# Soy Protein With or Without Isoflavones, Soy Germ and Soy Germ Extract, and Daidzein Lessen Plasma Cholesterol Levels in Golden Syrian Hamsters

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**Dietary isolated soy protein (ISP, containing approximately equal amounts of daidzein and genistein), ethanol-extracted ISP (ISP (-)), soygerm or soygerm extract (containing large amounts of daidzein and glycitein and little genistein) and the isoflavone, daidzein, were hypothesized to lessen plasma cholesterol in comparison with casein. Sixty male and 60 female golden Syrian hamsters (6–8 weeks of age) were randomly assigned to six treatments fed for 10 weeks. Four of the experimental diets (ISP, daidzein, soygerm, and soygerm extract) contained 1.3 mmol total isoflavones/kg. The ISP (-) diet contained 0.013 mmol isoflavone/kg, whereas the casein diet contained no isoflavones. Hamsters fed ISP, ISP (-), daidzein, soygerm, and soygerm extract had significantly less plasma total cholesterol (by 16%–28%), less non-HDL cholesterol (by 15%–50%) and less non-HDL/HDL cholesterol ratios compared with hamsters fed casein ($P < 0.01$). For male hamsters, there were no differences among treatments in plasma HDL concentrations. Female hamsters fed ISP (-) had significantly greater HDL levels ($P < 0.01$) than females fed casein or daidzein. Triglyceride concentration was significantly less in hamsters fed ISP (-) compared with the casein-fed females. Because soy protein with or without isoflavones, soygerm and soygerm extract, and daidzein lessened plasma cholesterol to an approximately equal extent, soy protein alone, varying mixtures of isoflavones, and other extractable components of soy are responsible for cholesterol-lessening effects of soy foods, mainly due to their effects to lessen LDL cholesterol.** Exp Biol Med 228:1063–1068, 2003

**Key words:** isoflavones; daidzein; soygerm; soy protein hamsters; cholesterol; cholesterol-lowering effects

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Elevated plasma LDL-cholesterol represents a major risk factor for the development of atherosclerosis (1). A number of dietary factors, such as dietary fiber or soy protein, counteract this effect. Consumption of soy protein decreases serum total and LDL cholesterol concentrations in humans (2–4), rats, hamsters, guinea pigs, rabbits, monkeys, and baboons (5–10). A meta-analysis of the effects of soy protein intake on serum lipid levels (11) showed a significant relationship between soy intake and decreased total and LDL cholesterol and less risk of coronary heart disease. However, the components of soy responsible for these cholesterol lowering effects have not been determined.

Nonprotein components in soy, including isoflavones, saponins, dietary fiber, and phenolic acids may be responsible for the hypocholesterolemic effect of soy protein (12–15). Some human (3, 4) and animal (12, 16, 17) studies indicate that isoflavones and/or other components extracted with isoflavones lessen cholesterol or atherosclerosis. Soybeans and soy foods are the major source of isoflavones in human diets, as daidzein, genistein, glycitein, and their glycoside forms, at concentrations from 0.25 to 3 mg/g (18). Soy isoflavones are estrogenic (19) and as estrogen agonists, may upregulate LDL receptor expression. The administration of oral estrogens or the synthetic antiestrogen, tamoxifen, decreased total serum cholesterol and LDL cholesterol levels in postmenopausal women (20). An ethanol extract from soy protein containing isoflavones and saponins reduced serum LDL cholesterol levels and increased LDL receptor activity in mice (21). Anthony *et al.* (16) showed that an isoflavone-rich soy protein diet significantly lowered total and LDL cholesterol in Rhesus monkeys when compared with ethanol-extracted soy protein from which more than 90% of the isoflavones had been extracted. Soy isoflavone extracts containing 50% to 60% isoflavones, when added to diets with casein as protein source, significantly lowered total and LDL cholesterol levels in rats and hamsters compared with casein-fed controls (22). Male obese Zucker rats fed high isoflavone (578 mg/kg) soy protein or low isoflavone (38 mg/kg) soy protein for 70 days

significantly lowered total cholesterol by 29% or 21%, respectively, compared with rats fed casein (23). These data are consistent with the hypothesis that the hypocholesterolemic effect of soy protein is due to soy isoflavones. However, none of these studies used purified isoflavones. Ethanol extracts from soy proteins contain soyasaponins and phenolic acids as well as isoflavones. Soyasaponins are also hypocholesterolemic (15, 24).

