

Soy: A Complete Source of Protein

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Soybeans contain all of the essential amino acids necessary for human nutrition and have been grown and harvested for thousands of years. Populations with diets high in soy protein and low in animal protein have lower risks of prostate and breast cancers than other populations. Increasing dietary whole soy protein lowers levels of total cholesterol, low-density lipoproteins, and triglycerides; may improve menopausal hot flashes; and may help maintain bone density and decrease fractures in postmenopausal women. There are not enough data to make recommendations concerning soy intake in women with a history of breast cancer. The refined soy isoflavone components, when given as supplements, have not yielded the same results as increasing dietary whole soy protein. Overall, soy is well tolerated, and because it is a complete source of protein shown to lower cholesterol, it is recommended as a dietary substitution for higher-fat animal products. (*Am Fam Physician*. 2009;79(1):43-47. Copyright © 2009 American Academy of Family Physicians.)

One recent consumer survey found that 33 percent of Americans consume soy food or beverages at least once per month, and 85 percent rate soy products as healthful.¹ Soybeans are second only to corn as the largest crop produced in the United States, with U.S. soy representing 42 percent of the world's soybean trade, and 75 percent of all the edible fats and oils consumed in the United States.² Compared with Asian diets, which may contain 30 to 60 mg per day of the isoflavones component of soybeans, the average American diet contains only about 1 to 3 mg per day.³ The recommended intake of dietary whole soy protein is 25 g per day, and 40 to 80 mg per day for soy isoflavones.^{4,5}

Available in a wide variety of products, soybeans are one of the few vegetarian sources of total protein containing all of the essential amino acids required in the human diet.⁴ Common food preparations include edamame (whole soybeans), tofu (soybean curd), soy milk, soy flour, tempeh (cooked and fermented soy), miso (fermented soybean paste), and soy sauce (*Table 1*^{6,7}). Refined soy components are also available as nutritional supplements in the form of isolated soy protein and as the soy-derived isoflavones genistein, daidzein, and glycitein.^{4,8} Soy has been a staple source of protein in Asian diets for thousands of years and received significant attention when studies showed that Asian populations have a lower risk of breast and prostate cancers.³ Studies of soy mainly

focus on three areas: dietary whole soy protein intake (e.g., soybeans, tofu); isolated soy protein supplements, which are alcohol-washed to remove components; and dietary supplementation with soy isoflavones.

Pharmacology

Soybeans contain many biologically active compounds, including saponins, lecithin, phytates, protease inhibitors, phenolic acids, phytosterols, isoflavones, and omega-3 fatty acids.⁹ Much of the attention around the active compounds in soy focuses on the isoflavones genistein and daidzein. These two phytoestrogens weakly bind to the estrogen receptors alpha and beta, but preferentially bind to the estrogen receptor beta, where they may act like selective estrogen receptor modulators.¹⁰ In vitro and animal studies suggest that soy may also decrease absorption of cholesterol and bile acid from the gastrointestinal tract, increase antineoplastic enzyme activity, regulate apoptosis and the cell cycle, inhibit tyrosine kinase proteins, and serve as an antioxidant.^{9,11,12} Many of the studies on mechanisms include refined soy components, which are often equated to whole soy. However, it is difficult to assume that the effects of individual soy components equate to the effects of whole soy protein.¹³

Uses and Effectiveness

Soy has been most widely studied for improving lipid levels; however, soy and its components have also been evaluated for

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
A daily diet containing 25 g of whole soy protein lowers levels of total cholesterol, low-density lipoprotein, and triglycerides.*	C	4, 8, 14-20
Whole soy protein and soy isoflavone supplementation may decrease menopausal hot flashes.	B	25, 26
A diet high in whole soy protein may help maintain bone mineral density and prevent fractures in postmenopausal women.	B	8, 28-31
There is no clear evidence to recommend for or against changes in soy intake for women who have a history of breast cancer.	C	4, 35

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

**—Although the evidence is high-quality, the outcomes are disease-oriented.*

Table 1. Nutritional Information for Selected Soy Food Products

<i>Soy product</i>	<i>Serving size</i>	<i>Protein (g)</i>	<i>Total fat (g)</i>	<i>Carbohydrates (g)</i>	<i>Fiber (g)</i>	<i>Calories</i>
Edamame (cooked, whole soybeans)	1 cup (180 g)	22	12	20	8	254
Margarine (hydrogenated soybean)	1 tsp (4 g)	0	4	0	0	32
Miso (fermented soybean paste)	1 tbsp	2	1	5	1	40
Soybean vegetable oil	1 cup (218 g)	0	218	0	0	1,664
Soy flour (defatted)	1 cup (105 g)	48	9	37	17	394
Soy milk (all flavors, enhanced)	1 cup (243 g)	7	5	8	1	109
Soy protein bar	1 bar (30 g)	4	6	16	3	130
Soy protein isolate	1 oz (28 g)	26	1	0	0	109
Soy sauce	1 tbsp (18 g)	2	0	1	0	11
Soy veggie burger	1 patty (70 g)	11	4	10	3	124
Tempeh (cooked and fermented soy)	1 oz (28 g)	5	3	3	0	55
Tofu (soybean curd; silken, firm)	1 slice (84 g)	6	2	2	0	52

Information from references 6 and 7.

their effects on menopausal symptoms, bone health, and cancer prevention.

