suggests that short-term administration of SP containing isoflavones or SL significantly improves the lipid profile in healthy postmenopausal women, whereas effects on endothelial function remain inconclusive. Further study is warranted to determine whether soy isoflavones and/or SL confer vascular benefit to particular subgroups of postmenopausal women, notably those with established cardiac or diabetic risk factors. Further study of these soy products using vehicles with lower sugar content is also warranted.

REFERENCES


**APPENDIX A**

<table>
<thead>
<tr>
<th>Product</th>
<th>Serving size</th>
<th>Protein g/serv</th>
<th>Fat g/serv</th>
<th>Calcium mg/serv</th>
<th>Isoflavones (aglc) mg/serv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanilla Soy DBB (w/ Alpha 5800)</td>
<td>30</td>
<td>12.5</td>
<td>0.5</td>
<td>87.3</td>
<td>56.6</td>
</tr>
<tr>
<td>Chocolate Soy DBB (w/ Alpha 5800)</td>
<td>27</td>
<td>12.5</td>
<td>0.6</td>
<td>92.6</td>
<td>56.4</td>
</tr>
<tr>
<td>Average</td>
<td>28.5</td>
<td>12.5</td>
<td>0.6</td>
<td>90.0</td>
<td>56.5</td>
</tr>
<tr>
<td>Vanilla Caseinate DBB (w/ 50:50 blend calcium/sodium caseinate)</td>
<td>30</td>
<td>13.7</td>
<td>0.2</td>
<td>104.4</td>
<td>NA</td>
</tr>
<tr>
<td>Chocolate Caseinate DBB (w/ 50:50 blend calcium/sodium caseinate)</td>
<td>30</td>
<td>14.1</td>
<td>0.3</td>
<td>104.1</td>
<td>NA</td>
</tr>
<tr>
<td>Average</td>
<td>30.0</td>
<td>13.9</td>
<td>0.3</td>
<td>104.3</td>
<td>NA</td>
</tr>
</tbody>
</table>

Analysis is per serving (2 servings per day).

Product data as analyzed by Nestle Analytical Labs (data received February 20, 2006).