We hypothesized that isoflavones and soy extract components fed in amounts similar to those found in soy protein were significantly hypocholesterolemic. To test this hypothesis, we fed purified daidzein and a soygerm extract to hamsters and assayed blood lipids. Soygerm was used because it is a rich source of isoflavones (>20 mg/g) (25). Golden Syrian hamsters were selected because there are several general similarities in cholesterol metabolism between hamsters and humans, including a low basal rate of hepatic cholesterol synthesis and a comparable bile acid pool composition (26, 27). Hamsters fed a diet enriched with saturated fat show a substantial increase in plasma total and LDL cholesterol, thus making them a good model to assess cholesterol metabolism (28).

## Materials and Methods

**Chemicals and Diets.** The isoflavone, daidzein, was synthesized according to Song *et al.* (25). The purity of daidzein, determined by HPLC chromatograph peak area percentage and Beckman Gold HPLC System peak purity software, was greater than 98%. Soygerm was generously donated by Schouten USA, Inc. (Minneapolis, MN). Isolated soy protein (ISP) was purchased from Protein Technologies International (St. Louis, MO). The soygerm extract was prepared by using ethanol and acetone extraction according to Balmir *et al.* (22). The isolated soy protein (ISP (–)) with isoflavones removed was prepared by extracting ISP with 70% ethanol at weight to solvent ratio of 1 g ISP: 4 ml of aqueous ethanol 4 times, stirring the extraction mixture overnight at room temperature each time. The isoflavone contents of ISP, soygerm, soygerm extract, and ISP (–) were analyzed by HPLC method (29) (Table I).

The control diet for hamsters was based on Terpstra *et al.* (28). Six treatments were fed: casein control, ISP, ISP (–), daidzein, soygerm or soygerm extract (Table II). Daidzein, soygerm, and soygerm extract diets were casein-based. The diets were formulated to contain the amount of daidzein, soygerm, or soygerm extract that provided total molar isoflavone content equal to that of ISP, 1.3 mmol/kg diet. Dietary cholesterol was 0.1%. Rice flour was used as a carbohydrate source to replace cornstarch in the standard rodent diet because rice flour prevents "wet tail" disease, a form of chronic diarrhea with a high rate of mortality for hamsters (28).

**Table I.** Isoflavone Concentrations[3] in Different Diet Components

| Components | Daidzein | Genistein | Glycitein | Isoflavone content[a] |
|---|---|---|---|---|
| | | (μmol/g) | | |
| ISP (Supro-670[2]) | 1.9 | 2.9 | 0.4 | 5.2 |
| Soygerm | 36.3 | 9.9 | 25.6 | 71.8 |
| Soygerm extract | 336.2 | 82.2 | 310.4 | 728.8 |
| ISP (–) | 0.015 | 0.02 | 0.015 | 0.05 |

[a] The total mole concentration of isoflavone was calculated as the sum of mole concentrations of daidzein, genistein, and glycitein. Minimum detection level was 1 μmol/g sample.