HYPERLIPIDEMIA

In 1999, the U.S. Food and Drug Administration (FDA) approved the health claim that a diet low in saturated fat and cholesterol that includes 25 g of soy protein per day may reduce the risk of heart disease.⁴ The FDA reached this conclusion after evaluating research from 27 studies. For an individual food product to qualify for a label containing this soy health claim, each serving must contain at least 6.25 g of soy protein, less than 3 g of fat (less than 1 g saturated), less than 20 mg of cholesterol, and less than 480 mg of sodium.⁴

Four meta-analyses (comprised of 38, 41, 22, and

eight studies) of randomized controlled trials (RCTs) of soy protein interventions showed a statistically significant reduction in total cholesterol levels (2.5 to 9.3 percent); a reduction of 3 to 12.9 percent in low-density lipoprotein levels; a reduction of 6 to 10.5 percent in triglyceride levels; and inconsistent improvement in high-density lipoprotein levels.¹⁴⁻¹⁷ These reductions appear to be greater for persons with higher starting cholesterol levels, and there is some support for a dose-response relationship between soy intake and cholesterol reduction.^{8,14-18} Studies of soy components (e.g., isoflavones) have not consistently demonstrated the same cholesterol-lowering effects as whole soy protein.¹⁹ In a recent RCT of postmenopausal women, substituting soy nuts for non-soy protein not only improved cholesterol

levels, but also lowered blood pressure in patients who were hypertensive or normotensive.²⁰ As a dietary intervention to lower cholesterol, the National Cholesterol Education Program recommends replacing higher-fat animal protein with soy protein.²¹

Although studies show an improvement in lipid levels, there have been no studies to prove that soy protein interventions improve cardiovascular outcomes. One study that included more than 16,000 women failed to show a reduction in cardiovascular risk with a diet high in phytoestrogens.²² Therefore, more data are needed before a definitive relationship between soy and cardiovascular outcomes can be established.

MENOPAUSAL SYMPTOMS

Because soy isoflavones bind weakly and preferentially to brain beta estrogen receptors, soy has been studied for the possible reduction of menopausal hot flashes.⁹ A meta-analysis of 11 randomized placebo-controlled trials of soy isoflavone extracts showed mixed results for a reduction in hot flashes.²³ Additionally, a randomized placebo-controlled trial of a dietary intervention of multibotanicals plus whole soy protein did not show the soy intervention to be better than placebo over one year in 165 women.²⁴ These two studies did not evaluate women based on the number of hot flashes per day. A newer meta-analysis (with 17 studies and 1,422 patients) including RCTs of isoflavone supplementation showed that patients with 10 or more hot flashes per day had a 20 percent reduction over the placebo groups, whereas patients with fewer than six hot flashes per day had no effect from soy isoflavones.²⁵ An RCT of 60 postmenopausal women compared therapeutic lifestyle changes only (control group) with an intervention group that received similar therapeutic lifestyle changes plus 2 cups per day of soy nuts (e.g., 25 g soy protein and 101 g isoflavones).²⁶ The study showed that the intervention group had a 45 percent decrease in hot flashes in women with more than 4.5 hot flashes per day, and a 41 percent decrease in women with fewer than 4.5 hot flashes per day. The women in the intervention group also showed improvement in menopausal quality of life.²⁶

Although a previous meta-analysis showed mixed results on the reduction of hot flashes,²³ newer studies have shown more favorable effects with isoflavone supplementation and with diets containing a combination of soy protein and isoflavones. One recent study showed a reduction in hot flashes of 43 percent at eight weeks and 52 percent at 12 weeks in the isoflavone group, with reductions ranging from 32 to 39 percent in the placebo group.²⁷

BONE HEALTH

In-vitro studies have shown that soy isoflavones modulate osteoblastic and osteoclastic activity in favor of decreased bone turnover.²⁸ A prospective epidemiologic study followed 24,403 postmenopausal Chinese women for a duration of 4.5 years.²⁹ The study found that women who had the highest soy intake (greater than 13.26 g per day) had a 36 percent lower risk of fracture compared with women who had the lowest soy intake (less than 4.98 g per day), after controlling for diet, age, socioeconomic status, and risk factors for osteoporosis. This reduction in fracture risk was not only statistically significant, but also showed a dose-response relationship across quintiles of daily soy intake.²⁹ A randomized, double-blind, placebo-controlled trial of 61 postmenopausal women found that women receiving soy protein isolate had statistically significant decreases in markers of bone turnover (i.e., serum C-terminal cross-linked telopeptides and bone-specific alkaline phosphatase) at nine months when compared with placebo. However, there was no change in bone mineral density.³⁰ A recent meta-analysis of 10 studies (n = 608) found that soy isoflavone consumption for six months attenuated bone loss of the spine in menopausal women, which was most pronounced in women consuming more than 90 mg per day of soy isoflavones.³¹