**Animals.** The animal experimental protocol was approved by Iowa State University Animal Use Committee. Sixty male and 60 female golden Syrian hamsters, 6 to 8 weeks old, 100 to 110 g, were obtained from Charles River Breeding Laboratories (St. Constant, Canada). They were housed individually in temperature-controlled rooms (23°C) with a 12-h light:dark cycle. Upon arrival, hamsters were fed a powdered AIN 93 M diet for 1 week to acclimate the animals and then randomly assigned to 6 treatments with 10 males and 10 females per treatment. Hamsters had free access to food and water during the 10-week experimental period. Body weights and food intakes were measured weekly. At the end of the feeding period, diets were withdrawn from hamsters 14 to 16 hrs before they were sacrificed under $CO_2$. Blood was collected by cardiac puncture and centrifuged at 5000 g for 10 min at 4°C to prepare plasma that was frozen at −20°C until analysis.

**Plasma Lipid Analysis.** Plasma total cholesterol, HDL cholesterol, and triglyceride (TAG) concentrations were measured with Sigma diagnostics kits (St. Louis, MO). Non-HDL cholesterol was calculated by subtraction of HDL cholesterol from total cholesterol and represented LDL+IDL+VLDL cholesterol.

**Plasma Isoflavone Analysis.** Plasma samples were combined within each group to give replicate pooled samples for each treatment; 2-ml 0.2 M acetate buffer (pH 5.5), 100 μl of H-3 type β-glucuronidase/sulfatase (Sigma Chemical Co., St. Louis, MO), and 10 μl internal standard, 2,4,4′-trihydroxydeoxybenzoin (THB, 4 mg/ml) prepared according to Song *et al.* (25) were added to 2-ml plasma samples. The mixture was incubated at 37°C for 16 hrs; 6 ml methanol was added to the mixture, mixed well, and centrifuged at 10,000 g for 20 min. Eight ml supernatant was dried under nitrogen and redissolved in 400 μl of 80% methanol. After centrifugation, 20 μl samples were taken for isoflavone analysis. A Beckman System Gold chromatograph with a Model 507 autosampler, a Model 126 dual pump, a Model 168 photodiode array detector, and an IBM 486 computer using Beckman System Gold HPLC data processing software (version 8, 1993) was used. A YMC-pack ODS-AM-303 analytical column (5 μm pore size, 25 cm × 4.6 mm, YMC, Inc., Wilmington, NC) was used. A linear gradient was composed of solvent A (0.1% acetic acid in water) and solvent B (0.1% acetic acid in acetonitrile). After injection of a 20-μl sample, the system was maintained at

**Table II.** Composition of Experimental Diets

| Ingredient | Casein | ISP | ISP (–) | Daidzein | Soygerm | Soygerm extract |
|---|---|---|---|---|---|---|
| | | | (g/kg) | | | |
| Casein[a] | 250 | 0 | 0 | 250 | 250 | 250 |
| ISP | 0 | 250 | 250 | 0 | 0 | 0 |
| Coconut oil | 100 | 100 | 100 | 100 | 100 | 100 |
| Safflower oil | 20 | 20 | 20 | 20 | 20 | 20 |
| Soybean oil | 40 | 40 | 40 | 40 | 40 | 40 |
| Cellulose | 75 | 75 | 75 | 75 | 75 | 75 |
| Wheat bran | 75 | 75 | 75 | 75 | 75 | 75 |
| Choline chloride | 3 | 3 | 3 | 3 | 3 | 3 |
| Vitamin mix[b] | 10 | 10 | 10 | 10 | 10 | 10 |
| Mineral mix[c] | 35 | 35 | 35 | 35 | 35 | 35 |
| Potassium bicarbonate | 20 | 20 | 20 | 20 | 20 | 20 |
| Cholesterol | 1 | 1 | 1 | 1 | 1 | 1 |
| Rice flour[d] | 371 | 371 | 371 | 370.67 | 353 | 369.22 |
| Daidzein | 0 | 0 | 0 | 0.33 | 0 | 0 |
| Soygerm | 0 | 0 | 0 | 0 | 18 | 0 |
| Soygerm extract | 0 | 0 | 0 | 0 | 0 | 1.78 |

[a] Vitamin-free casein (Harlan/Teklad, Madison, WI).
[b] Vitamin mixture #400160 (Harlan/Teklad, Madison, WI).
[c] Mineral mixture #170910 (Harlan/Teklad, Madison, WI).
[d] Rice flour (Bioserve, Frenchtown, NJ).

15% B for 5 min, then increased to 29% B in 31 min, and then to 35% B in 8 min. The system was recycled to 15% B after 45 min. The flow rate was 1.0 ml/min for the first 5 min, then increased to 1.5 ml/min for the next 40 min, and returned to 1 ml/min for recycling. The minimal detection level for daidzein, genistein, and glycitein was 1.6 μM in the injection solution by UV detector at 254 nm. Recovery based on the THB internal standard was 85%, and recovery-adjusted plasma isoflavone concentrations were reported.

**Statistical Analysis.** All data were analyzed by 2-factor ANOVA (SAS version 6.03, SAS Institute, Cary, NC). Because there were no interactions between gender and treatments, all analyses were redone separately for each gender by one-way ANOVA. Differences between treatments were determined by least significant difference test. An $\alpha$ of 0.05 was used to determine statistically significant differences.

## Results

**Hamster Body Weights and Food Intakes.** The powdered diets were well accepted by hamsters throughout the experiment. Daily food intakes did not differ among the groups for both males and females (Table III). Both male and female hamsters in all groups had similar initial mean body weight. The weight gain was 40 ± 3 g for males and 52 ± 4 g for females. There were no final weight differences among dietary treatment groups for females. For males, daidzein caused 10% less final body weight ($P < 0.05$) compared with other treatments (Table III).

**Plasma Lipids.** Two-way ANOVA showed that there were no interactions between diets and gender on total cholesterol, HDL cholesterol, non-HDL cholesterol, and TAG levels. Therefore, we separately analyzed the results for males (Table IV) and females (Table V). Total cholesterol, non-HDL cholesterol levels, and non-HDL/HDL cholesterol ratios were significantly less ($P < 0.01$) in hamsters fed ISP, ISP (–), daidzein, soygerm, and soygerm extract compared with hamsters fed the casein control diet, for both males and females. There were no differences among treatments in HDL cholesterol levels in males. However, female hamsters fed ISP (–) groups had 30% greater HDL choles-

**Table III.** Body Weight Change and Food Intake of Hamster's Fed Casein- or ISP-Based Diets with or without Soy Isoflavones[a,b]

| Treatment | Food intake g/d | | Initial body weight g | | Final body weight g | |
|---|---|---|---|---|---|---|
| | Male | Female | Male | Female | Male | Female |
| Casein | 7.2 ± 0.3 | 7.6 ± 0.3 | 104 ± 3 | 104 ± 7 | 145 ± 10[a] | 158 ± 12 |
| ISP | 7.5 ± 0.4 | 7.7 ± 0.5 | 105 ± 4 | 104 ± 5 | 150 ± 13[a] | 155 ± 15 |
| ISP (–) | 7.3 ± 0.2 | 7.6 ± 0.4 | 104 ± 4 | 103 ± 6 | 142 ± 12[a] | 154 ± 13 |
| Daidzein | 7.3 ± 0.5 | 7.5 ± 0.3 | 103 ± 3 | 102 ± 5 | 131 ± 7[b] | 155 ± 18 |
| Soygerm | 7.4 ± 0.2 | 7.8 ± 0.5 | 103 ± 8 | 103 ± 7 | 146 ± 13[a] | 158 ± 21 |
| Soygerm extract | 7.1 ± 0.3 | 7.6 ± 0.4 | 104 ± 4 | 104 ± 4 | 143 ± 16[a] | 152 ± 12 |

[a] Values represent means ± SEM, $n = 10$.
[b] Within a column, means with different superscripts are different ($P < 0.05$).