Overall, studies that include a soy intervention have not shown a consistent effect on bone mineral density, although they have shown variable reductions in markers of bone turnover. Most of these studies are limited by small numbers of participants and short durations.⁸

CANCER PREVENTION

Epidemiologically, prostate cancer is less prevalent in populations with high soy consumption, such as in China and Japan.⁹ However, Asian immigrants to the United States have similar rates of prostate cancer as other Americans.³² There are many factors that may contribute to this difference, but one possible factor is that Asian populations consume 10 to 15 times the amount of soy per day as U.S. populations.⁹ Clinical studies of soy and prostate cancer have been limited. In a meta-analysis of 24 trials using soy to prevent prostate cancer, none of the studies used development of cancer as an end point, and most used tumor-related markers only.⁸ No relationship between soy intake and tumor-related markers were demonstrated in these studies.

Studies of breast cancer deserve special attention because of the estrogenic effects of soy. In one meta-analysis of 18 epidemiologic studies, there was a 14 percent reduction in the risk of breast cancer among women with high soy intake compared with those with low soy

intake.³³ The effect was stronger in postmenopausal women and did not occur in studies with Asian women. However, the individual studies included in this analysis used different definitions of high-versus-low soy intake—high soy intake in the Western studies was considered low soy intake in the Asian studies. In a more recent meta-analysis of 21 epidemiologic studies, the pooled risk of developing breast cancer was reduced by 25 percent in women with high soy food intake, and reduced by 20 percent in women with isoflavone supplementation.³⁴

Questions have arisen about whether soy is safe in patients with breast cancer. Studies suggest that soy may act like a selective estrogen receptor modulator, and that isoflavone supplementation does not appear to change breast density in young women and may actually decrease breast density in postmenopausal women. However, current studies have shown neither a beneficial nor harmful effect of soy in women with breast cancer.³⁵

Contraindications, Adverse Effects, and Interactions

In general, soy and soy components are well-tolerated and have few adverse effects. In an analysis of 49 studies (n = 3,518), adverse effects were more common in the soy groups (soy diet, soy protein, and isoflavones) than in placebo groups.⁸ Gastrointestinal symptoms (e.g., diarrhea), followed by menstrual complaints (e.g., prolonged periods, amenorrhea) were the most commonly reported adverse events. Others included headache, dizziness, and musculoskeletal complaints.^{8,36}

One concern is that soy supplementation may cause endometrial hyperplasia. A recent review of the literature found that most studies do not support this concern. In one study of 120 women using high dosages of soy isoflavones (150 mg per day), four women developed endometrial hyperplasia after five years of therapy.³⁷ Most recommendations for isoflavone supplementation suggest much lower dosages of 40 to 80 mg per day.³⁷

As for drug interactions, soy extracts may be a weak inducer of the cytochrome P450 3A4 enzyme and, although reports of drug interactions with soy are uncommon, there has been one case of a possible lowered International Normalized Ratio in a patient taking warfarin (Coumadin) who added soy milk to his diet.^{5,38,39}

Studies have also shown that when babies taking a supplementation of iron or thyroid hormone are switched to soy infant formulas, the absorption of iron and thyroid hormone is decreased.⁴⁰ Also, there is a theoretical interaction with monoamine oxidase inhibitors because soy products contain tyramine.⁴¹

Soy allergy (often leading to bloody diarrhea) is reported

Table 2. Key Points About Soy

Effectiveness

Reducing total cholesterol, low-density lipoprotein, and triglyceride levels: 25 g per day of whole soy protein is effective; soy isoflavone components are less effective
 Reducing menopausal hot flashes: whole soy protein and isoflavones may be effective
 Improving bone mineral density: a diet high in whole soy protein may help prevent postmenopausal bone loss and fractures; possibly improves bone mineral density
 Preventing cancer: no clear evidence of effectiveness

Adverse Effects

Common: diarrhea
 Rare: prolonged menstruation, amenorrhea, headache, dizziness, musculoskeletal complaints

Interactions

Rare but potential interactions with iron, thyroid hormone, warfarin (Coumadin), and monoamine oxidase inhibitors

Contraindications

None

Recommended intake

25 g per day of dietary whole soy protein
 40 to 80 mg per day of soy isoflavones

Cost

Variable for dietary changes; \$10 to 40 per month for encapsulated soy components

Bottom Line

Soy, especially dietary whole soy protein, appears to improve lipid levels and may also improve menopausal hot flashes, help maintain bone density, and decrease risk of fractures in postmenopausal women

in about 1 percent of infants on soy formulas and usually resolves by three years of age, when most of these children begin to tolerate soy products. Allergy to soy in adults is uncommon and estimated to occur in about 0.2 percent of the U.S. population.⁴⁰ Anaphylaxis has been reported with soy, but is rare.⁴⁰

Table 2 lists key points about soy, including its effectiveness, interactions, and recommended intake.

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