**Table IV.** Plasma Cholesterol Levels in Male Hamsters Fed Casein- or ISP-Based Diets with or without Soy Isoflavones[1,2]

| Treatment | Total cholesterol (mmol/l) | HDL cholesterol (mmol/l) | Non-HDL[3] cholesterol (mmol/l) | Non-HDL/HDL | Triglyceride (mmol/l) |
|---|---|---|---|---|---|
| Casein | 6.22 ± 0.33[a] | 3.01 ± 0.18[a] | 3.21 ± 0.23[a] | 1.10 ± 0.11[a] | 2.88 ± 0.23 |
| ISP | 5.18 ± 0.30[b] | 2.71 ± 0.20[ab] | 2.47 ± 0.16[b] | 0.95 ± 0.06[ab] | 2.50 ± 0.18 |
| ISP (–) | 4.93 ± 0.29[b] | 2.79 ± 0.15[ab] | 2.14 ± 0.13[b] | 0.77 ± 0.02[bc] | 2.44 ± 0.28 |
| Daidzein | 4.74 ± 0.31[b] | 2.50 ± 0.16[b] | 2.24 ± 0.17[b] | 0.87 ± 0.03[bc] | 2.67 ± 0.17 |
| Soygerm | 4.83 ± 0.31[b] | 2.81 ± 0.17[ab] | 2.02 ± 0.17[b] | 0.72 ± 0.03[c] | 2.74 ± 0.18 |
| Soygerm extract | 4.77 ± 0.24[b] | 2.55 ± 0.12[ab] | 2.22 ± 0.17[b] | 0.88 ± 0.06[bc] | 2.56 ± 0.22 |

[1] Values represent means ± SEM, $n = 10$.
[2] Within a column, means with different superscripts are different ($P < 0.05$).
[3] Represents the VLDL + IDL + LDL fractions (by difference: Total – HDL).

**Table V.** Plasma Cholesterol Level in Female Hamsters Fed Casein- or ISP-Based Diets with or without Soy Isoflavones[1,2]

| Treatment | Total cholesterol (mmol/l) | HDL cholesterol (mmol/l) | Non-HDL[3] cholesterol (mmol/l) | Non-HDL/HDL | Triglyceride (mmol/l) |
|---|---|---|---|---|---|
| Casein | 5.61 ± 0.27[a] | 2.10 ± 0.09[b] | 3.51 ± 0.28[a] | 1.72 ± 0.18[a] | 1.53 ± 0.18[a] |
| ISP | 4.73 ± 0.31[bc] | 2.70 ± 0.21[ab] | 2.03 ± 0.21[b] | 0.81 ± 0.11[b] | 0.12 ± 0.12[ab] |
| ISP (–) | 4.91 ± 0.35[ab] | 2.82 ± 0.35[a] | 2.09 ± 0.25[b] | 0.84 ± 0.11[b] | 1.05 ± 0.17[b] |
| Daidzein | 4.37 ± 0.25[bc] | 2.18 ± 0.10[b] | 2.19 ± 0.11[b] | 1.01 ± 0.04[b] | 1.26 ± 0.14[ab] |
| Soygerm | 4.08 ± 0.30[c] | 2.32 ± 0.25[ab] | 1.77 ± 0.21[b] | 0.83 ± 0.11[b] | 1.25 ± 0.18[ab] |
| Soygerm extract | 4.28 ± 0.23[bc] | 2.13 ± 0.16[ab] | 2.16 ± 0.11[b] | 1.05 ± 0.08[b] | 1.10 ± 0.11[ab] |

[1] Values represent means ± SEM, $n = 10$.
[2] Within a column, means with different superscripts are different ($P < 0.05$).
[3] Represents the VLDL + IDL + LDL fractions (by difference: Total – HDL).

terol levels ($P < 0.01$) compared with females fed casein or daidzein. Triglyceride concentration was significantly less in female hamsters fed ISP (–) compared with casein-fed females.

**Plasma Isoflavones.** Daidzein, genistein, glycitein, and equol, a gut microbial metabolite of daidzein, were detected in most of the male hamster plasma samples but only in a few of the samples from females, ranging from 0.4 to 3.6 μM (Table VI).

**Table VI.** Plasma Isoflavone Concentrations in Hamsters[a]

| Isoflavone | ISP | ISP(–) | Daidzein (μmol/l) | Soygerm (μmol/l) | Soygerm extract |
|---|---|---|---|---|---|
| Daidzein | | | | | |
| Male | 1.4 | – | 0.4 | 2.3 | – |
| Female | – | – | 0.6 | – | – |
| Glycitein | | | | | |
| Male | 1.2 | – | – | 1.7 | – |
| Female | – | – | – | – | – |
| Genistein | | | | | |
| Male | 0.8 | – | – | 0.8 | 3.6 |
| Female | – | – | – | – | 3.6 |
| Equol | | | | | |
| Male | – | – | 1.6 | 0.5 | – |
| Female | – | – | 4.0 | – | – |
| Total | | | | | |
| Male | 3.4 | – | 2.0 | 5.3 | 3.6 |
| Female | – | – | 4.6 | – | 3.6 |

[a] (–) not detected, minimal detection level, 0.4 μM/plasma sample.

## Discussion

Our data showed that dietary soy protein, daidzein, and isoflavone-containing extracts lessened plasma cholesterol levels in hamsters. Daidzein, in a casein-based diet, significantly reduced total cholesterol, non-HDL cholesterol, and non-HDL/HDL ratios (Tables IV and V). This study confirmed our hypothesis that the soy isoflavone, daidzein, was a major contributor to the cholesterol-lessening effects of soy protein. However, other components of soy protein may be acting as well. In ISP, soygerm, and soygerm extract, saponins are also present in potentially significant amounts. Although saponins are well known to lessen plasma cholesterol by preventing cholesterol reabsorption from the gastrointestinal tract (30), saponin efficacy may require feeding 1% by weight of diet (24). Our diets are estimated to contain ~0.2% of the major soyasaponins (class B) for the ISP diet and ~0.04% group B saponins for soygerm or germ extract, according to values derived from Hu *et al.* 2002 (31). This suggests that isoflavones rather than saponins were the major contributors to cholesterol-lessening effects in our study, but saponins may be contributing to these effects.

The lesser final body weight caused by daidzein treatment of male but not of female rats compared with other treatments (Table III) suggests that this compound impairs energy utilization efficiency because food intake did not differ among treatments. Other isoflavones or components of soy protein must be counteracting this effect because the

other treatments were all similar in effects on body weight. This inexplicable gender-specific effect suggests a potential for daidzein toxicity that deserves further study.

Decreased plasma total and non-HDL cholesterol were observed in hamsters fed soy protein containing isoflavones compared with the casein control group. However, the removal of isoflavones from soy protein produced similar plasma cholesterol-lessening effects. These results were similar to that of Balmir *et al.* (22) where isolated soy protein, with or without soy isoflavones, had the ability to lower plasma cholesterol levels in rats. These data suggested that, in addition to isoflavones, soy protein amino acid composition or protein fragments produced cholesterol-lessening effects. The similar cholesterol-lessening effects of ISP and ISP (–) showed that cholesterol-lessening effects of soy protein cannot be attributed to isoflavones alone. Cholesterol-lessening effects of soy protein or soy isoflavones or extracts seemed to reach a plateau. Tovar-Palacio *et al.* (32) also showed in gerbils that soy protein lessened plasma cholesterol compared with casein, and when isoflavone extracts were added to the soy protein diet at 3 different doses of 8.0, 13.8, or 23.8 μmol isoflavone/g protein, they did not lessen cholesterol levels more than did soy protein alone. However, these diets significantly lessened cholesterol levels compared with casein. There was no additive effect for dietary soy protein and soy isoflavones in the current study. If lower levels of soy protein or isoflavone were used, additive effects might be revealed.

Soygerm, the hypocotyl of the soybean seed, is a naturally concentrated soy isoflavone source. Soygerm has a unique isoflavone profile, with daidzein accounting for 50% of the total isoflavones, glycitein for 35%, and genistein for 15%. This profile is very different from intact soybeans, where genistein accounts for 50% of the total isoflavones and glycitein for only 5% to 10%. The total isoflavone concentration in soygerm is 20 to 30 mg/g, much higher than soybeans or typical soy foods at 0.25 to 3 mg/g. Our study demonstrated the same magnitude of hypocholesterolemic effect of soygerm and soygerm extract as for ISP, ISP (–), or daidzein.

The cholesterol-lessening effects observed in the present study were mainly due to decreased non-HDL cholesterol, probably largely LDL cholesterol. Plasma LDL cholesterol levels depend upon the maximal rate of receptor-mediated uptake of LDL cholesterol by the tissues, the rate of LDL cholesterol production, the affinity of the LDL molecule for its receptor, and the rate of LDL cholesterol uptake through an LDL receptor independent process (33). Soy protein and soy isoflavones may influence plasma LDL cholesterol through any one of these factors. Dietary soy protein with isoflavones (1.33 mmol/kg diet) reduced plasma LDL cholesterol levels (30%) in C57BL/6 mice compared with the isoflavone-depleted soy protein but LDL receptor-deficient mice experienced no cholesterol lessening by soy (12). These data suggested that isoflavones affect LDL cholesterol levels through an LDL receptor dependent pathway. How isoflavones lessen LDL cholesterol production, which is increased by increased intake of saturated fat and cholesterol, should be investigated, including effects on LDL receptor activity.

Effects of soy protein on plasma HDL cholesterol concentrations are inconsistent. Anderson *et al.* (11) reported no significant changes in human HDL cholesterol with soy protein consumption. An increase in HDL cholesterol was seen only in female rhesus monkeys fed soy protein (16), similar to the present study in which female hamsters fed ISP (–) had higher HDL cholesterol levels compared with hamsters fed casein or daidzein. The mechanism for the effects on HDL cholesterol and the reasons for the gender difference are unknown. It has been postulated that the effect may be mediated by the interaction between isoflavones and estrogen receptors (34). Our results seem to rule out this hypothesis because there was no effect on HDL cholesterol concentrations when daidzein was added to the casein diet.

In the present study, there were no differences in triglyceride levels among treatments in males. However, triglycerides were significantly less in female hamsters fed ISP (–) compared with those fed casein, consistent with another report that soflavone-depleted soy protein isolate significantly lessened serum triglyceride concentrations in both sham-operated and ovariectomized female hamsters compared with casein (13). The cause of the different effects of protein sources on triglycerides in females is unknown and further studies are needed.

We detected all 3 isoflavones and equol in plasma samples, ranging from 0.4 to 3.6 μM, which were similar to the levels detected in human (35) and rat plasmas (36). We found both daidzein and its metabolite, equol, in plasma of daidzein-treated hamsters, which showed that hamsters had the ability to metabolize daidzein to equol. While isoflavones were detected in most of the male hamster plasma samples, only a few females had detectable plasma isoflavone levels. This suggested a gender difference in isoflavone absorption and metabolism in hamsters. However, there are no reports of more rapid glucuronidation (seemingly the main metabolic reaction of isoflavones) by female hamsters, which would increase clearance of plasma isoflavones. This remains to be determined.

The plasma cholesterol-lowering activity for the other isoflavones, genistein and glycitein, as well as the combinations of these 3 isoflavones, must be examined. The possible cholesterol-lowering effects of soy isoflavones suggest the potential to use these soy components as dietary cholesterol-lowering agents.

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